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New BIOTECHNOLOGY

TRANSGENIC PLANTS FOR FOOD SECURITY IN THE CONTEXT OF DEVELOPMENT

PROCEEDINGS OF A STUDY WEEK OF THE PONTIFICAL ACADEMY OF SCIENCES

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Editorial

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Preliminary remarks

During the 400 years of its existence, the Pontifical Academy of Sciences has carried out its statutory goals by employing various approaches. In the words of its 1976 reformed Statutes, it 'organises meetings to promote the progress of sciences and the solution of important scientific problems...and promotes scientific investigations and research which can contribute, in the appropriate places, to the exploration of moral, social and spiritual problems'.

Inspired by this idea, in October 1982 the Pontifical Academy held a Study Week on Modern Biological Experimentation. In this meeting, Professor J. Schell gave a paper on *Gene Transfers into Plants as a Natural and Experimental Phenomenon*. On this occasion, John Paul II addressed the participants with these words: "I wish to recall, along with the few cases which I have cited that benefit from biological experimentation, the important advantages that come from *the increase of food products* and from the formation of new vegetal species for the benefit of all, especially people most in need". The Holy Father John Paul II, who was well aware of what Paul VI called the tragedy of world hunger, concluded his message by asking God "to direct the application of scientific research to the production of new food supplies, since one of the greatest challenges that humanity must face, together with the danger of nuclear holocaust, is the hunger of the poor of this world". Encouraged by the Pope's message, in the Jubilee Year 2000 the Academy drafted its first Statement on Genetically Modified Food Plants to Combat Hunger in the World, which was then published in 2004. Ten years after this first Statement, the Council of the Academy, led by myself and counting on such authoritative members as Ingo Potrykus and Peter Raven, decided to update it with the meeting we are presenting in this volume. It is particularly significant that the new Statement was then signed by all the participants. It is our hope that this new effort will serve to clarify an issue which can undoubtedly and decisively contribute to solving the growing problem of world hunger.

The general view

Individual life times and population densities of any kind of living beings depend to a large extent on the availability of food, or in other words on food security. In archaeological times, humans found their nutrition as gatherers and hunters. About 10,000 years ago, our ancestors started to collect seeds and other plant materials from their preferred food plants. Agriculture then took its start by deliberate planting of the collected materials, growing the new plants up and harvesting their products. This neolithic or food-producing revolution must have taken place independently at different locations on the planet, both in the Old and in the New World. This cultural development allowed the human population to transform from small local or migrating tribes to larger, often resident communities which eventually developed into technologically advanced nations. A number of factors including food security contributed at various stages of this development to limit the ongoing population expansion.

A wide geographic exploration of our planet in the last millennium led stepwise to beneficial exchange of agricultural crops between continents of the Old and the New World. For example, Europe profited tremendously from the introduction of potatoes, tomatoes and maize from the Americas, while the New World introduced wheat, barley and rice, among other agricultural crops, from the Old World. None of these mass implantations led to serious ecological problems. As a result, food security generally improved and allowed the human population to continue to grow.

For a long time, agricultural management improved food security stepwise, largely through learning by doing and by learning from each other. Breeding methods became introduced and led to the selection of agricultural crops with higher yields and sometimes with higher nutritional values. It is mainly in the last century that increasing scientific knowledge and science-based technologies started to contribute to the improvement of food security, at least in parts of our planet. The green revolution boosted this development.

In the meantime scientific knowledge has tremendously increased, largely by the introduction of novel research strategies. Genomics, proteomics and metabolomics provide us with a rich scientific basis to understand better the sources and nutritional values of the products of many of our common food crops. In addition, research strategies, such as genetic engineering, have become available and can allow one to attempt experimentally to improve nutritional values and yields of food products. Site-directed mutagenesis of inherited genetic information and recombinant DNA techniques introducing carefully selected foreign genetic information into the genome of an agricultural target crop have recently become routine methodologies to reach envisaged improvements. Thanks to the set of actually available research strategies, selected products

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of such improvements can be assessed for their genetic setups and functional phenotypes before their introduction into the environment. In contrast to earlier practices, such as conventional plant improvement methodologies, today's molecular biological research strategies can confidently allow the researcher to obtain the envisaged genomic and functional abilities without introducing other, unexpected alterations into the developed product. There is no justification to assume that carefully carried out and controlled genetic engineering would principally go along with conjectural risks. Rather, molecular methodologies provide to the researcher highly secure and responsible approaches to improve crop properties such as higher nutritional values and improved health of the plant itself.

The good news given here can contribute to render agricultural practices more secure and also more sustainable. We must be aware, however, that the carrier capacity for agricultural crops is limited on our planet. Any longterm improvement of worldwide food security has to go hand in hand with a responsible and sustainable parenthood, together with the safeguard of the naturally given rich environmental diversity.

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Constraints to biotechnology introduction for poverty alleviation

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Poverty in developing countries is usually linked to low agricultural productivity. Inadequate quantity and quality of food impacts human development potential, physically and mentally. Reduced immunity to disease due to poor nutrition increases the burden and kills. Current technologies (fertiliser, improved seed, irrigation, pesticides) correctly applied can sustainably and safely increase crop yields. Purchase cost and infrastructural issues (lack of roads, credit, market access and market-affecting-trade-distortions), however, severely limit small scale farmers' ability to adopt these life sustaining and life saving technologies.

Plant Biotechnology has great potential to improve the situation. Delivery of the technology in the seed largely overcomes the logistical problems of distribution involved with packaged products: farmers can pass seed to each other. Once the initial research is completed the 'cost of goods' (that is of a biotechnologically delivered trait delivered in a seed) is zero. Total time to market is comparable between biotechnology products and conventionally bred seed. For some traits conventional breeding is not an option: the only way to introduce such a trait is by genetic engineering. Even for traits that can be improved by traditional breeding, genetic engineering may facilitate and speed up the process. Intellectual property issues are usually not a constraint in developing countries and in pro-poor agriculture.

It is notable that agricultural biotechnology uptake for commercially introduced traits has been extremely rapid, including in developing countries. However, for public good products from the public sector, despite much research in developing countries, this potential has not materialised. The politicisation of the regulatory process is an extremely significant impediment to use of biotechnology by public institutions for public goods. Costs, time and complexity of product introduction are severely and negatively affected (without such political impediment the technology is very appropriate for adoption by developing country scientists and farmers: it does not require intensive capitalisation). The regulatory process in place is bureaucratic and unwarranted by the science: despite rigorous investigation over more than a decade of the commercial use of genetically engineered (GE) plants, no substantiated environmental or health risks have been noted. Opposition to biotechnology in agriculture is usually ideological.

The huge potential of plant biotechnology to produce more, and more nutritive, food for the poor will be lost, if GE-regulation is not changed from being driven by 'extreme precaution' principles to being driven by 'science-based' principles. Changing societal attitudes, including the regulatory processes involved, is extremely important if we are to save biotechnology, in its broadest applications, for the poor, so that public institutions in developing as well as industrialised countries, can harness its power for good.

Against this background the programme of the study week was organised into the following sections. The *Introduction to the Study Week* presents the problem of increasing food insecurity in developing countries, the need for continued improvement of crop plants and agricultural productivity to address the problem, the track record and perspective of genetic engineering (GE) technology, and the roadblock to efficient use by the established concept of 'extreme precautionary regulation'. *Contributions From Transgenic Plants* will highlight what important contributions in the areas of tolerance to abiotic stress, resistance to biological stress, improved water use efficiency, improved nutritional quality, inactivation of allergens and reduction of toxins, are already in use or in the R&D pipeline. Following an account of the state-of-the-art of the technology and the world-wide, radical opposition on the use of the technology in agriculture, this session continues with the question of whether or not GE-plants diminish or promote biodiversity and describe what is necessary to achieve sustainable yield, including the contributions from the private sector.

In the section on the *State of Application of the Technology* concrete examples from Argentina show which products have made it over the hurdles of the regulatory regimes. This session concludes with a paper on the problems of and possible solutions

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in regard to intellectual property rights, and with a discourse on the ethics of the use and non-use of transgenic plants in the context of development. The session on the *Potential Impact on Development* will highlight what an important role transgenic plants could play if released from excessive regulation. The question of whether or not there is any scientific basis for an extreme precautionary attitude is analysed in the session on *Putative Risk and Risk Management*. A comparison of the molecular alterations to the genome by natural genetic variation and genetic engineering shows that there is *a priori* little reason to be concerned with genetic engineering of plants. In detailed case studies putative risks to the environment and the consumer are analysed, to explore whether in the history of use there was any case of real concern. This is followed by the lessons from 25 years of use, biosafety studies and regulatory oversight, and by an overview comparing GMO myths with reality.

A brief section on *Biofuels Must Not Compete With Food* indicates novel problems arising from the concept of biofuel production from agricultural land, already seriously affecting food security and concepts under study aiming at biofuel production from biological materials that will not compete with food sources. *Hurdles Against Effective Use For The Poor* describes which hurdles under the presently established regulatory regime prevent use of the technology for public good. The analysis focuses on (a) the political climate around GEs having been spread from Europe around the world; (b) the legal and trade consequences connected to regulation and political climate; (c) GMO over-regulation making use of GEs for the public sector inaccessible for cost and time reasons; (d) the financial support to professional anti-GE-lobby groups and (e) poor support for agricultural research in general.

The programme of the study week was designed (a) to present the potential of plant genetic engineering to contribute to food security, (b) to analyse the causes for the obvious exclusion of the public sector and projects from the delivery of public goods and (c) to develop concepts how to improve the situation to the benefit of the poor. The participants represented a wide and interdisciplinary range of scientific disciplines including philosophy, theology, political science, economy, agricultural law, agricultural economics, development economics, intellectual property rights, botany, ecology, plant pathology, evolution, botany, microbiology, agriculture, crop science, biochemistry, molecular biology, biotechnology, food safety, biosafety, and regulation. The participants jointly formulated and agreed unanimously to the following summary of the results of the study week in form of a 'STATEMENT' which summarises the scientific conclusions and recommendations following from those conclusions.

This STATEMENT is presented in five languages in print (English, Arabic, Chinese, Hindu, and Swahili) and in further 11 languages (Indonesia, Filippines, France, Germany, Italy, Japan, Korea, Portugal, Russia, Spain, and Turkey) in form of links to the internet. The English version is the authorised original, in case of inconsistencies in one of the translations, which have, however been carefully checked by Klaus Ammann.

The editors are very grateful to those who took care of the translations (English: Drafted and endorsed by all participants of the Conference, synthesized mainly by Ingo Potrykus, Peter Raven, Albert Weale, Chris Leaver

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Turkish: Selim Cetiner, Nadir Fayazoff). For more details see the translations.

Powerpoint presentations of the conference in pdf format are also available as hyperlink in the sequence of the original program.

Food insecurity, hunger and malnutrition: necessary policy and technology changes

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Ending food insecurity, hunger and malnutrition is a pressing global ethical priority. Despite differences in food production systems, cultural values and economic conditions, hunger is not acceptable under any ethical principles. Yet, progress in combating hunger and malnutrition in developing countries has been discouraging, even as overall global prosperity has increased in past decades. A growing number of people are deprived of the fundamental right to food, which is essential for all other rights as well as for human existence itself. The food and nutrition crisis has deepened in recent years, as increased food price volatility and global recession affected the poor. In a strategic agenda, it will be necessary to promote pro-poor agricultural growth, reduce extreme market volatility and expand social protection and child nutrition action.

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Ending hunger as a global priority

The current global architecture for governing food, nutrition and agriculture has not been able to adequately address the challenges the system now faces and ensure progress toward food security. Even when general ethical principles are understood and agreed upon, actors in the system do not take needed actions since they lack the right incentives for doing so [1,2]. A comprehensive new approach, founded upon strong ethical principles and right incentives, is needed to address persisting hunger and the rising challenges in the agri-food system. To realize the potential of technology and economic policies in reducing hunger and food insecurity, this approach should also give adequate attention to the role of institutions, including religious institutions.

The attention of the Catholic Church to poverty reduction and related actions has a long history. As stated in the Encyclical of Pope Leo XIII on capital and labor in 1891, the desire of the Church is that the poor should rise above poverty and wretchedness, and better their condition in life; and for this she makes a strong endeavor [3]. Fighting hunger seems to be one of the most obvious islands of consensus in world religions, and religious institutions, such as the Catholic Church, have an important role to play in advancing food security around the world. However, none of the global religious congregations can effectively address the hunger problem alone, and synchronized actions are needed on this issue.

Three different approaches have been developed for addressing food security and hunger. The *development* approach draws on economic, technological, and institutional strategies and innova-

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tions for hunger reduction. The *charity* approach emphasizes both private and public giving to the people in need, and the role of religious institutions is very strong. The *rights-based approach* focuses on prioritizing actions – including legal actions and advocacy – that enhance basic human rights, such as access to adequate food. All three approaches have an ethical base, and they all are intrinsically linked. Weaknesses in the development approach to hunger reduction, for example, undermine the rights-based approach in a way which cannot be easily compensated for by charitable actions. Technological innovations in food and agriculture are cutting across these different approaches for combating hunger. In the past, technological breakthroughs adopted on a large scale have had high positive social pay-offs – they have been a critical component in preventing Malthusian predictions of population growth outpacing agricultural production, and in instigating the Green Revolution in Asia in the 1960s and 1970s. New high-impact technologies such as biotechnology, biofortification and nanotechnology now offer further opportunities for boosting agricultural productivity and enhancing food quality and nutritional value. Science and technology alone, however, cannot eliminate hunger and malnutrition, and the power of agricultural technology is strengthened through related policies and institutions. At the same time, if agricultural innovations are blocked, development is also blocked, and hunger and poverty will be perpetuated.

The food and nutrition crisis expands and deepens

Global progress in combating malnutrition has been slow in past decades, with dramatic differences among countries and regions. The 2008 Global Hunger Index (GHI) score fell to 15.2 compared to 18.7 in 1990, indicating a slight improvement in the overall hunger situation [4]. (The GHI is a combined measure of three equally weighted components: (i) the proportion of undernourished as a percentage of the population, (ii) the prevalence of underweight in children under the age of five and (iii) the under-five mortality rate. The 2008 GHI is based on data until 2006 – the last year with data available at the time of publication.) But the absolute number of undernourished people in developing countries actually increased from 823 million in 1990 to 848 million in 2002–2005, and an estimated one billion in 2009 [5]. Even before the food price crisis in 2007–2008 hit the poor, roughly 160 million people were living in ultra poverty, on less than 50 cents a day [6]. In a worrying trend, the most severe deprivation is increasingly concentrated in Sub-Saharan Africa, which has experienced a significant increase in the number of the ultra poor since 1990 and is currently home to three-quarters of the world's ultra poor [6].

At their peaks in the second quarter of 2008, world prices of wheat and maize were three times higher than at the beginning of 2003, and the price of rice was five times higher. In response to high food prices, poor households had to limit their food consumption, shift to even less-balanced diets, and spend less on other goods and services that are essential for their health and welfare, such as clean water, sanitation, education and health care [7]. Food price hikes have also worsened micronutrient deficiencies, with negative consequences for people's nutrition and health, such as impaired cognitive development, lower resistance to disease and increased risks during childbirth for both mothers and children. Since children's nutrition is crucial for their physical and cognitive development and for their productivity and earnings as adults, the health and economic consequences of insufficient food and poor diets are lifelong – for the individuals as well as for society. A 2008 Lancet article shows that men who benefited from a randomized nutrition intervention when they were young children earned wages that were 50% higher than those of nonparticipants three decades later [8]. Thus, it must be assumed that even when a multiyear price shock ends, the adverse consequences for the poor and food insecure continue for decades.

The global financial crisis and recession are now adding to the burden on the poor as wages are lost, many small farmers find themselves unable to pay off their debts and capital for agriculture is further limited. With food and general costs of living on the rise, people in more than 60 countries turned to the streets in protest in 2007 and 2008. IFPRI estimates that recession and reduced investment in agriculture could raise international grain prices by 30% and push 16 million more children into malnutrition in 2020 compared with continued high economic growth and maintained investments [7]. At a global scale, the decline in investments leading to cuts in agricultural supply seems to be stronger than the demand decline due to the recession. These trends might soon put again strong upward pressure on food prices combined with increased price volatility.

The challenge of feeding the world has greatly increased. The recent hikes in food prices are not exceptionally high from a historical perspective but they have greatly increased the challenge of feeding the world's growing population [7]. Since the time of notoriously high food prices in the 1870s, world population has increased more than five times reaching 6.7 billion today and it is expected to reach 9 billion by 2050. To overcome existing hunger, feed an additional 2 billion people and accommodate rising demand from income growth, food production would have to be doubled by 2050.

Science and technology for hunger and poverty reduction

Existing land and water constraints, as well as further challenges for natural resources such as climate change, make the task of doubling food production in the next four decades additionally challenging. There is only about 12% or less of available arable land which is not presently forested or subject to erosion and desertification. The area of land in farm production could in principle be doubled, but only by massive destruction of forests and loss of biodiversity and carbon sequestration capacity. The other consequence of doubling food production this way is significant increases in the marginal costs of investment, which would translate in increased food prices.

Numerous studies have shown that spending on agricultural research and development (R&D) is among the most effective types of investment for promoting growth and reducing poverty. For example, for every 1 million rupees spent on agricultural R&D in India in the 1990s, 323 poor people were lifted above the poverty line [9]. Plant-breeding programs, in which the centers of the Consultative Group on International Agricultural Research (CGIAR) play a leading role, have developed more than 8000 improved crop varieties in the past 40 years.

The opportunities offered by agricultural science for the future are also wide. In an assessment of the key technological innova-

tions needed for advancement by 2020, 9 of the 16 technological innovations relate to agriculture and rural development, such as genetically modified crops and rural wireless communications [10]. Biofortification – the breeding of new varieties of staple crops that are rich in micronutrients – allows the poor to receive the necessary amounts of vitamin A, zinc and iron via their regular staple-food diets. Biofortification provides a means of reaching malnourished populations in relatively remote rural areas and delivering naturally fortified foods to people with limited access to commercially marketed fortified foods or supplements. New high-impact technologies such as nanotechnology and its applications, might allow people to eat foods without absorbing harmful allergens and cholesterol, and modify food taste and nutritional value. For such technologies, however, research efforts should be devoted to carefully studying both benefits and hazards early on in the application process.

Genetic modification has been successful in creating beneficial traits such as disease resistance, higher nutritional value and increased yields – traits which can be difficult to achieve through traditional breeding techniques. Biotechnology can increase small farmer productivity and equity in poor communities threatened by extreme weather, crop pests and different types of malnutrition. In addition, it can ameliorate environmental degradation by developing high-yield varieties, which require less use of chemical pesticides and do not require mechanical tilling. Since 1996, biotechnology has decreased the environmental impact associated with herbicides, and insecticide use has significantly reduced pesticide spraying. As a result, it has decreased the environmental impact associated with herbicide and insecticide use on these crops [11]. For consumers, biotechnology can improve health outcomes and reduce food and health expenditures.

Even though genetically modified foods currently available on the international market have passed risk assessments and are not likely to present risks for human health [12] opposition against genetically modified crops persists and has provoked wide attention and debate. On the surface, it appears as if interest group activism against genetically modified foods is motivated by precaution. However, a deeper look into the issue reveals that it is predominantly an issue of preferences. Therefore, the constructive solution would not be to enter into an exchange of dogmas, but an examination of the rationality of consumer preferences and improved information for customers.

From an ethical standpoint, the risks of growing genetically modified crops should be weighed against the risks of nonadoption. Rejection of genetically modified crops leads to negative externalities that hurt the poor. To sustainably save human lives without biotechnology investments, two options exist: use more environmental capital and undermine sustainability, and invest more in safety nets and direct social programs.

Both are very high-cost alternatives which are not sustainable.

Despite the benefits and the associated opportunity costs, agricultural growth in many developing countries continues to be hampered by lack of appropriate agricultural technologies. While in 2008, about 12.3 million farmers in 15 developing countries were growing biotech crops [13] these farmers still represent a small fraction of those working on the 400 million small farms globally. Dissemination of technology in agriculture requires much more upfront investment in the foundations of effective technology utilization, such as rural education, infrastructure and extension services.

However, public R&D investments have been stagnating since the mid-1990s, and the gap between rich and poor nations in generating new technology remains [14]. From 1992 to 2006, funding for the CGIAR, which is a major contributor to agricultural innovation in partnership with national research systems, increased by only 2% per year [15]. The current resources are hardly enough to work at the frontiers of new science, and the recent financial crunch further constrains the availability of capital for agriculture science in the developing world.

Strategic agenda for science and policy

At the global level, a science and technology initiative is needed to respond to risks such as rising food prices, economic recession, increased competition for natural resources and climate change. Its agenda should focus on increasing agricultural productivity, but also include increasing small farm incomes, sustainability of agricultural practices, natural resources management, international competitiveness, and food quality and health. Priorities should be set with a clear focus on the poor and food insecurity. For example, in the areas of agriculture, health and nutrition, focus should be placed on increasing lives saved and livelihoods improved, as well as economic productivity, growth and returns on investment. In addition, the proposed science and technology initiative would need to increase investments in R&D, explore new technologies, including biotechnology, and strengthen partnerships.

The renewed focus on agriculture, food and nutrition should be supported by three sets of complementary policy actions:

Promote pro-poor agricultural growth. To enhance agricultural productivity, investments should be scaled up in the areas of R&D, rural infrastructure, rural institutions, and information monitoring and sharing. Doubling investments in public agricultural research from US$5 to US$10 billion from 2008 to 2013 would significantly increase agricultural output and millions of people would emerge from poverty. If these R&D investments are targeted at the poor regions of the world – Sub-Saharan Africa and South Asia – overall agricultural output growth would increase by 1.1 percentage points a year and lift about 282 million people out of poverty by 2020 [15]. On a global scale, an evidence-based functional system is needed to ensure biosafety.

Reduce extreme market volatility. To prevent extreme volatility, it is essential to ensure open trade. In addition, two global collective actions for food security are needed: first, a small, independent physical reserve should be established exclusively for emergency response and humanitarian assistance. Second, a virtual reserve and intervention mechanism should be created to help avoid the next price spikes. The organizational design of the virtual reserve would include a high-level technical commission that would intervene in future markets and a global intelligence unit that would signal when prices head toward a spike [16].

Expand social protection and child nutrition action. To protect the basic nutrition of the most vulnerable and improve food security, agricultural growth and reducing market volatility must be accompanied by social protection and nutrition actions. Protective actions are needed to mitigate short-term

risks (incl. conditional cash transfers, pension systems and employment programs), and preventive actions are needed to avoid long-term negative consequences (including preventive health and nutrition interventions such as school feeding and programs for improved early childhood nutrition and strengthened and expanded to ensure universal coverage). In the formulation of global policy and technology promotion strategies, the different innovation needs and (risk) preferences of poor and rich need to be reconciled. To achieve this, first, innovation must not be compartmentalized as a need of a specific group, country or region, since such categorizations stop innovation in its tracks. Second, survival and basic needs should be acknowledged and treated as absolute, and must not be weighed against relative preferences. Third, solutions to overcome conflict must be found in the interest of the poor in terms of access to technology, which is implicit in the right to food, active development of pro-poor technology and access to product benefits.

Given that prioritization, sequencing, transparency and accountability are crucial for successful implementation, policy and governance practices in many developing countries must be strengthened. To achieve maximum effectiveness of policy and technology strategies, it is essential to close information gaps of credible and up-to-date data on the impacts of food and nutrition insecurity and the effects of policy responses. Technology, including biotechnology, for agricultural productivity growth is necessary for food and nutrition security. Making biotechnology available for developing countries' farmers is called for from all three approaches that ethically underpin the fight against hunger – development, charity and rights-based approach.

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Achieving food security in times of crisis

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In spite of several World Food Summits during the past decade, the number of people going to bed hungry is increasing and now exceeds one billion. Food security strategies should therefore be revisited. Food security systems should begin with local communities who can develop and manage community gene, seed, grain and water banks. At the national level, access to balanced diet and clean drinking water should become a basic human right. Implementation of the right to food will involve concurrent attention to production, procurement, preservation and public distribution. Higher production in perpetuity should be achieved through an ever-green revolution based on the principles of conservation and climate-resilient farming. This will call for a blend of traditional ecological prudence with frontier technologies, particularly biotechnology and information communication technologies.

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Mahatma Gandhi said in 1948 "God is bread to the hungry".

Food security involves physical, economic, social and environmental access to balanced diet, and clean drinking water for every child, woman and man. Physical access is a function of the

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availability of food in the market and is related to both in-country production and imports, when needed. Economic access is related to purchasing power and employment opportunities. Social access is conditioned by gender equity and justice. Environmental access is determined by sanitation, hygiene, primary healthcare and clean drinking water. Thus, both food and non-food factors determine food security.

The hunger crisis

In spite of the highest priority accorded to hunger elimination among the UN Millennium Development Goals (UN-MDGs), the FAO (Food and Agriculture Organisation) estimates that the number of people going to bed hungry is increasing. When UN-MDGs were adopted in 2000, about 820 million were estimated to be under-nourished. Now, it is over a billion. Why are we in this condition? The hunger crisis facing us has the following principal short-term dimensions:

- Environment
- Economics
- Equity
- Employment
- Energy

The long-term dimension relates to global warming and climate change.

Dealing with crisis

Environment

Among the key areas needing attention are:

- Conservation of prime farm land for agriculture, soil healthcare and enhancement
- Irrigation water availability and quality and rain water harvesting
- Biodiversity loss
- Damage to ecosystem services
- Ecological footprint (related to life styles) and population supporting capacity of ecosystems

Aristotle said long ago that the soil is the stomach of the plant. Exploitative agricultural practices lead to soil mining and damage to the physical, chemical and microbiological properties of the soil. Every farm family should have a soil health card giving integrated information on all aspects of soil health, like organic matter status, macro- and micro-nutrient availability and the hydraulic conductivity of the soil. Mobile Soil Health Vans should be organised. A national land care movement should deal with both the conservation of prime farm land for agricultural purposes and the prevention of soil erosion and degradation. The fertility of waste or wasted land should be restored. Building a sustainable water security system involves concurrent attention to supply augmentation and demand management. Supply augmentation involves harnessing all the major sources of irrigation water, namely rain, ground, surface, effluents and waste water and seawater. Rain water harvesting through a pond in every farm must become a way of life. Sea water constitutes over 97% of the water resources available in our planet. There is vast scope for sea water farming through agri-aqua farms. Conjunctive use of water like fresh water and treated industrial effluents should become institutionalised. Industry should give back the water it consumes in a good condition.

Demand management in agriculture should come from the adoption of 'more crop and income per drop of water' techniques. Agronomists should indicate in their publications not only yield per hectare, but also yield per unit of water. Micro-irrigation methods need to become universal.

Biodiversity loss and damage to ecosystem services is taking place at an alarming rate. This has serious implications in relation to our capacity to deal with the new challenges arising from climate change and transboundary pests. The loss of every gene and species limits our options for the future, particularly when recombinant DNA technology affords an opportunity to create novel genetic combinations capable of conferring resistance to abiotic and biotic stresses.

An institutional method to address environmental threats to food security is the organisation of community managed food and water security systems at the village level. This will comprise field **gene bank** through *in situ* on farm conservation of local land races, **seed bank** for ensuring the availability of seeds during times of drought and flood, **grain bank** involving storage of local food crops (often belonging to the category of orphan crops) and **water bank** in the form of ponds and reservoirs capturing rain water. Thus, conservation, cultivation, consumption and commerce can be linked into a **food security continuum**. A reason why malnutrition is increasing in the world is the centralised approach to both analysis and action. A decentralised, community centred approach to food security will help us to reach our nutrition goals speedily and surely.

Economics in relation to food security

The cost-risk-return structure of farming determines the decisions of farmers with reference to the choice of crops and investment on inputs. Input costs are going up partly due to the escalation in the price of petroleum products. Output prices are not increasing in tandem with a rise in the cost of production. Due to inadequate availability of institutional credit and effective insurance, small farmers get caught in a debt trap, with much of the borrowing coming from private money lenders at very high interest rates. **If farm ecology and economics go wrong, nothing else will have a chance to go right.** Public policies in the field of agriculture should give over-riding priority to safeguarding and improving the ecological foundations essential for sustainable agriculture, on the one hand and assured and remunerative marketing opportunities, on the other.

Equity

The social, economic, environmental and gender dimensions of equity must receive integrated attention. An area in intra-generational equity which needs urgent attention is the elimination of maternal and foetal under-nutrition resulting in the birth of children with low birth weight (LBW). Such LBW children suffer from several handicaps including impaired cognitive abilities. At the other end is the growing damage to our life support systems of land, water, biodiversity and climate, leading to reduced opportunities for a healthy and productive life to the children yet to be born.

A method of overcoming problems in the areas of environmental, social and gender inequity is to subject all the development programmes to a matrix analysis designed to ascertain whether the

programme is pro-nature, pro-poor and pro-woman. A pro-nature, pro-poor and pro-woman orientation is also essential in the area of technology development and dissemination.

Employment

The famine of jobs or purchasing power is often the cause of famine of food at the household level. Modern industry often leads to jobless economic growth. Agriculture including crop and animal husbandry, fisheries, forestry, agro-forestry, agro-processing and agri-business promotes job-led growth. Crop-livestock integrated farming systems enhance both income and nutrition security. In the developing countries of the Asia-Pacific Region, what we need is job-led economic growth, so that the goal of food for all coupled with human dignity can be achieved. The economics of human dignity demands that everyone should have an opportunity to earn his/her daily bread.

There are several successful models of promoting job-led economic growth in this region. One model relates to the successful experience in China of promoting higher small farm productivity and profitability on the one hand, and opportunities for skilled and remunerative non-farm employment through township–village–enterprises (TVE) on the other. This two pronged strategy has helped China to achieve both high farm productivity and impressive manufacturing capacity. 'Jobs for All' then becomes a reality.

The other model, developed at the MS Swaminathan Research Foundation (MSSRF), is known as the 'Biovillage' model of human-centred development. The Biovillage model involves the following three concurrent steps.

- Conservation and enhancement of the ecological foundation for sustainable agriculture, with particular attention to soil health care, rain water harvesting and efficient water use, biodiversity conservation and sustainable and equitable use, climate risk management, and the protection and development of village common property resources.
- Improving on-farm productivity based on ever-green revolution principles, which help to enhance farm productivity in perpetuity without associated ecological harm. This calls for mainstreaming ecological principles in technology development and dissemination.
- Generation of skilled and market-driven non-farm employment opportunities through improved post harvest technology and value addition to primary products.

Processing, storage and marketing require greater investment of technology and finance.

The Biovillage Council, which manages the biovillage activities through group co-operation, ensures that every adult in the village has an opportunity for a healthy and productive life

Energy

Each Biovillage Council develops a strategy for energy security involving a feasible and affordable blend of renewable and non-renewable sources of energy. Among the renewable sources solar, wind, biogas and biomass are particularly important.

Bridging the technology divide

Starting from the industrial revolution in Europe nearly 4 centuries ago, technology has been a major factor in North–South, rich–poor, rural–urban and gender divides. **If technology has been the primary cause of such divides, we should now enlist technology as an aid to bridging the divides.** An important requirement for promoting the 'Bridging the Divides Movement' is knowledge and skill empowerment. Harnessing modern Information and Communication Technologies (ICT) is a powerful method of empowerment of rural communities. The Village Knowledge Centre movement, launched in India by MSSRF in partnership with a multi-stakeholder National Alliance for Village Knowledge Revolution, is based on the principles of community ownership, demand driven and dynamic information, use of local language and capacity building. Capacity building and content creation are two key elements of this programme.

Biotechnology is becoming an important tool in creating novel genetic combinations. Action is needed at two ends of the spectrum for harnessing novel genetic combinations to meet current and future challenges arising from global warming and climate change. First, in village schools DNA Clubs should be organised to spread genetic literacy. Second, each Nation should have a statutory, professionally led National Biotechnology Authority. The bottom line of a Nation's Biotechnology Regulatory Policy should be:

> ***"the economic well being of farm families, food security of the nation, health security of the consumer, protection of the environment, biosecurity of the country and the security of national and international trade in farm commodities".***
>
> ***(Report of the M S Swaminathan Committee, 2004)***

Developing countries should develop regulatory procedures which ensure the safe and responsible use of biotechnology, particularly recombinant DNA technology. In India, a National Biotechnology Regulatory Authority is being created through an Act of Parliament.

From green to an ever-green revolution: Indian experience

In India, the 20th century was a period of agony and ecstasy on the farm front. The colonial period (1900–1947) was characterised by insignificant growth in food production and frequent famines. The last part of the colonial period witnessed the Bengal Famine of 1942–1943, when over 2 million children, women and men died from hunger. This led to Jawaharlal Nehru's famous statement soon after independence in 1947, **'everything else can wait, but not agriculture'**.

The Nehru period (1947–1964) was marked by emphasis on irrigation, power generation, production of mineral fertilisers, chemical pesticides, community development, national extension service, and above all strengthening of agricultural research and education through the establishment of agricultural universities. A post-graduate school was set up at the Indian Agricultural Research Institute, New Delhi, which was conferred in 1958 the status of a deemed university under the UGC Act of 1956. The first Agricultural University based on the Land Grant University system of the United States of America started functioning in 1960 at Pant Nagar in Uttar Pradesh (now in Uttarakhand).

In spite of all the measures taken to strengthen agricultural research, education, extension and development, the gap between

food production and food requirement continued to grow between 1950 and 1960. Consequently, food imports, largely under the PL-480 programme of the United States, grew year after year, reaching a peak level of 10 million tonnes in 1966. Globally and nationally, there was scepticism about India's capacity to feed its growing population.

To meet this challenge, an Intensive Agriculture District Programme (IADP) was started in the early 1960s to maximise the output of cereals like rice and wheat in districts where irrigation water was available. The strategy was to provide seeds, fertiliser and other inputs to improve productivity. During the first 15 years after independence, production increase was largely associated with area expansion and not due to higher yield. Consequently, the average yield of rice and wheat continued to stagnate at less than 1 tonne per hectare. It is under such circumstances, that I pointed out that the IADP, also referred to as the package programme, had one important missing ingredient, namely a genetic strain which can respond to the rest of the package, particularly soil nutrients and irrigation water.

The search for high-yielding varieties which can convert sunlight, water and nutrients into grains in an efficient manner first began in rice with the initiation of the *indica–japonica* hybridisation programme at the Central Rice Research Institute, Cuttack, in the early 1950s. Similar work was started in wheat in the mid-1950s, using mutation breeding techniques as well as hybridisation between *Triticum aestivum* varieties and sub-species *compactun* and *sphaerococum*. The *indica–japonica* hybridisation programme resulted in varieties like ADT-27 in Tamil Nadu and Mashuri in Malaysia. The programme did not make much headway due to sterility problems. In the case of wheat also, the expected improvement in yield potential did not take place because a short plant stature was also associated with short panicles and reduced yield potential. Fortunately, Japanese scientists led by Dr. Gonziro Inazouka identified Norin 10 and other genes which helped to break the negative correlation between plant height and panicle length. The Norin dwarfing gene was used by Dr. Orville Vogel in Washington State University, Pulman, to breed high-yielding winter wheats like Gaines. The same genes were used by Dr. Norman Borlaug in Mexico to develop semi-dwarf spring wheats. By adopting a shuttle breeding technique, Dr. Borlaug also made the wheat plant insensitive to photo-period and temperature. This gave birth to high-yielding spring wheat varieties Lerma Rojo-64A, Sonora 63, Sonora 64, Mayo 64 and other strains in Mexico. We obtained seeds of these varieties, as well as a wide range of segregating material from Dr. Borlaug in September 1963. The details of the semi-dwarf wheat programme initiated with the Norin dwarfing genes are contained in the publication 'Wheat Revolution – a Dialogue' [1]. Production advances were rapid resulting in the green revolution in 1968, due to the growth of a **Green Revolution Symphony**, consisting of mutually reinforcing packages of technology, services, public policy in input and out pricing and marketing, and above all farmers' enthusiasm.

In the area of technology, some of the significant steps taken included (a) the organisation of multi-location trials with 4 Mexican Semi-dwarf varieties during 1963–1964; (b) the organisation of National Demonstrations in the fields of resource poor farmers with small holdings from 1964 to 1965 onwards; (c) the import of 200 tonnes of seeds of Lerma Rojo-64A and Sonora 64 during 1965–1966 to expand the National Demonstration Programme throughout the wheat growing areas; (d) import of 18,000 tonnes of seeds from Mexico, mainly of the variety Lerma Rojo-64A for increasing the area under semi-dwarf wheat varieties; (e) selection of amber grain wheat varieties from the segregating populations sent by Dr. Borlaug and development of high-yielding amber wheats like Kalyan Sona and Sonalika, and initiation of a dynamic programme of cross-breeding both in *aestivum* and *durum* wheats to incorporate the Norin dwarfing genes into high quality Indian Wheat varieties like C306, bred by Chaudhury Ram Dhan Singh in the Punjab.

In the area of services, the important measures taken included (a) the setting up of a National Seed Corporation, (b) rural electrification, (c) rural communication, and (d) enlarged credit supply. The public policy measures led to the establishment of an Agricultural Prices Commission, the enforcement of a minimum support price through the Food Corporation of India, and the building up of grain reserves to feed the public distribution system. Because the new technologies are scale neutral but not resource neutral, special programmes like the small and marginal farmer support programmes were initiated. The aim was to ensure social inclusion in access to high-yield technologies.

The integrated packages of technology, services and public policies ignited farmers' enthusiasm and a small government programme became a mass movement. Writing in the Illustrated Weekly of India (May 11, 1969), I made the following remarks on the Punjab Wheat Miracle.

"Brimming with enthusiasm, hard-working, skilled and determined, the Punjab farmer has been the backbone of the revolution. Revolutions are usually associated with the young, but in this revolution, age has been no obstacle to participation. Farmers, young and old, educated and uneducated, have easily taken to the new agronomy. It has been heart-warming to see young college graduates, retired officials, ex-army men, illiterate peasants and small farmers queuing up to get the new seeds. At least in the Punjab, the divorce between intellect and labour, which has been the bane of our agriculture is vanishing".

To bring this significant development in India's agricultural evolution to public attention, the then Prime Minister Smt. Indira Gandhi released a special stamp titled 'The Wheat Revolution' in July 1968.

Similar opportunities for enhancing production through productivity improvement soon became available in rice, maize, sorghum and peal millet. Hence, the US scientist Dr. William Gaud coined the term 'Green Revolution' to indicate productivity triggered production increase. To ensure that a productivity based agriculture does not result in ecological harm due to the unsustainable exploitation of land and water, adoption of mono-culture and excessive use of mineral fertilisers and chemical pesticides, I appealed to farmers in the following words, not to harm the long-term production potential for short-term gains in my address to the Indian Science Congress held on Varanasi in January 1968:

"Exploitative agriculture offers great dangers if carried out with only an immediate profit or production motive. The emerging exploitative farming community in India

should become aware of this. Intensive cultivation of land without conservation of soil fertility and soil structure would lead, ultimately, to the springing up of deserts. Irrigation without arrangements for drainage would result in soils getting alkaline or saline. Indiscriminate use of pesticides, fungicides and herbicides could cause adverse changes in biological balance as well as lead to an increase in the incidence of cancer and other diseases, through the toxic residues present in the grains or other edible parts. Unscientific tapping of underground water will lead to the rapid exhaustion of this wonderful capital resource left to us through ages of natural farming. The rapid replacement of numerous locally adapted varieties with one or two high-yielding strains in large contiguous areas would result in the spread of serious diseases capable of wiping out entire crops, as happened prior to the Irish potato famine of 1854 and the Bengal rice famine in 1942. Therefore the initiation of exploitative agriculture without a proper understanding of the various consequences of every one of the changes introduced into traditional agriculture, and without first building up a proper scientific and training base to sustain it, may only lead us, in the long run, into an era of agricultural disaster rather than one of agricultural prosperity."

I pleaded for converting the *green revolution* into an *ever-green revolution* by mainstreaming the principles of ecology in technology development and dissemination. I defined 'ever-green revolution' as increasing productivity in perpetuity without associated ecological harm [2–5]. I pleaded for avoiding the temptation to convert the green revolution into a greed revolution. Unfortunately, ecologically unsound public policies, like the supply of free electricity, have led to the over-exploitation of the aquifer in the Punjab, Haryana and Western UP region. The heartland of the green revolution is in deep ecological distress [6]. The need for adopting the methods of an ever-green revolution has therefore become very urgent.

There are two major pathways to fostering an ever-green revolution. **The first is organic farming.** Productive organic farming needs considerable research support, particularly in the areas of soil fertility replenishment and plant protection. Soils in most parts of India lack organic matter and are also deficient both in macro- and micro-nutrients. A majority of farmers cultivate one hectare or less. Crop-livestock integrated farming will help to build soil fertility, but most small farm families have only 1 or 2 farm animals like cows, buffaloes and bullocks. Green manure crops and fertiliser trees can help to build soil fertility. Also, commercially viable organic farming methods will spread only if there is a premium price for organic products. Organic farming should be promoted in the case of vegetable and fruit crops and medicinal plants, where the danger of pesticide residues should be avoided.

The second pathway to an ever-green revolution is **green agriculture**. In this case, ecologically sound practices like conservation farming, integrated pest management, integrated nutrient supply and natural resource conservation and enhancement, are promoted. Green agriculture techniques could include the cultivation of crop varieties bred through the use of recombinant DNA technology, in case such varieties have advantages like resistance to biotic or abiotic stresses, or other attributes like better nutritive quality. In organic farming, the cultivation of genetically modified crops is prohibited. The cultivation of varieties bred with the help of molecular marker assisted selection is however allowed.

New possibilities can be envisaged by a combination of organic farming and high-yield agriculture. **Eco-agriculture** aims at mutually reinforcing relationships between agricultural productivity and conservation of nature. Innovative eco-agriculture approaches can draw together the most productive elements of modern agriculture, new ecological insights and the knowledge that local people have developed from thousands of years of living in harmony with nature. Eco-agriculture is defined as an approach that brings together agricultural development and conservation of biodiversity as explicit objectives in the same landscapes [4,7,8].

For resource poor farmers, green agriculture is the method of choice for producing more in an environmentally benign manner. The smaller the farm, the greater is the need for marketable surplus. Research on efficient micro-organisms which can help to build soil fertility, as well as fertiliser trees like *Faidherbia albida* will help both organic farming and green agriculture. The National Commission on Farmers NCF recommended in 2006 the initiation of a conservation farming movement in the heartland of the green revolution, to halt the damage now occurring to the ecological foundations essential for sustainable agriculture. NCF suggested the allocation of Rs. 1000 crores (US$ 200 million) to start with, for achieving a paradigm shift from exploitative to conservation farming in the Punjab-Haryana-Western UP region.

Sustainable food security

Despite the large number of nutrition safety net programmes introduced by the Central and State Governments from time to time, India still remains the home for the largest number of malnourished children and adults in the world. We should ask why we are in this regrettable and unacceptable situation. The answer lies in the basic structure of our consumption pattern.

Nearly two thirds of our population lives in rural areas. A majority of them are small and marginal farmers and landless labourers. They fall under the category **producer–consumer**. We have thus two categories, that is about 700 million **producer–consumers** and about 400 million **consumers**. In industrial countries, consumers will be about 97% and producer–consumers will be about 3%. Therefore widespread malnutrition and endemic hunger will persist unless the producer–consumer can consume a balanced diet. This situation also prevails in most countries in the Asia-Pacific Region. This will call for higher small farm productivity and profitability, on an environmentally sustainable manner. **An ever-green revolution accompanied by a small farm management revolution are hence vital components of a freedom from hunger movement.** How can we develop a sustainable and equitable food security system?

As pointed out earlier, food security at the level of each individual child, woman and man involves physical, economic and social access to balanced diet, including the needed macro- and micro-nutrients, safe drinking water, primary health care, sanitation and environmental hygiene. Thus, concurrent attention is needed to both food and non-food factors. Any national legislation related to food security should deal with production, access and absorption in a holistic manner. The following three steps are

urgently needed for ensuring adequate availability of home-grown food.

- First, we must take steps to **defend the gains** already made. This will involve integrating ecological principles in technology development. At the same time, public policies should promote the sustainable use of land, water, biodiversity and common property resources through conservation farming. If the regions, which now provide most of the grain for the public distribution system, do not shift to an ever-green revolution pathway of productivity improvement, the nation's food security system will be jeopardy.
- Second, we must **extend productivity gains** to the 'green but no green revolution' areas like the entire eastern India, where there is adequate water availability. These areas constitute the 'sleeping giant' of Indian agriculture and should be enabled to take to green agriculture in a big way through appropriate packages of technology, services and public policies.
- Third, we should **make new gains**, particularly in rainfed areas, which constitute 60% of the farm area in the country. Available data show that the yield gap (i.e. gap between potential and actual yields) in such rainfed semi-arid areas is as high as 200–300% in the case of pulses, oilseeds, millets, semi-arid horticulture, etc. Work on 'more crop and income per drop of water' and on planting a billion fertiliser trees like *Faidherbia albida* should be promoted. Water harvesting and efficient water use should become a way of life in such areas. A *Pond in Every Farm* should become a habit and where appropriate, labour from the National Rural Employment Guarantee Act (NREGA) programme should be utilised for constructing farm ponds in the fields of small and marginal farmers in drought-prone areas.

India has nearly a billion farm animals including poultry. Livestock and livelihoods are intimately inter-related in all major agro-ecosystems, but more particularly in arid and semi-arid areas. Also, the ownership of livestock is more egalitarian than that of land. Therefore, crop-livestock integrated farming systems should be promoted because this confers multiple benefits, like income and nutrition security.

There are several other areas involving a blend of technology and social engineering which need immediate attention.

The first area relates to giving the power and economy of scale to small and marginal farmers, who constitute the large majority of the farming population of this region. The average size of holding is declining year after year. Yet, Green Agriculture, involving Integrated Pest Management IPM, Integrated Network solutions INS, rain water harvesting and watershed management, requires cooperative efforts among the farm women and men living in a watershed or the command area of an irrigation project. Hence, efforts to promote either cooperative or group farming or the formation of Small Farmers' Self-help Groups, should be intensified with the help of Agricultural and Animal Sciences Universities. Contract farming can be promoted if it represents a win–win situation to both producers and purchasers.

Second, there is increasing feminisation of agriculture. All agricultural research and development programmes must be gender sensitive. Taking into consideration the multiple burdens on a woman's time, every effort should be made to reduce the number of hours of work of rural women and increase their earning per hour of work. Also, support services for women in agriculture like crèches and day care centres, as recommended by the National Council of Farmers, should be provided. The gender dimensions of the impact of climate change should be studied because women generally tend to be in charge of water, fodder, fuel wood and livestock.

Third, 70% of populations in rural India are young women and men below the age of 35. A survey of the National Sample Survey Organization (NSSO) has revealed that over 45% of farmers would like to quit farming, if there is any other livelihood option. Attracting and retaining youth in farming are hence major challenges. This is where a technological upgrading of agriculture and multiple livelihood occupations become important. We must make agriculture economically rewarding and intellectually satisfying. This will call for blending traditional wisdom and ecological prudence with frontier technologies like biotechnology and information and communication technologies.

Fourth, we should enhance the coping capacity of farm families to the adverse impact of climate change. For this purpose, at least one woman and one male member of every local self-governing bodies should be trained as **Climate Risk Managers**. They should become well versed in the art and science of monsoon and climate management. '**Weather information for all**' should become a reality through the establishment of a national grid of mini-agro-meteorological stations.

Fifth, there are new pathways offered with the help of modern breeding technology in the area of biofortification of crops, such as the golden rice.

Overcoming hidden hunger caused by micronutrient deficiencies

The challenge of micronutrient deficiencies in diet is becoming great especially for the chronically poor. Iodine, vitamin A and iron deficiencies are serious in many parts of the developing world. Worldwide, iron deficiency affects over one billion children and adults. Recent analyses from the United States Institute of Medicine [9–12] highlight the effect of severe anaemia in accounting for up to one in five maternal deaths. Maternal anaemia is pandemic and is associated with high MMR; anaemia during infancy, compounded by maternal under-nutrition, leads to poor brain development. Iron deficiency is also a major cause of permanent brain damage and death in children and limits the work capacity of adults [12–17]. There is not enough appreciation of the serious adverse implications to future generations arising from the high incidence of low birth weight among newborn babies. LBW is a major contributor to stunting and affects brain development in the child. The new millennium will be a knowledge century, with agriculture and industry becoming more knowledge intensive. Denial of opportunities for the full expression of the innate genetic potential for mental development even at birth is the cruelest form of inequity that can prevail in any society [15]. We must take steps to eliminate as soon as possible such inequity at birth leading to a denial of opportunities to nearly one out of every three children born in South Asia, for performing their legitimate role in the emerging knowledge century.

Wherever rice is the staple, a multi-pronged strategy for the elimination of hidden hunger should be developed by rice scientists. IRRI has undertaken research on enriching rice genetically

with iron and other micro-nutrients. Fortification, promotion of balanced diets, new semi-processed foods involving an appropriate blend of rice and micro-nutrient rich millets as well as genetic improvement, could all form part of an integrated strategy to combat the following major nutritional problems in predominantly rice eating families:

- Protein-energy malnutrition
- Nutritional anaemia (iron deficiency)
- Vitamin A deficiency
- Iodine deficiency
- Dietary deficiencies of thiamin, riboflavin, fat, calcium, vitamin C and zinc, as I suggested [12] that the International Rice Commission could include nutrition security aspect as an integral part of the International Network.

We must fight the serious threat to the intellectual capital of developing countries caused by low birth weight children and hidden hunger [18]. Some of the research areas worthy of attention in this context are described below.

Breeding for nutritional quality

Nutritive quality is as important as cooking quality for countries in tropical Asia, where rice is the principal source of dietary protein, vitamin (B_1) and minerals (Fe, Ca) [19]. Rice provides about 40% of the protein in the Asian diet. Among the cereal proteins, rice protein is considered to be biologically the richest by virtue of its high digestibility (88%), high lysine content (+4%) and relatively better net protein utilisation. Yet, it is nutritionally handicapped on account of two factors *viz*: (i) its inherently low protein content (6–8%) and (ii) inevitable milling loss of as much as 15–20%. Unlike other cereals, increased protein content in rice does not result in decreased protein quality as all of its fractions (glutelin 65%, globulin and albumin 15% and lysine–cysteine-rich prolamin 14%) are rich in lysine and other essential amino acids. Even a marginal increase of 2 percentage points of protein, therefore, would mean 10–15% increase in the nutritionally rich protein intake in our diet.

Genetic engineering approaches for correcting micronutrient deficiencies

Breeding for Nutritional Improvement was recommended at the 19th Session of the International Rice Commission, which called for an increase in focus on strategies to combat malnutrition [20,21]. There are four categories of direct intervention believed to be successful in reducing micro-nutrient malnutrition; supplementation, fortification, dietary diversification and genetic enhancement [22]. Nutritional status of populations will focus on the potential for improving malnutrition, primarily micronutrient malnutrition through genetic improvement.

Golden rice

About 250 million people worldwide are deficient in vitamin A. Over five million children in South and South-east Asia are reported to suffer from the serious eye disease 'xerophthalmia' every year and about 5,00,000 of them eventually become partially or totally blind due to deficiency of vitamin A. Besides affecting vision, vitamin A deficiency predisposes children to varied respiratory and intestinal diseases resulting in high mortality. Researchers from Swiss Federal Institute of Technology inserted these genes from daffodil and a bacterium into temperate rice plants to produce a modified grain, which has sufficient β-carotene (precursor of vitamin A) to meet total vitamin A requirements in a typical Asian diet [23]. Golden rice technology was made available to developing nations for research. If this technology can be moved to the production stage, it could represent an important contribution to improved human nutrition. In particular, rice fortified genetically with vitamin A and iron will be very useful to improve the nutritional status of pregnant and nursing women.

Iron deficiency

Iron deficiency anaemia (IDA) is the world's most common nutritional deficiency. It affects pregnant and nursing women and young children most commonly. IDA in mothers predisposes to still births, neonatal mortality, anaemia and low birth weight in infants, and increases the risk of maternal mortality [10,12]. Regular intake of iron or administration of iron prevents anaemia. Daily supplementation with iron–folic acid tablets is a low-cost and effective intervention. Genetic enrichment of iron in rice has also been accomplished through recombinant DNA technology [24].

To sum up, Indian agriculture is at the crossroads. Our population may reach 1750 million by 2050. Per capita crop land will then be 0.089 ha and per capita fresh water supply will be 1190 m^3/year. Food grain production must be doubled and the area under irrigation should go up from the current 60 million ha to 114 million ha by 2050. Degraded soils should be restored through increase in carbon pools in soils. How are we going to achieve a match between human numbers and human capacity to produce adequate food for all? To quote Edward O. Wilson [25] in *The Future of Life:*

> ***"The problem before us is how to feed billions of new mouths over the next several decades and save the rest of life at the same time without being trapped in a Faustian bargain that threatens freedom from security. The benefits must come from an evergreen revolution (as proposed by Swaminathan). The aim of this new thrust is to lift production well above the levels attained by the Green Revolution of the 1960s, using technology and regulatory policy more advanced and even safer than now in existence".***

Making hunger history in the Asia-Pacific Region

With the spread of democratic systems of governance in most parts of the world, a world without hunger is an idea whose time has come. Access to balanced diet and clean drinking water must be a fundamental right of every human being. **This will call for a shift from a charity based approach to hunger elimination to a right based one.** The Government of India is currently developing legislation to ensure food security for all. Such a National Food Security Act, to be effective, should deal with food availability, access and absorption in an integrated manner. Food availability can be ensured by launching a 'bridge the yield gap' movement, which is designed to help in narrowing or eliminating the gap between potential and actual yields through packages of technology, services and public policies.

Food access can be ensured through making food availability at affordable cost and by generating sustainable livelihood oppor-

tunities in the farm and off-farm sectors. **A rights based approach to access can provide for common and differentiated entitlements.** The common entitlement should aim to ensure adequate availability of food in the market coupled with an effective public distribution system which will enable all citizens to access essential quantities of staple grains at a reasonable price. Differentiated entitlement will refer to providing food at low price to the socially and economically underprivileged sections of the society. Thus, there will be universal access to the needed calories and proteins, making the goal of food for all a reality.

A National Food Security Act should in addition to aiming to end poverty induced protein–energy malnutrition, should also provide for the following:

- Elimination of hidden hunger caused by the deficiency of micro-nutrients like iron, iodine, zinc, vitamin A and vitamin B_{12} through a food cum fortification approach. In particular, emphasis should be placed on providing horticultural remedies for the nutritional maladies prevailing in an area, based on local foods.
- Provision of clean drinking water to ensure food assimilation in the body.
- Attention to non-food factors like primary health care, environmental hygiene and sanitation.
- Launching of a nutrition literacy movement and training one woman and one man in every village as 'Hunger Fighters'.

In the ultimate analysis we will succeed in achieving food security in an era of global change, only through a well planned and concerted endeavour at the global, national and local levels. Centralised goals and resource allocation should be coupled with decentralised planning and action. Community food and water security systems involving the establishment of local level gene, seed, grain and water banks will facilitate both as ever-green farm revolution and sustainable food and nutrition security. Such local level Food Security systems will also help to enlarge the shrinking food basket by including a wide range of millets, legumes and tubers in the diet.

FAO is the flagship of the global resolve to end hunger. The Asia-Pacific Region is the home of the largest number of under-nourished children, women and men. Hunger can be overcome if there is the requisite fusion of professional skill, political will and action, farmers' enthusiasm and above all, people's participation. The FAO Regional office for the Asia-Pacific Region has the unique opportunity for promoting a Food Security Symphony to generate the needed degree of convergence and synergy among the numerous nutrition safety net programmes in operation in our region.

Finally, we should develop and spread climate-resilient cropping and farming systems. Gene Banks for a Warming Planet are necessary [26]. Breeding strategies should give priority to developing varieties of crops, characterised by a high per-day productivity because global warming will lead to a reduction in the duration of crops like wheat and rice under sub-tropical conditions [26]. *A National Climate Management Movement* should include appropriate mitigation and adaptation measures. This is an essential requirement for an ever-green revolution [27].

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The past, present and future of crop genetic modification

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The introduction of science and technology into agriculture over the past two centuries has markedly increased agricultural productivity and decreased its labor-intensiveness. Chemical fertilization, mechanization, plant breeding and molecular genetic modification (GM) have contributed to unparalleled productivity increases. Future increases are far from assured because of underinvestment in agricultural research, growing population pressure, decreasing fresh water availability, increasing temperatures and societal rejection of GM crops in many countries.

Introduction

The world has experienced a succession of shocks over the past two years: a global food crisis, spiraling energy costs, accelerating climate change and most recently, a financial meltdown. The food crisis sparked riots in countries on every continent (http://www.time.com/time/world/article/0,8599,1717572,00.html).

But even as each crisis sweeps the previous one out of awareness, it is crucial to recognize that the food crisis is not a transient phenomenon. Indeed, crisis is a misnomer.

The current situation developed over a very long time as a result of relentlessly increasing demand pushing against a shrinking natural resource base, even as investment in agricultural research and development declined decade by decade. The oil price spike combined with widespread droughts in 2007 and 2008 to aggravate the underlying trends and send grain prices spiraling. Prices have come down since, but the overall upward trend persists. Indeed, the adequacy of the food supply will increasingly be a crucial issue, if not *the* crucial, of the 21st century [1].

Integration of science and technology into agriculture

Food security is not a new concern. In recent times, it was Thomas Malthus' famous 1798 Essay on Population that crystallized the problem of balancing food and human population [2]. Indeed, Malthusian has entered the language to denote the prophecy that humanity is doomed to poverty and famine because the growth of the human population must inevitably outstrip mankind's ability to increase food production. Malthus penned his essay at about the time that science began to enter agriculture in earnest. Late 18th century milestones were Joseph Priestley's discovery that plants emit oxygen [3] and Nicholas-Théodore de Saussure's definition of the chemical composition of plants [4]. Malthus could not have envisioned the extraordinary increases in productivity that the integration of science and technology into agricultural practice would stimulate over the ensuing two centuries.

Both organic and mineral fertilization of plants have ancient roots. Long before the reasons were understood, people knew that certain chemicals, such as saltpeter and lime, as well as a wide variety of biological materials ranging from fish and oyster shells to manure and bones stimulated plant growth [5]. Justus von Liebig laid the foundation for the modern chemical fertilization methods in the early 19th century by identifying the major chemical requirements for plant growth [6]. Although it was known by mid-century that biological sources of nitrogen could be replaced by chemical sources, supplying nitrogen in the reduced or oxidized forms that plants use remained a major limitation until the development early in the 20th century of the Haber–Bosch process for fixing atmospheric nitrogen on an industrial scale [7]. Today agriculture in the developed world relies primarily on chemical fertilizers.

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Crop domestication

Long before chemistry entered agriculture, people were doing what we now call genetic modification (GM), transforming inedible wild plants into the crop plants that feed people and their animals today. Corn, also known as maize (*Zea mays*), remains arguably the most spectacular feat of genetic engineering ever accomplished. Its huge ears, packed with starch and oil, provide one of humanity's three top food and feed crops. Corn bears little resemblance to its closest wild relative, teosinte. Indeed, the two are so dissimilar that when teosinte was first discovered in 1896, it was assigned to a different species and named *Euchleana mexicana.* Although it was already known in the 1920s that teosinte and corn have the same number of chromosomes and readily produce fertile hybrids, controversies about their relationship and about the origin of corn continued throughout most of the 20th century.

It was the work of Dr John Doebley and his colleagues starting with the genetic analysis of teosinte–corn hybrids that precisely defined the genetic changes that transformed teosinte into modern corn (http://www.teosinte.wisc.edu/publications.html). Perhaps the most remarkable outcome of his genetic sleuthing is that the difference between teosinte, a grass with hard, inedible seeds and modern corn resides in just a handful of genes. Fossilized cobs recovered from caves in Mexico and dated as more than 6000 old already have the multirowed character of the modern corn ear, as do almost 4000 year-old cobs from the Ocampo Caves in northeastern New Mexico [8]. Doebley's later work with the evolutionary geneticist Svante Paabo traced the key genetic changes that transformed teosinte into corn to the Balsas River Valley in Mexico and dated them to roughly 6–10,000 years before the present. What is even more remarkable is that once this handful of mutations had been brought together, the suite of genetic changes stayed together and spread very rapidly, so that the same group of alleles had already penetrated into the American Southwest more than 3000 years ago.

Perhaps the most important insight that has been gained through the molecular analysis of crop domestication is that people have vastly changed wild plants to transform them into crop plants and that this has been done over many thousands of years. All of the changes are genetic changes. This is as true of wheat and rice as it is of tomatoes, cabbage and oranges. Each crop has its own interesting history [9]. Among the most important traits that distinguish wild from domesticated plants is the retention of mature seeds on the plant. Plants have a variety of mechanisms for dispersing their seeds, central to which are the shattering of the seed structure upon maturation. It is much easier for people to harvest seeds if they remain attached to the plant, hence the selection of genetic changes, technically known as *mutations*, that prevent seed dispersal is thought to be among the earliest steps in crop domestication.

Among the many other traits altered during domestication are the size and shape of foliage, tubers, berries, fruits and grains, as well as their abundance, toxicity and nutritional value. The underlying genetic differences that distinguish a domesticated crop plant from its wild progenitors are many, but molecular analysis is revealing that key changes are often in genes that encode transcription factors, proteins that regulate the expression of many other genes [10]. Differences in nutrient composition among varieties of the same crop are attributable to mutations in genes coding for proteins of certain biosynthetic pathways. For example, mutations in genes for enzymes involved in the conversion of sugar to starch gave rise to sweet corn varieties.

Modern crop improvement

Crop improvement benefited from both the Mendelian and the molecular genetic revolutions of the 20th century. Austrian monk Gregor Mendel's pioneering observations on inheritance, published in 1865, were made independently by Dutch botanist Hugo de Vries, only then gaining the interest of other geneticists [11]. Indeed, a simple demonstration project to illustrate Mendelian inheritance led to the discovery of hybrid vigor, a phenomenon whose incorporation into crop breeding resulted in a dramatic expansion of the corn ear and, thereby, crop yield. The discovery is attributed to George Harrison Shull, working at the Carnegie Institution of Washington's Station for Experimental Evolution. He was asked by the Station's director to develop a demonstration of Mendel's rules of inheritance. In the course of these experiments, he grew curious about why some kinds of corn made more rows of kernels than others, so he inbred the respective varieties and then crossed them to see whether row number trait segregated in the simple way that Mendel had observed with round and wrinkled peas. What he discovered instead is that when he crossed the inbred lines to each other, he got tall healthy uniform plants with much bigger ears [12]. This phenomenon, called hybrid vigor or heterosis, is the basis of today's extraordinarily productive hybrid corn varieties [13].

Curiously, when they were first introduced in the US during the 1930s, corn hybrids faced a good deal of the kinds of resistance that biotech crops face today. They were complex to produce and agriculture experiment stations were not interested. Eventually a company was formed to produce hybrid seed. But farmers accustomed to planting seed from last year's crop saw no reason to buy it. It was only when farmers realized the yield benefits and the drought-resistance of hybrid corn during the 1934–1936 dust-bowl years that hybrid corn was rapidly adopted in the mid-west [14].

Techniques for accelerating mutation rates with radiation and chemicals and through tissue culture were developed and widely applied in the genetic improvement of crops during the 20th century [15]. Such techniques introduce mutations rather indiscriminately and require the growth of large numbers of seeds, cuttings or regenerants to detect desirable changes. Nonetheless, all of these approaches have proved valuable in crop improvement and by the end of the 20th century, more than 2300 different crop varieties, ranging from wheat to grapefruit, had been developed using radiation mutagenesis [16].

Mechanization of agriculture

Another major development whose impact Malthus could not have envisioned is the mechanization of agriculture. Human and animal labor provided the motive force for agriculture throughout most of its history. Early tractors powered by steam engines were large and unwieldy, but the invention of the internal combustion engine at the turn of the 20th century led to the development of smaller and more maneuverable machines. The mechanization of plowing, seed planting, cultivation, fertilizer and pesticide distribution and harvesting accelerated in the US,

Europe and Asia following World War II [17]. Agricultural mechanization drove major demographic changes in all developing countries. In the US, 21% of the workforce was employed in agriculture in 1900 [18]. By 1945, the fraction had declined to 16% and by the end of the century the fraction of the population employed in agriculture had fallen to 1.9%. At the same time, the average size of farms has increased and farms have increasingly specialized in fewer crops.

The Green Revolution

Malthus penned his essay when the human population of the world stood at less than a billion. The population tripled over the next century and there was a resurgence of Malthusian predictions of mass famines in developing countries that had not yet incorporated science-based and technology-based advances into their agricultural systems. Perhaps the best known of the mid-century catastrophists was Paul Ehrlich, author of The Population Bomb [19].

It took the work of just a handful of scientists, principally plant breeders Borlaug, Swaminathan and Khush, to avert the predicted Asian famines [20]. The Green Revolution was based on the development of rice and wheat varieties with mutations in genes that controlled their growth rate, resulting in dwarf varieties able to respond better to fertilizer application without falling over. Subsequent breeding for increasing yield continued to increase the productivity of these crops by as much as 1% per year. Instrumental in these discoveries were the first two institutes established by the Consultative Group on International Agricultural Research (CGIAR), the International Rice Research Institute (IRRI) (http://www.irri.org/) in the Phillipines and the International Maize and Wheat Improvement Center (CIMMYT) (http://www.cimmyt.org/). Remarkably, the Green Revolution innovations of the late 20th century reduced the fraction of the world's hungry from half to less than a sixth, even as the population doubled from 3 to 6 billion.

Molecular genetic modification (GM) of crops

A genetic revolution that began in the 1960s led to the development of a new set of methods for modifying plants. Research in the 1950s and 1960s identified the existence of tiny chromosomes, called plasmids, in bacteria that could replicate themselves independently [9]. Other discoveries led to the identification of proteins, called restriction enzymes, that cut the small chromosomes in a way that made it possible to insert a piece of genetic material from a completely different organism, then reseal the plasmid. The new 'recombinant' plasmid could then be reintroduced into a bacterium, where it replicated itself many times over, even as the bacteria multiplied. This amplification of the recombinant plasmids yields enough copies of the gene of interest to permit its sequence analysis and its modification. The techniques of cloning and sequencing DNA underlie today's genomic revolution, in which the genetic information has been decoded for literally hundreds of different organisms, from viruses and bacteria to plants, animals and humans.

Additional techniques were developed for the introduction of genes into plants. These generally use either the soil bacterium *Agrobacterium tumefasciens*, which naturally transfers a segment of DNA into wounded plant cells, or mechanical penetration of plant cells using tiny DNA-coated particles [21]. This combination of techniques has made it possible to introduce into plants genetic material from either the same or a related plant or even an unrelated organism, such as a bacterium or a different species of plant.

Several crop modifications achieved using these methods are now in widespread use. Perhaps the best known of these are crop plants into which a gene from the soil bacterium, *Bacillus thuringiensis*, has been introduced. *B. thuringiensis* has long been used as a biological pesticide because it produces a protein that is toxic to the larvae of certain kinds of insects, but not to animals or people (http://www.extension.umn.edu/distribution/cropsystems/DC7055.html). The gene coding for the toxin is often called 'the Bt gene' for its bacterial origin. The Bt toxin genes, which constitute a family of closely related proteins, have been introduced into several different crops, primarily corn and cotton. In the US and Europe, pest-protected crop varieties are produced almost exclusively by companies such as Monsanto, DuPont and Syngenta. In other parts of the world, including in China and India, such crop modifications are being done by both the public and private research sectors.

Another widely accepted crop modification is the introduction of genes that confer resistance to herbicides. Herbicides are chemical compounds that kill plants by blocking physiological processes that are necessary for plant growth and survival (http://www.hort.wisc.edu/cran/pubs_archive/../HowHerbicideWork.pdf). These are generally processes unique either to all plants or certain kinds of plants. Among the most widely used today are compounds that interfere with the production of amino acids that plants make, but animals do not [22]. Herbicide-tolerant crop plants make it possible to control weeds with an herbicide without damaging the crop and have been derived through natural and induced mutations, as well as by introduction of genes from either bacterial sources or modified genes from plant sources. Today, herbicide-tolerant varieties of many crops, most importantly soybeans and canola, are widely grown.

Papaya ringspot virus-resistant papayas are a remarkable GM achievement that saved the Hawaiian papaya industry [23]. Papaya ringspot virus (PRSV) is a devastating insect-borne viral disease that wiped out the papaya industry on Oahu in the 1950s, forcing its relocation to the Puna district of the big island. By the 1970s, the Puna district was producing 95% of Hawaii's papayas. PRSV was first detected in the Puna district in 1992; by 1995 it was widespread and threatening the industry. However, Dennis Gonsalves and his colleagues at Cornell University began a project in 1985 to introduce a viral gene into papayas based on the observations made in Roger Beachy's group at Washington University that introducing a viral gene could make a plant resistant to the virus from which the gene came [24].

The first transgenic papaya plants expressing a PRSV gene were ready in 1991, small field tests began in 1992 and large-scale field tests began in 1994. Approvals from the Animal Plant Health Inspection Service (APHIS) of US Department of Agriculture (USDA), as well as the Environmental Protection Agency (EPA) and the Food and Drug Administration (FDA) for release of the seeds to farmers took another three years, by that time many papaya farmers had gone out of business. Transgenic seeds were released in 1998 and by 2000, the papaya industry had come back to pre-1995 levels. Although it was not known at the time, recent

studies have shown that the resistance is attributable to post-transcriptional gene silencing, a process in which a small RNA derived from a double-stranded version of the viral gene transcript initiates the cleavage of invading viral RNA [25]. This remarkable method of crop protection enhances a mechanism present in plants and responsible for protecting the plant from further infection by the same and closely related viruses, much as the development of immunity protects people and animals from reinfection by pathogens.

Adoption of GM crops

Although the use of molecular modification techniques in crop improvement engendered controversy from the beginning, GM crops have experienced unprecedented adoption rates since their initial introduction in 1996. By 2008, the latest year for which statistics are available, roughly 10% of cropland was planted in GM crops [26]. Transgenic crops were grown on more than 300 million acres in 25 countries by more than 13 million farmers, 90% of whom were small-holder, resource-poor farmers. The vast majority of transgenic cropland is devoted to just four transgenic crops: cotton, maize, soybean and canola, but the list of transgenic crops is growing and already includes papaya, tomato, poplar, petunia, sweet pepper, squash, alfalfa and, for the first time in 2008, sugar beet.

Few of the widely anticipated adverse effects have materialized. While some resistance to the Bt toxin has developed, it has not been as rapid as initially feared and second-generation, two-Bt gene strategies to decrease the probability of resistance are already being implemented [27]. Predicted deleterious effects on nontarget organisms, such as monarch butterflies and soil microorganisms have either not been detected at all or are not significant. Moreover, while conventional pesticides use decreases the abundance of beneficial insects, Bt crops do not.

The many studies that have been done to assess the safety of foods containing or consisting of GM crops have reached the conclusion that GM foods are at least as safe as non-GM foods [28]. This is in part because of the close scrutiny paid during product development to the potential for toxicity and allergenicity of the proteins encoded by genes being added.

To date, the unexpected effects have been beneficial. For example, many grains and nuts, including corn and peanuts, are commonly contaminated by mycotoxins, toxic compounds made by fungi that follow boring insects into the plants. Two of these, fumonisins and aflatoxin, are extremely toxic and carcinogenic. Bt corn, however, shows as much as a 90% reduction in mycotoxin levels because the fungi that follow the boring insects into the plants do not get into the Bt plants [29].

As well, there is evidence that planting Bt crops reduces insect pressure in other crops growing nearby. Bt cotton has been widely planted in China. Analysis of the population dynamics of the target pest, the cotton bollworm, showed that Bt cotton not only controls the bollworm on transgenic cotton designed to resist this pest, but also reduces its presence on other host crops and thereby decreases the need for insecticide sprays in general [30].

Future challenges in agriculture

The scientific and technological advances in agriculture of the 19th and 20th centuries have been nothing less than spectacular. Since Malthus' time, the human population has expanded more than sixfold. In the developed world, agriculture has become less labor-intensive and has kept apace of population growth worldwide. Today, less than 1 in 50 citizens of developed countries grows crops or raises animals for food. On the one hand, this means that most people live in cities and find livelihoods that pay higher wages than farming. Those remaining on farms often also work in off-farm jobs, raising average farm income. On the other hand, this means that most citizens of developed countries have little knowledge of what it takes to create the bounty of foods that stock contemporary supermarkets.

Moreover, after a half-century's progress in decreasing the fraction of humanity experiencing hunger from half to less than a sixth, the food crisis and the more recent global financial crisis have again begun to swell the ranks of the hungry [31]. Population experts anticipate the addition of another two to four billion people to the planet's population within the next three to four decades [32]. However, the amount of arable land has not changed appreciably in more than half a century, increasing by only about 10% [33]. And it is not likely to increase much in the future because we are losing it to urbanization, salinization and desertification as fast or faster than we are adding it.

Another variable that is becoming crucial is the availability of fresh water for agriculture. Today, about one-third of the global population lives in arid and semiarid areas, which cover roughly 40% of the land area. Climate scientists predict that in coming decades, average temperatures will increase and dryland area will expand [34]. Even now, inhabitants of arid and semiarid regions of all continents are extracting ground water faster than aquifers can recharge and often from fossil aquifers that do not recharge [35].

Thus the challenges to agriculture in the 21st century are profound: increasing agricultural productivity on land largely already under cultivation at higher temperatures using less water. Can it be done? The truth is, we do not know. The impediments are both biological and cultural.

The major crops that now feed the world – corn, wheat, rice and soy – require a substantial amount of water. For example, producing a kilogram of wheat requires between 500 and 2000 L, largely lost through transpiration [36]. But because half of the grain currently produced worldwide is fed to animals, five to ten times as much water is consumed to produce a kilogram of meat as is required to produce a kilogram of grain.

The optimal growth temperature to produce maximal yields of our major crop plants is determined by the temperature optimum for photosynthesis, the process by which plants convert solar energy into chemical energy, and other physiological processes. It is also determined by the temperature range that supports optimal development of the harvested storage organs (grain, bean and kernel) that accumulate starches, proteins and fats [37]. A recent study reports that yields increase with temperature up to 29°C for corn, 30°C for soybeans and 32°C for cotton, but then decline precipitously at higher temperatures [38]. This study predicts that yields of these crops in their current growing areas will decline by 30–46% by the end of the 21st century under the most moderate climate change scenario and by 63–82% under the most rapid warming scenario.

The expected pressures on water availability and increasing temperatures present crucial challenges to agricultural researchers to increase crop water efficiency and heat tolerance. Whether our current highly productive food and feed crops can be modified and adapted to be even more productive at the higher temperatures expected or at more northern latitudes is simply not known. It would therefore be wise to increase investment in research on alternative forms of agriculture based on plants not now used in agriculture, but capable of growing at higher temperatures and using brackish or salt water for irrigation. Indeed, the array of molecular tools and knowledge available today might make it possible to design a wholly new kind of agriculture for a more arid, hotter world.

But even though the molecular tools, physiological knowledge and genomic information available today are extraordinary, there are also political and cultural barriers to their widespread use. Japan and most European and African countries remain largely opposed to growing GM crops and even, in some countries, importing GM food and feed. Moreover, even where there exists a regulatory framework that supports the testing and introduction of GM crops, the regulatory process is both extended and expensive. These factors have largely eliminated the participation of university and other public sector researchers in molecular crop improvement in many countries around the world. It is difficult to predict the progress that can be made in crop adaptation and improvement without the use of contemporary molecular technology.

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Review

Lessons from the 'Humanitarian Golden Rice' project: regulation prevents development of public good genetically engineered crop products

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Compared to a non-Genetically Engineered (GE) variety, the deployment of Golden Rice has suffered from a delay of at least ten years. The cause of this delay is exclusively GE-regulation. Considering the potential impact of Golden Rice on the reduction in vitamin A-malnutrition, this delay is responsible for an unjustifiable loss of millions of lives, mostly children and women. GE-regulation is also responsible for the fact that no public institution can deliver a public good GE-product and that thus we have a *de facto* monopoly in favour of a few potent industries. Considering the forgone benefits from prevented public good GE-products, GE-regulation is responsible for hundreds of millions of lives, all of them, of course, in developing countries. As there is no scientific justification for present GE-regulation, and as it has, so far, not prevented any harm, our society has the urgent responsibility to reconsider present regulation, which is based on an extreme interpretation of the precautionary principle, and change it to science-based regulation on the basis of traits instead of technology. GE-technology has an unprecedented safety record and is far more precise and predictable than any other 'traditional' and unregulated breeding technology. Not to change GE-regulation to a scientific basis is considered by the author 'a crime against humanity'.

Contents

Background: the Humanitarian Golden Rice project

The following analysis is based on ten years of day-to-day experience with the public good project 'Humanitarian Golden Rice' [1]. This project from the public sector follows the successful proof-of-concept work [2–6] in which GE-technology was used to engineer the biochemical pathway for the synthesis of pro-vitamin A into the starch-storing tissue of the rice seed, the endosperm, which is consumed in the form of 'polished rice'. Polished 'Golden Rice' thus contains substantial amounts of pro-vitamin A (which the body converts into vitamin A). This concept of 'bio-fortification' [7] (defined as using the potential of genetics to improve the micro-nutrient content of food) was applied to save eyesight and lives of the numerous vitamin A-deficient children dependent on rice as their basic diet [1]. As polished rice does not contain pro-vitamin A, rice-dependent poor populations, which cannot afford

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a diversified diet, suffer from vitamin A-malnutrition. 'Yellow rice' (yellow indicating pro-vitamin A) was, therefore, on the wish-list of rice breeders since the early 1980s, but could not be attained via traditional breeding because of the lack of natural variability in this trait [1]. This trait became an option only with the advent of 'genetic engineering' [8] and is still beyond the reach of traditional breeding. Subsequent to the early proof-of-concept work by the teams of my collaborator Peter Beyer and my own, which produced the first Golden Rice in 1999, research by the private sector [9] and traditional breeding by the public sector (e.g., Cuu Long Delta Rice Research Institute, Vietnam and International Rice Research Institute, The Philippines amongst other institutions) [1] has led to substantial increases in the accumulation of pro-vitamin A in polished Golden Rice, such that the routine and standard daily diet of Golden Rice instead of white rice could prevent vitamin A-malnutrition [1].

Figure 1 illustrates, with the typical example of Bangladesh, how different dietary components contribute to vitamin A and pro-vitamin A to the daily diet. Rice-dependent poor societies typically receive between 40% and 80% of their food calories from rice and the remaining calories from fruit and vegetables (providing pro-vitamin A), and fish and poultry (providing vitamin A) [1]. Figure 1a shows that neither women nor children reach the 50% line of the recommended daily allowance, the minimum required to be protected from malnutrition [1]. Figure 1b indicates how a shift to Golden Rice would raise the vitamin A-level across this critical line. The concept of Golden Rice represents, therefore, a sustained intervention for a reduction in vitamin A-deficiency.

The concept of using the potential of genetics and GE-technology in a public sector project to fight a severe public health problem affecting poor societies was welcomed with much enthusiasm by the scientific community, the private sector, the media and the public, and Golden Rice has been featured in numerous international print media, including the cover of the Asian and US (but not the European) editions of TIME Magazine [10]. However, it also provoked heavy opposition by anti-GE-advocates, largely as the project undermined this opposition's views that GE-technology was only for industrialised farmers in industrialised countries for multinational profit. Rather, Golden Rice is to be free of any charge to growers and consumers in poor developing countries, to address one of the great public health travesties of our time – vitamin A-deficiency. Expectations were high and it was generally expected that Golden Rice would be in the fields 'soon' [11]. On the Basis of the experience with traditional variety development with such a clear and single locus trait, experienced rice breeders were predicting that eight backcross generations (three years at IRRI for example, or even less if marker-assisted breeding were to be applied) would be sufficient to develop and register Golden Rice varieties [12]. The International Rice Research Institute, Philippines (IRRI), and other public rice research institutions in developing countries were keen to progress variety development and registration [1]. According to these expectations Golden Rice should have reached the farmers' fields in Asia by 2002. It is now 2009 and it will take at least until 2012 before Golden Rice can be handed over to the farmers in the first Asian countries.

Hurdles preventing the use of GE-technology for public good projects

What then were the hurdles which, in comparison to a comparable non-GE-variety, delayed the deployment of Golden Rice for more than ten years? How can we understand a ten-year delay for a case with so much public support and such high expectations of social benefits? And what can we learn from this experience for the numerous other public good projects in the pipeline around the world?

It turned out that, under the enthusiasm of the scientific breakthrough, neither the scientists involved, nor the scientific community, nor the media, nor the public were aware of the specific requirements associated with development of a GE-crop variety. There were numerous problems which came as a surprise to the 'naïve' public sector scientists, who followed the idealistic concept of using their scientific breakthrough to fight vitamin A-malnutrition. In retrospect, however, it turned out that one single problem was responsible for nearly all of the delay. This outstanding problem was (and still is) the political dimension of GE and particularly its effect on GE-regulation. The rules and regulations established worldwide for the handling and use of 'transgenic plants' (genetically engineered plants, GEs) and the expectations of the regulatory authorities are so demanding that even with best support it takes ten years to prepare for and assemble all the data required for a regulatory dossier, not to mention the exorbitant costs involved. In the following I will briefly describe the various

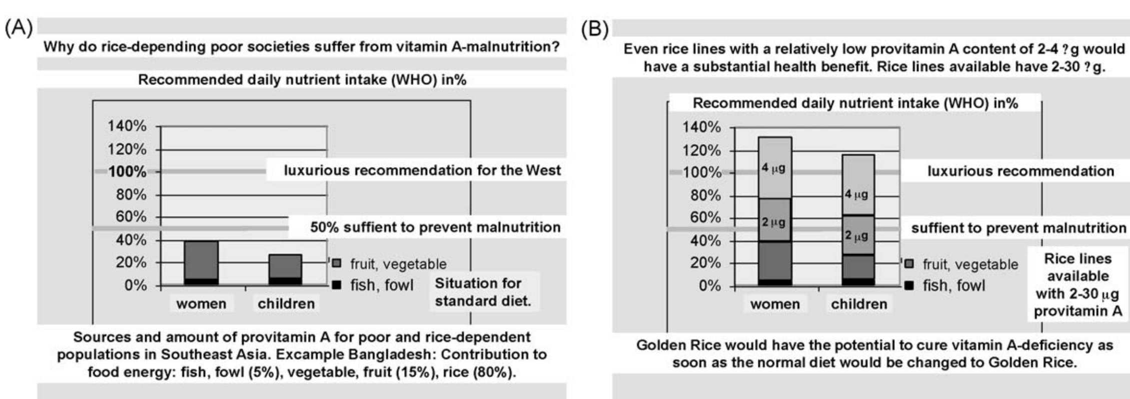

FIGURE 1

Contribution of vitamin A from the routine diet in rice-dependent poor populations without and with Golden Rice with the example of Bangladesh.

hurdles and their contribution to the 'unexpected' delay of more than ten years.

Intellectual property (IP) rights were the first and apparently 'insurmountable' hurdle we were faced with. As long as working for proof-of-concept, scientists can effectively ignore IP rights. Patents do not play a role. Scientists are free to exploit the public knowledge provided by patented inventions. We had no idea, which patents we were using for our task. The best scientific breakthrough, however, cannot rescue a single child from vitamin A-malnutrition, if a product is not developed on its basis. From this moment on, however, patents count. As we intended that Golden Rice would be handed over to the farmers free of charge, we had to organise free licences for the IP involved. It turned out that the number of patents was dramatically high [13,14]. Free licences, as it turned out, for 70 patents belonging to 32 patent holders appeared, not only to us, like the end of our idea. Under the specific circumstances of our 'humanitarian' project [1] however, the support within a 'public–private partnership' [1], and the experience and engagement of our partner from the private sector, Dr. Adrian Dubock, it was possible to solve this supposedly 'insurmountable' problem within less than half a year and in such a way that it did not delay the project for even a day [15]. Another important early contribution from Dr Dubock to the humanitarian project's long-term viability was the concept of the Humanitarian Golden Rice Board & licensee Golden Rice Network [1].

Lack of financial support from the public domain was the next hurdle. It turned out that within the public domain there was no funding beyond proof-of-concept. Financial support for 'product development' is probably beyond the philosophy of any academic institution. Academic institutions are set up to finance basic or strategic research for 'scientific novelty'. Product development is considered a task for the private sector. As a result of that situation, we were caught in an institutional 'dead end road': our concept was to use the results from our proof-of-concept work for a public good project on the reduction of vitamin A-deficiency, and this required developing a 'product'. There is no question that the responsibility for public good projects are within the public sector. But the public sector does not support – and has no expertise in – product development, and expects the private sector to take care of product development. This concept works for cases where the private sector has an interest and can expect a financial return for the investment required to develop a product on the basis of a public sector result. Humanitarian projects do not offer a chance for such a return. Therefore, the private sector cannot afford to develop such a public good product. So, again this looked like the end of our concept of a 'Humanitarian Golden Rice'.

The only way out was to find some mutual interest which could encourage the private sector to support the humanitarian project. As we had patented our invention, we could accept a proposal by the private sector (Zeneca, now Syngenta) to grant them the rights for *commercial* exploitation of our invention in return for rights to additional necessary technology from Syngenta and defined support for clearly and precisely defined *humanitarian* exploitation. This concept worked out [1]. The rights for our invention were transferred to Zeneca/Syngenta. We licensed back, together with other necessary technology and defined support, the rights for 'humanitarian use', and agreed a 'sublicense agreement' to be used as the basis for collaboration with numerous partner institutions on the basis of a 'sub-sub-license agreement'. We benefited from this 'public–private partnership' through substantial in-kind support and solution of the patent problems, and received very valuable donations for the humanitarian project from work done by Syngenta while working towards the development of a commercial Golden Rice product. Much to our regret, the company stopped the commercial project because the chance for a financial return at the level of the investment was too low. We learned the hard way what it means to develop a product and what it means to manage such a task effectively.

Nothing from these activities was holding back the development of a Golden Rice product. Financial support was received from philanthropic and other visionary organisations such as The Rockefeller Foundation, USAID, and the Syngenta Foundation under Mr Andrew Bennett. But no support was available from any public European or any UN institution. Thanks to the existence of altruistic organisations, although it was not easy to find financial support, it was possible, and lack of financial support was not a factor blocking the development of our product.

There were further disturbing factors such as the negative political climate around GE-technology [16], anti-GE-activists [17], the negative attitude of developmental aid organisations to GE crops [18], which all had strong negative effects on possible governmental support and especially on putative support from UN-organisations, even those having a specific mandate to reduce vitamin A-malnutrition, who did not reply to written invitations to engage in some way. But all this did not slow down Golden Rice development.

How GE-regulation delays GE-variety deployment by ten years

The only and dramatic bottleneck was, and is, *GE-regulation*. As there was no experience in the public domain with deregulation of a GMO-product, we followed advice from the private sector with appropriate expertise. Regulation affects a GE-product long before the collection of data for a regulatory dossier starts, and much longer before a complete dossier can be handed in to national authorities for the actual process of deregulation. The actual process of regulatory clearance, once a dossier is in line with the regulatory requirements, can be relatively fast. Which are then the practical GE-stumbling blocks which interfere with the development of a product long before regulatory authorities work on the regulatory clearance?

(1) **Deletion of selectable marker (two years)**: GE-technology requires use of selectable marker genes, which allow the selection, from amongst millions of cells, of a few which have integrated the novel genes of interest. Regulatory authorities prefer, under public scrutiny, that antibiotic selectable marker genes be deleted. This is technically possible, but takes a lot of time and effort. This has to be done despite the fact that there is a wealth of scientific literature documenting that the antibiotic marker genes in use have no effect on consumer and environmental safety [19].

(2) **Screening for streamlined integration (two years)**: Regulatory authorities do not accept complicated integration patterns of the 'transgenes'. The argument is that this can have unexpected and unforeseeable consequences. As inte-

gration of genes is a random event, the only way to achieve clean integration is to repeat the experiment so often until such an event has been found. This requires endless repetitions of the same experiment. Use of *Agrobacterium*-mediated transformation is helpful, but does not guarantee clean integration. This request is maintained for GE crops despite the fact that any 'traditional' standard breeding process leads to uncontrolled integration as well, especially if prior mutagenesis by radiation or chemical means is involved, yet such random mutagenesis goes unregulated if no new genes have been introduced from other organisms.

(3) **Screening for regulatory clean events (two years)**: 'Regulatory clean' events are DNA integration events which combine all the features which make them unproblematic for regulatory authorities, in all molecular genetic aspects. The gene cassette for one transgene is integrated in an ideal and perfect manner when there is: (a) one copy only, (b) no alterations of the construct, (c) no read-through on both sides possible, (d) no disturbance of existing reading frames, (e) no activation or inactivation of neighbouring genes or expression signals, (f) no activation of possible mobile elements, (g) stable expression at the predicted level and under the predicted conditions. Such 'ideal' events are rarities. To find them requires not only hundred-fold repetitions of the same experiment with regulatory clean constructs and technology, but also sequencing for all candidate events not only of the construct but also of the adjacent host DNA, which by itself is not as problematic as the discovery of such an event amongst thousands. We were in the fortunate situation that Syngenta was screening for them with an enormous effort during their, later abandoned, 'commercial' Golden Rice phase and was donating the material to the humanitarian project under the terms of the original licence. All final Golden Rice varieties are based on such 'regulatory clean' events.

(4) **Trans-boundary movement of seeds (two years)**: Golden Rice is, of course, an international breeding exercise. Rice breeders within the Golden Rice network [1] in the different countries, using traditional and marker-assisted breeding, develop agronomically improved, locally optimised Golden Rice varieties on the basis of the most popular varieties in their countries. This requires free exchange of breeding seed material between countries. The conditions set up by the Cartagena protocol [20] make exchange of transgenic seed so complicated that it took more then two years to transfer, for example breeding seed from The Philippines to Vietnam; and one year from USA to India, during which time 30 politically loaded questions were asked in the Indian Parliament. These Cartagena conditions are enforced, despite common sense suggesting that it is extremely difficult to construct a hypothetical risk from seed transfer between two breeding stations in different countries, especially for Golden Rice.[1]

(5) **Obligatory sequence from growth chamber to green-house to screen-house to field (two years)**: Permission for work in the field is given, if at all, only after intensive testing and data collection in (a) a contained growth chamber, (b) followed by the same in a contained glasshouse, and (c) followed by the same in a contained screen-house. This means that tests can begin on small plots only after 18 months, according to the regulatory requirement. Whether permission is given, however, also has a political component. We waited until late 2008 for the first permission for the first small-scale field plot in a developing country. Fortunately, we carried out initial field tests in Louisiana, USA, in 2004, where granting of the permission did not even require half a year. Variety development, however, means 'breeding'; breeding depends upon large numbers of offspring; large numbers are possible only in the field. Breeding also requires response to the natural environment to explore response to the natural stress conditions. Neither the necessary numbers nor the environmental conditions can be achieved under artificial conditions. This most severe impediment of normal, efficient breeding is the automatic consequence of regulation. It does not matter that nobody has ever come up with a hypothetical scenario arguing for any hypothetical environmental risk from Golden Rice. Every GE case has to follow all rules and regulations, independently of whether there is any putative risk or not. Again, we lost far more than two years to ideology-based regulation!

(6) **Requirement for one-event selection (two years)**: Preparing a regulatory dossier for a single transgenic event is so demanding and expensive that it is totally impossible to deregulate several independent transgenic events. This forces any GE-product developer to base all variety development on a single transgenic event. To be able to select the single event and then invest all resources in it requires collection of numerous data from many events. To collect these data without extended work in the field is impossible. Event selection can come only after permission for field experiments (see above for the problems!). Different varieties developed from a single transgenic event can be deregulated on the basis of the same regulatory dossier, if they are derived by traditional breeding. Therefore, all Golden Rice varieties are derived from one single transgenic event more than half a decade ago and all subsequent steps are the result of traditional plant breeding in the different partner institutions in the different countries. We definitely would prefer to have varieties based on different events, but the conditions for deregulation leave no choice, despite the whole basis of the applicable rules being a one-time transitory necessity to overcome the limitations of conventional breeding all those years and seed generations before.

(7) **Requirements for the regulatory dossier (four years)**: I will not describe all the hundreds of expensive studies in molecular genetics, biochemistry, nutrition, protein identity, -digestibility, -immunogenicity, gene expression, anti-nutrients, and agronomy required, at publication level quality, for the final regulatory dossier. These requirements keep an entire team of specialists busy for at least four years. Part of the studies can already be done during the course of develop-

[1] Incidentally, free movement of cereal seed between different countries seed breeding systems was absolutely at the heart of the success of the green revolution of the 1960s and 1970s in introducing new genes to countries, increasing biodiversity, and increasing food productivity and reducing malnutrition.

ment, but an essential part has to be done with the final variety to be released. This also means that ten years of expensive experimentation has to be performed with no guarantee that at the end everything will be in accordance with the regulatory requirements. Not to be in line with the regulatory requirements, however, does not need to constitute a realistic risk. It just means no permission for release.

(8) **Deregulation procedure (one year)**: Once a complete regulatory dossier, especially one based on a regulatory clean event, has been assembled, the actual procedure for regulatory clearance has a fair chance of taking less than a year. Therefore, it is neither the regulatory authorities, nor the final regulatory process, which has to be blamed for delaying registration of GE varieties. It is the rules and regulations themselves for the use of transgenic plants and, of course, the political attitude enforcing its 'extreme precautionary application'.

The putative impact of Golden Rice

The definite impact of Golden Rice will be monitored in epidemiological studies following release to the farmers and consumption by vitamin A-deficient and rice-dependent populations. Because of regulation this will not be possible before 2013. Socio-economic studies, however, allow one to get an educated estimate already now, by performing state-of-the-art *ex ante* studies. Because solid data about human bioconversion and bio-availability of pro-vitamin A from Golden Rice have been generated [21,22], the predictions can be relatively precise. There has also been a series of economic *ex ante* studies with Golden Rice in different countries. In the following paragraph I refer to the detailed study on the putative impact of Golden Rice in India, published by the team of Professor Matin Qaim, Göttingen [23].

The annual burden of vitamin A-deficiency in India is characterised by the loss of 71,600 lives or 2,328,000 'DALYs'. (A DALY is a technical term used by economists to quantify, and allow comparison between the impacts of interventions and refers to a standardised disability-adjusted life year.) The potential annual impact of Golden Rice is presented in two scenarios, one 'pessimistic' and the other 'optimistic'. Three years after this publication, we know that the optimistic scenario is a realistic one. According to these scenarios, Golden Rice could save up to 40,000 lives per year, or in DALYs, up to 1,382,000 healthy life years annually. The lives saved would represent 95% of those rice-dependent poor in danger of losing eyesight and life. As only half of the Indian poor depend upon rice and the other half upon wheat, Golden Rice could not save more than half of the 71,600. (For the others 'Golden Wheat' might be an option.)

The World Bank's benchmark cost of saving one 'disability-adjusted life year', valued at \$620–\$1860 by the Bank, is \$200. The actual costs for the, so far most effective, traditional intervention – the free distribution of vitamin A-capsules – is between \$134 and \$559. Golden Rice is expected to do the same thing for only \$3. And this \$3 cost would include all the money spent in ten years of proof-of-concept work, plus all the money spent on product development, deregulation, variety registration and social marketing. These unprecedented low costs are the consequence of the fact that there are no recurrent costs, once a variety has been released. This is the major reason why this intervention based on 'biofortification' is highly sustainable as well as cheap.

Once cleared for adoption by the national authorities, seeds of agronomically optimised and locally adapted Golden Rice varieties will be provided to the farmers by public seed distribution units or by licensed seed multiplications units, free of charge for the trait and within the framework of the humanitarian project. The farmer will be free to grow, harvest, sell, consume and store Golden rice without restrictions, including to use part of the harvest for the next sowing and to pass seeds on to neighbours. The rice farmers will continue to use their traditional farming practices and will not require any additional input in the form of agrochemicals or fertiliser. The costs of production will be the same as for any other variety of rice The yield of Golden Rice varieties is at least as good as other popular non-GE varieties and there is no off-taste which would discourage consumers from eating Golden Rice. The only difference is the yellow colour. Initial but in depth social marketing research has shown that households have no problem with the colour when they understand it is associated with good nutrition.

Lessons learned from the Humanitarian Golden Rice project

From ten years work with the development of the first public sector GE-product we can derive a series of lessons which apply to any further public sector GE project. These lessons are probably new to most colleagues in academia as well as to the public sector in general. As they have, however, far-reaching consequences for all those projects in the public domain, financed with the vision of contributing to the solution of altruistic problems (much of basic science in plant molecular biology and biotechnology is financed with this argument in mind), those financing and working on such problems should at least be aware of what stands between a pleasing, academic, proof-of-concept result and the practical impact it claims to achieve.

A. Negative attitudes to GE crops:
   1. The European negative attitude to GE has a very strong negative effect on governments in developing countries.
   2. The negative attitude is prevalent within several NGO's, a small part of the public, much of the media, many development aid organisations and most European governments.
   3. This effect is exacerbated by the financial support of the EU to NGO groups paid to lobby the EU against GE crops
   4. This effect is exacerbated by the financial support by European NGOs to NGOs in developing countries.
B. Regulatory process:
   1. Justification for present regulation is based on the notion that the technology leads to 'unpredictable and uncontrolled modifications of the genome'.
   2. This argument ignores the fact that all traditional breeding has been and is doing exactly the same (e.g., [24–28]).
   3. In the entire history of GMO-technology development and application there is not a single documented case of harm, which could be used to argue for maintenance of the present regulatory situation [29].
   4. There is no scientific justification for present regulation.

C. The financial and time cost implications of excessive regulation:
   1. The costs for the development of a GE-variety are currently so immense, due to politics, not science, that it is difficult to identify a product which offers a fair chance for financial return of the investment for non-industrial crops.
   2. In addition, GE-regulation delays delivery of GE-based products for about ten years, compared to non-GE varieties and carries a huge financial penalty.
   3. Time and costs for delivery of a GE-product to the market are, therefore, so immense that neither public institutions, nor any small- or medium-sized enterprise, can afford the investment in funds and/or personnel.

D. Impact on food security of unscientific regulation:
   1. Food security for developing countries, however, requires, besides the best of traditional agriculture, also the best of novel technologies. GE-regulation excludes a very potent and promising technology.
   2. There is, in addition to Golden Rice, excellent progress within the Bill & Melinda Gates Foundation funded biofortification projects within *Grand Challenges in Global Health No. 9* [30] with regard to high-iron-, high zinc-, high protein-rice, and exactly the same in cassava, banana, and sorghum, which have the potential to save further millions of lives per year.
   3. All these projects suffer from the same consequences of regulation as described for Golden Rice, increasing the number of lives lost to the tens of millions per year. And there are *drought-*, *salt-*, *flooding-*, *virus-*, *bacterial- fungal-*, *insect-*, *nematode-resistance* projects too, not only with the major crops, but also with staple crops important for food security in developing countries, and there is improved exploitation of natural resources which could all substantially contribute to food security [31], if only GE-regulation did not prevent public good GE-product development.
   4. Numerous other public projects for, for example, improved food security, including many from developing country laboratories and with orphan crops, have – under these conditions – no chance to make it to the market place.
   5. GE-potential is, therefore, blocked for public good projects. The often-raised complaint (especially by the GE-opposition) that GE-technology has been only exploited for industrial projects, has its only cause in the GE-regulatory system, and politicisation of this useful technology.

E. The social cost of over regulation:
   1. According to the *ex ante* study mentioned above [21] Golden Rice could save in India alone ca. 40,000 lives per year. The social costs as the consequence of GE-regulation, calculated only for the case of Golden Rice, India and the delay of deployment of ten years, would add up to a loss of about 400,000 lives.
   2. However, there are further countries with vitamin A-deficiency problems and poor, rice-dependent poor populations, such as The Philippines, Bangladesh, India, Vietnam, Indonesia, and China for which Golden Rice is under development [1]. Delay of deployment raises the social costs of regulation to a loss of lives far beyond one million.
   3. A conservative estimate of the social costs of all those blocked public good projects indicated above, and considering just the ten years of delay, amounts to astronomic losses of hundreds of millions of lives.
   4. And this is not everything with regard to social costs, because the great majority of the public good projects will not just be delayed; they will never make it to the market place, thus adding further loss in lives.
   5. In addition to the unacceptable and astronomic social costs, there are also enormous economic losses which cannot be recovered because the loss of lives and healthy life years (DALYs) are irreversible.
   6. A World Bank study [32] calculates the annual economic loss of GDP due to lack of adoption of ‘Golden Rice technology’ to be ca. $15.6 billion in Asia alone, with utmost $300m of exports to Europe at risk.

F. The role and limitations of the public sector:
   1. The public sector, not the private one, is responsible for public good, altruistic and humanitarian projects.
   2. The public sector has competence for proof-of-concept work, but is totally incompetent and unwilling to deliver public good GE-products from its own successful research.
   3. The public sector, therefore, depends upon partnership with the private sector for the exploitation of its achievements in science and technology.
   4. In contrast to the private sector, academic personnel survive on publications. All the work necessary for product development and deregulation does not offer the slightest chance of publication.
   5. New ways of recognising merit need to be developed to address this shortcoming, which impedes academic involvement in pro-poor product development.

G. The role of the private sector and those with broad based commercial experience in the private sector:
   1. The consequence of the above is a *de facto* monopoly for GE-products among a few financially potent companies and for industrial crops.
   2. There is goodwill in, and from those individuals with experience of, the private sector to support development of public good products with expertise and intellectual property, as long as this does not interfere with commercial interests.

H. The role of public–private partnerships:
   1. Public–private partnerships function only, if there is a strong mutual interest also for the private partner and if the public partner can be considered reliable.
   2. Public–private partnerships require clear definition of, and the related contractual basis for, those mutual interests and reliable management structures on the public side, to minimise liability risks for the private sector and to ensure that the public sector gets what it needs consistently from the private sector, despite changing personnel and business situations.

I. The moral imperative:
   1. The damage to lives and welfare from GE-regulation is enormous, and affects the poor, and not the rich Western societies, which are responsible for the establishment and maintenance of these regulations.

2. The West ignores a moral imperative to make these technologies available to the poor, including its application to orphan crops [33,36] and therefore carries responsibility for the consequences.

Considering the above and the additional fact that there is a scientific consensus that transgenic plants pose NO novel risk as compared to non-transgenic plants derived from traditional plant breeding [34], it is difficult to understand that our society continues with the practice of extreme precautionary regulation, exclusively of those plants which have been produced with the most precise and predictable technique of genetic modification and which have the safest track record compared to any other technology [35].

Are those opposing the technology and those politically responsible for existing regulation willing to take responsibility for the economic losses? Or, far more importantly, are they ready to take responsibility for the astronomic social costs?

What else is necessary to open the eyes of those, who carry political responsibility, to understand that not changing GE-regulation from extreme precautionary to science-based regulation, guided by considerations of the risks and benefits of the trait instead of regulating a technology on ideological terms, constitutes a 'crime against humanity' [28]?

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Transgenic crops coping with water scarcity

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Water scarcity is a serious problem that will be exacerbated by global climate change. Massive quantities of water are used in agriculture, and abiotic stresses, especially drought and increased salinity, are primary causes of crop loss worldwide. Various approaches may be adopted to consume less water in agriculture, one of them being the development of plants that use less water yet maintain high yields in conditions of water scarcity. In recent years several molecular networks concerned with stress perception, signal transduction and stress responses in plants have been elucidated. Consequently, engineering some of the genes involved in these mechanisms promises to enhance plant tolerance to stresses and in particular increase their water use efficiency. Here we review the various approaches used so far to produce transgenic plants having improved tolerance to abiotic stresses, and discuss criteria for choosing which genes to work on (functional and regulatory genes) and which gene expression promoters (constitutive, inducible, and cell-specific) have been used to obtain successful results.

Contents

Introduction

According to the Food and Agriculture Organization the planet has approximately 1400 million km^3 of water [1]. However, after subtracting the salt water of the oceans and the freshwater locked up in ice caps, only around 9000–14,000 km^3 of freshwater is potentially available for human use [1].

The success of agricultural production depends crucially on water availability. Over 80% of global cropland is rain-fed; however irrigated cropland, constituting about 16% of the total, produces about 40% of the world's food [2]. Agriculture currently uses over 70% (86% in developing countries) of available freshwater [3,4].

The global population is projected to increase from the current 6.7 billion to over 9 billion by 2050. Rising living standards have increased meat consumption, with consequent increased demand for grain for animal feed, which will have a significant impact on agricultural land use [5]. Increased food production implies increased demand for and consumption of water.

Water scarcity, typically accompanied by increasing salinity, is the one of the major causes of poor plant performance and limited

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crop yields worldwide [6] and is the single most common cause of severe food shortage in developing countries. Even in most of the agriculturally productive regions, short periods of water deficiency are responsible for considerable reductions in seed and biomass yields each year [5]. Global climate change, which is increasing temperatures worldwide and changing rainfall patterns, is expected to exacerbate the negative effects of water deficiency in agriculture [7].

To meet the growing demand for food and to contrast the detrimental effects of climate change on crop yields, it is imperative to develop new crops that have improved water use efficiency and have improved resistance to drought stress. These goals might be attained by conventional plant breeding approaches. In fact using the traditional methods of crossing and selecting progeny, breeders have produced new varieties with improved ability to resist stresses [8]. However modern plant biotechnology has a much greater potential by far to produce substantial improvements [9,10].

Mechanisms of drought resistance

Plants are sessile and have had to evolve various mechanisms to enable them to adapt to ever-changing environmental conditions. They have developed two strategies to resist drought: drought avoidance and dehydration tolerance [11]. Drought avoidance refers to a plant's ability to maintain high water status even when water is scarce, for example by growing long roots to reach deep soil moisture, or reducing water loss by restricting the aperture of the stomata on leaf surfaces. In fact, stomata play a major role in plant adaptation to stress. Dehydration tolerance is well illustrated by the so-called 'resurrection plants' which are able to withstand loss of around 90% of their water content yet remain viable and re-grow when moist conditions return; most other plants can withstand only moderate dehydration (about 30% water loss) and still remain viable. Breeding programs have generally sought to improve dehydration avoidance rather than dehydration tolerance as strategies for producing new varieties able to cope with drought stress [11].

At least six signal transduction pathways in plants are involved in responses to drought and closely related responses to high salinity and cold stress [12]. The hormone abscisic acid, synthesized in response to abiotic stress, plays a key role in three of these pathways [12].

The elucidation of mechanisms involved in stress responses has provided valuable insights into how plant responses to abiotic stresses might be improved by genetic engineering. Following the application of microarray technology, several hundred stress-induced genes, mainly in the model plant *Arabidopsis thaliana*, have been identified as candidates for manipulation [12] and have been classified into three groups [13]: (a) genes encoding proteins with a known enzymatic or structural function. Examples include enzymes for synthesis of osmoprotective compounds, late embryogenesis abundant (LEA) proteins, osmotins, chaperons, channels involved in water movements through cell membranes, ubiquitins, proteases involved in protein turnover, and detoxifying enzymes; (b) genes with as yet unknown functions; and (c) regulatory genes, such as those coding for kinases, phosphatases and transcription factors.

Numerous studies have investigated drought resistance mechanisms at the vegetative stage, and such studies are important for improving resistance in plants subject to continuous or sub-continuous water deficit. However for major cereals, resistance to drought is more important at the reproductive stage, to ensure pollen fertility and grain development, and more recent studies have therefore focused on identifying genes that can be modified to improve drought tolerance at this crucial stage [14–18].

In the following we review the various genetic engineering approaches used in recent years to obtain drought-tolerant plants.

Improving response to water stress by manipulating single action genes

Early attempts to develop transgenic plants resistant to water stress focused on single action genes responsible for the modification of a single metabolite or protein that would confer increased tolerance to drought stress. Recent reviews [13,19] document progress in this area.

Osmoregulation is one of the most effective ways evolved by stress-tolerant plants to combat abiotic stress, but most crop plants lack the ability to synthesize the osmoprotectants naturally produced by stress-tolerant plants. Therefore genes concerned with the synthesis of osmoprotectants have been incorporated into transgenic plants to confer stress-tolerance (reviewed in [13,19]). Overproduction of compatible solute osmoprotectants such as amino acids (e.g. proline), quaternary and other amines (e.g. glycinebetaine and polyamines), and sugars and sugar alcohols (e.g. mannitol, trehalose and galactinol) has been achieved in various target plants. Glycinebetaine in particular has been extensively studied as a compatible solute, both by genetically engineering its biosynthesis in agriculturally important species and by its exogenous application [20]. When maize plants were transformed with the *betA* gene from *Escherichia coli* that encodes choline dehydrogenase, they accumulated glycinebetaine in tissues and were more tolerant to drought stress than wild-type plants at different developmental stages. Most importantly their grain yield was 10–23% higher than that of wild-type plants after three weeks of drought stress [21].

In some cases the accumulation of compatible solutes also protects plants against damage by reactive oxygen species (ROS) [22]; in other cases the solutes have chaperone-like activities that protect other proteins maintaining their structure and function [23,24].

Genes coding for heat-shock proteins, molecular chaperones and LEA proteins (reviewed in [13,19]) have been extensively used to improve drought responses in plants. An interesting recent example is the use of RNA chaperones of bacterial origin by Castiglioni *et al.*, to confer abiotic stress tolerance in several species, and improved grain yield in maize under water-limiting conditions [25]. These authors demonstrated that constitutive expression of two cold shock proteins – CspA from *E. coli* and CspB from *Bacillus subtilus* (both RNA chaperones) – conferred abiotic stress tolerance to transgenic *Arabidopsis*, rice, and maize. They obtained a greater than 20% increase in maize grain yield under water-limiting conditions in field trials, without observing pleiotropic effects on plant development. The improvement in drought response was observed in the late vegetative/flowering period as well as the grain-fill period: during these periods, three consecutive days of wilting can reduce grain yield by 30–50% [26]. Stress tolerance conferred by manipulation of cold shock proteins

is not only novel, but also appears as a highly promising approach to improving plant productivity in suboptimal growth conditions.

Improving response to water stress by manipulating regulatory genes

The transference of a single gene encoding a specific stress protein does not always result in sufficient expression to produce useful tolerance, because multiple and complex pathways are involved in controlling plant drought responses [27] and because modification of a single enzyme in a biochemical pathway is usually contrasted by a tendency of plant cells to restore homeostasis [28]. Targeting multiple steps in a pathway may often modify metabolite fluxes in a more predictable manner. Another promising approach is therefore to engineer the overexpression of genes encoding stress-inducible transcription factors. Transcription factors typically regulate several genes and are likely to be used extensively in the next generation of genetically modified crops [29,30]. Numerous transcriptional regulators are known to be involved in plant responses to drought stress [31]; most fall into one of the large transcription factor families (AP2/ERF, bZIP, NAC, MYB, MYC, Cys_2His_2 zinc-finger, NFY and WRKY); and some *cis*-elements, bound by these transcription factors, have been identified [31]. For example abscisic acid-responsive elements (ABRE) [32] are 5′ upstream regions of abscisic acid-responsive genes that are bound by AREB/ABF transcription factors belonging to the basic leucine zipper family. These mediate at least one of the abscisic acid-dependent pathways involved in responses to drought stress. Another *cis*-element is the dehydration responsive element/C-repeat (DRE/CRT) which is involved in one of the abscisic acid-independent pathways [29]. Various DRE/CRT-binding proteins, coding for ERF/AP2 transcription factors, are induced by desiccation, salt treatment, and cold in some plant species [31].

The first examples of transcription factor engineering to improve abiotic stress tolerance were overexpression of the ERF/AP2 factors CBF1, DREB1A and CBF4. Overexpression of these factors resulted in cold, drought and salt tolerance in *Arabidopsis* [33–35] and it was later shown the similar tolerance could be induced in many crop plants by overexpression of these factors [36,37]. Numerous transgenic *Arabidopsis* varieties with improved drought tolerance due to overexpression of various stress-regulated transcription factors have been reported, but similar results have also been obtained in crop plants [38].

Typically a gene coding for a transcription factor in *Arabidopsis* is isolated, characterized and shown to improve drought response when overexpressed. The gene is then transferred to a crop plant where it often confers the same drought-tolerant phenotype. The *HRD* gene, coding for an AP2/ERF-like transcription factor [39] exemplifies this approach. *Arabidopsis* plants with a gain-of-function mutation in the *HRD* gene (*hrd-D* mutants) are drought-resistant, salt-tolerant, and overexpress abiotic stress marker genes. Overexpression of the same gene in rice significantly improves water use efficiency both under well-watered conditions (50–100% increase) and under drought (50% increase). These plants also show enhanced photosynthetic assimilation and reduced transpiration [39]. *HRD* gene overexpression conserves drought tolerance in both dicots and monocots.

In other cases a gene coding for a transcription factor is isolated and characterized in *Arabidopsis,* but its orthologue gene in the crop plant of interest is identified and made to overexpress. For example Nelson *et al*. [40] showed that overexpression of the *Arabidopsis* CAAT box-binding transcription factor AtNF-YB1 confers improved performance in *Arabidopsis* under drought conditions. They next overexpressed the orthologue of AtNF-YB1 (called ZmNF-YB2) in maize and found that, under simulated drought conditions, the altered maize plants produced up to 50% more than unmodified plants [40].

In other cases, studies of responses to abiotic stress directly on the crop plant of interest have contributed to the identification of candidate genes to overexpress. A recent example is the study of Oh *et al*. [17], which showed that independent constitutive expression of the stress-inducible genes *AP37* and *AP59* in rice – which code for transcription factors belonging to the AP2 family – resulted in increased tolerance to drought and salinity at the vegetative stage. This study also provides a good example of how gene modification can result in opposing effects in response to drought in the reproductive and vegetative organs of a plant. Thus in plants transgenic for AP37, grain yield increased by 16–57% over controls under severe drought conditions, whereas in plants transgenic for AP59 grain yield was reduced by 23–43% compared with controls, under both normal and drought conditions [17], while at the vegetative stage overexpression of the two genes resulted in increased tolerance.

In recent years much attention has focused on the transcription factors involved in regulating stomatal movements [41–44]. Stomata are pores in the plant epidermis that regulate CO_2 uptake for photosynthesis and water loss by transpiration; pore size is controlled by turgor-driven volume changes in the two guard cells that surround each stoma [45]. The highly specialized guard cells integrate signals from the plant and from the environment to regulate aperture size and help ensure plant survival under various conditions [46].

The transcription factor SNAC1 (stress-responsive NAC1) influences stoma aperture size in the rice plant. Transgenic plants that overexpressed SNAC1 had improved drought resistance and a 22–34% increase in seed-setting (both compared to control) during severe in-the-field drought conditions at the reproductive stage [42]. Such plants show increased sensitivity to abscisic acid and have more stomata closed under both normal and drought conditions than wild-type plants [42]. The rice variety in which this work was done is not widely grown commercially, so the team is now generating transgenic plants from commercial rice varieties [47].

Constitutive, inducible and cell-specific promoters

All the approaches to improving water stress tolerance reviewed above involved constitutive overexpression of genes. This implies that the gene construct introduced into the target plant also contains a gene promoter that ensures constitutive transcription of the gene. Commonly used promoters are Cauliflower mosaic virus 35S (CaMV35S) [48] or promoters for constitutively expressed plant genes like ubiquitin [49], actin [50], and cytochrome c [51]; these are usually effective in producing transgenic plants with the required stress-tolerant properties. In some cases however, constitutive expression of a gene normally only induced by stress has negative effects – so-called pleiotropic effects [34,52–54] – on growth and development when stress is not present. One

solution is to use inducible (rather than constitutive) promoters that allow expression of a transgene only when it is required, while it is silenced otherwise. For example constitutive expression in *Arabidopsis* of *DREB1/CBF3*, a gene coding for a transcription factor induced by osmotic stress, confers tolerance to stress, but causes severe growth retardation under normal growth conditions [34]. However, if this gene is expressed under the control of an osmotic stress-inducible promoter – RD29A was the promoter used – no growth retardation occurs, while the plant is highly resistant to several stressing conditions when these occur [34].

Similar results have been obtained in crop plants. In tomato, overexpression of the *Arabidopsis CBF1* gene, encoding a transcription factor belonging to AP2/ERF family, confers increased drought, cold and oxidative stress tolerance compared to wild-type plants, but plant growth is severely affected [52]. By contrast, when the same gene was placed under the control of a synthetic promoter derived from the barley *HVA22* gene, it was expressed mainly under abiotic stresses, so that the plant had the same tolerance characteristics towards stresses, but plant growth under normal conditions was not affected [53]. This approach was also applied to the rice *OsNAC6* gene, which codes for a transcription factor involved in responses to abiotic stresses. Its overexpression under the control of the CaMV35S promoter resulted in decreased plant growth and productivity, while expression of the same gene under the control of either of the two stress-inducible promoters *LIP9* or *OsNAC6*, improved stress tolerance, without affecting plant growth [54].

Stress-inducible promoters usually maintain low levels of expression of the downstream genes under normal growth conditions, but even low expression levels may have negative effects if the gene of interest has pleiotropic effects under conditions in which its expression is not necessary. A promoter that is completely silenced under normal growth conditions, but is active in response to drought, abscisic acid and increased salinity, is that of the rice *OsLEA3-1* gene [55]. However this promoter also has the drawback that it is activated only after 6 days of drought stress, or after 18 hours of salt treatment. These times are too long for an efficient response. An ideal stress-inducible promoter would be completely silenced under normal conditions, but induced by stress in a fairly short time (a few hours) after stress onset. The promoter of the *Arabidopsis AtMYB41* gene, which is not expressed in any tissues under standard growth conditions but is highly induced in response to drought, salt and abscisic acid [56], may therefore be a very useful promoter.

Cell-specificity is another aspect that needs to be considered in choosing a promoter. Because of the fundamental role played by guard cells in integrating internal and environmental signals, they appear to be attractive targets for engineering drought response. Genetic engineering of target genes in guard cells requires effective expression systems with suitable promoters, because constitutive promoters (e.g. CaMV35S) are not always functional or can have negative effects on plant growth and productivity. However, very few guard cell-specific plant promoters have been identified. One that has been investigated is the *Arabidopsis AtMYB60* promoter which shows high guard cell-specificity [41]. As *AtMYB60* expression is rapidly down-regulated by abscisic acid and dehydration stress, it is promising as a research tool for the targeted guard cell gene silencing of negative regulators of stress response (see below). Constitutive guard cell-specific promoters are also promising for engineering positive stomata responses to drought. Examples include pGC1 [57] and pCYP [58,59].

Gain of function versus loss of function

Most approaches to abiotic stress resistance have introduced genes with a constitutive or inducible promoter, resulting in gene overexpression. In some cases, however, stress resistance has been conferred by gene down-regulation. This may be achieved by RNA interference [60], co-suppression [61] or loss-of-function mutants [41–43]. The major role of short single-stranded RNA molecules (miRNAs) in stress responses has only been recently elucidated and is reviewed in [62].

Use of loss of function to achieve stress resistance is exemplified by an *Arabidopsis* mutant harboring a knock-out mutation in the *AtMYB60* gene, coding for an R2R3MYB transcription factor [41]. As noted above, the *AtMYB60* gene is guard cell-specific. Stoma size in the mutant is 30% smaller than in wild-type plants, so transpiration is reduced resulting in greater tolerance to dehydrating conditions than wild-type plants. The exact role of the AtMYB60 transcription factor has not been fully elucidated. Its expression is up-regulated by signals that induce stoma opening, like white and blue light, and negatively down-regulated by desiccation and abscisic acid treatment – signals that promote stoma closure. It is possible that this transcription factor is an up-regulator of stoma opening that is silenced in stress conditions. Technological transfer of the AtMYB60 strategy to crop plants is in progress.

A similar phenotype has recently been described in a rice *dst* mutant [43]. The corresponding gene encodes a zinc finger drought and salt tolerance (DST) transcription factor that down-regulates stoma closure through modulation of H_2O_2 homeostasis. In the mutant, stoma closure is increased and stoma density reduced, resulting in enhanced drought and salt tolerance.

Conclusion

The green revolution of the 20th century markedly increased crop production through genetic improvements to major food crops, increased mechanization, improved pest control and improved soil fertility. In April 2000, Kofi Annan, then Secretary General of the United Nations, called for a blue revolution in agriculture to generate 'more crop per drop' [1]. Although this revolution is not yet with us, 'the seeds have at least been planted' as recently noted by Pennisi [47].

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Golden Rice and 'Golden' crops for human nutrition

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Abstract

Micronutrients are essential for a healthy life. Humans do not produce micronutrients, and hence they must obtain them through the foodchain. Staple crops are the predominant food source of mankind, but need to be complemented by other foodstuffs because they are generally deficient in one or the other micronutrient. Breeding for micronutrient-dense crops is not always a viable option because of the absence of genetic variability for the desired trait. Moreover, sterility issues and the complex genetic makeup of some crop plants make them unamenable to conventional breeding. In these cases, genetic modification remains the only viable option. The tools to produce a number of micronutrients in staple crops have recently become available thanks to the identification of the genes involved in the corresponding biochemical pathways at an unprecedented rate. Discarding genetic modification as a viable option is definitely not in the interest of human wellbeing.

Contents

Nutritional genomics

Owing to the rapid development of sophisticated molecular techniques over the past decades, progress in gene discovery has been extraordinary, and the knowledge of biosynthetic pathways has grown tremendously. The main reason is that all organisms share a good proportion of their genes and metabolic functions, making it possible to draw conclusions from one species to another and to do research on model organisms with short life cycles while taking advantage of an exhaustive genetic infrastructure already available, such as sequenced genomes and gene expression data [1,2].

The elucidation of plant metabolic pathways and their interconnections still remains a significant challenge, not least because of sheer numbers. Plants are extremely versatile chemical factories. An Arabidopsis leaf contains no fewer than 2000 different substances, and the entire plant kingdom can produce 200 000 or more different chemical compounds [3]. Many of these are so-called secondary metabolites and relevant for the plant's adaptation to specific environments. However, some of these are also relevant from a human nutritional perspective. Being essential

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components of the diet, these are termed 'vitamins' when organic, and 'trace minerals' when inorganic, and together are referred to as 'micronutrients'. 'Nutritional Genomics' is a discipline of modern biology that focuses on elucidating the biochemical pathways (vitamins) or physiological processes of uptake and mobilization (minerals) that are needed in plants to sustain human health.

Unequal distribution of micronutrients in plant tissues

As a whole, plants can provide all human dietary macro and micronutrients needed to live a healthy life as a vegetarian. However, micronutrients are usually unevenly distributed not only between plant species but more importantly also within different tissues of a given plant. Leaves often contain all necessary micronutrients, while the specialised storage tissues of grain, roots, and tubers – which make up most staple foods – show only limited biochemical diversity and at levels often insufficient for human nutritional needs.

For example, in the rice endosperm, the edible part of the rice grain, the micronutrients iron, folate, provitamin A, and vitamin E are present only at minimal levels while in the rice leaf they are present in quantities which would be adequate if rice leaves were apt for human consumption. For rice endosperm to meet human nutritional requirements it is, therefore necessary to modify the plant so that the endosperm accumulates the required nutrients. Alternatively, supplementation and fortification can and are being used to cope with the deficiency problems that arise from an unbalanced diet owing to reliance mainly on micronutrient deficient food staples. Predominant consumption of staples is a consequence of extreme poverty. Unfortunately, large parts of the world's population survive on less than two dollars a day and hence can neither diversify their diets nor buy supplements.

Biofortification: Breeding vs. genetic modification

Micronutrient malnutrition is a continuing and serious public health problem in many countries. Supplementation and fortification-based interventions have been applied for decades. Although such interventions have shown considerable success in the past, they have not been able to eradicate the problem, mainly owing to the significant and expensive distribution logistics required which are insufficiently developed in poorer countries. Moreover, such interventions are not economically sustainable, requiring ongoing funding which may falter upon economic crisis or political turmoil. Experience with vitamin A supplementation programs, for instance, revealed that coverage achieved over the last decade in 103 priority countries has stagnated at 58%, with high year-to-year fluctuation [4]. In India, the 'Nutritional Anaemia Control Programme', mostly designed to address iron deficiency, has been in place since 1970 with little impact, because of mismanagement, underfunding, logistical problems, and poor compliance [5]. In recent years, coverage with iron folate supplements was around 30% for pregnant women and 10% for adolescent girls [6].

Biofortification, much advocated by the HarvestPlus research consortium (see http://www.harvestplus.org), is potentially a cost-effective and sustainable intervention, either as a stand-alone solution or in combination with supplementation and fortification. Biofortification denotes the 'fortification' of agronomically important crop plant tissues by means of their own biochemical capacity. Once the crops are developed the costs of biofortification – including development costs – constitute only a fraction of supplementation costs. Biofortified crops are intended to be distributed through the traditional pathways of agriculture and local trade. Golden Rice, for instance, should require little more than the costs of the normally reliable seed production systems for its continued deployment following introduction. Production costs will be no different from any other rice.

The costs of breeding are moderate – in the range of $4m per variety spread over 10 years – amounting to approximately 0.2% of the global vitamin A supplementation expenditures in the scenario described above over the same period [7]. The development and regulatory approval of a transgenic crop can be 5–8 times higher [8,9], still representing only a fraction of the sustained costs necessary for a classical public health intervention. These higher costs have the potential to be substantially reduced once a more scientifically based regulatory requirement is introduced.

Given these advantages, the often-debated question is whether all of the biofortification needs can be achieved by breeding techniques alone, including 'precision (smart) breeding' relying on genetic markers associated with the desired trait. The simple answer is 'no'. There are two main reasons for the need for genetic modification. In cases where the genetic variability for a given trait is too low to meet the target levels, breeding is not an option and one needs to resort to the knowledge gained in nutritional genomics research (see above) in order to apply recombinant DNA technology. The other case is with crop plants which are impossible or very difficult to breed.

In other words, biofortification of staple crop plant tissues can be achieved through breeding where this is possible, while recombinant DNA technology must be applied in all other cases. Some examples will be given in the subsequent paragraphs.

Some plants do not show adequate trait variability: the case of provitamin A rice (Golden Rice)

Accumulation of provitamin A carotenoids in rice grains cannot be achieved through breeding. Germplasm screening conducted at the International Rice Research Institute (IRRI) and elsewhere did not reveal any cultivar of rice capable of accumulating provitamin A in the grain that could be used as a parental line for further breeding. Consequently, genetic engineering needed to be applied to biofortify rice, with the aim of helping combat vitamin A deficiency (VAD) induced diseases, which are widespread in the tropics.

Vitamin A denotes a group of C_{20} carotenoid derivatives (retinal, retinol and its esters, and retinoic acid), which play an essential role in vision, immune response, epithelial cell growth, bone growth, reproduction, maintenance of the surface linings of the eyes, embryonic development, and regulation of adult genes. In humans, provitamin A carotenoids are cleaved in the centre of the molecule and converted into vitamin A retinoids. An early symptom of vitamin A deficiency is night blindness. Structural alterations of the conjunctiva and the cornea (xerophthalmia, keratomalacia) may follow, and subsequent inflammation and infection result in irreversible blindness. Depression of the immune system increases the severity of measles and diarrhoea, leading to a nine-fold increase in child mortality, which is apparent even before the appearance of xerophthalmia. According to WHO, an estimated 127 million preschool children are affected by vitamin A deficiency, with 250 000–500 000 becoming blind every

year, half of whom die within 12 months of losing their sight (WHO database of vitamin A deficiency; http://www.who.int/vmnis/vitamina/data/en/index.html).

The Golden Rice technology currently being developed – known as GR2 – employs two provitamin A pathway genes (see [10], for review). One codes for the enzyme phytoene synthase, which has turned out to be the major rate-limiting step in carotenoid production in most plant tissues. The essential improvement in the development of GR2 over the previous GR1 version was to exchange the phytoene synthase from daffodil with the one from maize, thus leading to increased provitamin A formation [11]. The second gene (which codes for a carotene desaturase) is CrtI from the bacterium *Pantoea ananatis* (formerly named *Erwinia uredovora*). CrtI was used because plants utilise four genes (two carotene desaturases and two carotene *cis–trans* isomerases) to carry out the same reaction sequence leading to the provitamin A precursor lycopene. One single bacterial transgene can thus substitute for four plant transgenes. The enzyme activities upstream of phytoene and downstream of lycopene in the carotenoid pathway are all actively expressed in wild-type rice endosperm. Thus all that is needed is to reconstitute the overall biosynthetic sequence is to 'bridge the gap' [12].

During the past few years the trait has been transferred from the original cultivar into selected locally adapted rice varieties. This was done by a consortium of partner institutions in the Philippines, Vietnam, and India. Concomitantly, the event to be carried through the regulatory process was determined based on the datasets collected during the breeding process and instructed by the bioconversion numbers obtained, which showed that bioavailability of the provitamin A in GR2 is very high [13].

The case of folate and iron in rice

Folate, or vitamin B9, is an essential coenzyme involved in one-carbon metabolism. Folate deficiency is associated with a higher risk to newborns of neural tube defects, spina bifida, and anencephaly, and an increased risk of cardiovascular diseases, cancer, and impaired cognitive function in adults. Mandatory fortification of wheat flour with folic acid in the United States in 1998 was followed by a significant reduction in the prevalence of neural tube defects [14]. Folate deficiency also causes widespread megaloblastic anaemia during pregnancy and often exacerbates already existing iron deficiency anaemia [15], see also [17–19].

As with provitamin A, folate levels are very low in rice endosperm and so is the genetic variability of the trait. Thus, folate biofortification is another case for which genetic modification is required. A successful proof-of principle rice has recently been reported [16]. Here, the transformation of two pathway genes from *Arabidopsis thaliana* shifted folate production to levels in the grains which can be expected to meet the requirements necessary to combat its deficiency. Product development would be required but, inexplicably, has so far not met the interest of donor agencies. Other results demonstrate that recommendations for folic acid supplementation alone did not appear to succeed in reducing the incidence of open NTDs in Nova Scotia, whereas the fortification of grain products with folic acid did result in a significant reduction in the incidence [20].

Iron is a redox-active constituent of the catalytic site of heme and non-heme iron proteins. More than one-third of the world's population suffers from anaemia; half of it caused by iron deficiency [21]. Endemic infectious diseases exacerbate the incidence of iron deficiency anaemia in developing countries. Iron deficiency adversely affects cognitive development, resistance to infection, work capacity, productivity, and pregnancy. Children of anaemic mothers have low iron reserves, requiring more iron than is supplied by breast milk, and suffer from physical growth and irreversible mental development impairment [21]. It is estimated that 800 000 deaths are attributable to iron-deficiency anaemia annually.

Rice endosperm is a very poor source of iron, the variability between cultivars ranging from ca. 1 to 8 ppm. Although a study conducted with rice containing 6 ppm can have a positive impact on nutritional status [22], there is consensus that significantly higher levels would be very desirable. The lack of adequate variability in iron content of seed calls for transgenic approaches capable of increasing iron partitioning in favour of the grains. However, the knowledge base for this trait is still meagre; 39 genes are thought to control iron homeostasis in rice [23] of which the rate-limiting ones are currently unknown. More research in the field of nutritional genomics is required to answer this question.

In contrast to iron, a significantly higher variability has been found for the zinc content of polished rice grains (G. Barry, P. Virk, IRRI, personal communication) which makes this trait a likely candidate for precision breeding.

Some plants cannot be bred or breeding is very difficult

Banana (cooking banana: 'plantain') is the staple food in more than 50 countries; in Uganda, for instance, consumption is approximate to 220 kg per person per year. However, banana fruit as eaten contains only low levels of vitamins and minerals. Bananas constitute sterile triploids selected from the wild. This makes conventional breeding extremely difficult, which explains why bananas are propagated vegetatively. For this reason the species has been genetically static for thousands of years and is consequently susceptible to changing environments and biotic stresses, such as attack by fungal diseases, as well as by bacteria and viruses. The banana variety 'Gros Michel' has been lost almost entirely to the so-called 'Panama Disease' caused by the fungus *Fusarium oxysporum* because breeding for resistance was not possible. Because banana-based diets are deficient in provitamin A, iron, and vitamin E, a project employing genetic transformation is underway to increase the level of these micronutrients. The project is being led by the Queensland University of Technology, Australia, in partnership with scientists at the National Agricultural Research Organization of Uganda (see http://www.grandchallenges.org).

Cassava ranks number five among human staple foods. In sub-Saharan Africa, however, it is number one because of its ability to provide food security in drought conditions. However, the micronutrient content is low and there are other problems with this crop such as the content of toxic cyanogenic glycosides and post-harvest deterioration, which minimises shelf-life. Cassava is vegetatively propagated, like banana. By contrast, however, it can be bred but has never been pushed to produce genetically uniform inbred lines. Cassava plants therefore, possess a very complex, heterozygous genetic makeup, which renders varietal recovery very difficult. Long breeding cycles and asynchronous flowering

represent further hindrances to breeding cassava for specific traits [24]. Consequently, projects employing genetic modification are underway at several institutions, such as The Danforth Plant Science Center (USA) partnering with several Universities and African institutions (see http://www.grandchallenges.org), and at CIAT (Colombia), partnering with the University of Freiburg, Germany. All of these have made significant progress (Richard Sayre, Danforth Center, personal communications) on all fronts and have developed proof-of-principle results showing that nutritionally improved versions of cassava can be produced through genetic modification.

Potato, as a vegetatively propagated crop plant, shares the issue of genetic complexity with cassava and has also been targeted to increase provitamin A content. This was successful; however the installation of a 'mini-pathway' was required to arrive at high provitamin A levels [25].

Needs for the development of nutritionally improved crop plants in the public sector

The examples given above are not at all comprehensive; the list could be extended by further cases of product-focused transgenic research conducted by public-sector scientists both in industrialised countries as well as in developing nations.

The public sector needs to resource these developing country targeted projects as they do not represent commercially valuable targets and therefore cannot be a commercial priority for the private sector. However, the private sector does have a potentially valuable role to play in pro-poor projects if skill is applied to structuring public–private partnerships so that all parties benefit. Golden Rice is an example where crucial phases of technology development have been mastered for pro-poor purposes by partnering with Syngenta AG (Basle) and by carefully defining complementary commercial and non-commercial (humanitarian) exploitation rights of combined technologies originating from both the public and the private sector.

Public-sector research funding is needed in basic science to further improve the arsenal of identified genes, together with molecular and genetic knowledge of pathways involved in the biosynthesis and biodegradation of nutritionally important micronutrients or in mineral homeostasis. However, the detailed knowledge gained from model systems must also be more effectively extended to crop plants, such as by understanding rate-limiting steps of metabolic pathways and pathway regulation. Where genetic modification is needed, better toolsets need to be developed for many crop plants grown in the tropics, such as promoters conferring precise tissue specificity of gene expression or more effective plant transformation protocols.

With genetically modified plants, the public sector also needs to learn and apply the skills required to proceed beyond the purely scientific or proof-of-principle state of their work. A complete set of highly specialised skills, not currently common in the public sector, is required to drive a genetically modified plant through the processes involved in regulatory approval and beyond. For example, more specialised knowledge is needed in the areas of community engagement, communication, social marketing, and nutritional extension and education, requiring partnerships across disciplines as well as considerable management skills.

These public–private and multidisciplinary partnerships and their management require sustained funding, given the fact that for many traits and crop plants genetic modification is not an option, but rather a necessity to deliver sustainable nutrition in staple crops in developing countries.

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Review

Inactivation of allergens and toxins

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Plants are replete with thousands of proteins and small molecules, many of which are species-specific, poisonous or dangerous. Over time humans have learned to avoid dangerous plants or inactivate many toxic components in food plants, but there is still room for ameliorating food crops (and plants in general) in terms of their allergens and toxins content, especially in their edible parts. Inactivation at the genetic rather than physical or chemical level has many advantages and classical genetic approaches have resulted in significant reduction of toxin content. The capacity, offered by genetic engineering, of turning off (inactivating) specific genes has opened up the possibility of altering the plant content in a far more precise manner than previously available. Different levels of intervention (genes coding for toxins/allergens or for enzymes, transporters or regulators involved in their metabolism) are possible and there are several tools for inactivating genes, both direct (using chemical and physical mutagens, insertion of transposons and other genetic elements) and indirect (antisense RNA, RNA interference, microRNA, eventually leading to gene silencing). Each level/strategy has specific advantages and disadvantages (speed, costs, selectivity, stability, reversibility, frequency of desired genotype and regulatory regime). Paradigmatic examples from classical and transgenic approaches are discussed to emphasize the need to revise the present regulatory process. Reducing the content of natural toxins is a trade-off process: the lesser the content of natural toxins, the higher the susceptibility of a plant to pests and therefore the stronger the need to protect plants. As a consequence, more specific pesticides like Bt are needed to substitute for general pesticides.

Contents

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The dangers of nature and food

Toxic substances abound in living beings, plants included. Humans use plants (or products made from them) as a source of food, fiber, fuel, tools or drugs and therefore are constantly exposed to toxins and allergens of plant origin. The plant world can thus be viewed as a 'minefield'. A short walk both in cultivated fields and wild areas in many places in Italy, for which I have some experience, and more generally everywhere in the world, allows one to meet plants which have caused poisoning or even fatalities in humans or animals (see some examples in Table 1). For instance, castor bean (*Ricinus communis*) is common in southern Italy and produces ricin, a poison among the most potent known to man. The lethal oral dose in humans is approximately eight beans; even half a bean was enough to cause death [1]. Other highly toxic encounters in Mediterranean countries are oleander (*Nerium oleander*) and most plants in the Ranunculaceae, Scrofulariaceae and Solanaceae (nightshade) families. For references on common toxic plants in Italy [2]; for North America [3]; for a general treatise [4]; for a recent compilation [5]; for a website [6]. The common names for several members of the Solanaceae are quite explicit in their message: angel's trumpet or devil's weed (*Datura stramonium*), the apple of Sodom (*Solanum sodomeum*), bittersweet nightshade or poisonberry (*Solanum dulcamara*), black nightshade or devil's little tomatoes (*Solanum nigrum*) and deadly nightshade (*Atropa belladonna*). Some of the fruits or flowers are quite attractive in appearance and therefore become more dangerous for people raised in urban settings and who are unaware of the risks, children in particular, for example [7–9]. One author suggests that 'about 2% of plant species can severely poison people who happen to ingest them', with alkaloids being the major cause [10]. Some toxins are quite widespread among plants, like cyanogenic glucosides, which are reported in at least 2500 different species [11]. Many toxic plants are weedy, wild plants which need not human's intervention to survive.

Likewise, many crops have dangerous substances (Table 1), some in edible part and some in organs not used as food. For instance potato tubers or ripe tomato fruits usually have low levels of glycoalkaloids, but leaves, diseased tubers and fruits (a small berry) of potato or leaves and immature fruits of tomato are more

TABLE 1

Examples of wild and crop plants with toxic substances and their effects

Common name	Latin name	Toxic substance[a]	Effect[b]	Dose[c]|content[d]
Giant fennel	*Ferula communis*	Prenylated coumarins	Lethal	
Jimson weed	*Datura stramonium*	Atropine (and other alkaloids)	Lethal	100 seeds|0.1 mg/seed
Tobacco	*Nicotiana tabacum*	Nicotine	Lethal	1 mg/kg|3–6%
Apple of sodom	*Solanum sodomeum*	Solasonine, solanidine	Toxic	30 mg/kg|0.3 mg/g
Castor bean	*Ricinus communis*	Ricin/ricinoleic acid	Lethal	Half a seed
Pepper	*Capsicum* spp.	Capsaicin	Lethal	|0–2 mg/g
Tomato	*Solanum lycopersicum*	Tomatine	Toxic	
Potato	*Solanum tuberosum*	Solanine	Lethal	|3–6 mg/kg
Cassava (Yucca)	*Manihot esculenta*	Cyanogenic glucosides	Paralysis–stunting	|15–400 mg HCN/kg
Soybean	*Glycine max*	Protease/amylase inhibitors	Toxic	
Almond	*Prunus dulcis*	Cyanogenic glucosides	Lethal	20 seeds|29 mg/kg
Brussel sprouts	*Brassica oleracea*	Glucosinolates	Lethal-goiter	|1–2 mg/g
Cotton	*Gossypium hirsutum*	Gossypol	Cardio/hepatotoxic	0.3–3 mg/kg|10 mg/g
Vetch	*Lathyrus sativus*	Oxalyl-diaminopropionic acid	Neurotoxin/paresis	|0.3–3.2%
Lima bean	*Phaseolus lunatus*	Cyanogenic glucosides	Lethal	|2–3 mg HCN/kg
Poppy	*Papaver somniferum*	Morphine	Lethal	100 mg|10 mg/g
Bamboo	Several species	Cyanogenic glucosides	Toxic	|1–8 g HCN/kg

[a] Only the main toxic components are listed. Most of the plants in the table are mentioned in [14], but see also [1–13]. For the giant fennel toxicity, see [147], for Jimson weed [148], for pepper [149]. Many other toxic substances can often contaminate plants or food, but are not considered in this list.
[b] The effect is obviously dependent on the dose. When a substance or a plant is defined as lethal in the table, there are reports in the literature of fatal cases for humans or grazing animals (e.g. [147]). For other examples of toxicity in animals, see http://www.ansci.cornell.edu/plants/ (plant poisonous to livestock and other animals).
[c] The lethal dose reported is usually the minimum observed and may not be always lethal. The dose is expressed as the amount of plant (e.g. number of seeds) or as the amount per kg of body weight able to cause the effect.
[d] The content refers to the main active principle causing the toxic effect and it is expressed per plant part or weight.

toxic. Cases of severe poisoning, sometimes fatal, are reported in the literature for several of the edible plants listed in Table 1 (e.g. [12,13]; for a compilation [14]).

Most of the toxic substances in plants are known to men since time immemorial and were identified by modern science according to their chemical characteristics (alkaloids, glucosides, aminoacids, proteins, lipids, etc.). Their toxicology and mode of action have been described (for a comprehensive compilation see [4,5]). Although some (e.g. digitoxin) have a long history of use as pharmaceuticals and are still used today, most have been abandoned because of the short interval between therapeutic and toxic dose.

The ability of humans to survive and thrive depends on their capacity to recognize and avoid or inactivate most of these toxic compounds. Especially for plants used as food, this is achieved by a combination of proper storage and processing (e.g. maceration and fermentation) among which cooking is the most prominent for its major effect of heat inactivation. Knowledge in this context can be likened to a precise map handed down from generation to generation through culture and education, warning of the dangers of the minefield, while technology becomes similar to a metal detector to reveal, avoid or inactivate toxic substances. Knowledge and technology buffer us from the toxic effect of nature and allow a far wider spectrum of plants or plant parts to be used to our benefit than those 'naturally' available. The widespread belief in the superior goodness of nature and the evil of manipulations by human is causing harm and death (e.g. [15–17]).

Cultivated plants seem to have fewer toxins than their wild relatives, as the result of selection for better-tasting plants [18]. For example, the wild potato *Solanum acaule* has three times more glycoalkaloids than cultivated potato and is more toxic [19–21]. Cultivated Brassicaceae (cabbage, broccoli and cauliflower), when compared to wild species, have less glucosinolates, a major class of secondary metabolites [22,23] and this affects the survival of herbivore insects and their parasitoids [24,23]. The wild bean *Phaseolus lunatus* contains about three times cyanogenic glucosides when compared to the cultivated bean [25]. Wild and cultivated beans have different levels of antinutritional factors [26]. Cyanogenic glucosides in white clover (a forage crop) act as a deterrent against herbivores [27], but cultivars devoid of cyanogenic glucosides have been bred to obtain better palatability for grazing animals. Similar reductions have been reported for other crops [28]. The issue is complicated by the effect of the environment and pest pressure [29]. Whether this is a general rule remains to be demonstrated, but it seems an acceptable hypothesis and might contribute to the general susceptibility of crop plants to pests. Nevertheless, the point remains that humans can clearly tolerate at least low levels of toxins in their diet without ill effects. In fact, the ability to safely consume a low level of toxins has been a key element in the survival of all omnivores. The most appealing explanation for the observed crop–wild differences is that humans selected loss of function mutations leading to a reduced toxin content during the domestication process on the basis of feeding 'tests'. Most presumably it was a long process of trial and error (or trial and death). At least in one case it seems that not only the overall quantity of toxic glucosinolates is reduced, but also that inducibility by wounding is lost in the cultivated species [23].

Thus many crops still produce the same kind of toxins as their wild relatives, albeit in lower quantity, at least in edible parts. This means that the biosynthetic capacity is there. Indeed sometimes crops are fatal for humans [12,13,30]. Moreover, toxin content might increase spontaneously or during the breeding process, the so-called 'unintended effects'. Cases are known where commercial varieties caused health problems for this reason: rashes from celery [31,32], vomiting, stomach cramps, diarrhea or collapse from zucchini [33,34], potato [35] and bottle gourd [36]. Therefore testing for known toxins is routinely performed in crops known to contain toxic compounds, irrespective of the breeding method used. A problem relevant both to the developing and developed world is mycotoxin contamination of foodstuffs. Mycotoxins are not actually produced by plants, but are a byproduct of fungal growth on plants or foods. While there are several strategies (both conventional and transgenic) to control mycotoxins, this is outside the scope of my review. Other authors discuss mycotoxins in this issue (W. Parrot, B. Chassy).

Improving food safety and food security

The presence of toxic substances is still problematic for a few crop plants, which might be ameliorated by a further reduction, as well as for wild plants, in those cases for which a rapid domestication process might be desirable, such as for some biofuel crops [37]. To give a perception of the relevance of crop amelioration in economical as well as human terms, I provide three examples: rapeseed, cassava and cotton.

Rapeseed is widely grown and the annual production in 2007 was 50 Mt. The seeds are used mainly for oil production. After extraction, the resultant meal (35 Mt/year) is a good source of protein for animal feed, but its use is often limited by the amount of glucosinolates that can be ingested because of their toxicity. Glucosinolates themselves are not toxic, but upon cell disruption, they are hydrolyzed by plant myrosinases (specific esterases) and their hydrolysis products have been shown to be deleterious to rat, pig, poultry, rabbit, cow, sheep and fish, with effects on health, growth, productivity and reproduction (reviewed in [38]). In several cases, high-level intake results in increased mortality. Part of the negative effects on animals can be reduced by iodine supplementation, because some of the glucosinolates hydrolysis products interfere with thyroid hormone production. Classical breeding was used to create varieties low in glucosinolates: the so-called 'double zero' varieties are low in (but not devoid of) both erucic acid and glucosinolates. Also several treatments are available to reduce glucosinolate content [38]. Processing like heat inactivation further reduces the toxicity of glucosinolates, but also reduces lysine availability and thus the quality of the feed [39]. Thus genetic engineering gives a possibility of improving the meal through selective removal/reduction of glucosinolates in seeds beyond the reductions already obtained by breeding. The problem of toxicity might be less relevant in developed countries where most varieties have already a reduced glucosinolate content, but further improvements at the genetic level can translate into increased feed utilization efficiency, even in developed countries, making intensive agriculture more sustainable.

Cassava is a staple food for around 700 million people in the world, mainly Africa and Latin America. The starchy tuberous roots are poor in protein and contain varying amounts of two cyanogenic glucosides (linamarin and lotaustralin) which can be converted to HCN upon hydrolysis of the glucoside. Chronic

exposure to sublethal levels of HCN is responsible for konzo (irreversible paralysis of legs [40–42]), goiter and cretinism, stunting of children [42] and possibly Tropical Ataxic Neuropathy [43]. Some of these effects are exacerbated by diets poor in iodine and/or protein. On the history and sufferings connected to goiter due to iodine deficiency, I recommend the book by Hetzel [44]. Both bitter and sweet cassava (with a reduced content of cyanogenic glucosides) are available [45], but the preference of consumers and farmers depends also on traits such as cooking quality, starch texture and resistance to disease. Therefore the availability of plants combining certain characteristics with reduced cyanogen content might be better achieved by transgenesis rather than breeding. Given the rising consumption of cassava, especially in Africa [46] there is the case for improving varieties as well as education on the methods to process cassava tubers to remove cyanogens [46].

The third example is cotton, a crop primarily grown for fiber with an annual production in the range of 25–28 Mt of fiber in recent years. Interestingly, for each kg of fiber the plant produces 1.65 kg of seed (41–46 Mt/year) which contains 21% oil and 23% protein. The meal left after oil extraction contains high-quality protein (8–10 Mt/year), but it is unsuitable for consumption by monogastric animals, humans included, because of the presence of gossypol, a cardio- and hepato-toxic terpenoid [47]. It is therefore used as feed for ruminants, which are less sensitive to gossypol, either as meal after oil extraction or more rarely as whole seeds. Costly chemical, biological and physical procedures (see [48] for some references) are used to remove gossypol from cottonseed products to allow their use as food for non-ruminant animals, including solvent extraction with different solvents, ferrous sulfate or calcium hydroxide treatment, microbial fermentation and mechanical processing. It is clear that the development of varieties without gossypol would completely eliminate the need for gossypol removal and could potentially satisfy the daily protein requirement for half a billion people. A glandless cotton mutation was discovered in 1954 and immediately attracted the attention because gossypol accumulates in epidermal glands, located in seeds and aerial plant parts. Several commercial glandless varieties were developed by conventional breeding but they turned out to be extraordinarily susceptible to several insect pests, presumably because they lack protective terpenoids [49,50].

Targeting the genes rather than the proteins

The overwhelming majority of toxins are either protein themselves or are synthesized by proteins. The dogma of molecular biology states that 'DNA makes mRNA and mRNA makes protein'. This is normally represented as: Gene → mRNA → Protein. If we target the gene or the mRNA coding for a certain protein, then we end up not making the protein at all or making a nonfunctional protein. Therefore, the most sensible approach to reduce/inactivate a toxin in a living being is targeting the gene coding for (i) the toxin (if this is a protein synthesized through mRNA/ribosomes), (ii) a component of the specific machinery/pathway responsible for its production/accumulation (as is the case for toxic metabolites) or (iii) a regulator of the expression of the toxin, either directly (for a toxic protein) or indirectly (if it is a metabolite). Other strategies are the pharmacological or physical inactivation of the protein (e.g. by heat through cooking and food processing) or the stimulation of its degradation, but these strategies will not be dealt with here. I shall focus on inactivation at the gene/mRNA level as a safe and cheap alternative. The power of this approach is that mutations are inherited and usually quite stable. All the progeny of a plant with a disrupted gene will carry the same inactive allele. This implies that protein inactivation through gene inactivation is a once-for-all approach and needs not to be repeated at each generation or harvest. In a few cases, mutations could revert to the original status, but this is a spontaneous process whose frequency depends on the type of mutation. Selecting the appropriate mutation can make the reversion frequency extremely low. The next question is: how it is possible to inactivate a gene or its corresponding mRNA?

Direct and indirect gene inactivation strategies

Mutations arise spontaneously in any organism and by several means. Some of the causes are inevitable, such as background radiation, the endogenous production of reactive oxygen species or the mutagenic effect of DNA replication and cell division, while others can be induced or strengthened by environmental conditions. Mutation frequency can be enhanced for experimental purposes by various treatments: UV, X- and γ-rays, chemical mutagens and mitogens (indirectly), just to name a few. Mutants arise for instance because transposons can move around and 'jump' into genes. Similar results can be obtained by natural transposons or T-DNA/engineered transposons [51–54]. Genes have been inactivated through mutation (broadly defined as base changes, insertion or deletion) all the time. A mutation can involve just a single base or entire chromosomes. The importance of this process is particularly evident during domestication whereby the expression of certain genes was altered. For instance, loss of shattering, a trait of great importance in agriculture, is attributed to a disruption in the development of the abscission zone between grains and pedicles [55,56]; for more examples, see [57,58]. Many mutations involved in domestication are recessive, consistent with a loss of function and are deleterious in the wild (see contribution by P. Raven in this issue). Whether a similar phenomenon applies to the reduction in toxin content that happened during domestication, it is too early to tell for the lack of molecular data, but it seems quite a plausible mechanism.

Mutations resulting in inactivation of a protein can be classified into two broad categories (Fig. 1): mutations in the targeted gene and mutations involving another gene, but which affect the targeted gene via an RNA intermediate. The first class of mutations strike at the gene itself (box in Fig. 1a) thereby compromising the ability to produce a functional/stable mRNA or affecting the functionality or stability of the corresponding protein. The other class (RNA-mediated, Fig. 1b) interferes with the expression of the target gene by means of a double-stranded RNA (dsRNA), but leaves the gene sequence unchanged. This second class is collectively referred to as post-transcriptional gene silencing (PTGS), different variants of which are possible (antisense, RNAi, miRNA, hpRNA, etc.) and often involve epigenetic changes [59–61]. To be precise, the direct inactivation of a gene coding for a regulator (e.g. transcription factor) of a metabolic pathway is a protein-mediated strategy and therefore should be classified as an 'indirect gene inactivation', but for the sake of simplicity it will be treated as a direct gene inactivation strategy, because the targeted gene is directly inactivated.

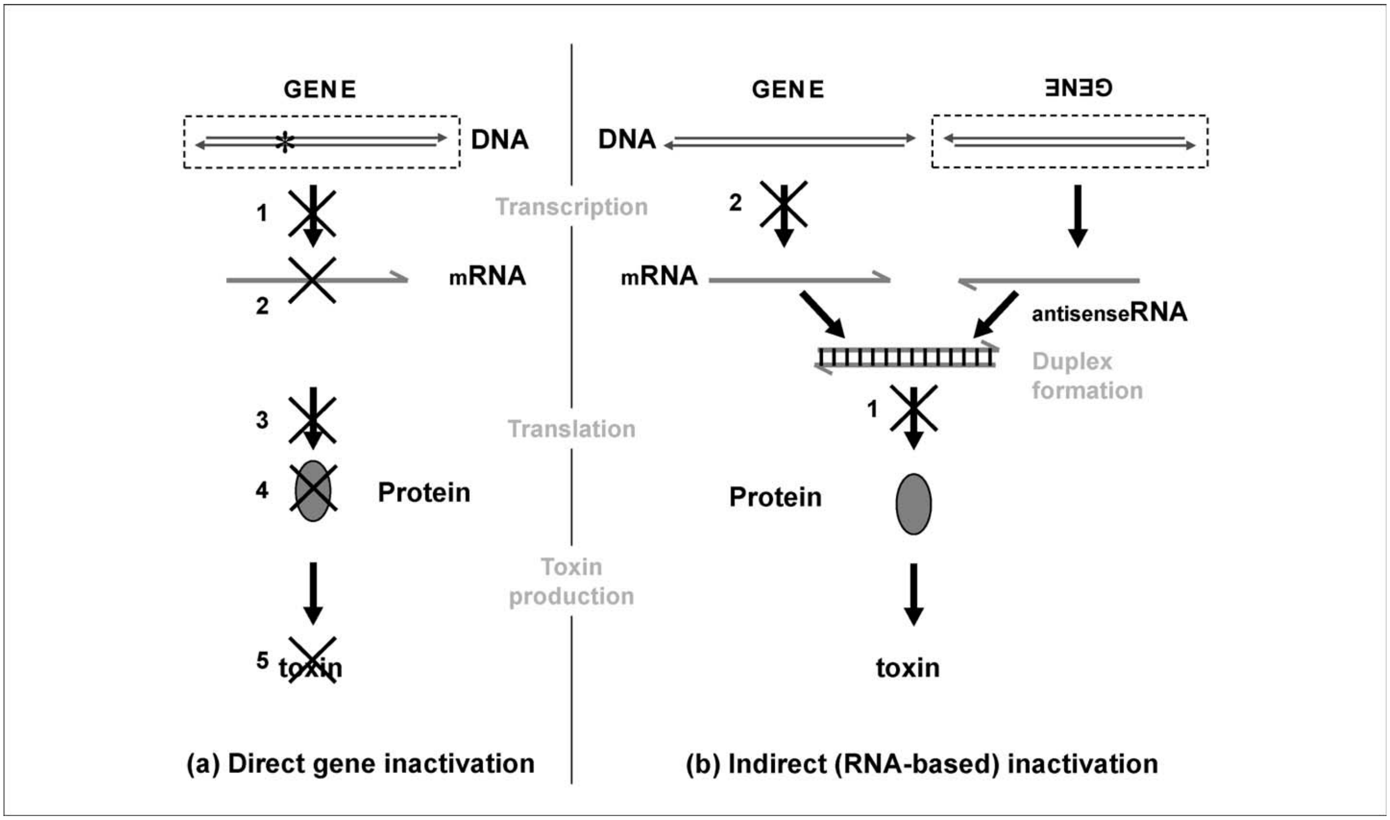

FIGURE 1

Classification of gene inactivation strategies. Strategies can be broadly assigned to either to **(a)** direct or **(b)** indirect category. The former indicates all those situations where the gene itself (within dashed box) is inactivated by the mutation, which is depicted as an asterisk at the DNA level and representing any change in the DNA sequence; large × represent all the potential levels where the inactivation may reveal itself: transcription (1), mRNA processing or stability (2), translation (3), protein folding or stability (4) or function (5). Indirect strategies (b) leave the original gene intact, but introduce another gene (dashed box) which produces an RNA molecule complementary to the mRNA of the gene that is going to be silenced. For this reason the introduced gene is depicted in the antisense orientation and the RNA produced is called antisenseRNA, often abbreviated in asRNA. The mRNA (sense) and the antisenseRNA pair together forming a duplex (dsRNA) which inhibits translation directly (1) or prevents transcription (2, indirectly, at the chromatin level, via the production of small RNAs).

The different methods to obtain a mutant are listed in Table 2, together with advantages/disadvantages of each method. It is noteworthy to stress that different methods might end up exactly in the same result – lack of a (functional) protein – and could be mediated by the same or a similar change at the DNA level, irrespective of the agent performing the modification (be it a human being or a bacterium or the plant itself) or the method by which the mutation is produced. It is therefore hard or impossible to distinguish natural/non-natural mutations (see contributions by W. Arber and by W. Parrott in this issue). Moreover what is relevant is the phenotype, the effect of the modification, and not the method used for achieving it. It is plausible that different direct

TABLE 2

Kinds of mutation and their advantages/disadvantages

Origin	Advantages[a]	Disadvantages[b]
Spontaneous mutation	No/little regulation	Low frequency/restricted choice
Induced mutation	No/little regulation	Low frequency/restricted choice
Mutagenic oligonucl.	Specific, quick, little/no regulation	Restricted choice
Transposon	May be specific	May be reversible, single target, low frequency
T-DNA insertion	Specific/irreversible	Single target, low frequency
Antisense RNA	Specific, dominant, sequence-based, many targets	Silenced gene intact (reversible), may be leaky
RNAi (hpRNA)	Specific, dominant, sequence-based, many targets	Silenced gene intact (reversible), may be leaky
miRNA	Specific, dominant, sequence-based, many targets	Silenced gene intact (reversible), may be leaky

[a] *Advantages*: specificity of inactivation might have different degrees of intensity and might concern different tissues. Both depend on the construct and the transformation event. Irreversibility depends also on the technique and on the event. 'Sequence-based' means that only the sequence is required to obtain the desired mutant (and the frequency of the mutant is usually high.

[b] *Disadvantages*: by frequency it is meant the number of mutants with the desired phenotype compared to the number of mutants generated. Leaky means that small amount of toxin might still be produced (e.g. [63]) in the tissue.

mutations (e.g. a deletion spanning the whole gene, the insertion of a T-DNA or of a transposon or a point mutation) produce the same effect by affecting a similar target, like, for instance (1) the promoter region (eliminating transcription) or (2) the coding region (introducing an early stop codon or a missense mutation, affecting protein stability, folding or activity) or (3) a splice site (abolishing the splicing) or (4) determinants of mRNA stability (causing rapid mRNA degradation). The extent (length of the DNA involved), nature (insertion, deletion or change) and site of action (transcription, splicing, mRNA stability, translation, protein folding or stability or catalysis) of the mutation can be very different. Similarly for indirect mutations, the origin of the asRNA, its length, position and extent of pairing with the mRNA can vary greatly between different indirect strategies. Also the ultimate level of action for the asRNA can be different: in some cases the duplex formation targets the mRNA for destruction and inhibits translation, in other cases the small RNA fragments can lead to an alteration in the methylation pattern of the gene and ultimately in the silencing of transcription.

No one method suites all situations (of pros and cons)

Gene inactivation is an excellent means to study gene function and it has been applied to basically all processes in living organisms since the discovery of mutations and their hereditability. More recently, systematic insertional mutagenesis was applied to *Arabidopsis* (e.g. [53,54,62] and other plants to study gene function in all aspects of their biology. This paper deals only with strategies aiming at inactivating toxin and allergens.

In the case of direct gene inactivation, some methods like X-rays or T-DNA insertion very often cause irreversible mutations which are stably inherited. Both characteristics are obviously advantageous for breeding. Other mutations, caused by chemical mutagens, spontaneous to base change or transposon insertion, might be more prone to reversion and less desirable compared to stable ones. Certain methods (insertional mutagenesis with T-DNA or transposons) are ineffective or slow when multiple gene codings for similar proteins need to be inactivated at the same time. In these cases, approaches like RNAi or antisense are more effective. Another big advantage of this approach is that knowledge of the sequence is the only requirement. Once the target gene is known, the construction of a transgenic organism affected in the expression of the gene is relatively easy. However, in the case of indirect gene inactivation, the target gene remains intact and therefore the phenotype might revert completely when the 'interfering' gene is inactivated or removed. Very interestingly, RNA-based inactivation methods allow for gene inactivation in specific tissues or developmental stages, as well as multiple targets, goals much more difficult (but not impossible in principle) to achieve with other methods.

In short, the best method depends on the specific combination of trait/crop one wants to achieve. The strong regulation required for mutants produced by some method is of course a self-imposed disadvantage that has no scientific basis (see contribution by H. Miller in this issue).

Examples of inactivation of toxins in transgenic plants

The seed-specific inactivation of the biosynthetic pathway for gossypol is the most striking example of the potential of biotechnology for toxin inactivation. Sunilkumar *et al.* [63] cloned a fragment of δ-cadinene synthase, the first step in gossypol biosynthesis, into a hpRNA vector and obtained tissue-specific silencing of the corresponding gene by restricting the expression with the seed-specific α-globulin B gene promoter. All transgenic seeds show a strong reduction in the level of gossypol, within the limits approved by the World Health Organization (WHO). The trait strictly co-segregates with the transgene and is stably maintained in the RNAi lines. The levels of gossypol and other protective terpenoids (hemigossypolone and heliocides) in leaves are not altered. Earlier attempts to reduce gossypol via antisense RNA did not yield a strong reduction or were unconvincing (see [63,64] for other references).

The authors demonstrated that it is possible to disrupt gossypol biosynthesis in seeds (and in seeds only) by interfering with the expression of a biosynthetic gene during seed development. Targeted gene silencing can thus be used to modulate biosynthetic pathways in a specific tissue to obtain a desired phenotype. Traditional breeding was unable to achieve this goal. Most remarkably, the authors hope to get reduced-gossypol cotton through regulatory approval process in the U.S., but, due to the very high costs (estimated in the range of 50 M$, see contribution by I. Potrykus in this issue) they 'do not know where the money is going to come from' (K. Rathore, pers. commun.). The foregone benefits of a delay in delivering this variety to farmers are evident with around a billion hungry people on the planet.

Another example is the reduction of glucosinolates in *Arabidopsis*. Several groups have recently identified regulators of the biosynthetic pathway [65–71]. Overexpression and gene inactivation/silencing studies have revealed that Myb28, 29 and 76 control the aliphatic pathway. Myb28 is responsible for the basal transcription of the biosynthetic genes together with Myb29. Inactivation of the former effectively eliminates long-chain aliphatic glucosinolates, while inactivation of the latter reduces the amount of short-chain glucosinolates. Elimination of both gene functions results in the complete loss of aliphatic glucosinolates. Myb76 seems to be relevant in the induction of the pathway following wounding, but does not play a major role in the basal transcriptional regulation. By contrast, Myb34, 51 and 122 control the aromatic (indolic) branch. There appears to be a complex cross regulation between the two branches because a reduction in flux in one branch stimulates the flux in the other one. Even though *Arabidopsis* is not a crop, research findings with this species are easily transferred to other brassicas (e.g. [72]). A precise manipulation of glucosinolate content in seeds needs a better understanding of the full regulatory circuitry and transport. As for cotton, seed-specific silencing might be a desirable approach to avoid an overall increase in pest sensitivity.

As a third example there is again cassava. Different transgenic strategies have been attempted to reduce cyanogenic glucosides [73–77]. Antisense inhibition or RNA interference in leaves of the first step of cyanogen biosynthesis reduces linamarin levels by 60–94% in leaves and by 99% in roots. These plants however are impaired in growth or tuber formation in the absence of a reduced nitrogen source, presumably due to the role of cyanogen hydrolysis in aminoacid biosynthesis [73,77]. A more promising strategy is expressing the leaf-specific enzyme hydroxynitrile lyase (HNL) in roots to accelerate cyanogenesis and cyanide volatilization

during processing [74]. Several other examples of reductions of toxin have been published, but they have little relevance to food (nicotine in tobacco [78], morphine in Poppy [79,80]). Of interest is the reduction of antinutritional factors like phytic acid in maize [81] for environmental benefits, even if it decreases germination.

Room for improvement of orphan crops

Lathyrus sativus is a hardy tropical/subtropical legume also known as grass or Indian pea. Beans from this so-called 'famine crop' are an important source of nutrition for poor people in Asia and Africa, but contain a neurotoxin: oxalyldiamino-propionic acid (ODAP). This compound causes lathyrism, a lower limbs paralytic disease prevalent among adults in Central India who consume large quantities of seeds for several months [82]. Safe content for ODAP is <0.2%, while content in germplasm ranges between 0.3 and 3.3 [83]. Soaking and boiling of seeds reduce ODAP levels but effective detoxification often results in a decrease of nutritional quality. Classical breeding and tissue culture approaches have already produced varieties with greatly reduced ODAP levels (see references in [84], but the substantial outcrossing rate for this crop means that low ODAP lines must be multiplied in isolation and provided to farmers every year [85]. A biosynthetic pathway has been proposed for ODAP [86] and it is thus feasible to attempt its silencing only in the seed using a transgenic approach, as done for gossypol biosynthesis in cotton. Antisense or RNAi construct, due to their dominance, would reduce the need for segregation in seed production.

Other examples are two millet species, fonio and pearl millet, which are cultivated for food in sub-Saharan Africa and India with an annual production of 22 Mt (80% of the world total). High consumption of these two species is known to cause goiter (see references in [87]) with its burden of suffering [44] due to the flavonoids apigenin and vitexin, respectively in fonio and pearl millet, which are strong inhibitors of thyroid peroxidase. Available knowledge allows one to attempt the targeted inactivation of the biosynthetic pathway in seeds and suggest that genetic engineering approaches are more reasonable than conventional ones [87].

Trade-offs for toxin reduction

Reduction in toxin content usually comes with a price: plants become more susceptible to pests [70,71,27,88] sometimes to the point of making them unsuitable for cultivation [49,50]. Several natural pesticides are quite general in their mode of action [89] and natural pesticides account for 99.99% of our dietary pesticide intake [90]. For example, benzoxazinones, secondary metabolites from cereals, are important in the defense against insects, fungi and bacteria [91,92] and the same is true for the glucosinolates/myrosinase system in brassicas [93]. Similarly cyanogenic glucosides seem generally toxic against insects and animals [11,94,95] and protect plants from herbivores [27,28], even though several insects might have evolved specific resistance. On the contrary, accumulating new pesticides into a plant increases pest resistance (e.g. cyanogenic glucosides [96]). This strategy is indeed the key to the success of insect resistance based on Bt toxins engineered into cotton and maize [97], as well as many other species (e.g. [98,99]). The environmental and safety price bargained through the more precise tools of genetic engineering is expected to be substantially lower than those obtained with classical genetic approaches, because of the use of pesticides (e.g. Bt or avidin, see [100]) targeting only specific classes of pests, and a much wiser alternative to the application of synthetic chemicals.

Plant-derived allergens

Allergens are of widespread occurrence and one might not be aware of their presence until experiencing their effects. It is not only a nuisance and/or a cost, but it could be a deadly threat. Minute amounts of allergens might cause a life-threatening event called an anaphylactic reaction. This might occur after ingestion, skin contact, injection or inhalation of an allergen. In the UK alone, allergens in food are reported to have caused 48 deaths over a 7-year period between 1999 and 2006 [101]. Half of the eight foods accounting for 90% of all food-allergic reactions (milk, egg, fish, shellfish, peanut, tree nut, soy, and wheat) are of plant origin [102]. Products containing them are quite widespread and difficult to avoid in a standard diet. Beyond them, pollen is the major cause of respiratory allergy, with at least 40% of type 1 allergic patients who are sensitized against grass pollen allergens.

Contrary to common perception, transgenic plants never caused allergic reactions to consumers. In one case a gene for a 2S albumin from the Brazil nut (a known allergenic food) was expressed in soybean [103]. The resulting transgenic soybean was tested for allergenicity and it was ascertained that the 2S albumin is indeed a major Brazil-nut allergen. The development of this product was abandoned, no product was ever commercialized or released and no consumer suffered any allergic reactions. This was not a serendipitous finding, because if a gene used for transgenesis comes from a plant containing allergens, the transgene has to be checked for allergenicity. A similar situation was found for transgenic peas expressing the bean α-amylase inhibitor [104]. The transgenic peas elicited an immune response in mice upon feeding, but the reaction could be ascribed to changes induced in the plant by the transformation and regeneration procedure or by the changes detected in the α-amylase inhibitor between bean and pea [105] regarding the glycosylation pattern and the removal of amino acid residues of the protein. The guidance rules adopted in the EU require a risk analysis for potential allergenicity for any gene that is being used for transformation [106,107].

Examples of inactivation of allergens in transgenic plants

There are several examples of manipulations for the reduction of plant allergens content (apple, peanut, wheat, soybean, ryegrass and birch). In this paper I discuss one example each from soybean and apple. Several papers describing or reviewing other cases are available [108–112] (M. Schenk, Birch pollen allergy: molecular characterization and hypoallergenic products, Ph.D. thesis, Wageningen University, 2008 (http://www.library.wur.nl/wda/dissertations/dis4391.pdf)).

In the US/Europe: 5–8% of babies and 2% of adults are reported to be allergic to soybeans. The dominant soybean allergen is a protein named P34 or Gly m Bd 30 K, with more than 65% of soy-sensitive patients reacting only to it. Mutagenesis and breeding allowed the removal of some soybean allergens [113,114], but not the dominant allergen P34. Transgenic soybeans without P34 were readily obtained by gene silencing [115,116]. Apart P34, the authors found no difference in composition, development, struc-

ture, polypeptide pattern or ultrastructure when comparing the silenced line with control plants. However, using the very same words of the authors, 'regulatory difficulties and the lack of acceptance of GM soybeans by the baby food and formula industry makes using such an allergen-suppressed soybean difficult at the present time', a euphemism to mean nearly impossible. Therefore an alternative approach was used to achieve the same goal: identify soybeans lacking the allergen. The entire USDA national soybean germplasm collection was screened and out of more than 16,000 accessions screened, they found 12 lines (2 of which are cultivated soybean) with no P34 allergen [117]. Based on the sequence analysis, it is possible to guess the reason why these soybean plants lack the allergen. It is however possible that the expression of many other genes is altered with concomitant unintended effects (e.g. expression of new allergens). By contrast, the suppressed soybean line was thoroughly investigated by 2D gel electrophoresis and the only change detected concerns the targeted polypeptide out of the 1400 examined. Beyond any logic, the approval for the transgenic event will be far more complicated and costly than for the conventional mutant lines (E. Herman, pers. commun.).

Apple allergy is dominated by protein Mal d 1, which is also found in birch pollen. Allergenicity depends on the amount of specific Mal d 1 isoforms, whose quantity varies among apple cultivars. Because of this, classical breeding might be used to create new hypo-allergenic cultivars, but this is complicated by the fact that Mal d 1 is encoded by a gene family comprising at least 18 members (loci) arranged in several gene clusters. The expression of Mal d 1 in apple was inhibited by RNAi [118] and this translated into a reduced *in vivo* allergenicity. In another study [119], the allelic diversity of the seven Mal d 1 genes was investigated in several apple cultivars. It is clear that few alleles associate strongly with differences in allergenicity, suggesting that the production of new varieties by breeding is a feasible target. However, it takes over 15 years to produce a marketable cultivar out of a cross and therefore the direct production of clones with reduced amount of an allergen by transformation of existing cultivars seems a reasonable shortcut, except for the exorbitantly high hurdles associated with present regulatory regime.

It is often feared in non-scholarly sources that plant biotechnology would inadvertently introduce new allergens in foods. The examples presented here, as well as the available literature, make it clear that biotechnology is part of the solution to allergies rather than a cause of increased concern.

An example of insanity in regulation: percent similarity is not everything

Biosafety regulations require that if a protein shares at least 35% identity over 80 amino acids to an allergen, then any transgenic plant or product expressing it must be labeled as 'potential allergen', even if there is no evidence for any allergenicity [107], unless it can be proved that the protein is not an allergen. Phaseolin is a protein from bean which is not recognized as an allergen or listed in the official allergenonline.com website, even if it shares a substantial similarity (53% identity) to β-conglycinin, a minor soybean allergen. Moreover phaseolin is safely eaten by around one billion people everyday. The 27 kDa γ-zein is a storage protein from maize which is also not recognized as allergenic and consumed by hundreds of millions of people everyday. Zeolin, a chimera between phaseolin and 89 amino acids of γ-zein has been produced [120] and expressed in transgenic cassava (C. Fauquet, pers. commun.). However, zeolin-expressing cassava should be labeled as a 'potential allergen' because the similarity of phaseolin to β-conglycinin is well above the limit and it would be impossible to demonstrate that zeolin cannot be an allergen. Actually it would only be possible, as well as difficult and expensive, to demonstrate that the risk is below a certain level. This cassava shows a 350% improvement in protein content and a 55% reduction in cyanogenic glucoside, an unintended but welcome effect. It would be made freely available in developing countries if regulations would allow it. The labeling requirement, an obviously impossible (as well as ridiculous) task in places like Africa, makes this transgenic cassava another victim of present day regulation and a rather enlightening example of its insanity.

To stress the point, let us take an example of poetry (the first verses of Dante's Paradise, Canto I, v. 1–3): 'The glory of Him who moveth everything/Doth penetrate the universe, and shine/In one part more and in another less.' If we now substitute 40% of the letters in the words (changes underlined), we could get the following as one of the many examples: The <u>st</u>ory of him who <u>belie</u>veth everything/Do<u>es</u> <u>infil</u>trate <u>di</u>verse <u>lies</u> and <u>causes</u>/one part <u>of farmers or</u> another <u>to die</u>. Obviously the result is not poetry any longer and the meaning is substantially different. A similar thing happens with protein sequences. Two proteins could have 80% identity and yet perform different functions or have different structures. Conversely, proteins with little or no sequence identity could have similar structures or perform similar functions. The % of sequence identity is often a poor indicator of the protein properties and it is unreasonable to rely on it for predictions, if other evidence is at hand.

Conclusions

Plant-derived allergens and toxins are ubiquitous, abundant and essentially unavoidable components of our diet and environment. Tools are available to reduce them at the genetic level, either by conventional or transgenic approaches. However, strategies must be reasonable, that is accept some level of risk, and effective, that is the benefits have to be balanced against cost. For instance, it is unreasonable to require demonstration that zeolin is not an allergen when both phaseolin and zein are not. Similarly, it is unfair to demand multigenerational feeding tests on insect resistance Bt maize but not on maize varieties more resistant to several insects because accumulate more benzoxazinones [121]. Overcautious regulation goes in the opposite directions on both issues: a zero risk tolerance requires endless testing (and infinite costs) to obtain approval for innovative products as substitutes of older technologies. Moreover, reducing the content of natural toxins is often a threshold issue (the dose makes the poison). Accepting low levels of toxins seems a sensible option [89,90] and even a beneficial choice [122].

The insanity of present regulation is more evident with so-called 'loss of function' mutations, that is mutations inactivating gene function, such as many of those mentioned in this review, but similar arguments can be put forward for other kinds of genetic changes. The fact that genetic engineering easily achieved something that conventional breeding was unable to do – for example

maintain gossypol in leaves, where it is useful, and eliminate it in seeds [63], see also [123,124] – is the demonstration of the higher precision of this technology, not a proof of its unnaturalness, because it is conceivable that screening a larger number of conventional mutants might eventually deliver the same phenotype. An overcautious attitude might kill the technology altogether and its associated benefits. Comparing the techniques adopted for reducing toxins and allergens, usually transgenesis shows superior characteristics: it is not only more efficient in obtaining the desired phenotype (both in time and trial numbers) but also more precise. Natural null mutants for the P34 soybean allergen [117] have a frequency of 2/14,000 in cultivated soybean, that is 0.014%, and the exact reason for the lack of P34 is uncertain. Conversely, the frequency of soybeans coming out of a transformation showing P34 cosuppression is in the 10–20% range (E. Herman, pers. commun.). The possibility of 'unintended effects' is obviously smaller for the transgenic mutant, because a detailed analysis revealed only one change in composition (one protein missing out of around 1400 examined), the reason of which is the transgene. In other words safety testing of transgenic varieties must be compared against testing of varieties developed by conventional means.

Breeding approaches allowed in the past the creation of new varieties with lower toxin levels: erucic acid and glucosinolates in brassicas [39], cyanogenic glucosides in clover, cassava, almonds and cotton just to name a few [27,46,49,125,126]. Transgenesis is another tool which can be employed for the same purpose (e.g. [63,73]) and seems particularly suited for reducing the allergenic content of foods and plants in general, especially in fruit trees, where the use of conventional means, like mutagens or crosses among natural variants, is discouraged for practical reasons (e.g. the method takes too long a time or would alter the peculiar characteristics of the cultivar).

Other specific problems still await a solution or optimization. Several legumes must be heat treated before consumption especially for monogastric animals because they contain one or more toxic compounds: trypsin inhibitors, amylase inhibitors and lectins (in legumes [127]), saponins, vicine and convicine (pyrimidine glucosides from broad beans) responsible for favism in humans [128], just to name a few. The possibility of reducing single or multiple toxins in food and feed could improve food safety, food security and conversion efficiency. Other compounds like phytate are not toxic, but reduce availability of phosphate and iron in legumes and, to a lesser extent, in cereals [81]. The evident consequence of this further domestication is the need to substitute general pesticides for new, more specific pesticides like Bt to counter plant pests. Several new plant toxic proteins with insecticidal properties have potential in this respect [129–131] some of which are commonly found in foods we already eat (e.g. [132]) and we know how to inactivate them. A particular appealing strategy is the use of RNAi in plants to silence pest genes [133,134].

Sometimes it could be desirable to modulate the content of specific compounds. Glucosinolate hydrolysis products seem also to be responsible for the anticarcinogenic activity of brassica vegetables in humans [135], but the beneficial dose window of glucosinolate hydrolysis products can be rather narrow. It is amazing how fully acceptable is a new 'superbroccoli' variety obtained by conventional breeding through a cross with a wild variety [136] with a 10-fold increase in a specific glucosinolate content and a 100-fold inducing potency of a marker of phase II detoxification enzymes in mammalian systems. This is obviously considered to be a good thing by the popular press [137]. Another variety, named 'Booster Broccoli™', with a smaller but substantial increase in sulforafane, has just been launched on the market and its purported non-GM status is highlighted together with the benefits of a high sulforafane diet [138]. One wonders what would the reaction be if a transgenic canola (engineered for instance for herbicide tolerance) with minor alteration in glucosinolate profile was to be introduced in the market.

It is conceivable that new almond or peach varieties might accumulate much more cyanogenic glucosides and new potato varieties might accumulate more or new glycoalkaloids. From a few cases in the past [31–35] we know classical breeding can cause problems and yet, in the EU, new varieties with a real toxic potential (e.g. potato) require no regulatory scrutiny (no compulsory measurement of toxic compounds and no safety tests) before release, cultivation or commercialization if they are produced by conventional means. And we also know that conventionally bred crops might present far more changes at the genomic level than transgenic ones [139–144] or might contain new allergens [145]. Therefore there is a strong case for demanding a more science-based regulation (see also contribution by H. Miller in this issue).

Gene technology could further improve food safety, food security and wellbeing as well as reduce environmental impact of agriculture and other human activities. Regulation is a major obstacle because (rewording an Italian common way of saying) 'where logic ends, biotech regulation begins'. Technology is of course a constant source of new problems and challenges as it has been since the beginning of human society. As examples, think of the dangers of moving at high speed or, more recently, the hypothesis that the rise in allergies is linked to a reduced microbial exposure [146]. But rather than reverting to older and less safe technologies, we need to think of more technology as the solution. To state it more humorously in the words of F. Salamini: 'Everybody wants to return to nature, but not by foot'.

Note added in proof

An interesting approach to insect 'resistance' is reported in Ref. [150].

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Review

Modifying agricultural crops for improved nutrition

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The first generation of biotechnology products commercialized were crops focusing largely on input agronomic traits whose value was often opaque to consumers. The coming generations of crop plants can be grouped into four broad areas each presenting what, on the surface, may appear as unique challenges and opportunities. The present and future focus is on continuing improvement of agronomic traits such as yield and abiotic stress resistance in addition to the biotic stress tolerance of the present generation; crop plants as biomass feedstocks for biofuels and ''bio-synthetics''; value-added output traits such as improved nutrition and food functionality; and plants as production factories for therapeutics and industrial products. From a consumer perspective, the focus on value-added traits, especially improved nutrition, is undoubtedly one of the areas of greatest interest. From a basic nutrition perspective, there is a clear dichotomy in demonstrated need between different regions and socioeconomic groups, the starkest being inappropriate consumption in the developed world and under-nourishment in Less Developed Countries (LDCs). Dramatic increases in the occurrence of obesity and related ailments in affluent regions are in sharp contrast to chronic malnutrition in many LDCs. Both problems require a modified food supply, and the tools of biotechnology have a part to play. Developing plants with improved traits involves overcoming a variety of technical, regulatory and indeed perception hurdles inherent in perceived and real challenges of complex traits modifications. Continuing improvements in molecular and genomic technologies are contributing to the acceleration of product development to produce plants with the appropriate quality traits for the different regions and needs. Crops with improved traits in the pipeline, the evolving technologies and the opportunities and challenges that lie ahead are covered.

Contents

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The 2008 World Bank Development Report emphasized that ''Agriculture is a vital development tool for achieving the Millennium Development Goals that call for halving by 2015 the share of people suffering from extreme poverty and hunger'' [1]. The Report notes that three out of every four people in developing countries live in rural areas and most of them depend directly or indirectly on agriculture for their livelihoods. It recognizes that overcoming abject poverty cannot be achieved in Sub-Saharan Africa without a revolution in agricultural productivity for resource-poor farmers in Africa, many of whom are women. New and innovative techniques will be required to improve the efficiency of the global agriculture sector to ensure an ample supply of healthy food. To confound this situation the inequity between the affluent and developing countries will continue to grow and only a handful of technologies are sufficiently scale neutral to help with redressing this imbalance.

The first generation of the products commercialized from one of those technologies, namely biotechnology, were crops focusing largely on input agronomic traits primarily in response to biotic stress. The coming generations of crop plants can be generally grouped into four broad areas. The present and future focus is on continuing improvement of agronomic traits such as yield and abiotic stress resistance in addition to the biotic stress tolerance of the present generation; crop plants as biomass feedstocks for biofuels and 'bio-synthetics'; value-added output traits such as improved nutrition and food functionality; and plants as production factories for therapeutics and industrial products. Developing and commercializing plants with these improved traits involves overcoming a variety of technical, regulatory and perception challenges inherent in perceived and real challenges of complex modifications. Both the panoply of traditional plant breeding tools and modern biotechnology-based techniques will be required to produce plants with the desired quality traits. Table 1 presents examples of crops that have already been genetically modified with macro- and micronutrient traits that may provide nutritional benefits.

Nutrition versus functionality

At a fundamental level, food is viewed as a source of nutrition to meet daily requirements at a minimal to survive, but with an ever greater focus on the desire for health optimization. From the basic nutrition perspective, there is a clear dichotomy in demonstrated need between different regions and socioeconomic groups, the starkest being injudicious consumption in the developed world and under-nourishment in Less Developed Countries (LDCs). Both extremes suffer from forms of malnourishment, one through inadequate supply, the other, in many but not all instances, through inappropriate choices, the latter often influenced by economic considerations. Dramatic increases in the occurrence of obesity, cardiovascular disease, diabetes, cancer and related ailments in developed countries are in sharp contrast to chronic under- and genuine malnutrition in many LDCs. Both problems require a modified food supply, and the tools of biotechnology, while not the sole solution, do have a significant part to play. Worldwide plant-based products comprise the vast majority of human food intake, irrespective of location or financial status [2]. In some cultures, either by design or default, plant-based nutrition comprises almost 100% of the diet. Given this, one can deduce that significant nutritional improvement can be achieved via modifications of staple crops.

While the correlative link between food and health, beyond meeting basic nutrition requirements, has only been unequivocally proven in several cases, a growing body of evidence indicates that food components can influence physiological processes at all stages of life. Nutrition intervention from a functionality perspective has a personal dimension. Parsing individual response is at least as complex a challenge as the task of increasing or decreasing the amount of a specific protein, fatty acid, or other component of the plant itself [3]. There is also evidence that early food regimes can effect later life health, for example, some children that survived famine conditions in certain regions of Africa grew into adults battling obesity and related problems, presumably due to the selective advantage of the thrifty gene in their early food-stressed environment becoming a hazard during more abundant times especially if later diets are calorie dense. Functional food components are of increasing interest in the prevention and/or treatment of several leading causes of death: cancer, diabetes, cardiovascular disease, and hypertension. Many food components are known to influence the expression of both structural genes and transcription factors in humans [4,5]. Examples of these phytochemicals are listed in Table 2. The large diversity of phytochemicals suggests that the potential impact of phytochemicals and functional foods on human and animal health is worth examining as targets of biotechnology efforts.

From a health perspective, plant components of dietary interest can be broadly divided into four main categories, which can be further broken down into positive and negative attributions for human nutrition.

- macronutrients (proteins, carbohydrates, lipids [oils], and fiber),
- micronutrients (vitamins, minerals, and phytochemicals),
- antinutrients (substances such as phytate that limit bioavailability of nutrients),
- allergens, intolerances, and toxins.

The technology

There are approximately 25,000 metabolites (phytochemicals), of the 200,000 or so produced by plants, with known value in the human diet [4]. Analysis of these metabolites (most specifically metabolomic analysis) is a valuable tool in better understanding what has occurred during crop domestication (lost and silenced traits) and in designing new paradigms for more targeted crop improvement that is better tailored to current needs [6]. In addition, with modern techniques, we have the potential to seek out, analyse and introgress traits of value that were limited in previous breeding strategies. Research to improve the nutritional quality of plants has historically been limited by a lack of basic knowledge of plant metabolism and the challenge of resolving complex interactions of thousands of metabolic pathways. A complementarity of techniques both traditional and novel is needed to metabolically engineer plants to produce desired quality traits. Metabolic engineering is generally defined as the redirection of one or more reactions (enzymatic and otherwise) to improve the production of existing compounds, produce new compounds or mediate the

TABLE 1

Examples of crops in research and/or development with nutritionally improved traits intended to provide health benefits for consumers and animals[a].

Trait	Crop (trait detail)	Reference
Protein and amino acids		
Protein quality and level	Bahiagrass (protein↑)	[63]
	Canola (amino acid composition)	[64]
	Maize (amino acid composition; protein↑)	[29,34,65,66]
	Potato (amino acid composition; protein↑)	[67–70]
	Rice (protein↑; amino acid)	[71]
	Soybean (amino acid balance)	[32,72]
	Sweet potato (protein↑)	[31]
	Wheat (protein↑)	[33]
Essential amino acids	Canola (lysine↑)	[30]
	Lupin (methionine↑)	[73]
	Maize (lysine↑; methionine↑)	[74,75]
	Potato (methionine↑)	[76]
	Sorghum (lysine↑)	[77]
	Soybean (lysine↑; tryptophan↑)	[30,78]
Oils and fatty acids		
	Canola (lauric acid↑; γ-linolenic acid↑; +ω-3 fatty acids; 8:0 and 10:0 fatty acids↑; lauric + myristic acid↑; oleic acid↑)	[64,74,79–82]
	Cotton (oleic acid↑; oleic acid + stearic acid↑)	[25,83]
	Linseed (+ω-3 and −6 fatty acids)	[84]
	Maize (oil↑)	[34]
	Oil Palm (oleic acid↑ or stearic acid↑; oleic acid↑ + palmitic acid↓)	[85,86]
	Rice (α-linolenic acid↑)	[87]
	Soybean (oleic acid↑; γ-linolenic acid↑)	[18,88]
	Safflower (γ-linoleic acid GLA↑)	[89]
Carbohydrates		
Fructans	Chicory, (fructan↑; fructan modification)	[90–92]
	Maize (fructan↑)	[93]
	Potato (fructan↑)	[94]
	Sugar beet (fructan↑)	[91]
Frustose, raffinose, Stachyose	Soybean	[95]
Inulin	Potato (inulin↑)	[36]
Starch	Rice (amylase ↑)	[96,97]
Micronutrients and functional metabolites		
Vitamins and carotenoids	Canola (vitamin E↑)	[98]
	Maize (vitamin E↑; vitamin C↑)	[99–101]
	Mustard (+β-carotene)	[102]
	Potato (β-carotene and lutein↑)	[103]
	Rice (+β-carotene)	[104]
	Strawberry (vitamin C↑)	[105]
	Tomato (folate↑; phytoene and β-carotene↑; lycopene↑; provitamin A↑)	[14,53,106–109]
Functional secondary metabolites	Apple (+stilbenes)	[110]
	Alfalfa (+resveratrol)	[111]
	Kiwi (+resveratrol)	[112]
	Maize (flavonoids↑)	[113]
	Potato (anthocyanin and alkaloid glycoside↓; solanin↓)	[114]
	Rice (flavonoids↑; +resveratrol)	[98,115]
	Soybean (flavonoids↑)	[116]
	Tomato (+resveratrol; chlorogenic acid↑; flavonoids↑; stilbene↑anthocynanins↑)	[17,109,117–119]
	Wheat (caffeic and ferulic acids↑; +resveratrol)	[120,121]
Mineral availabilities	Alfalfa (phytase↑)	[122]
	Lettuce (iron↑)	[49]
	Rice (iron↑)	[123]
	Maize (phytase↑, ferritin↑)	[48,56]
	Soybean (phytase↑)	[124]
	Wheat (phytase↑)	[125]

[a] Excludes protein/starch functionality, shelf life, taste/aesthetics, fiber quality and allergen reduction traits. Modified from Refs. [15,126].

degradation of undesirable compounds. It involves the redirection of cellular activities by the modification of the enzymatic, transport, and/or regulatory functions of the cell. Significant progress has been made in recent years in the molecular dissection of many plant pathways and in the use of cloned genes to engineer plant metabolism.

Although progress in dissecting metabolic pathways and our ability to manipulate gene expression in genetically modified

TABLE 2

Examples of plant components with suggested functionality[a].

Class/components	Source[b]	Potential health benefit
Carotenoids		
Alpha-carotene	Carrots	Neutralizes free radicals that may cause damage to cells.
Beta carotene	Various fruits, vegetables	Neutralizes free radicals.
Lutein	Green vegetables	Contributes to maintenance of healthy vision.
Lycopene	Tomatoes and tomato products (ketchup, sauces)	May reduce risk of prostate cancer.
Zeaxanthin	Eggs, citrus, maize	Contributes to maintenance of healthy vision.
Dietary fiber		
Insoluble fiber	Wheat bran	May reduce risk of breast and/or colon cancer.
Beta glucan[c]	Oats	May reduce risk of cardiovascular disease (CVD).
Soluble fiber[c]	Psyllium	May reduce risk of CVD.
Whole Grains[c]	Cereal grains	May reduce risk of CVD.
Collagen Hydrolysate	Gelatin	May help improve some symptoms associated with osteoarthritis.
Fatty acids		
Omega-3 fatty acids – DHA/EPA	Tuna; fish and marine oils	May reduce risk of CVD and improve mental, visual functions.
Conjugated linoleic acid (CLA)	Cheese, meat products	May improve body composition, may decrease risk of certain cancers.
Gamma linolenic acid	Borage, evening primrose	May reduce inflammation risk of cancer, CVD disease and improve body composition.
Flavonoids		
Anthocyanidins: cyanidin	Berries	Neutralize free radicals, may reduce risk of cancer.
Hydroxycinnamates	Wheat	Antioxidant-like activities may reduce risk of degenerative diseases.
Flavanols: catechins, tannins	Tea (green, catechins), (black, tannins)	Neutralize free radicals, may reduce risk of cancer.
Flavanones	Citrus	Neutralize free radicals, may reduce risk of cancer.
Flavones: quercetin	Fruits/vegetables	Neutralize free radicals, may reduce risk of cancer.
Glucosinolates, indoles, isothiocyanates		
Sulphoraphane	Cruciferous vegetables (broccoli, kale), horseradish	Neutralizes free radicals, may reduce risk of cancer.
Phenolics		
Stilbenes – resveratrol	Grapes	May reduce risk of degenerative diseases; heart disease; cancer. May have longevity effect.
Caffeic acid, ferulic acid	Fruits, vegetables, citrus	Antioxidant-like activities; may reduce risk of degenerative diseases; heart disease, eye disease.
Epicatechin	Cacao	Antioxidant-like activities; may reduce risk of degenerative diseases; heart disease
Plant stanols/sterols		
Stanol/sterol ester[c]	Maize, soy, wheat, wood oils	May reduce risk of coronary heart disease (CHD) by lowering blood cholesterol levels.
Prebiotic/probiotics		
Fructans, inulins, fructo-oligosaccharides (FOS)	Jerusalem artichokes, shallots, onion powder	May improve gastrointestinal health.
Lactobacillus	Yogurt, other dairy	May improve gastrointestinal health.
Saponins	Soybeans, soy foods, soy protein-containing foods	May lower LDL cholesterol; contains anticancer enzymes.
Soybean protein	Soybeans and soy-based foods	25 g/day may reduce risk of heat disease.
Phytoestrogens		
Isoflavones – daidzein, genistein	Soybeans and soy-based foods	May reduce menopause symptoms, such as hot flashes, reduce osteoporosis, CVD.
Lignans	Flax, rye, vegetables	May protect against heart disease and some cancers; may lower LDL cholesterol, total cholesterol, and triglycerides.
Sulfides/thiols		
Diallyl sulfide	Onions, garlic, olives, leeks, scallions	May lower LDL cholesterol, helps to maintain healthy immune system.
Allyl methyl trisulfide, dithiolthiones	Cruciferous vegetables	May lower LDL cholesterol, helps to maintain healthy immune system.
Tannins		
Proanthocyanidins	Cranberries, cranberry products, cocoa, chocolate, black tea	May improve urinary tract health.
		May reduce risk of CVD, and high blood pressure

Modified from Ref. [127].

[a] Examples are not an all-inclusive list.

[b] U.S. Food and Drug Administration approved health claim established for component.

(GM) plants has progressed apace, attempts to use these tools to engineer plant metabolism have not quite kept pace. Since the success of this approach hinges on the ability to change host metabolism, its continued development will depend critically on a far more sophisticated knowledge of plant metabolism, especially the nuances of interconnected cellular networks, than currently exists. This complex interconnectivity is regularly demonstrated. Relatively minor genomic changes (point mutations and single-gene insertions) are regularly observed following metabolomic analysis, to lead to significant changes in biochemical composition [7–10] used a genetic modification approach to study the mechanism of light influence on antioxidant content (anthocyanin and lycopene) in the tomato cultivar Moneymaker. However, other, what on the surface would appear to be more significant genetic changes, unexpectedly yield little phenotypical effect [11].

Likewise, unexpected outcomes are often observed, for example significant modifications made to primary Calvin cycle enzymes (fructose-1, 6-bisphosphatase and phosphoribulokinase) have little effect while modifications to minor enzymes (e.g., aldase which catalyzes a reversible reaction) seemingly irrelevant to pathway flux, have major effects [12,13]. These observations demonstrate that caution must be exercised when extrapolating individual enzyme kinetics to the control of flux in complex metabolic pathways. With evolving ''omics'' tools, a better understanding of global effects of metabolic engineering on metabolites, enzyme activities, and fluxes is beginning to be developed. Attempts to modify storage proteins or secondary metabolic pathways have also been more successful than have alterations of primary and intermediary metabolism [14]. While offering many opportunities, this plasticity in metabolism complicates potential routes to the design of new, improved crop varieties. Regulatory oversight of engineered products has been designed to detect such unexpected outcomes in biotech crops and, as demonstrated by Chassy *et al.* [15] existing analytical and regulatory systems are adequate to address novel metabolic modifications in nutritionally improved crops.

Several new approaches are being developed to counter some of the complex problems in metabolic engineering of pathways. Such approaches include use of RNA interference to modulate endogenous gene expression or the manipulation of transcription factors (TFs) that control networks of metabolism [16–18]. For example expression in tomato of two selected transcription factors (TFs) involved in anthocyanin production in snapdragon (*Antirrhinum majus* L.) led to high levels of these flavonoids throughout the fruit tissues, which, as a consequence, were purple. They also stimulated genes involved in the side-chain modification of the anthocyanin pigments and genes possibly related to the final transport of these molecules into the vacuole processes that are both necessary for the accumulation of anthocyanin [17]. Such expression experiments hold promise as an effective tool for the determination of transcriptional regulatory networks for important biochemical pathways. Gene expression can be modulated by numerous transcriptional and post-transcriptional processes. Correctly choreographing the many variables is the factor that makes metabolic engineering in plants so challenging.

In addition there are several new technologies that can overcome the limitation of single-gene transfers and facilitate the concomitant transfer of multiple components of metabolic pathways. One example is multiple-transgene direct DNA transfer, which simultaneously introduces all the components required for the expression of complex recombinant macromolecules into the plant genome as demonstrated by a number including [19] who successfully delivered four transgenes that represent the components of a secretory antibody into rice [20], constructed a minichromosome vector that remains autonomous from the plant's chromosomes and stably replicates when introduced into maize cells. This work makes it possible to design minichromosomes that carry cassettes of genes, enhancing the ability to engineer plant processes such as the production of complex biochemicals. It was demonstrated [21] that gene transfer using minimal cassettes is an efficient and rapid method for the production of transgenic plants stably expressing several different transgenes. Since no vector backbones are required, this prevents the integration of potentially recombinogenic sequences insuring stability across generations. They used combinatorial direct DNA transformation to introduce multi-complex metabolic pathways coding for beta carotene, vitamin C and folate. They achieved this by transferring five constructs controlled by different endosperm-specific promoters into white maize. Different enzyme combinations show distinct metabolic phenotypes resulting in 169-fold beta carotene increase, six times the amount of vitamin C, and doubling folate production effectively creating a multivitamin maize cultivar [22]. This system has an added advantage from a commercial perspective in that these methods circumvent problems with traditional approaches which not only limit the amount of sequences transferred, but may disrupt native genes or lead to poor expression of the transgene, thus reducing both the numbers of transgenic plants which must be screened and the subsequent breeding and introgression steps required to select a suitable commercial candidate.

As demonstrated ''omics''-based strategies for gene and metabolite discovery, coupled with high-throughput transformation processes and automated analytical and functionality assays, have accelerated the identification of product candidates. Identifying rate-limiting steps in synthesis could provide targets for modifying pathways for novel or customized traits. Targeted expression will be used to channel metabolic flow into new pathways, while gene-silencing tools will reduce or eliminate undesirable compounds or traits, or switch off genes to increase desirable products [23–25]. In addition, molecular marker-based breeding strategies have already been used to accelerate the process of introgressing trait genes into high-yielding germplasm for commercialization. Table 1 summaries the work done to date on specific applications in the categories listed above. The following sections briefly review some examples under those categories.

Macronutrients: protein

The FAO estimates that 850 million people worldwide suffer from undernutrition, of which insufficient protein in the diet is a significant contributing factor [26]. Protein-energy malnutrition (PEM) is the most lethal form of malnutrition and affects every fourth child worldwide [27]. Most plants have a poor balance of essential amino acids relative to the needs of animals and humans. The cereals (maize, wheat, rice etc.) tend to be low in lysine, whereas legumes (soybean, peas) are often deficient in the

sulfur-rich amino acids, methionine and cysteine. Successful examples of improving amino acid balance to date include high-lysine maize [28,29] canola and soybeans [30]. Free lysine is significantly increased in high-lysine maize by the introduction of the dapA gene (cordapA) from *Corynebacterium glutamicum* that encodes a form of dihydrodipicolinate synthase (cDHDPS) that is insensitive to lysine feedback inhibition. Consumption of foods made from these crops potentially can help to prevent malnutrition in developing countries, especially among children.

Another method of modifying storage protein composition is to introduce heterologous or homologous genes that code for proteins containing elevated levels of the desired amino acid such as sulfur containing (methionine and cysteine) or lysine. An interesting solution to this to create a completely artificial protein containing the optimum number of the essential amino acids methionine, threonine, lysine, and leucine in a stable, helical conformation designed to resist proteases to prevent degradation. This was achieved by several investigators, including sweet potato modified with an artificial storage protein (ASP-1) gene [31]. These transgenic plants exhibited a two- and fivefold increase in the total protein content in leaves and roots, respectively, over that of control plants. A significant increase in the level of essential amino acids such as methionine, threonine, tryptophan, isoleucine, and lysine was also observed [15,31]. A key issue is to ensure that the total amount and composition of storage proteins is not altered to the detriment of the development of the crop plant when attempting to improve amino acid ratios [32].

Some novel indirect approaches have also been taken to improve protein content. An ancestral wheat allele that encodes a transcription factor (NAM-B1) was ''rescued'' [33], that accelerates senescence and increases nutrient remobilization from leaves to developing grains (modern wheat varieties carry a nonfunctional allele). Reduction in RNA levels of the multiple NAM homologs by RNA interference delayed senescence by more than three weeks and reduced wheat grain protein, zinc, and iron content by more than 30%. Yet another approach to indirectly increase protein and oil content has been used [34]. They used a bacterial cytokinin-synthesizing isopentenyl transferase (IPT) enzyme, under the control of a self-limiting senescence-inducible promoter, to block the loss of the lower floret resulting in the production of just one kernel composed of a fused endosperm with two viable embryos. The presence of two embryos in a normal-sized kernel leads to displacement of endosperm growth, resulting in kernels with an increased ratio of embryo to endosperm content. The end result is maize with more protein and oil and less carbohydrate [15].

Macronutrients: fiber and carbohydrates

Fiber is a group of substances chemically similar to carbohydrates that nonruminant animals including humans poorly metabolize for energy or other nutritional uses. Fiber provides bulk in the diet such that foods rich in fiber offer satiety without contributing significant calories. Current controversies aside, there is ample scientific evidence to show that prolonged intake of dietary fiber has various positive health benefits, especially the potential for reduced risk of colon and other types of cancer.

When colonic bacteria (especially *Bifidobacteria*) ferment dietary fiber or other unabsorbed carbohydrates, the products are short-chain saturated fatty acids. These may enhance absorption of minerals such as iron, calcium, and zinc, induce apoptosis preventing colon cancer and inhibit 3-hydroxy-3-methylglutaryl coenzyme-A reductase (HMG-CoAR) thus lowering low density lipoprotein (LDL) production [35]. Plants are effective at making both polymeric carbohydrates (e.g., starches and fructans), and individual sugars (e.g., sucrose and fructose). The biosynthesis of these compounds is sufficiently understood to allow the bioengineering of their properties and to engineer crops to produce polysaccharides not normally present. Polymeric carbohydrates such as fructans have been produced in sugar beet and inulins and amylase (resistant starch) in potato [36] without adverse affects on growth or phenotype. A similar approach is being used to derive soybean varieties that contain some oligofructan components that selectively increase the population of beneficial species of bacteria in the intestines of humans and certain animals and inhibit growth of harmful ones [37].

Macronutrients: novel lipids

Genomics, specifically marker assisted plant breeding combined with recombinant DNA technology, provides powerful means for modifying the composition of oilseeds to improve their nutritional value and provide the functional properties required for various food oil applications. Genetic modification of oilseed crops can provide an abundant, relatively inexpensive source of dietary fatty acids with wide ranging health benefits. Production of such lipids in vegetable oil provides a convenient mechanism to deliver healthier products to consumers without the requirement for significant dietary changes. Major alterations in the proportions of individual fatty acids have been achieved in a range of oilseeds using conventional selection, induced mutation and, more recently, post-transcriptional gene silencing. Examples of such modified oils include: low- and zero-saturated fat soybean and canola oils, canola oil containing medium chain fatty acids (MCFA) whose ergogenic potential may have application in LDCs, high stearic acid canola oil (for *trans* fatty acid-free products), high-oleic acid (monounsaturated) soybean oil, and canola oil containing the polyunsaturated fatty acids (PUFA), λ-linolenic (GLA; 18:3 n-6) stearidonic acids (SDA; C18:4 n-3) very-long-chain fatty acids [38] and omega-three fatty acids [39]. These modified oils are being marketed and many countries have a regulatory system in place for the premarket safety review of novel foods produced through conventional technology.

Edible oils rich in monounsaturated fatty acids provide improved oil stability, flavor, and nutrition for human and animal consumption. High-oleic soybean oil is naturally more resistant to degradation by heat and oxidation, and so requires little or no postrefining processing (hydrogenation), depending on the intended vegetable oil application. Oleic acid (18:1), a monounsaturate, can provide more stability than the polyunsaturates, linoleic (18:2) and linolenic (18:3). Antisense inhibition of oleate desaturase expression in soybean resulted in oil that contained >80% oleic acid (23% is normal) and had a significant decrease in PUFA [18]. Dupont have introduced soybean oil composed of at least 80% oleic acid, and linolenic acid of about 3%, and over 20% less saturated fatty acids than commodity soybean oil. Monsanto's Vistive contains less than 3% linolenic acid, compared to 8% for traditional soybeans. These result in more stable soybean oil, and less need for hydrogenation.

Review

A key function of α-linolenic acid (ALA) is as a substrate for the synthesis of longer-chain ω-3 fatty acid found in fish, eicosapentaenoic acid (EPA; C20:5 n-3) and docosahexaenoic acid (DHA; C22:6 n-3) which play an important role in the regulation of inflammatory immune reactions and blood pressure, brain development *in utero*, and, in early postnatal life, the development of cognitive function. Stearidonic acid (SDA, C18:4 n-3), EPA, and DHA also possess anticancer properties [40–42]. Research indicates that the ratio of n-3 to n-6 fatty acids may be as important to health and nutrition as the absolute amounts present in the diet or in body tissues. Current Western diets tend to be relatively high in n-6 fatty acids and relatively low in n-3 fatty acids. Production of a readily available source of long-chain-PUFA, specifically ω-3 fatty acids, delivered in widely consumed prepared foods could deliver much needed ω-3 fatty acids to large sectors of the population with skewed n-6:n-3 ratios. In plants, the microsomal ω-6 desaturase-catalyzed pathway is the primary route of production of polyunsaturated lipids. Ursin *et al*. [129,130] have introduced the δ-6 desaturase gene from a fungus (*Mortierella*) succeeding in producing ω-3 in canola. In a clinical study James [128] observed that SDA was superior to ALA as a precursor by a factor of 3.6 in producing EPA, DHA and docosapentaenoic acid (DPA, C22:5 n-3). Transgenic canola oil was obtained that contains >23% SDA, with an overall n-6:n-3 ratio of 0.5.

Structural lipids also have positive health benefits for example in addition to their effect in lowering cholesterol, membrane lipid phytosterols have been found to inhibit the proliferation of cancer cells by inducing apoptosis and G1/S cell cycle arrest through the HMG-CoAR as noted above [43]. In addition to this and the above-specialty oils may also be developed with further pharmaceutical and chemical feedstock applications in mind.

Micronutrients: vitamins and minerals

Micronutrient malnutrition, the so-called hidden hunger, affects more than one-half of the world's population, especially women and preschool children in developing countries [44]. Even mild levels of micronutrient malnutrition may damage cognitive development and lower disease resistance in children, and increase incidences of childbirth mortality. The costs of these deficiencies, in terms of diminished quality of life and lives lost, are large [45]. The clinical and epidemiological evidence is clear that select minerals (iron, calcium, selenium, and iodine) and a limited number of vitamins (folate, vitamins E, B6, and A) play a significant role in maintenance of optimal health and are limiting in diets.

As with macronutrients, one way to ensure an adequate dietary intake of nutritionally beneficial phytochemicals is to adjust their levels in plant foods. Using various approaches including genomics, Vitamin E levels are being increased in several crops, including soybean, maize and canola, while rice varieties are being developed with the enhanced vitamin A precursor, β-carotene, to address vitamin A deficiency that leads to macular degeneration and impacts development. A similar method was used by Monsanto to produce β-carotene in canola and by Fauquet *et al*. [46,47] in cassava. The latter is being field tested in Nigeria. Ameliorating another major deficiency in LDCs, namely minerals such as iron and zinc, has also been addressed. Iron is the most commonly deficient micronutrient in the human diet, and iron deficiency affects an estimated 1–2 billion people. Anemia, characterized by low hemoglobin, is the most widely recognized symptom of iron deficiency, but there are other serious problems such as impaired learning ability in children, increased susceptibility to infection, and reduced work capacity. Endosperm-specific co-expression of recombinant soybean ferritin and *Aspergillus* phytase in maize has been demonstrated [48] which resulted in significant increases in the levels of bioavailable iron. A similar end was achieved with lettuce [49].

A rather interesting approach was taken by [50] to increase the levels of calcium in crop plants, by using a modified calcium/proton antiporter (known as short cation exchanger 1 (sCAX1) to increase Ca transport into vacuoles. They also demonstrated that consumption of such Ca-fortified carrots results in enhanced Ca absorption. This demonstrates the potential of increasing plant nutrient content through expression of a high-capacity transporter and illustrates the importance of demonstrating that the fortified nutrient is bioavailable. Other targets include folate-enriched tomatoes and isoflavonoids [14,51].

Micronutrients: phytochemicals

Unlike for vitamins and minerals, the primary evidence for the health-promoting roles of phytochemicals comes from epidemiological studies, and the exact chemical identity of many active compounds has yet to be determined. However, for select groups of phytochemicals, such as nonprovitamin A carotenoids, glucosinolates, and phytoestrogens, the active compound or compounds have been identified and rigorously studied. Epidemiologic studies have suggested a potential benefit of the carotenoid lycopene in reducing the risk of prostate cancer, particularly the more lethal forms of this cancer. Five studies support a 30–40% reduction in risk associated with high tomato or lycopene consumption in the processed form in conjunction with lipid consumption, although other studies with raw tomatoes were not conclusive [52]. In a study by [53] to modify polyamines to retard tomato ripening, an unanticipated enrichment in lycopene was found, with levels up by 2- to 3.5-fold compared to conventional tomatoes. This is a substantial enrichment, exceeding that so far achieved by conventional means. This approach may work in other fruits and vegetables. Likewise, as noted, [17] used snapdragon transcription factors to achieve high levels of the reactive oxygen scavengers, anthocyanins expression in tomatoes.

Other phytochemicals of interest include related polyphenolics such as resveratrol which has been demonstrated to inhibit platelet aggregation and eicosanoid synthesis in addition to protecting the sirtuins, genes implicated in DNA modification and life extension; flavonoids, such as tomatoes expressing chalcone isomerase that show increased contents of the flavanols rutin and kaempferol glycoside; glucosinolates and their related products such as indole-3 carbinol (I3C); catechin and catechol; isoflavones, such as genistein and daidzein; anthocyanins; and some phytoalexins (Table 1). A comprehensive list of phytochemicals is outlined in Table 2. To reiterate, although there is a growing knowledge base indicating that elevated intake of specific phytochemicals may reduce the risk of diseases, such as certain cancers, cardiovascular diseases, and chronic degenerative diseases associated with aging, further research and epidemiological studies are still required to prove definitive relationships.

Antinutrients, allergens, and toxins

Plants produce many defense strategies to protect themselves from predators. Many, such as resveratrol and glucosinate, which are primarily pathogen protective chemicals, also have demonstrated beneficial effects for human and animal health. Many, however, have the opposite effect. For example, phytate, a plant phosphate storage compound, is considered an antinutrient as it strongly chelates iron, calcium, zinc and other divalent mineral ions, making them unavailable for uptake. Nonruminant animals generally lack the phytase enzyme needed for digestion of phytate. Poultry and swine producers add processed phosphate to their feed rations to counter this. Excess phosphate is excreted into the environment resulting in water pollution. When low-phytate soybean meal is utilized along with low-phytate maize for animal feeds the phosphate excretion in swine and poultry manure is halved. Several groups have added heat- and acid-stable phytase from *Aspergillus fumigatus* inter alia to make the phosphate and liberated ions bioavailable in several crops [54]. To promote the reabsorption of iron, a gene for a metallothionein-like protein has also been engineered. Low-phytate maize was commercialized in the USA in 1999 [55]. In November 2009, the Chinese company Origin Agritech announced the final approval of the world's first genetically modified phytase expressing maize [56]. Research indicates that the protein in low-phytate soybeans is also slightly more digestible than the protein in traditional soybeans. In a poultry feeding trial, better results were obtained using transgenic plant material than with the commercially produced phytase supplement [57]. Poultry grew well on the engineered alfalfa diet without any inorganic phosphorus supplement, which shows that plants can be tailored to increase the bioavailability of this essential mineral.

Other antinutrients that are being examined as possible targets for reduction are trypsin inhibitors, lectins, and several heat-stable components found in soybeans and other crops. Likewise strategies are being implied to reduce or limit food allergens (albumins, globulins, etc.), malabsorption and food intolerances (gluten) and toxins (glycoalkaloids, cyanogenic glucosides, and phytohemagglutinins) in crop plants and aesthetics undesirables such as caffeine [58]. Examples include changing the levels of expression of the thioredoxin gene to reduce the intolerance effects of wheat and other cereals [59]. Using RNAi to silence the major allergen in soybeans (P34 a member of the papain superfamily of cysteine proteases) and rice (14–16 kDa allergenic proteins). Blood serum tests indicate that p34-specific IgE antibodies could not be detected after consumption of gene-silenced beans [24,60].

Biotechnology approaches can be employed to down-regulate or even eliminate the genes involved in the metabolic pathways for the production, accumulation, and/or activation of these toxins in plants. For example, the solanine content of potato has already been reduced substantially using an antisense approach, and efforts are underway to reduce the level of the other major potato glycoalkaloid, chaconine [61]. Work has also been done to reduce cyanogenic glycosides in cassava through expression of the cassava enzyme hydroxynitrile lyase in the roots [62]. When ''disarming'' plants natural defenses in this way one must be aware of potentially increased susceptibility to pests, diseases and other stressors, so the recipient germplasm should have input traits to counter this.

The future of crop biotechnology

Research to improve the nutritional quality of plants has historically been limited by a lack of basic knowledge of plant metabolism and the almost insurmountable challenge of resolving intersecting networks of thousands of metabolic pathways. With the tools now available through the field of genomics, proteomics, metabolmics and bioinformatics, we have the potential to fish *in silico* for genes of value across species, phyla and kingdoms and subsequently to simultaneously study the expression and interaction of transgenes on tens of thousands of endogenous genes. With these newly evolving tools, we are beginning to dissect the global effects of metabolic engineering on metabolites, enzyme activities and fluxes. For essential macro- and micronutrients that are limiting in various regional diets, the strategies for improvement are clear and the concerns such as pleiotropic effects and safe upper limits are easily addressed. However, for many putative health-promoting phytochemicals, clear links with health benefits are yet to be demonstrated. Such links, if established, will make it possible to identify the precise compound or compounds to target and which crops to modify to achieve the greatest nutritional impact and health benefit. With rapidly emerging technologies, the increase in our understanding of and ability to manipulate plant metabolism during the coming decades should place plant researchers in the position of being able to modify the nutritional content of major and minor crops to improve many aspects of human and animal health and wellbeing.

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Knowledge and technologies for sustainable intensification of food production

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Knowledge and technologies will always continue to be developed, as they have always, to bring new efficiencies to plant breeding and crop production, which suffer from many constraints and inefficiencies. These constraints need to be overcome throughout the world to help increase the rate of improvements in food production and intensify production on less land. The recent discoveries and technical innovations that are revealing the full complement of genes in crops, the ability to define genetic variation and use DNA markers to follow chromosome segments with known functions through breeding programmes are leading to new efficiencies in breeding. The ability to isolate and redesign genes and transfer them into different plants also offers the breeder solutions to several key limitations. These benefits are described together with some of the current issues associated with the use of transgenes. Generation after generation can look forward to new knowledge and technologies, many of which we cannot know at present, and thus there is no reason to be despondent about meeting future goals, if the right decisions and investments are made globally and locally. These decisions include putting optimal use of land at the top of the world agenda to sustain both the planet and an adequate quality of life for mankind. As always has been the case, more investments are urgently required into the dissemination of successful technologies in crop breeding and production, into teaching and training as well as into innovative research. Failure to invest adequately in innovative technologies will leave future decision-makers and citizens with fewer options and greatly enhance the risks for mankind and a healthy planet.

Contents

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Introduction

It is understandable that citizens who have not had the chance to gain knowledge and insight into the frontiers of genetic technologies should be wary of the innovative technologies being built to improve food production. But we must learn from history, the ancestral farmers and entrepreneurs who have brought us the food we enjoy. Without their genetic innovations we would not have corn, wheat or almost any of the foods we enjoy and that keep alive a global population. The world would be in a hopeless position. Mankind would still be in the dark ages. To bring about a better world where people have enough healthy food to eat and our planet is sustainable, we need wise decision-making and new technologies to make food production more efficient. We also need to transfer the best of existing technologies to food production worldwide.

Progress often depends on new technologies and it has always been so in the breeding of crops and in their production by farmers. It takes some 10 years to breed, test and commercialise a new variety starting with two parent plants. Ten years ago plant genetics and genomics were in their infancy compared with now. Also we had no Google, no Facebook, no You Tube, no blogs nor twitters. Farmers in poorest Africa were not in touch with the outside world. Today we are in a new enlightenment in plant genetics and breeding and have all these personalised communication systems that empower the individual, decentralise societies and bring people together with knowledge, systems and choices as never before. In consequence, the African farmer is in touch with the outside world via the cellphone and small villages in India have a computer and the World Wide Web. Where will societies be in 10, 20, 30, 40 and 60 years in the poorer parts of the world? What will the farmers and citizens be achieving and demanding, having become connected to global communication systems, knowledge and new markets. What will be the standards in plant breeding and farming? Not as today, that is certain. Many of today's technologies will be seen as old fashioned, hopelessly short of what is possible and required. Plant breeding and farming need to change radically in many parts of the world and will do so, driven by new knowledge and innovations in technology.

The idea that technology will stand still over the coming decades is obviously nonsense. Many thoughts today may seem fanciful, including some mentioned in this paper, but then so to people in Europe and USA in the early years of the 20th century would have been civil aviation, space exploration, organ transplants, nuclear power, computers, the Internet, nanotechnology and mobile phones. While plant breeding and solving the food and energy crop production issues may seem daunting to the average citizen, science will evolve beyond ways we understand today, to provide new options. Placing today's needs in the context of what has been overcome in the past, the opportunities of technology development and where we seek to be in the future can legitimately generate optimism, providing wise decision-making and appropriate investments are sustained. When wise decisions are not made, then technical developments have to be even more successful to meet the needs. Planners and opinion formers need to have all this at the heart of their decision-making. This paper seeks to draw attention to the new knowledge and technologies that are available and will become available to increase food production sustainably and more intensively so that all are fed and land is available for sustaining the planet and quality of life. It is recognised that hunger is most often a consequence of poverty, absence of markets, inadequate land reform and poor education systems. However, sound agriculture is a source of wealth for many rural people and societies in general. This justifies the focus of this paper on the knowledge and technologies associated with agriculture as one of the sources of relief from hunger. The paper is not designed to be in any sense a technical handbook for practitioners. Other treatises fulfil this need [1–3].

The issues we all face

There are many examples of successful increases in food production over the past 40 years, especially in Asia [4]. Figure 1 illustrates the large increases in total food production in different continents [5]. This means that breeders have produced suitable varieties, farmers have heard about them, invested in them and thereby increased food production. Much of Asia's food production increases have involved the use of modern varieties [6]. Even in Africa yields have increased. This would be a very satisfying position, except that food increases have not kept pace with population increases and so the increases *per capita* shown in Figure 1B are less positive. Africa is now only just beginning to restore the *per capita* food position that it had 40 years ago. Thus in spite of all these increases and successes there are still 1 billion people suffering from poverty and lack of food [4].

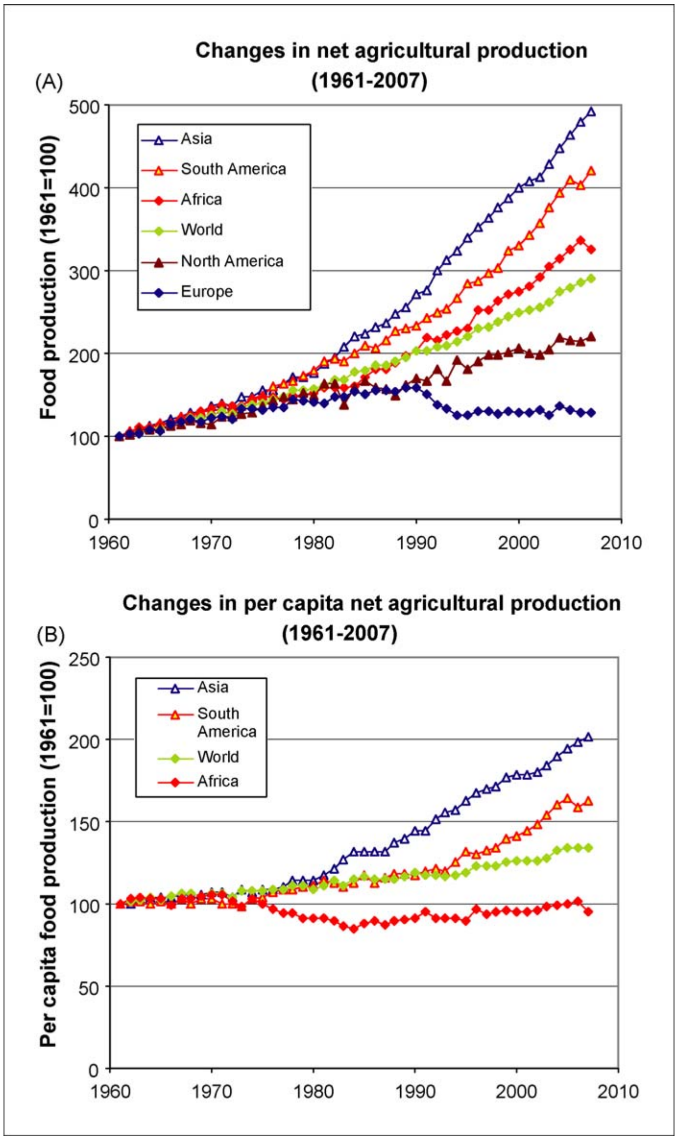

FIGURE 1

(A) Changes in net agricultural production in continents. **(B)** Changes in *per capita* net agricultural production. From Jules Pretty and Royal Society, 2009.

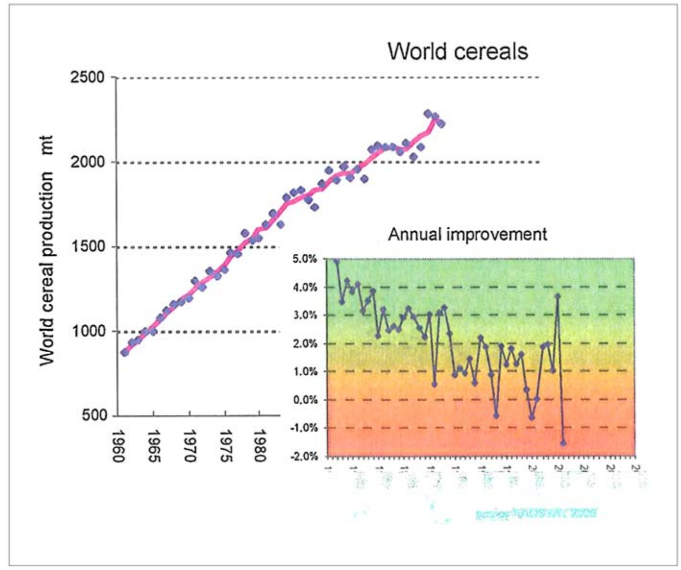

FIGURE 2

Changes in world cereal production and annual rate of improvement (FAOSTAT, 2008).

Can we sustain the good increases illustrated in Figure 1A throughout the world in all environments? If plant breeding were easy and we could simply make higher yielding crops more quickly by scaling up existing methods then the outlook would be more hopeful. However the results for world cereal production show that the *per capita* gains produced have fallen since 1985 and the rate of annual increase is declining (Figure 2). Thus plant breeders and farmers are not making gains. This is a serious position, given that we need to increase global food production by 40% in the next 20 years [4,7]. Figure 1 shows this to be an enormous challenge. Also these trends do not reveal the levels and the diversity of food needed to bring a healthy and satisfying life for all. Furthermore they do not draw attention to the amounts of land required to keep the planet and its populations sustainably healthy by the growing of biomass for biofuels, managing greenhouse gas levels, sustaining adequate biodiversity and providing essential amenities. In summary, we need to increase the rate of gain in food production and reverse the positions in Figure 2, intensify food production on less land and free up land for other needs. To do this, plant breeding and food production need to be supplied with a constant stream of new knowledge, tools and systems that will lead to more sustainable intensification of agriculture, just as what occurred with US corn production and Asian wheat and rice breeding during the Green Revolution [8]. The needs are urgent and the options for success are visible. It is recognised that many other factors are necessary, in addition to new varieties, for successful adoption of innovations [4,7]. They include numerous financial and policy factors, but discussion of these is outside the scope of the paper.

What is the technical basis of plant breeding?

Plant breeding involves the bringing together of new versions of genes to create plants with new properties. During the formation of eggs and pollen in plants, new gene assortments are created by existing chromosomes becoming recombined and then, as a consequence of the fertilisation of eggs by pollen, new combinations of genes from the two parents are brought together to form embryos and the new generation. There are from 30 000 to over 60 000 different genes in a plant species. Fortunately, there are also many different versions of each gene in a species, created by natural mutations, and it is the reassortment of these variants that is achieved in plant breeding. Following the creation of new combinations of gene variants the breeder grows large numbers of offspring and seeks plants that perform better than the parents and existing varieties. Because there are so many genes and variants of each, there is almost an infinite number of possible combinations that could be made. In addition, there are so many environments in which the plants need to be successful, the process of improving plants by plant breeding and demonstrating the improvements in farmers' fields is statistically very inefficient, time-consuming and relatively expensive [9].

When seeking progeny that are better than those already available, breeders have to optimise a large number of traits. Some of

TABLE 1

Traits that are commonly assessed directly or indirectly by breeders

• Architecture-height, number of leaves, tillers, branches, leaf angle, number of flowers and seeds, seed size, root structure, surface area.
• Optimum planting density.
• Flowering time and photoperiod responses.
• Growth rate regulation.
• Growth responses to light quality and quantity.
• Photosynthesis-rates and overall carbon fixed during the growing season.
• Heterosis.
• Fertility and seed production.
• Nitrogen use efficiency-uptake, translocation, storage, reduction and portioning between plant parts.
• Water use efficiency-uptake, storage, transpiration rates, loss, tolerance to chronic drought and bursts of drought.
• Disease, pest and virus resistances.
• Tolerance to heat shock and sustained heat.
• Tolerance to cold shock and sustained cold.
• Seed germination in cold.
• Tolerance to freezing.
• Tolerance to flooding.
• Tolerance to oxidative stress.
• Amounts of key nutrients in seeds, roots, leaves, fruits and stems.

these are listed in Table 1. Each of these traits is specified by many genes interacting in very complex circuits. Thus the reassorting of genes and gene variants in each breeding cycle affects almost every trait in every generation. This complexity also makes plant breeding inefficient. Where there are no genes for a particular desired trait in the species, the improvements dependent on such genes cannot be achieved, no matter how large the investment. Most traits in most crops are still suboptimal, especially resistance to pests and diseases. Shortcomings in managing all these traits in breeding programmes lead to inadequate products. What can be learnt from successful breeding programmes, past and present, that can be applied more widely? One of the most successful breeding programmes has been corn breeding in the USA [10–12]. I will use this example to make many key points in relation to knowledge and technology development for crop improvement. Other examples from rice [13] and wheat [14] could also have been chosen but even these examples do not display some of the key innovations in US corn improvement.

The sustainable intensification of US corn production

The extensive gains in yield per acre made over the past 60 years by corn breeders and farmers in the USA are well known [10–12] and are illustrated in Figure 3. What have been the innovations behind this progress? One of the most extraordinary series of innovations took place centuries earlier by the Indian enterpreneurs of Central America. They transformed an ancestral perennial species into what we now know as corn. The plants look very different and the genetic changes selected by the Indians are becoming understood from comparisons of all the genes in the ancestor and modern corn. In the US, yields stayed the same until after the 1940s (Figure 3), when innovative crosses and genetic understanding had been developed. It was discovered that if certain plants were crossed, the F1 hybrids were much more vigorous than the parents. This so-called heterosis has been the basis of many yield gains since [15]. While the plant breeders were making better and better heterotic hybrids, the use of fertilisers and herbicides helped the farmers get higher yields. The makers of farm machinery also helped by making a succession of improved machines to increase the efficiency and scale of agricultural production. In the late 1990s knowledge of how to measure genetic variation in DNA sequences at scale (see below) became

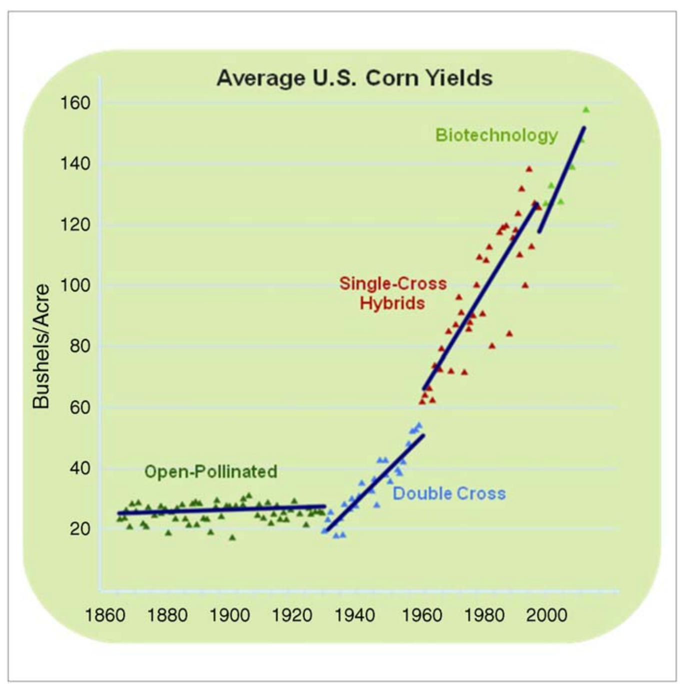

FIGURE 3

Increases in corn yields in US. The periods when open pollination and when the use of double and single cross hybrids were introduced are shown. The introduction of transgenic hybrids occurred towards the end of the 1990s when biotechnology started to make its impact.

available and this led to the commercial adoption of marker-assisted breeding. Genetic engineering emerged during the 1980s and genes were selected, purified, redesigned and then introduced into corn plants (see later) that conferred tolerance to herbicide (Roundup) and resistance to feeding insect larvae (corn stem borers). Elite transgenic lines were commercialised to be among the first transgenic row crops [16]. More recently, genes conferring resistance to root worm have been added. Today's corn lines have up to nine transgenes in them [16]. The herbicide tolerance and insect tolerance genes brought environmental benefits, because Roundup is more benign to the environment than herbicides used previously and because of the reduced use of insecticide sprays. It has also been found that protecting corn from root damage brings some drought tolerance too.

The increases in yields in Figure 3 are the results of sustained investment by government and the private sector combined with government subsidies and incentives. All these working in combination enabled and stimulated the stream of technical improvements behind breeding and the growth in production intensity. Yet over the past 15 years the farmers have applied less nitrogen, phosphate, herbicide and insecticide per bushel and adopted no-till practices to conserve water, soil structure and reduce erosion [17]. Thus, the farmers have addressed the issues of sustainability during the latter years of intensification, even while output gains have continued.

This example of the intensification of corn in the USA points the way ahead for all other crops and breeding programmes because it has both driven innovations and adopted new tools from nature, breeders and farmers as they have been developed. It has not been without its difficulties. For example, hybrids made using cytoplasmic male sterility in the late 1960s and early 1970s were susceptible to a fungus [18], but difficulties and setbacks must be expected en route to success. If all this knowledge and new technologies were incorporated into all the other breeding programmes worldwide then yield gains would be very substantial. This is emphasised by the comparative yield figures for corn in different countries shown in Figure 4. While many local features including soil and climate prevent the best yield figures being achieved everywhere, the large discrepancies revealed in Figure 4 are due to lack of sustained investments equivalent to those made in the US.

Corn Yield Trends (Bushel Per Acre)

	1990	2000	2005
World Average	59	70	75
USA	113	137	149
Argentina	60	93	109
China	74	78	80
Brazil	33	47	54
India	23	29	31
Sub-Saharan Africa	22	24	25

FIGURE 4

Comparisons of average corn yields between countries since 1990.(Monsanto/Doane Forecast).

Comparisons of the toolkits of nature, the breeders of the past and the breeders of today and tomorrow

Progress in evolution by natural selection depends on genetic variation. This variation has its origins in genetic mistakes that survive in individuals and are inherited. They are then either selected during evolution, carried along as neutral mutations and spread in populations by accident or spread because of being linked to other favourable mutations under selection. The naturally occurring mistakes include chromosome duplications, gene loss, gene duplication, mutations in genes that change the protein or RNA products or change gene activity during plant development, and the movement of specialised gene elements, so-called transposable elements, that occur in large numbers in plant genomes and move around the genome. Such mutations become mixed in populations by sexual recombination. Occasionally, but importantly, evolution involves the rare hybridisation between different but related species to form a new hybrid. Thus the toolkit of nature is confined to the natural variation accumulated in populations during evolution and the rare hybridisation between distant individuals.

Plant breeders use this variation and recombine it as noted above, also using the processes of sexual recombination. Thus breeders use nature's toolkits, albeit augmented by other technologies. Occasionally breeders are able to force interspecies recombinations that do not occur or are inviable in nature and then select stable progeny that carry genes from both species. Breeders try this approach to introduce or improve a trait that is needed. A problem for breeders is that when seeking to add better versions of genes by making crosses between dissimilar parents that carry useful genes, they also have to import large numbers of deleterious genes. This makes improving plants in specific ways difficult, time-consuming and inefficient.

These toolkits can be contrasted with those devised by the molecular biologist. The innovations from molecular biology provide the means of isolating and defining any gene from any organism, creating any kind of mutation in any gene and designing and making new genes. The novel genes can then be inserted into any plant. Thus, with these tools and techniques, the modern breeder can overcome the serious limitations of (1) only having the mutations found in nature to solve food production and quality problems, (2) not being able to move defined genes between species to add specific traits and avoid the introduction of other deleterious traits, (3) not being able to modify varieties one step at a time and (4) not being able to track favourable and deleterious genes through breeding programmes. All of these innovations have emerged over the past 30 years. The first transgenic plants were created and bred around 1982 [19]. The technologies developed by molecular biologists when integrated into plant breeding programmes change dramatically our abilities to improve plants for agriculture. This fact should not be underestimated, but rather be the reason to make new investments and train new breeders to meet the needs of societies, especially those with poverty and hunger. The technologies bring new optimism.

Advances in gene and genome discoveries and their applications to breeding

Genome and gene sequencing

In 2000, the complete genome sequence of Arabidopsis, the first plant genome to be sequenced, was announced following a large international effort [20]. The rice genome sequence was also announced in 2002 [21,22]. Since then several plant genomes have been essentially completely sequenced, including those of corn, soybean and sorghum [23–25]. While thousands of genes were identified from the first genome sequence, their function was not understood. Also many important genes were missed in the initial interpretation of the genome sequences. Thus in 2003, there were about 5000 genes defined (by sequence and a function) in plants. In 2008, the number had grown to 200 000 and was increasing exponentially. Similarly the number of gene products (proteins) recognised was a few thousand in 1998 but is now over 1 000 000. This rapid growth in knowledge happened because of technical innovations in DNA sequencing methods and cost reductions, as a number of radically new sequencing technologies have come into commerce [26,27]. These created dramatic increases in output of DNA sequence per machine and slashed costs by miniaturising the processes and performing millions of reactions in parallel. In the year 2000, about 10 bases could be identified per dollar. In 2005, it grew to about 40 bases per dollar and in 2015 it might be 1 000 000. There is a race to deliver 'a complete (human) genome sequence for $1000'. Six or seven companies appear today to be firmly in the race. Competition in this race to capture the global market of being able to read the DNA sequence of a person at prices that individuals and healthcare systems can afford is likely to become increasingly intense. So, within the next few years, the $1000 human genome sequence will become a reality. For a plant breeder to be able to sequence the genome of a large number of potential parents and selected plants, to know the variation within them and to check his product is an extraordinary concept but is clearly almost with us [27]. It is worth noting that this innovation, perhaps the one with the largest impact for increasing commercial crop production, has come from the private sector entrepreneurs and investors in the medical and IT industries, that are not concerned with agriculture and plant science.

Cataloguing and mapping genetic variation in chromosomes using DNA markers

Plant improvement is based on, and necessarily exploits, genetic variation. Thus, being able to characterise the variation in every gene in the plants of a breeding nursery can bring powerful knowledge to the breeder, as noted above. Recombination in gamete formation in egg and pollen cells occurs only a few times per chromosome in any one generation. This results in blocks of genes being inherited together. Thus to follow which chromosome segments, and therefore constituent genes, are in a progeny plant requires only a marker for each of the chromosome regions that are inherited intact and not divided by recombination. Plant breeding is therefore greatly aided by having DNA markers for each version of the chromosome segment (haplotype) introduced via the different parents [28–30].

Finding markers today is easily achieved using the genome sequencing described above. Using these methods, the variant DNA sequences that allow the chromosomal segments to be distinguished are discovered. High throughput assays are then designed for this subset of markers. The commercial technologies for doing all this are advancing rapidly—millions of data points can be gathered in a day [28]. They are evolving in synchrony with the DNA sequencing technologies. Technical advances will arise year-on-year over the next 10 years. Therefore the goal to provide breeders with haplotype maps of essentially all the germplasm of a crop, easily accessible in databases, with full details of all the plant accessions possessing each of these haplotypes, is within reach. This too will revolutionise breeding.

As with DNA sequencing described above, the generation of large datasets of marked chromosomes needs to go hand-in-hand with IT and software innovations and development of user-friendly databases to enable the benefits of all new information to be useful to the breeders. This is a major activity by world experts and is also advancing rapidly [31].

Establishing gene–trait associations

Geneticists have long sought to define the genes that influence traits on genetic maps. The genes are embedded in quantitative trait loci or QTLs. The use of polymorphic genetic markers covering all the chromosome sets allows linkage between a chromosome segment (QTL) and a trait in populations to be sought easily when the trait is segregating [32,33]. The establishment of huge datasets of mapped sequence polymorphisms means that DNA markers need no longer be limiting. What is rate-limiting is measuring the traits. The plant breeder often needs to do this in hundreds or thousands of progeny from a large number of crosses for each species to reveal tight associations. It is also desirable to do this with plants grown in multiple environments. To measure certain traits such as those affecting disease, stresses and so on, there is the need to expose the plants to the stresses. All this adds up to an enormous task that needs considerable investment.

An alternative is to achieve gene–trait associations by comparing markers and traits in a large number of accessions of a crop that are as unrelated as possible [34–37]. If sufficient recombination events have taken place during the separate evolution of the accessions then it may be possible to infer that deviations from random linkage signify a close physical relationship between marker/gene and the trait. This newer approach of 'association mapping' is being studied in corn in detail. Nevertheless, it still leaves the necessity to measure a large range of traits (Table 1) in a large number of accessions. While it is an immense volume of work to determine gene–trait associations, they will be known for all time and this will be an enduring platform for underpinning plant breeding for ever. A different version of this approach is to find markers that correlate with selection of a given trait in breeding programmes where the genetic location of the genes is ignored [38–40]. When models built upon markers that give a high selection coefficient for the traits in question are obtained, then the markers can be deployed to drive a breeding programme, for the relevant combinations of traits. These approaches, only possible by the discovery and large-scale measuring of DNA markers, are likely to have a high impact on plant breeding in the future.

Gene–trait associations have been established extensively in Arabidopsis, corn, rice and many other crop species by mutant analysis [41] and also inferred by linking gene expression patterns

with a trait. They have also been established by QTL analysis [32,33]. All this information from multiple species can be brought together to establish hypotheses for one crop species using the results from other plant species. The future value for comparative genetics is likely to be substantial, especially where the species are closely related, for example, corn and sorghum.

Many gene–trait associations have also been established by observing the effects on traits of adding known transgenes to a plant [42,43]. Complete linkage between the added, known transgene and the new trait provides direct evidence for a gene–trait association. It remains to be seen to what extent these gene–trait associations coincide with the associations derived from genetic variation in natural populations.

Gene transformation into plants

There are two principal ways genes are introduced into plants [44,45]. The first exploits the natural process of gene transfer evolved in the soil bacterium, *Agrobacterium tumefaciens*. The second is by bombardment of plant cells capable of division with particles coated with genes. In the first, genes designed and reconstructed *in vitro* and propagated in *Escherichia coli* are transferred into agrobacteria on specifically designed plasmids that contain the DNA signals that are recognised by the bacterial transfer process. When the agrobacteria are mixed with plant cells, the gene transfer process is activated and pieces of DNA containing the genes to be transferred are passed into the plant cells and become integrated into plant chromosomes. The plant cells are stimulated to divide and those containing the new genes are selected owing to the presence of genes transferred from the bacteria that provide resistance to some chemical, such as a herbicide. When many cell divisions have taken place, then the plant cells are stimulated to differentiate into shoot and roots and so new plants are formed. In such plants, each cell should carry one or a few copies of the new genes. In the second method the genes propagated in *E. coli* are forced into plant cells and internal processes lead to the incorporation of the pieces of DNA into the plant chromosomes. Thereafter the processes adopted are similar to those in the first method.

Today any plant species can be transformed with new genes in these ways but the efficiency of regeneration of a whole plant from the initially transformed cells can vary greatly, including between lines of the same species. Where the efficiencies are low, research to increase the efficiencies is usually effective. Furthermore some transgenes have been found that increase transformation/regeneration frequencies, and these are in use commercially [46].

The ability to add new genes to a species fulfils, in principle, the dreams of most plant breeders who constantly seek to add new traits more efficiently and effectively. But, much more is emerging as the technology grows from its infancy.

Advances in plant breeding emanating from the deployment of transgenes

The combinations of genetic analyses using genomics and markers will improve plant breeding immensely, but there is substantial recognition that the deployment of transgenic technologies can achieve more far-reaching and beneficial products in agriculture. Some of these advances are listed in Table 2. They are outlined here firstly to provide some details of the technologies, but secondly to illustrate steps along a path towards a radically different kind of plant improvement that we should work towards to rid the world of the food, feed and fibre shortages and ensure the availability of land to provide other services to mankind and to manage the planet optimally.

Addition of novel traits not already in the crop species or in need of improvement

The addition of new traits, such as herbicide tolerance, insect resistance, novel omega 3 fatty acids, provitamin A and hundreds

TABLE 2

Opportunities for improvements in crop plants and breeding by the use of transgenes
• Development of a new strategy for breeding and selection of improved traits using a few, known, dominant transgenes instead of many recessive QTLs for each trait.
• The ability to substitute any allele by another using homologous recombination to optimise varieties.
• The ability to change the expression pattern of any gene by changing promoters and upstream regulatory sequences using homologous recombination.
• The ability to control the rates and places of recombination in crop chromosomes to enable new gene combinations to be produced and at much greater rates and so reduce the number of progeny that need to be produced to achieve specific kinds of products; and alternatively to reduce recombination to fix desired genotypes.
• The ability to delete unwanted transgenes by specific recombination using cre-lox or flip recombinase systems.
• The ability to control major diseases by creating novel genetic systems based on, for example, non-host resistance, pathogen recognition systems and production of downstream resistance mechanisms.
• Development of sentinels and rapid assays to reveal the health of the production crop.
• The ability to add and sustain banks of specific transgenes in one locus via a novel chromosome or chromosome segment.
• The ability to fix hybrids showing heterosis using the principles of apomixis.
• The ability to switch traits using simple reagents based on particular weather patterns and needs, such as the need for a protein rich crop as opposed to a carbohydrate crop. Switching technologies based on novel promoters that can be activated by specific chemicals are already available.
• The ability to make transformation and regeneration trivial for all crops by improvements in, for example, agrobacterium vectors and strains that include genes that stimulate regeneration, but which can be silenced or deleted when regeneration has been achieved.
• The ability to target genes to dividing cells to make regeneration more efficient.
• Optimisation of crops for their nutritional content such as provitamin A as in 'Golden Rice' and the equivalent in other crops.

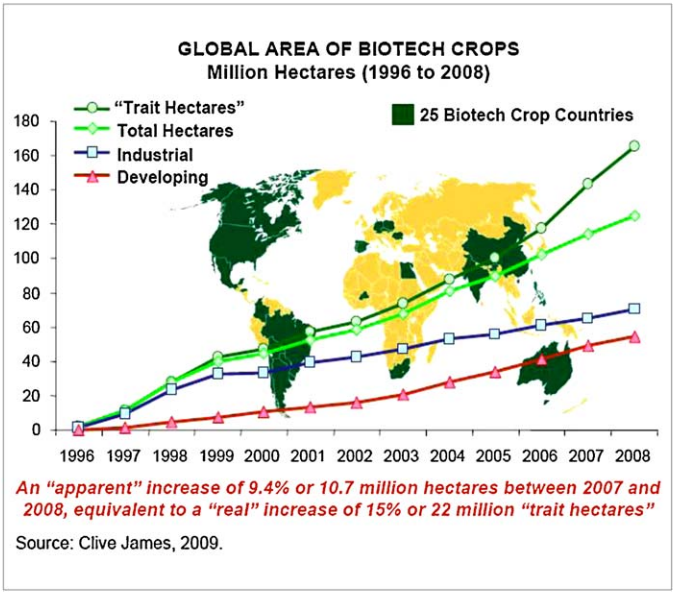

FIGURE 5

The cumulative adoption of transgenic crops into agriculture since 1996.(James, 2009).

of other valuable traits, including those listed in Table 1, will bring enormous benefits to consumers and growers of tomorrow's food [16,47]. These are already exemplified by Roundup ready and Bt soybean, corn and cotton crops. These transgenic crops are manifestations of the fastest take-up of any agricultural product (Figure 5) and over 14 million farmers are growing such crops today [16]. There are already many traits in various crops and model plants that have been 'improved' in the laboratory by the addition of transgenes. Improvements in tolerance to stresses have been a particular focus. It is likely that drought tolerance will be the first commercial product in this category [48,49]. Much research is also focused on tolerance to acid soils, better nitrogen utilisation efficiency (Figure 6) and, of course, seed yield.

FIGURE 6

Comparison of field-grown rice plants illustrating effect of adding an Arabidopsis gene, under the control of a broadly active promoter, that stimulates height and biomass accumulation without significantly affecting flowering time (Ceres, unpublished).

Silencing and inactivation of genes in the crop

While many traits are more readily 'improved' by the addition of new functions, some improvements are made by the inactivation of existing genes and processes. This can be sometimes achieved by random mutagenesis and then seeking plants that have a particular gene inactivated. The process of 'Tilling' achieves this [50]. Large populations of mutated plants are created and then the sequence of the gene to be mutated is used to devise a polymerase chain-based assay that enables rare mutant versions of the gene to be discovered. This is a non-transgenic approach but suffers from two sorts of deficiencies. Firstly, the gene activity is lost in all cells and this can be lethal. Secondly, many genes are duplicated in plant genomes and the redundancy results in the mutation not having any effect on a trait. Often it is more desirable to down-regulate the levels of expression in particular tissues and from all copies of a gene. Here a transgene possessing sequences that match those of the gene to be down-regulated can be inserted and the RNA products of the transgene activate the RNAi pathways that result in degradation of the mRNA of the natural gene(s) [51,52]. Where gene activity is required to be down-regulated in a particular tissue, then placing the transgene under a promoter active only in that tissue should achieve the desired effect. Selection of particular transgenic events should enable the right levels of reduction to be achieved although instabilities of gene expression are difficult to manage and may change from one generation to the next. Particular genes can also be silenced by the insertion of a transgene into it as described below.

Substitution of any allele, including its promoter, by another using homologous recombination

Breeders consider the ability to replace one or a few alleles in a successful variety with another one of the most powerful additions to plant breeding. The technology would enable specific traits to be improved in the most precise way possible, using essentially the plant's own genes, without the need to either tolerate or eliminate large numbers of deleterious genes from another parent. Recent experiments and the development of novel systems to achieve homologous recombination imply that this goal is within reach and is being investigated in several crops [53,54]. The ability to replace one allele with another also provides the geneticist with the ability to compare the function of specific genes and thus prove their role. Another potentially powerful utility of this sort of technology is to change promoters and so alter the activities of resident genes in a precise way. Given that variation in gene expression is an important source of variation in breeding populations the ability to change promoters precisely is likely to have a very significant future.

Efficient homologous recombination relies on the existence of a double strand break in the chromosome. Such a break can increase the efficiency of homologous recombination several thousand-fold at that site. Thus, the challenge has been to learn how to create double strand breaks at the desired site of insertion in the defined gene. Zinc finger nucleases (ZFNs) and meganucleases are tools that have been designed to achieve this [55–57]. Zinc finger nucleases consist of a DNA-binding zinc finger domain covalently linked to the non-specific DNA cleavage domain of a restriction endonuclease. ZFNs bind as dimers to the specific DNA site and the nuclease catalyses the double strand break.

Targeting of transgenes to pre-determined sites by specific recombination systems

The sites of insertion of transgenes are not generally under the geneticist's control at present. However, transgenes can be integrated into chromosomes at particular sites using site-specific integration systems. These rely on proteins that specialise in recombining two identical, specific sequences. This enables, for example, multiple novel genes to be inserted at a target site. The so-called cre-lox recombination system from bacteriophage lambda has been used for site-specific integration of DNA into tobacco and rice [58]. Here the lox target site is inserted into the chromosome (at random) and the desired transgene is then integrated into this genomic target via recombinase-mediated site-specific integration. The cre/lox site-specific recombination system has also been used successfully in wheat and rice to target single copy insertions into lox sites placed in the genome [59]. Another system, flp-frt, involves the flippase recombinase derived from yeast. Flp recognises a pair of frt target sequences that flank a genomic region of interest. The flp recombinase system has been used in corn [60,61] for site-specific gene replacement, while the lambda and phiC31 integrases have also been used [62]. These approaches facilitate the potential to stack new traits at valuable transgenic loci in a modular fashion and can integrate new genes at a site in the genome already found to support strong constitutive expression, avoiding the disruption of existing genes and negative agronomic impacts.

Control of the rates and places of recombination in chromosomes

Progress in plant breeding depends on the recombination of different genes. How often particular genes become recombined depends on the frequency of recombination and the positions of the genes in the chromosomes in relation to the position of recombination. Given the difficulties in changing the positions of genes with respect to one another there is great appeal in being able to control the position and frequency of recombination during meiosis. This will surely become possible [63]. The ideal is that recombination can be greatly increased to generate more variation efficiently and then reduced back to current levels to maintain genetic stability and integrity. Such an advance will be brought about by the use of specific transgenes under the control of promoters that can be activated by the breeder using, for example, an externally supplied chemical.

Construction of chromosomes for stacking many transgenes in a defined order

A vision of improving plants with a large catalogue of transgenes necessarily raises the question should all the transgenes reside together to aid their regular expression and to make it easy for the breeder to select them altogether? Also should they be arranged so that individual genes can be deleted and new versions added easily? While these issues are addressed partly by development of the homologous integration systems (C and D above) other technologies may be preferable. These are being explored and evaluated in agricultural crops. A novel mini chromosome has been built for maize by combining the genes of interest with a larger piece of maize DNA that encodes satellites, retro-elements and other repeats commonly found in maize centromeres and that confer the ability of a chromosome to be divided regularly between daughter cells at mitosis and meiosis [64]. The mini chromosome, when introduced into maize cells by particle bombardment and plants regenerated containing the new chromosome, shows regular inheritance most of the time. The availability of many valuable genes for crop improvement is starting to accelerate and so there is the need to address questions of where and how to organise many genes for optimum long term utility.

Simplification of the genetic basis of traits

While the application of DNA sequencing and molecular marker technologies to plant breeding will bring about huge gains in efficiency and increases in the rate of improvement, the breeder still has to wrestle with the genetic complexities underlying the traits. It turns out frequently that variation in traits is determined by many genes and variation in each gene usually makes only a relatively small difference in the trait. Such differences are hard to measure without large-scale replication. The bringing together of many such genes by recombination and their subsequent maintenance during other breeding cycles can be very difficult. Such complexities are very hard to overcome because they are inherent in the genetic wiring of the species. If the trait could be reduced to one or a few variant genes of large effect, then such traits would be much easier to detect and manage in breeding programmes.

These issues have been a major driver for the discovery and use of single transgenes for important traits. Ceres, as well as many other laboratories, has inserted thousand of genes with high levels of expression into Arabidopsis and rice to discover single genes that make a major change in an important trait (Figure 6). When such genes are found the large trait change is inherited along with the transgene. It is then easy to track both the gene and the trait in subsequent breeding programmes. If it becomes possible to specify each of the traits listed in Table 1 by a few transgenes, then this simplification in complexity would be a huge advantage to plant breeding. Furthermore, it may be that the same or very similar genes would be able to make similar improvements in multiple crops. This would avoid the necessity to repeat the primary genetic analyses in each and every species separately, as is the case at present.

Any one of these uses of transgenes could provide extraordinary improvements in plant breeding and the quality of products, but it is the combination of these that will provide the dramatic opportunities in crop production and a rapid rise in the pace of development of new, improved varieties. Some of the technologies can be developed for application in the near term while others are high risk and it will take brilliant, inspired science to bring these about, even for the longer term. Nevertheless, since plant improvement with these crops will be needed for all time the progress envisaged here will have relevance for all time. Knowing how to improve crops and production more efficiently will never be irrelevant information.

Significant issues associated with the use of transgenes

The successful deployment of transgenes is not without its difficulties: financial, technical and social. Some of these are listed in Table 3. It is expensive to develop all the knowledge to find the relevant genes. When transgenic plants are created, they usually show variation in the expression of the trait. This is undoubtedly due to the ways in which the gene becomes modified by methylation in the cell, the chromatin configuration adopted in the chromosomes and/or the activation of RNAi protection mechan-

TABLE 3

Current issues with the deployment of transgenes

• Variable expression and instability over generations.
• Silencing of their expression.
• Desirability of removing the selectable markers.
• Inefficient transformation processes in certain genotypes.
• Consumer and political acceptance, even when improvements are valuable.
• Cost of regulation and additional time taken for these processes.
• Outcrossing to non-transgenic relatives.
• Intellectual Property and Freedom To Operate issues.
• Costs if crops have to be kept separate from non-transgenics in commercial agriculture.

isms that lead to degradation of transgene RNA or silencing of transcription [52,65,66]. Transgene expression is not always stable during generations probably for the same reasons. Any transgene for a trait will interact with the existing genes and metabolic networks in the cell. This may lead to differences in expression of the trait in different genetic backgrounds and present challenges for the breeder. Indeed all these issues are problems for the breeders but are they any more challenging that all the existing problems with improving plants? I suspect not and in any case they will be managed and overcome as more knowledge accrues.

Different sorts of problems are created by consumers and legislators who are wary of using new technologies, especially where breeding and food are concerned. While understandable in some ways, we should recognise that many of such views are the result of pressure groups against the technology who have advertised and misled societies profusely. It is the case that some of the transgenic options do have potentially far-reaching effects—that is the message of this paper. Societies are poorly equipped to evaluate them because they have insufficient knowledge of the substantial genetic changes behind selection of our current crops. The views that should prevail will surely emerge in the end from the 14 million, and increasing, farmers around the world who grow transgenic plants and the people who are eating transgenic food today. Much is said about this topic elsewhere in this volume.

Other concerns are based on the transfer of transgenes into other non-transgenic varieties by pollination. This is a complex subject with biological and legal aspects. While definitions of organic products do not allow the presence of transgenes, there will always be concerns about chance pollinations from neighbouring transgenic crops. Collection of transgenic pollen by bees and its accumulation into honey is an issue that has been fought in the courts by organic honey vendors. There are concerns about the accumulation of transgenes into wild species by pollinations from related crop plants and the consequential loss of 'clean' wild species. The concerns are often amplified where the transgenes are conferring a beneficial trait, such as drought tolerance, that could be strongly selected for in the wild species and thus increase its fitness and weediness [67]. The statistics and probabilities of pollinations, seed set and subsequent selection of new transgenic wild forms are complex and rarely addressed properly. The hazards and risks are even more rarely weighed against the benefits of boosting agricultural production levels and releasing land that can serve as a habitat for the wild species. Such issues are beyond the scope of this paper.

Many have become disturbed by the patenting of genes and generating difficulties for others to use the technologies commercially without licenses. This is addressed elsewhere in this volume.

The Future—a series of breakthroughs and radical improvements

This paper emphasises that technical advances on the frontiers that change the opportunities and processes of plant breeding are occurring rapidly. Such innovations will continue, and history tells us that numerous innovations will come along that we cannot predict at present. Would the Wright brothers, as they celebrated their success of the first flight in 1903, been able to predict that in 66 years there would be a man on the moon? Many innovations for plant breeding will come from other fields, not plant breeding, as has been mentioned several times above. Thus it is legitimate to speculate and predict that there will be additional stunning breakthroughs in the future. This is implied in Figure 7. There will be waves of discoveries involving single or small number of genes, more complex combinations of genes and entirely novel gene systems that specify extraordinary improvements in crops and production. Maybe the improvements will be novel forms of photosynthesis that harness solar energy much more efficiently [68]. Maybe they will be roots that optimise growth with less fertiliser and water, or bring nitrogen fixation into cereal crops. They will surely include understanding and exploitation of heterosis in the major crops [69,70]. They probably will enable plants to be resistant to diseases and pests. Ultimately there will surely be the creation of new crops, via synthesis of entirely new genomes, that do not suffer from the deficiencies of the species evolved in nature. Crops did not evolve to serve man. It is to be expected that many crops are not well designed for agriculture. Man must continue to seek to make the crops he needs. Such advances will enable mankind to avoid relying on natural biodiversity for food. While such advances are many, many decades away, we should believe in their potential and the contribution they will make to providing high quality food for all in sustainable ways, leaving as much land as possible for other purposes and especially for managing the survival of the planet. This scenario means we should look

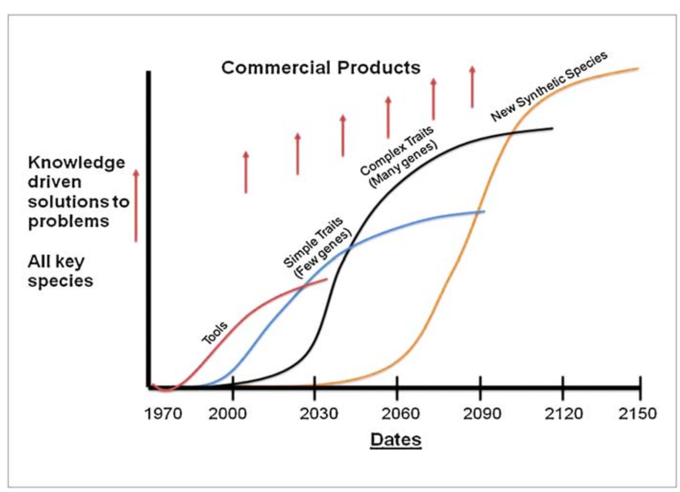

FIGURE 7

Hypothetical adoption of new technologies that provide solutions to major agricultural constraints.

at the current technologies and addition of the first few transgenes to crops as the 'tip of the iceberg'. They are the first few baby steps along a road of discovery and application. It is very important therefore not to judge the current technical achievements and difficulties in ways that undermine the future use of the technologies. This would deny mankind the benefits of huge innovations.

Can we do without the use of transgenes?

Of course we can, because we did not have commercial applications of gene transfer before the 1990s. (However, it is important to note that evolution and the development of our crops as we know them could not have taken place with transfer of genes between species over evolutionary time.) As noted earlier, if all the knowledge and kinds of non-transgenic technologies that have been deployed in US corn production, for example, were applied to cereal grain crops in the different environments around the world, then food production would be very much higher. Indeed this paper draws attention to the fact that much is starting to be achieved in increasing food production by adopting all the analytical, non-transgenic tools from molecular biology, such as molecular markers. This will undoubtedly continue, at some pace, dependent on investments and human capital. But, also as noted above, transgenic crops have already been adopted by some 14 million farmers [16] and it is naïve to believe that it will be possible to turn back the clock and withdraw these crops with their advantages. The insect resistance traits supplied by the transgenes in corn and cotton cannot be supplied by other means. To deny such traits would make many farmers poorer—in any case the farmers would surely prevent withdrawal of the crops. If societies choose not to deploy solutions involving transgenes then advances will come more slowly and some societies will lose significantly, especially where alternative solutions are not readily possible, for example, provitamin A production in rice. The losses include loss of life, sustained poverty, misery and stress and all the things that accompany poor health and reduced education. The over-riding importance of such tragedies in societies and the moral and ethical issues associated with their continuing existence prompt the necessity to change the question from 'can we do without the use of transgenes?' to 'should we do without the use of transgenes?'.

Should we do without transgenes?

The answer to this question depends on where mankind is seeking to take human existence and the planet. To me there is only one way forward and that is towards sustaining the highest quality of life for mankind consistent with sustaining the planet for all time. This means working rapidly and purposefully towards intensifying agriculture sustainably to produce the amounts and diversity of food needed using as little land as possible. This is to leave plenty of land to sustain the planet, manage greenhouse gases, provide renewable energy from biofuels, maintain adequate biological diversity and land and water for recreation and other amenities. To achieve this requires, firstly, wise decision-making from governments working together down to the smallest villages and individuals and, secondly, the deployment of safe technologies to improve food production as rapidly as possible. Nothing less is acceptable. We should not condemn future generations to more poverty and hunger or make more difficult the survival of life on the planet by not developing and using all relevant technology streams. Risks will always be with us, but the risk of not developing and deploying technologies to give better options for the future is the biggest risk. This means accelerating investments in training, education and the dissemination of valuable proven technologies in societies.

Concluding comments

From all that is written above, it should be clear that our responsibilities are much more obvious now, because we know what previous generations did not know. We now know every gene in the major crop plants and have the ability to learn them for any new plant. We know how genes have evolved in nature and what gene systems breeders have selected to adapt our crops to our uses and fields across the world. We know how to speed up rates of improvement, create improvements where none were possible before and produce more on less land. We can describe this information in great detail and are beginning to design improvements. With all this knowledge our responsibilities have become sharpened. Of course there are risks in deploying any technology but to employ the precautionary principle routinely in agriculture where so many are hungry and enveloped in poverty is condemning societies to even greater misery and possibly compromising the ability to manage the planet in beneficial ways for ever. Fortunately agriculture is practised by many millions of farmers all over the world and so experiments involving new technologies are being adjudicated year-on-year millions of time. This puts a huge quality control into the system. All should recognise this. The fast growing global wireless communication systems will increasingly enable farmers and consumers, rich and poor, to know what works well and what does not, what is available elsewhere and what should be adopted. May the farmers, knowledge generators and entrepreneurs of the world teach us all, and especially disconnected decision-makers and citizens, how to overcome our current challenges, decade by decade and create the sustainable promised land for 9 billion people.

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Genetic engineering compared to natural genetic variations

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By comparing strategies of genetic alterations introduced in genetic engineering with spontaneously occurring genetic variation, we have come to conclude that both processes depend on several distinct and specific molecular mechanisms. These mechanisms can be attributed, with regard to their evolutionary impact, to three different strategies of genetic variation. These are local nucleotide sequence changes, intragenomic rearrangement of DNA segments and the acquisition of a foreign DNA segment by horizontal gene transfer. Both the strategies followed in genetic engineering and the amounts of DNA sequences thereby involved are identical to, or at least very comparable with, those involved in natural genetic variation. Therefore, conjectural risks of genetic engineering must be of the same order as those for natural biological evolution and for conventional breeding methods. These risks are known to be quite low. There is no scientific reason to assume special long-term risks for GM crops. For future agricultural developments, a road map is designed that can be expected to lead, by a combination of genetic engineering and conventional plant breeding, to crops that can insure food security and eliminate malnutrition and hunger for the entire human population on our planet. Public–private partnerships should be formed with the mission to reach the set goals in the coming decades.

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Introduction

Genetic engineering was introduced around 1970 as a highly potent strategy for genetic research at the level of DNA molecules, the carriers of genetic information. This strategy consists principally of introducing nucleotide sequence alterations into DNA molecules, such as by site-directed mutagenesis and by splicing DNA segments from different locations in the genome or from different kinds of organisms (recombinant DNA molecules). Genetic engineering has rapidly become an efficient strategy for structural and functional studies in genomics.

Already at an early time, scientists raised the question of conjectural risks of their experimental approach. This led in February 1975 to an international conference held in Asilomar, California. There, conjectural risks were seen at two levels. On the one hand, short-term, rapidly manifested risks were proposed to be investigated, case-by-case, under laboratory conditions in analogy to the medically relevant diagnosis of pathogens and to investigations on the effects of toxic substances, avoiding any impact on the health of the investigators. On the other hand, long-term risks could be expected to become of evolutionary relevance after deliberate release of organisms carrying genetically modified (GM) DNA. For the assessment of such conjectural risks, monitoring was envisaged, as well as a comparison between the deliberate alteration of genetic information by genetic engineering and the naturally occurring spontaneous generation of genetic variants, which are the drivers of biological evolution. This comparison is the aim of the present article. It is a follow-up of earlier publications ([1,2]; see also [3,4]).

Principles of the Neo-Darwinian theory of evolution

Any large population of living organisms contains individuals having suffered a genetic variation. Such variants can be identified by specifically altered phenotypic traits. These spontaneous mutants drive biological evolution. Together with their parental forms, their traits are the substrate for natural selection. The latter results from the environmental constraints that are exerted on living organisms by the physico-chemical composition of the environment and by the activities of other kinds of living beings in the natural ecosystems. Natural selection, together with the available genetic variants, guides the direction of biological evolution. Reproductive and geographic isolations represent the third pillar (besides genetic variation and natural selection) of biological evolution and they modulate the process of evolution.

Towards molecular Darwinism

It is thanks to experimental work on microbial genetics [5] and in structural biology [6] that we have known for about 60 years that long filamentous molecules of DNA are the carriers of genetic information.

The genetic script

DNA molecules are composed of linearly arranged sequences of four different nucleotides that form specific base pairs in the double-stranded form of DNA. Genetic information is contained in the linear sequences of these building blocks, comparable to the linear sequences of letters in our writing. Remaining with this metaphor, the genome (i.e. the entire genetic information) of a bacterium corresponds to one book, whilst the genomes of higher organisms correspond to many books, ranging up to encyclopedias of several hundreds to a thousand books. A classical gene, the determinant for a specific gene product, ranges between a few lines to about one page. As we will see below, this metaphoric comparison can help us in the comparison of genetic variations caused either spontaneously or by genetic engineering.

Definition of the term mutation

Note that we use here the terms ‘mutation’ and ‘genetic variation’ synonymously. In classical genetics a mutation is identified by an altered phenotype that becomes transmitted to the progeny. By contrast, in molecular, reverse genetics a mutation is defined as an altered nucleotide sequence. Thus, it is advisable to be aware of this difference in the use of the term mutation.

Effects of mutations

It is generally known that altered nucleotide sequences turn out to be only rarely favourable, useful for the organism that has suffered the mutation. Often, a mutation provides selective disadvantage by inhibiting to some degree the life processes. In extreme cases this can be lethal. Also quite often a new alteration in the nucleotide sequence has no immediate influence on the life processes. These are neutral, silent mutations. Consequently, we cannot identify evidence for a directedness of spontaneous mutations and the rates of spontaneous mutagenesis must be kept quite low under natural conditions not to eradicate life.

Molecular mechanisms of genetic variation

Textbooks often state that spontaneous mutations represent errors or accidents which occur in the DNA, for example, upon DNA replication. In view of the now available, more profound knowledge on singled-out events of genetic variation, this concept of errors does not correspond to the reality. Particularly from experimental research with microorganisms, but increasingly also from DNA sequence comparisons involving evolutionally more or less closely related organisms, we know that many different specific molecular mechanisms contribute to overall genetic variation.

Some mutations are due to intrinsic infidelities of DNA replication. Short living isomeric forms of biological molecules represent a prominent source of replication infidelities. For example, a tautomeric imino form of the nucleotide adenine can no longer pair with thymine, but it can pair with cytosine. After returning

into its standard form, adenine's partnership with cytosine becomes a mispairing [7]. It is thanks to specific activities of repair enzymes that most such mispairings, sources for nucleotide substitutions, are rapidly eliminated after the passage of the DNA replication fork. Other disturbing effects on local nucleotide sequences, such as deletion or insertion of one or a few adjacent nucleotides and the scrambling up of a few neighbouring nucleotides, can also be attributed to intrinsic properties of the replication machinery.

Other genetic variations are attributed to intragenomic rearrangements of DNA segments. Such reshuffling of DNA segments is generally mediated by recombination enzymes (see 'Rearrangement of intragenomic DNA segments').

Still other genetic variations are due to the uptake of segments of foreign DNA. As a rule, this is also mediated to a large part by specific gene products (see 'DNA acquisition by horizontal gene transfer').

Natural strategies of genetic variation

On the basis of our knowledge of specific molecular mechanisms contributing to spontaneous genetic variation, one can conceptually attribute each particular mechanism to natural strategies for generating genetic variants. As we will see, each of the three strategies here described contributes with a different quality to the occasional formation of genetic variants and thus to biological evolution.

Local sequence changes

Replication infidelities, such as those described in 'Molecular mechanisms of genetic variation', represent local sequence changes affecting usually only one or a few adjacent nucleotides. Chemical mutagens, either internal or environmental, often cause local sequence changes as well. Such changes can affect open reading frames, gene expression control signals or other sequences that are directly or indirectly involved in cellular functions. One can expect that only rather rarely will a local sequence change represent a favourable alteration and provide a selective advantage. But the rare, beneficial mutations represent, in general, a stepwise improvement of an available biological function.

Rearrangement of intragenomic DNA segments

Contributions to this kind of natural strategy of genetic variation are usually brought about by the action of recombination enzymes, that is specific gene products that we call here variation generators. Such enzyme systems with various specificities are found in all living organisms.

In the general recombination, more or less extended homologous stretches of nucleotides (often involving one line to about one page of the genomic library), become aligned, cut and repasted, so that recombinants are formed.

Mobile genetic elements, often involving a few lines to one page of the genomic library, are widespread in living organisms. These elements can occasionally transpose to another chromosomal location. Depending on the characteristics of the involved enzymes, this process may or may not involve further DNA sequence alterations. In the microbial world, one has already identified a large number of specific mobile genetic elements, each following its own specific mode of recombinant activities (e.g. see Ref. [8]).

Whilst site-specific recombination, in general, reproducibly splices DNA segments together at relatively short specific or consensus sequences, the underlying enzymes can very occasionally also use one of a large number of different secondary crossover sites. These latter, quite rare activities are a good source of evolutionally relevant fusions of different functional domains in the genetic information [8].

With regard to their contributions to the process of biological evolution, all these enzymatic variation generators can bring about an improvement or novel uses of available genetic capacities. For example, fusion between two previously separated functional domains (gene fusion) may lead to a novel ability, and the fusion of an open reading frame with a previously separated expression control signal can lead to a higher or a lower yield of the gene product concerned.

DNA acquisition by horizontal gene transfer

Microbial genetics took its fulgurant start some 70 years ago. It unravelled within one decade the basic principles by which prokaryotic microbial organisms can exchange genetic information. In transformation, free extracellular DNA can be taken up by so-called recipient bacteria [5]. In conjugation, a donor cell can pair with a recipient cell and thereby transfer parts of its genetic information into its partner cell [9]. In bacteriophage mediated transduction, a bacterial virus can serve as a gene vector after having incorporated donor DNA into infectious progeny viral particles [10]. Studies of these processes were facilitated by the availability of microbial mutants, so that recombinants could be identified between the involved donor and recipient bacterial strains. Whilst these processes proved to be efficient as long as donor and recipient strains belong to the same kind of bacteria, they also promote genetic exchange between more or less related microbes, although with much lower rates. As a matter of fact, several different natural barriers keep the rates of this so-called horizontal gene transfer at very low levels. Important barriers are, on the one hand, surface incompatibilities hindering the penetration of donor DNA into recipient bacteria, and on the other hand, DNA restriction-modification systems enabled to identify foreign DNA and to cut it into fragments. Only rarely can such a fragment find its way to integrate into the recipient genome before its rapid exonucleolytic digestion [11]. A last barrier acts at the level of expression of acquired genetic information: the functional harmony of the resulting hybrid must not be disturbed, otherwise natural selection will sooner or later eliminate hybrid forms from the concerned microbial population. Qualitatively, horizontal gene transfer can represent an extremely effective step in biological evolution, but for the abovementioned reasons, in reality it is allowed to occur only very rarely. Success of DNA acquisition is best if it occurs in small steps, involving some lines up to about one page of the book of bacterial genetic information.

The tree of evolution

With regard to the evolutionary contributions brought about by the DNA acquisition strategy, we draw the classical evolutionary tree with occasionally placed connectors between branches [12]. Hence, living organisms must have not only a common past, but also a common future, at least to some degree. As a matter of fact, there is increasing evidence that the strategy of DNA acquisition is

not limited to the world of microorganisms, but it also contributes to the biological evolution of higher organisms, sometimes spanning wide distances of evolutionary relatedness.

A new evolutionary synthesis

On the basis of specific knowledge on molecular mechanisms and natural strategies for the generation of genetic variants, one can envisage incorporating this knowledge into the Neo-Darwinian theory, in analogy to the modern evolutionary synthesis which around 1940 brought classical genetics together with the Darwinian theory of evolution and which resulted in the Neo-Darwinism [13]. The result of the new evolutionary synthesis can be called *molecular evolution* or *molecular Darwinism*.

Natural reality actively takes care of biological evolution

As we have seen, the overall genetic variation depends both on the availability of specific enzymes (acting as variation generators and as modulators of the rates of genetic variation) and on non-genetic elements including structural and functional flexibility of nucleotides, environmental mutagens and random encounter.

Enzymes are gene products. For the microbial world it has become clear that many of these gene products are inessential for the normal life of a cell from one generation to the next. Their biological function is clearly to foster biological evolution. We therefore call their genetic determinants evolution genes.

The duality of the genome

Unexpectedly we realise that not all of the genes carried in a genome serve for the fulfilment of the life of an individual during its lifetime. The products of evolution genes serve mainly for a constant, but slow evolutionary development at the population level. They serve for an expansion of life, for biodiversity. In other words, thanks to a well-balanced synergy between products of evolution genes on the one hand and non-genetic, intrinsic properties of matter and random encounter on the other, biological evolution steadily proceeds and nevertheless ensures to individuals a certain genetic stability, without which life would not be possible. We assume that in the long evolutionary history of life on our planet, evolution genes have been fine-tuned for their activities by second-order selection [14]. Organisms which had become genetically able to drive evolution by the three described, qualitatively different, natural strategies of genetic variation and to limit genetic variation to tolerably low rates, had an advantage over others, and this may have led to the functionally fine-tuned activities that we now observe in today's living organisms.

From classical to modern biotechnologies

Biotechnology takes advantage of biological functions and frequently uses the available knowledge to facilitate human life. Increasingly, care for sustainability of the development serves as guidance for biotechnological applications.

In classical biotechnological approaches, organisms were normally used as found in nature. Improvements of their envisaged activities could sometimes be reached by breeding techniques between related organisms. In more recent times, mutagens served to increase mutation rates and thus to procure a random improvement of the functions concerned and their availability.

The impact of reverse genetics on modern biotechnology

Reverse genetics makes use of components from genetic engineering. The sorting out of a particular segment of a genome and the carrying out of structural and functional studies with such a DNA segment, can lead to an understanding of its biological functions. This can be seen as fundamental research. In view of envisaged innovative applications, scientists may try in translational research to obtain improvements by site-directed mutagenesis, affecting the open reading frame of the gene in question. This can alter the gene product in a particular functional property. Alternatively, such mutagenesis exerted on the expression control signal may alter the yield of the envisaged product. In contrast to the possibilities of classical biotechnology, one can try in modern biotechnology to introduce the specific genetic information into another organism that might be more appropriate for the biotechnological production and further use of the envisaged products. These novel possibilities make modern biotechnological applications increasingly attractive.

Evaluation of conjectural long-term evolutionary risks of genetic engineering

Let us now compare the kinds of genetic variations carried out in genetic engineering with those acting in the natural, spontaneous generation of genetic variants. In both cases, the same three strategies of genetic variation are involved: small local sequence changes, intragenomic DNA reshuffling and acquisition of external, foreign DNA by horizontal gene transfer. Both in genetic engineering and in natural biological evolution, similar amounts of nucleotides are thereby generally involved, ranging from one letter to one or at most a few pages of the genomic encyclopaedia. In view of the implication of similar molecular mechanisms and similar amounts of DNA sequences involved in these genetic variations, one can expect that conjectural risks are also comparable for the natural biological evolution (including classical breeding techniques) and for genetic engineering. There is no scientific reason to claim that genetic engineering, as an efficient research strategy, would bear particular conjectural evolutionary risks. From our long-term experience, we know that neither natural evolution nor classical breeding activities have caused major, noted disasters in the living world. It is thus highly unlikely that such disasters could result from genetic engineering.

In this context, it is, nevertheless, advisable to maintain carefulness in human contributions to the process of biological evolution. This responsibility should equally concern contributions by genetic engineering and by classical breeding. Scientific know-how is today available to test carefully in a case-by-case approach the kinds of alterations introduced into DNA sequences, and thus also into functional gene products, before their release into the environment for the benefit of humankind and of our natural environment. Available scientific knowledge and potent investigation methodology represent an efficient and effective basis for *a priori* responsibly carried out technology assessments before GM-organisms, either as produced by genetic engineering or as selected by classical breeding, become released into the environment. Any decision taken on such releases should be based on the specific biological functions involved, not on the ways by which the selected organisms were produced.

A road map for future agricultural biotechnologies

In the long past history of agriculture, selection of food plants did largely follow the principle of trial and error. Random mutagenesis in the absence of knowing the physico-chemical basis of genetic information can nowadays be seen as blind genetics. As we have discussed in 'The impact of reverse genetics on modern biotechnology' and 'Evaluation of conjectural long-term evolutionary risks of genetic engineering', much more powerful research strategies are now available, both to stepwise alter genetic information and to assess the effects that such alterations can cause. In addition, rapid advances in genomics, proteomics and metabolomics provide us a wealth of knowledge on genetic functions and on nutritional requirements for our daily diets. This situation enables us to envisage programmes to specifically improve nutritional values of our common food plants. A convincing example is the so-called golden rice which provides us the required amounts of vitamin A [15]. In following this example, one can expect that it should be possible to enrich the nutritional values of our common food plants with various capacities to ensure nutritional requirements for the entire human population of our planet. At the same time, one should also envisage improving the health of the food plants themselves, both during their growth and during storage.

With this idealistic goal in mind, a road map has been described [16] that might serve as a guiding principle for the next few decades of agricultural development. The proposed road map respects environmental constraints such as the limited availability of fertile soils and of fresh water, and it also respects the preservation of a rich biodiversity and of the climate. In other words, the envisaged development is expected to be highly sustainable.

Under these conditions, priorities must be set for agricultural biotechnologies. A high priority should be given to the production of food for humankind. As we have already outlined, GM crops should be envisaged to have good health themselves and to ensure high nutritional values, vitamins, minerals, essential amino acids, etc., which provide healthy, well-balanced food to the worldwide human population. If this goal can be attained, one can expect that eating habits may tend to shift towards largely vegetarian food. This will consequently render less pressing the production of animal food. The use of fertile soils for growing animal food can then be given a low priority.

High priorities could also be given to agriculture for biopharming, the growth of appropriately modified plants yielding products of medical relevance. Responsibly designed plants for bioremediation (amelioration of soil quality) should also be given a high priority. By contrast, and in view of ensuring food security without interfering with the goal for sustainability, low priority should be given for growing crops for obtaining commodities such as cotton and bioplastics. And last, but not least, low priority should be given to the production of biofuels.

It will be advisable for the political leadership, as speakers for the civil society, to form partnerships with the scientists and economists, to follow the road map drawn with the aim of guiding agriculture towards a sustainable future. This can ensure, on the one hand, durable food security for the human population and, on the other hand, the preservation of the environmental richness of the inanimate and the animate worlds. Scientific methodology and knowledge are rich enough to attain the set goal. Genetic engineering can contribute hand-in-hand with conventional breeding techniques to the envisaged development. A responsible, reliable assessment of envisaged introductions of GM crops can also be based on scientific methodology and knowledge. One can expect that the realisation of the envisaged development will have a good chance to be accomplished within a very few decades, provided the politicians drive the proposed action and favour the appropriate, scientifically based information of the general public.

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Review

Needs for and environmental risks from transgenic crops in the developing world

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The developing world has many unique constraints to crop production and, lacking inputs, they are best overcome if solutions are seed borne. Classical breeding cannot overcome many of these constraints because the species have attained a 'genetic glass ceiling', the genes are not available within the species. Transgenics can supply the genes, but typically not as 'hand me down genes' from the developed world because of the unique problems: mainly parasitic weeds, and weedy rice, stem borers and post-harvest insects, viral diseases, tropical mycotoxins, anti-feedants, toxic heavy metals and mineral deficiencies. Public sector involvement is imperative for genetically engineering against these constraints, as the private biotechnology sector does not see the developing world as a viable market in most instances. Rice, sorghum, barley, wheat and millets have related weeds, and in certain cases, transgenic gene containment and/or mitigation is necessary to prevent establishment of transgenes in the weedy relatives.

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Introduction

The least developed areas of the world are dependent on a small number of crops for caloric input: S.E. Asia depends predominantly on rice; Africa on maize, sorghum or cassava; with strong

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regional predominance of single crops. The world as a whole is not much less diverse with 80% of human and livestock calories coming from but four crops. This lack of crop biodiversity is frightening considering what a single new disease or other constraint might do to these four, wheat, rice, maize and soybeans.

The globalisation of a few crops is actually due to the greater genetic diversity within these few crops allowing them to be cultivated in many areas. Indigenous or other crops do not have the same genetic potential to spread and overcome constraints; if the necessary genes are lacking, no amount of traditional or sophisticated breeding can cause them to come forth; each crop has its own 'genetic glass ceiling' [1], which can only be breached by bringing the needed genes from wherever they might occur by genetic engineering. Even the four major crops have their own genetic glass ceilings, as demonstrated by the phenomenal success of engineering herbicide resistance or insect resistance into their genomes, allowing cost/environmentally friendly control of weeds and insects. The Irish potato famine could have been obviated and present extensive fungicide use can be replaced by transgenes conferring blight resistance that have been generated [2], but not commercialised.

A number of constraints to developing world agriculture are described below as examples of problems that have not been solved by breeding owing to lack of endogenous genes, with possible biotechnological solutions. One major constraint – the lack of pro-vitamin A from grain crops, is discussed in a separate paper in this issue. Many of these solutions will have to be developed by the public sector, as there is not enough interest by the large, major crop, developed world focused, multinationals. They will then have to be commercialised by public–local private sector cooperation. Only the agronomic constraints are discussed below, not the infrastructural problems that must be solved by politicians and cannot be solved by biologists and genetic engineers.

While all transgenic crops released so far are clearly devoid of environmental risks, and do bear environmental benefits [3], there are instances where there can be agro-environmental risks. These risks are limited to those cases where a crop has a weedy relative that could become more competitive should the transgene introgress (cross into) the weed. This is especially risky with herbicide resistance in rice, sorghum, wheat, barley and sunflowers, which do have such pernicious weedy, interbreeding relatives. Still, there are genetic engineering solutions to limit the gene flow and to mitigate it by preventing the weeds from being competitive.

Major weed problems requiring genetic engineering solutions

While there are many weeds that require control, most can be controlled by herbicides, whose use is becoming universal, except in Africa where manual (usually 'femanual') control predominates. Two such major weed problems not amenable to present herbicides or manual control nor to breeding, are described below.

Weedy rice in rice

Rice culture is rapidly being transformed from back-breaking, labour-intensive hand transplanting to direct seeding into the paddy. Hand transplanting gave rice a month head start over weeds. Most weeds in direct seeded rice can be controlled by herbicides, except one, a weedy form of rice that has evolved in farmers' fields to a form that spills its seeds before crop harvest ('shatters') and is taller than rice, and often the few seeds that remain and contaminate the crops seeds have an undesirable telltale red colour. The weedy rice problem is a major constraint where direct seeding started first: the Americas, Europe and now Thailand, Vietnam, Malaysia and elsewhere [4,5].

Solutions to weedy rice: All herbicides that control weedy rice also kill rice. They are botanically the same interbreeding species, and thus have the same metabolism. Only countries that heavily subsidise rice cultivation can use expensive machinery to transplant rice seedlings, and workers are unwilling/unavailable to return to transplanting, even in some of the poorest countries.

Developing herbicide resistant rice has been a proven solution. A mutant rice was found that was resistant to the acetolactate synthase (ALS-AHAS) inhibiting herbicides and has been widely commercialised as a solution [6]. Additionally, genetic engineers have developed rice resistant to the herbicides glyphosate [7] and glufosinate [8], and both kill the weedy rice.

Even though rice is 'cleistogamous', pollinating itself before the flowers open, there is some pollen transfer, and the ALS resistance gene has spread rapidly into weedy rice, wherever used [4]. In some places the herbicide resistant rice was withdrawn, and the transgenic herbicide resistant rice was not released, as it was demonstrated in the laboratory that there would be gene flow [9].

This gene flow can be mitigated, as described in a later section.

Parasitic weeds

Root parasitic weeds (*Orobanche* spp.; *Striga* spp.) are widespread. *Orobanche* spp. (broomrapes) attack grain legumes, vegetable crops and sunflower especially around the Mediterranean basin into Eastern Europe. The only solution to broomrapes was to fumigate the infested soil with the now banned methyl bromide, and was affordable only for expensive 'truck' crops. *Striga* (witchweed) species attack maize, sorghum, millet and grain legumes throughout much of sub-Sahara Africa, and are a major reason for the low productivity in these areas, where they have a 20–100% yield reduction in any given season [10,11].

These root parasites attach only to host crop roots, waiting for a host root to pass nearby, stimulating germination and attachment. They do most of their damage while still underground. When the flower stalk emerges late in season, it is a sign to the farmer that the crop has been devastated. Pulling up stalks by hand does not help this year's crop, and actually can damage the crop root system, but does prevent each stalk from dropping tens of thousands of tiny seeds back into the soil. Some herbicides can control the emerging stalks but few farmers can afford to spray when they know that this season's crop is partially or fully lost.

Solutions to parasitic weeds: Some crop rotations, sanitation, hand roguing to prevent spread can reduce the problem. One intercrop, *Desmodium* can prevent *Striga* development in limited geographical areas in Africa, and its foliage is excellent cattle/goat fodder [12].

There has been considerable success with breeding sorghum for *Striga* resistance, but it requires a complicated combination of separate recessive genes each on different chromosomes, controlling partial prevention of secretion of germination stimulation, partial inhibition of attachment structures and then attachment,

and partial inhibition of penetration of the crop vascular system [13]. This has been successful enough to rightly cause the super-breeder Gebisa Ejeta to be awarded the 2009 World Food Prize for this work. Sorghum co-evolved with *Striga* in Africa and thus possessed these modicums of resistance that could be combined. Maize was introduced to Africa and breeding for resistance was less successful, although periodically there are publications claiming some resistance, claims that later seem to vanish.

Biotechnology has been and can be helpful. Transgenic herbicide resistance is a simple workable solution, well demonstrated in the laboratory for *Orobanche* [5,14–17]. It has not made it to the field, except for transgenic glyphosate resistant maize, released in South Africa, where there is no *Striga*. A tissue culture derived, herbicide resistant maize mutation has been crossed into African maize varieties and hybrids and has been released [17–19]. It has a novel cost-saving technology advance; instead of spraying the herbicide over the whole field, the herbicide is applied to the seeds before planting [18], requiring over 90% less herbicide than that required when sprayed. A similar mutation was found in sorghum and is being readied for commercialisation [20].

Once the needed sorghum genes are isolated and cloned, they could be transformed in a single, dominantly inherited construct containing a group of clustered genes, which would be a very effective strategy. Such resistance could easily be backcrossed into local varieties and land races preserving crop biodiversity, because it is inherited as a single dominant gene and not four separate recessive genes. Perhaps the resistance genes from sorghum, once isolated, could be stacked with those responsible for *Desmodium* allelochemical production, along with resistance genes being found in cowpea [21] and rice [22], all into minichromosomes [23] or into the genome at one locus. It would be very hard for the parasitic weeds to overcome such resistance and many crop species could be engineered with the same gene cluster.

Other approaches are also beginning to work [24] after initial reports of failure [25]. RNAi constructs encoding genes that suppress parasite-only metabolic pathways have been engineered into the crop. The present constructs only lower the number of emerging *Orobanche* attachments on the transgenic tomatoes where this was tested [24], but presumably with different gene configurations and promoters, it will soon be possible to use this technology effectively.

What risks might resistance to parasites have? The parasite-affected crops with interbreeding weeds are rice, sorghum, sunflower and carrots. What parasite-resistance traits might confer a fitness advantage on the weeds? Clearly herbicide resistance would – but only where herbicides are widely used, and are sprayed. Little herbicide is actually used in Africa, and only when herbicide is used would there be an advantage. If the crop seed alone is treated with herbicide, only resistant weeds within less than 15 cm of a crop would be affected by the herbicide [26]. The rest would not, and there would be no advantage to the resistance genes. Those developing the non-transgenic herbicide resistant sorghum use the above as excuses why they do not fear gene flow. Conversely, one cannot prevent the mutant gene from moving, as a similar mutant moved in rice. There are ways to preclude such movement or mitigate its effects with transgenics, as discussed in a later section.

Insect constraints to crop production requiring biotech interventions

Stem borers

Lepidopterous insects are major problems on grain crops in the developed and developing world [27]. Besides the damage to yield by their feeding, winds easily knock over the larvae-hollowed stems, causing breakage before harvest. These insects are also vectors of disease causing fungi, including those *Fusarium* species that secrete fumonisins, that cause oesophageal cancer in humans and other syndromes in livestock.

These and other lepidopteran insects have been controlled by spraying organophosphate or other insecticides in the developed world, or as small pinches of granular insecticide by bare hands or as drops of liquid formulations with a medicine dropper into the leaf whorl of maize in Africa. Organic agriculture has used sprays of dried *Bacillus thuringiensis* (Bt) bacteria to control these insects. Genetic engineers isolated the gene encoding the active toxin in Bt and inserted the gene directly into the crop, obviating the need for the middleman. Such maize and cotton is widely grown in the developed world (the Americas, Spain, China, India and South Africa) [3], and maize varieties are being developed by the public sector for other areas of sub-Saharan Africa. The problem here though is one typical of how the developing world is given 'hand me down genes' that do not always fit. The strains of Bt genes that have been given to Africa are appropriate for the European corn borer and not for the African corn borer. The strains thus far developed have not been compared with the more limited approach to stem borers (and *Striga*) of co-cultivation with *Desmodium* [12]. Synthetic Bt strains that should be far more effective in Africa are not being used [28], probably because they would require undergoing new regulatory procedures. Various Bt genes are needed in other crops as well.

It is not clear whether such Bt genes in sorghum (for example) would confer a selective advantage to weedy sorghum should it move.

Grain weevils and moths

Post-harvest insects are especially bad pests, especially in humid tropical countries where grain cannot be properly dried and where closed storage facilities are lacking, especially on the farm. Not only do the insects wreak havoc on the grain, leaving it part-eaten and full of larvae, but also they are vectors for the *Aspergillus* species that produce aflatoxins [27]. These mycotoxins prevent liver adsorption of food at low doses, increase the risk of hepatitis, liver cancer at higher chronic doses and can cause rapid death at acute doses.

There is little published effort on finding transgenes that can prevent attack by these pests in cereal grains but there has been a modicum of success with legumes [29].

There should be Bt genes that deal with these pests, but such efforts to screen for them are unknown. When companies possessing huge libraries of Bt strains were canvassed in the past, they said they had no interest in making their libraries available for post-harvest insect control in the developing world [27].

Diseases where the breeders have not found resistance

There has been little effort to find transgenes that confer resistance to fungal diseases, even with the threat of new wheat rust strains

appearing out of Africa. This is less the case with viral diseases where one can use the viral genes either to produce coat protein in the plant, precluding viral growth, or using anti-sensing or RNAi constructs against viral genes transformed into the crop. There has been some success with this approach with cassava [30] and maize streak [31] viruses.

Mobilisation of minerals/prevention of mineral uptake

Many of the inputs that seem inexpensive in the developed world, are expensive in the developing world; fertiliser costs 4–6 times more in real terms and far more relative to farmers' income. Many soils contain considerable amounts of phosphate, which alas is unavailable to plant roots. Various transgenes are being tested that 'mobilise' soil phosphorus rendering it available to plants [32]. Similar genes are needed to mobilise iron, especially for crops cultivated in high pH soils. Conversely, some minerals are at toxic levels in many soils and gene systems are needed that can exclude them from the edible portions of plants. Minerals that need to be excluded include aluminium, arsenate and cadmium. This is an active research area [33].

Transgenes to deal with toxins/anti-feedants

Diets are often monotonous and bad in the developing world. Some foods are fine if mixed into a diet, but are basically poisonous if they are the sole or major source of nutrition. As discussed earlier, poor control of insects not only lowers yield, but also vectors pathogens that release mycotoxins. A few examples of such problems are described below to provide a feeling of how genetic engineering can overcome such problems. The reader should note carefully that most of these problems do not have a sufficient market value to justify involvement of private biotechnology companies (except to sell seed) whereas the public health aspect justifies public sector involvement.

Phosphorus fertiliser is expensive and resources are being rapidly depleted. Much of the phosphate in the plant ends up as a polymer, phytic acid, which cannot be degraded by monogastric animals, necessitating addition of phosphorus to feed. Phytic acid binds iron and zinc rendering them unavailable to monogastric animals (including humans), engendering dietary deficiencies despite the presence of these minerals. Genes preventing the biosynthesis of phytic acid in seeds can be transformed into crops, and/or a gene encoding phytase, which degrades phytic acid can be transformed into crops [34]. Either way one gets adequate dietary phosphorus, iron and zinc without added cost.

Pearl millet, when a major component of the diet, causes goitre because it contains vitexin, which inhibits thyroxin production [35]. The genes encoding vitexin biosynthesis are known [36], and using antisense technology can be suppressed, preventing this problem [1]. Grasspeas contain a compound causing a syndrome known as lathyrism [1]. Suppressing this transgenically will be harder than dealing with vitexin, as the genes encoding the pathway have yet to be isolated.

Soybeans contain allergens that cause severe diarrhoea in infants ingesting soy based milk. This can be crucial for mothers unable to afford more expensive cow's milk in poor countries. The genes that have been isolated can be used to suppress the production of the major allergen [37]. Hopefully the day will arrive when infant formula will bear the label 'contains only soybeans genetically engineered to contain no allergens – does not contain allergenic native soybean products'. This reduced allergy soybean will also allow the use of more soy meal in feed pellets for aquaculture, reducing the need for fish meal.

Genes that encode enzymes degrading mycotoxins have been isolated [38], but have not been deployed in crops for fear of public reaction. It is sad that it is perceived that the public prefers liver damage, cancer and so on over genetically engineered products. Those who mould public perception by misinformation and disinformation should have second thoughts about their ethics.

Wasted feed in biofuel crops proposed for the developing world

Much is being made of the efforts to attain fuel sufficiency by cultivating oilseed crops such as castor bean and *Jatropha* (common name: vomit nut) [39]. These related species produce related toxins, ricin and curcin, respectively, among the most potent toxins known. The literature about them uses understatement in saying that the residual material after oil extraction is 'inedible' (when it is poisonous). The high protein meal is to be used as 'manure' without any environmental impact studies to see what the long lasting poisons do to soil biota. To throw away what could be excellent animal feed seems scandalous in areas of the world where there is little animal protein in the diet. The genes encoding both curcin and ricin are known, which would allow facile genetic engineering suppression of toxin production [39]. Should these undomesticated species be cultivated without dealing with the toxins as well as other issues such as seed shatter, non uniform ripening, need for hand picking and other traits, which render these hard to cultivate?

Environmental biosafety considerations – gene flow

There has been a considerable amount of dissemination of disinformation on how transgenes might wander from crops and introgress into unrelated species (horizontal gene flow) as well as into related wild species [1]. These are specious claims; horizontal gene flow among unrelated species is very common among bacteria. While known in evolutionary time, it is virtually unknown in human time in higher species. Because both the number of pollen grains drops off exponentially with distance and pollen vitality also drops off with time, it is likely that only small amounts of pollen will go from a crop to a wild species in nature. This rare pollen will compete with native pollen. As the crop and wild species are different, the crop pollen would have to overcome species recognition barriers and even if successful, the hybrid would either be sterile or unfit to compete with the wild type. Survival of the fittest is fierce in plants where hundreds of seeds compete to replace a parent plant. Thus, transgenic crops crossing with wild relatives is not much more of a problem than non-transgenic crops crossing with wild relatives.

That does not mean that there can be no problems from gene flow; as discussed above with non-transgenic herbicide resistant rice there is indeed a problem. The problem is not of gene flow to a distant relative in the wild habitat, but to a weedy form of the crop, adjacent to it in the agro-ecosystem [40]. It is here where solutions to gene flow are needed, as described with non-transgenic rice. Fascinatingly, there are no regulatory restrictions to cultivating non-transgenic herbicide resistant rice owing to gene flow issues, but these issues are considered when, instead of a transgene, a

mutant gene is used. With the transgene, there are ways to prevent/delay gene flow; no such failsafe mechanisms exist with the mutant genes.

There are two ways to deal with gene flow; before it occurs (containment) and after it occurs (mitigation), as described below.

Containing gene flow

Many methods have been proposed but only some have been tested [1]. These include:

- Engineering the transgene onto the chloroplast genome instead of the nuclear genome. If there is maternal inheritance of chloroplasts, pollen from the crop cannot transfer the trait. This is incorrect about 0.4% of the time, as that amount of pollen transfers the chloroplast genome. More importantly, the proponents ignored that the related weed could pollinate the crop giving an identical hybrid, but with the transgene. The related weed can be the recurrent pollen parent transferring the trait into the weed.
- Use GURTs. Genetic Use Restriction Technologies (more expressively called 'Terminator Genes') are technologies that allow a crop to be cultivated for a single season, and progeny from outcrosses would also die. Still, the transgene could flow in the fields used to produce seed (<1% of agricultural fields). Whether GURTS are 100% suicidal is unclear, as they have not been deployed.
- Single generation transformations. Various attenuated plant viruses can be used as vectors to introduce transgenes into crops. Some of these viruses are not transmitted by seed or pollen, so the transgene DNA cannot be disseminated to weedy relatives of the crop. The technology is presently cumbersome and has not been commercially deployed.

Mitigation of transgene flow

Mitigation is based on co-inheritance of the transgene of choice, which may provide a selective advantage to a weedy relative, with a mitigating transgene that renders the weedy recipient unfit to compete with cohorts [40]. This mitigator gene can encode a trait that is either neutral or beneficial to the crop. These two (or more) transgenes are transformed into the crop in a tandem construct (are covalently bound to each other) and thus will be inherited together, and will very rarely segregate from each other. Wherever the gene of choice goes, so goes the unfit mitigator [41].

Typical mitigating genes are:

- Anti-shattering genes, which prevent seeds from falling to the ground, resulting in their being harvested.
- Dwarfing genes – increase yield of crops (e.g. the first green revolution) but render weeds non-competitive.
- Uniform germination genes – desired in a crop but prevent weeds from having a 'hedge'; if they all come up together they can be exterminated together.
- Susceptibility to a herbicide not used in the current season with the transgenic crop, but used in the following season [4].

Other genes can be used for special purposes, such as non-bolting (no premature flowering) with various root crops, or sterility for vegetatively propagated crops such as potato.

Concluding remarks

There are often ample alternative inputs to transgenic crops, and a great biodiversity of affordable food in the developed word. Such luxuries are not as widespread in the developing world. Thus, it is that transgenics have much more to offer the developing world than the developed. In some developing world crops, it will be necessary to insert failsafe mechanisms to mitigate gene flow from crops to weeds. The public sector will have to perform the product development needed in most instances, as the multi-national private sector does not understand the market or its needs. In the developed world, transgenics have not substantially increased yields, but have reduced inputs and thus increased profitability. In the developing world where the inputs were too costly, transgenic crops can vastly increase yields by inexpensively providing the input in the seed. It is not hard to double yields, when they are a third of the world average.

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Review

Does the use of transgenic plants diminish or promote biodiversity?

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The protection of biodiversity and of ecosystem services ought to be a top priority, taken into consideration in the course of all human activities, because we depend on it fully now and for the future. In this context, we note that the ecological problems related to the cultivation of GE crops fail to differ in any fundamental way from the ecological problems associated with agriculture in general, except that they usually involve the application of much lower quantities of chemicals and thus tend to leave the environments in and adjacent to where they are grown in better condition than do the conventional ones. Higher productivity on cultivated lands, which is one outcome of growing GE crops, protects biodiversity by sparing lands not intensively cultivated, whereas relatively non-productive agriculture practised is highly destructive to biodiversity, since it consumes more land in an often destructive way, even though more biodiversity may be preserved among the crops themselves than in industrialized, large fields, especially if hedgerows and woodlands are not encouraged in near proximity. The major preservation of biodiversity, however, does not take place among crops! If weeds are present that are closely related to the crops, they may acquire immunity to the effects from which the crops were protected and be more difficult to control among them. The production of superweeds as a result of hybridization between cultivated crops and their wild relatives is essentially a myth. The definition of 'organic' production in the U.S. and elsewhere unjustifiably rules out GE crops, often in such a way as to damage the environment more than would be the case otherwise. Unless the definition of 'organic' is a problem, or close relatives to the crops are weedy among them, there seems to be essentially no ecological risk involved in growing GE crops.

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For reasons that remain somewhat obscure, several institutions and well-intentioned individuals continue to oppose the use of contemporary genetic techniques to enhance the properties of crops. There is no scientific evidence that the process of transferring genes from one kind of organism to another poses intrinsic problems. Further, not a single one of the hundreds of millions of people who regularly consume foods produced by GE plants has become ill as a result of eating such foods. As I will review now, the ecological problems often supposed to be related to the cultivation of such crops do not differ in any fundamental way from the ecological problems associated with agriculture in general. Notwithstanding the evidence, all of these points continue to be cited as reasons that it supposedly problematical to grow crops with features that have resulted in part from the application of these particular methods.

Here we are concerned with direct and indirect effects of cultivating GM crops on biodiversity. The preservation of biodiversity is of major importance to human beings and to our prospects for the future. Our ancestors evolved as one of millions of species on earth and we are entirely dependent on biodiversity for our existence here. All of our food comes directly or indirectly from plants. Plants provide all of the medicines used by a large majority of the people on earth and a large fraction of prescription drugs came originally or still come from organisms. In communities and ecosystems, the relationships between organisms preserve topsoil, regulate the run off of water, and often determine local climates. The beauty of organisms supports us and uplifts our spirits, inspires our art and fills our days with delight.

During the half century in which we have enlarged our understanding of the functioning of genes and molecules, it has become evident, as Dick Flavell emphasized, that our hopes for the future rest, in large part, on our ability to understand and to utilize the properties of biodiversity wisely. Our level of understanding now is very poor. Of the estimated 12 million or more species of organisms other than bacteria or viruses, we have so far named 1.7 million and we know next to nothing about the great majority of these. We are naming approximately 10,000 additional species a year, so that it would take us more than a century to give names to those we believe exist now. That will not be possible, however, because of the rate at which species are disappearing. Comparing rates of extinction that can be measured in the fossil record with those estimated to be occurring now, we can state that the rate of disappearance of species has risen over the past 10,000 years, and especially recently, from about 1 species per million per year to at least hundreds of species per million per year.

At that rate, and considering the progressive destruction of habitat, the spread of invasive species in natural habitats and the loss of habitat to global warming, as many as two-thirds of all species in existence now could disappear within the course of this century. That would be a loss comparable to the one that occurred 65 million years ago, at the close of the Cretaceous Period. At that time, the nature of life on earth changed fundamentally and the tempo of evolution was not recovered for an estimated 10 million years. For us, it would mean an enormous loss of our capacity to benefit from the properties of those organisms and an impoverished, less sustainable, and less healthy earth. To ignore the loss we are causing is truly unwise from any perspective. The great American conservationist Aldo Leopold put it this way: 'The first rule of intelligent tinkering is to save all the cogs and wheels.'

What is the role of GE crops in driving the extinction of life at such frightening rates? Plainly, the spread of agriculture itself over the past 10,500 years has greatly lowered the survival rate for local biodiversity and of the world's biodiversity as a whole. A major effort is made in cultivated fields to exclude all organisms except for the one being grown. Exceptions are, of course, made for pollinating insects and some other beneficial forms, but the principle remains generally true. It is obvious that cultivating crops over an estimated 11% of the earth's land surface limits the extent of biodiversity both locally and generally. Considerations of the effects of GE crops on biodiversity must begin with an understanding of this relationship. Providing food for a rapidly increasing human population, currently estimated at 6.8 billion, has led to the elimination of a large fraction of the world's biodiversity over the past 10,500 years, as the human population increased and agriculture spread and intensified. When crops were first domesticated, the entire human population amounted to several million people, a number that has grown over approximately 400 generations (10,500 years) to its present level. As this rapid growth has taken place, the lowlands of tropical, subtropical and temperate regions have been stripped of more than half of their original vegetation, the remaining natural habitats often persisting only in relatively small patches.

With the exception of the agroforestry systems developed in recent decades, we may say that the more intensive the agriculture, the fewer weeds persist in cultivated fields; this in turn results in reductions in the populations of insects, birds and other animals that feed on the weeds or on the cultivated plants themselves. Traditional small fields may include more biodiversity than large, industrial-scale ones, because they are likely to fit into the natural landscape better and to be less intensively cultivated. The biodiversity that remains in a large field of hybrid maize or a rice paddy is limited, even though the crops in these cases are not products of genetic engineering. Agricultural fields have been increasing in size and intensity of cultivation for centuries, with the inevitable result that transgenic technologies are particularly useful there, although their use is in fact size neutral with respect to the fields. The effects of agriculture, often including the use of a high proportion of the regionally available water or the application of large amounts of pesticides or herbicides that drift regularly into the surrounding ecosystems, are profound and can be devastating [1]. When GE crops are grown, some of these negative effects can be avoided or ameliorated because of the particular characteristics of the GE crops (e.g. [2]). Are there also specific negative effects of the cultivation of GE crops on the environment? In the following, we shall review and evaluate the suggestions along these lines that have been offered by various authors.

Modern agriculture is more efficient and much more highly productive than earlier kinds of agriculture, which would not have been adequate to support the numbers of people that now inhabit the Earth. Milpas sprawling over the hillsides of southern Mexico have low yields of maize, but they also incorporate many other useful and medicinal plants. If human populations remain low, such methods of cultivation serve them well; as the population grows, the kind of production levels attained in the large fields of northern Mexico are necessary to keep pace with the need to feed

the higher numbers of people. Overall, the level of maize production in Mexico is insufficient to supply the amounts necessary for domestic consumption; the situation can be alleviated only by achieving increased productivity, but the conservative agricultural practices that are prevalent in various regions of the country have made it difficult to achieve an adequate yield.

Historically, agricultural improvements have tended to spread rapidly. When hybrid maize was planted on hundreds of thousands of acres in the central U.S. starting in the 1930s, few understood the principles of hybrid vigor or the double-cross method of producing the maize; yet there was relatively little objection to the large, high-yielding fields that resulted from this technical advance and a great deal of pleasure with the results. Clearly, the lower-yielding maize fields that existed up to that time had held more weeds and hence more biodiversity, but that was seen as an undesirable situation, holding back the implementation of a new kind of highly productive agriculture. Times change, and the degree of difficulty in achieving public acceptance of GE technology could not have been imagined a few decades ago.

Central to lessening the impact of agriculture on biodiversity is the way the bordering lands, roadsides, hedgerows, patches of woods, relict prairies and other natural communities persisting among the agricultural lands are managed. As mentioned above, and for example, herbicides drifting from the fields sometimes have very negative effects on the health of native vegetation, and pesticides may kill very large numbers of other organisms in the surroundings of the fields. There is ample evidence that maintaining a sort of overall balance in the countryside helps to support ecological services, such as those provided by healthy populations of predators (birds, insects, other animals that help control crop pests), as well as pollinators that visit the flowers of many crops and help to insure good seed set. Weeds may spread from the fields into neighboring habitats with results damaging to biodiversity, a topic to which we shall return.

The overall genetic diversity of the maize crops grown in the United States and eventually elsewhere was clearly decreased by the widespread planting of hybrid corn, but the insertion of transgenes to enhance the characteristics of particular crops is scale-neutral. Thus more than 700 varieties of soybeans grown in the United States have been made glyphosate resistant and the overall number of different strains grown is no different than it was before the more efficient methods of cultivation involving GE strains were developed. Similarly, the deployment of individual strains of hybrid corn, which does not involve the precise transfer of individual genes, means that many original parents are used to produce the strains that have the highest yields in particular, relatively small, regions. In short, the application of GE technology to the improvement of crops does not, in itself, limit the overall diversity of the crops, whereas the development of modern agriculture, in which certain genetically defined strains are grown over wide areas and other strains that were cultivated locally earlier may disappear, does. The preservation of genetic diversity in crops is important and of general interest, but the appearance of GE crops did not cause the problem or advance its spread.

A very limited amount of additional arable land is available for the spread of crop agriculture. It is of the utmost importance that the land cultivated now be utilized in the best possible way; doing so will do a great deal to protect biodiversity by preventing further incursions into formerly undisturbed habitats. To attempt a switch to the less productive forms of organic agriculture worldwide would, in this sense, be a tragic mistake, leading to the destruction of large areas where species survival would suffer greatly as a result. A special word about biofuels is in order at this point. If they can be cultivated in marginal lands not now cultivated, biodiversity will suffer greatly; if lands are taken out of conservation reserves to cultivate biofuels, biodiversity will again suffer greatly. Producing ethanol seems to require more energy than it generates, and while biofuels of some kind will clearly be a part of our future energy budgets, we must plan for it carefully and in view of the potential for further destruction of life.

Aside from the environmental effects of chemicals used in connection with growing GE crops, which we will treat subsequently, or the possible effects of toxins or other chemicals produced within crop species when the plants decay, also to be treated subsequently, the possible effects of GE crops on biodiversity include the following categories: (a) gene flow to weedy or wild relatives; (b) the transfer of genes from the GE crop to non-GE crops of the same species; (c) the possible production of new, aggressive weeds as a result of hybridization between the GE crop and wild or weedy relatives; (d) the effects of the chemicals produced by certain GE plants on non-target species. Each of these will be discussed in with respect to the probability of the events and the effects that might follow their occurrence.

Gene flow to wild or weedy relatives of crops

Gene flow between crops and their wild or weedy relatives has been a constant feature of agriculture ever since people began to cultivate plants. As many authors, starting especially with Edgar Anderson, have documented, hybridization of this kind has had a major role in enhancing the genetic variability of both the crops, facilitating the selection of suites of desired characteristics, and of their weedy or wild relatives. In some cases, as for example in the origin of hexaploid ($2n = 42$) bread wheat (*Triticum aestivum*), the hybridization has been followed by polyploidization, stabilizing the hybrid and its characteristics as an object for further selection through selective planting in the mixed fields. In others, as in the origin of maize (*Zea mays*), repeated backcrossing and selection of plants with improved characteristics from wild relatives, teosintes, has facilitated the assembly of the characteristics of modern maize over a period of perhaps 7000 years in southern Mexico. There are no naturally occurring plants that resemble either bread wheat or maize, and of course bread wheat can form fertile hybrids only with other hexaploids. Maize, by contrast, can hybridize with teosintes that have the same chromosome number ($2n = 20$) and the characteristics of the wild and cultivated plants can be recombined in different ways both in the crops and in their wild relatives. The diversity of local strains, land races, of maize in Mexico and elsewhere has a great deal to do with the recombination of these features following hybridization of the sort discussed.

The two examples just reviewed have parallels in the origin and subsequent improvement of virtually all cultivated crops; therefore, it should not be surprising that GE crops hybridize in the same way and to the same degree as takes place in the evolution of all other crops, reviews by Ellstrand and CAST [3,4]. When hybrid maize and other improved varieties were introduced into Mexican fields, their characteristics spread widely and were used by the

indigenous people for developing improved local strains. The diversity of races of maize that occurs across Mexico and elsewhere is continually evolving in a way one could imagine as the patterns in a kaleidoscope, with repeated inventories separated by decades yielding strikingly different results as a result of the continued selection and introduction of new forms into the specific areas. What the introduction of GE corn plants into the region would mean environmentally would depend on the particular characteristics of the genes involved and the selective forces encountered in different regions.

Considering maize or any other crop in context, and taking the main genes that are widespread in certain crops – Bt protection from pests; glyphosate-ready crops; and virus resistance – we may first ask what the consequences of these genes reaching wild or weedy relatives might be. If the weeds or wild plants gained Bt protection from their pests, and if the pests generated significant selective pressures in the particular environment, the genes might persist in the wild or weedy populations. If they did persist, the plants would be better protected from the pests that were attacking their cultivated relatives than they would be otherwise. A concrete example of the movement of a Bt transgene from cultivated to wild sunflowers (*Helianthus annuus*) reducing herbivory and increasing fecundity in wild populations of the same species is provided by Snow *et al.* [5] and Poppy and Wilkinson [6]. It is difficult to imagine why the acquisition of enhanced protection from herbivores by wild or weeds plant populations would pose an environmental problem and we are not aware of any demonstration that that would be the case.

The question of herbicide resistance is more complex. Whenever herbicides are used in agriculture, resistant strains of the target species and other species that are regularly exposed to the herbicides will eventually appear. For example, the widespread use of glyphosate has resulted in the appearance of several resistant strains of weeds in different areas. This is a general property of herbicide (or pesticide) use and in principle has nothing specifically to do with whether GE crops are the ones treated or not. Various strategies have been employed to deal with herbicide-resistant weeds, similar to the strategies used for dealing with antibiotic resistance in human beings or other animals; and they will continue to be needed in agricultural situations whether or not GE plants are involved.

In the case of bentgrass *Agrostis stolonifera*, glyphosate-resistant strains appeared up to 21 km from the plots where the GE plants were cultivated, although most of the gene flow took place within 2 km [7]. This is considered a problem in the sense that glyphosate is the principal means of controlling this introduced European grass, grown as turf but weedy for example in clearings in forests and parks. This example also demonstrates the fact that the mode of pollen dispersal greatly affects the effects of growing GE crops, or any cultivated crops, at certain distances from their wild or weedy relatives. Clearly alternative herbicides could be found for such infestations, but the advantages and disadvantages of planting glyphosate-resistant turf need to be considered on their own merits in the context of the environmental situation overall.

These examples illustrate some of the diverse situations that can arise with the transgenes that are currently in widespread use. As additional genes are introduced in various crops, they should be evaluated for their possible effects if they were transferred into wild or weedy relatives. In general, though, there appears to be no reason to fear gene flow from GE plants generally. In addition, most crops are not grown in areas where their wild relatives occur, so there is often no possibility for gene transfer. Only in Mexico and Guatemala, for example, are there wild relatives of maize with which the crop could hybridize; there is no possibility of gene flow elsewhere. Within the borders of the U.S., the only cultivated crops that have wild relatives with which they could hybridize are blueberries, sunflowers, some squashes, and pecans; for all other crops there is by definition no possibility of GE traits spreading to wild relatives. For some cultivated species, such as *A. stolonifera*, mustards (*Brassica*), radishes (*Raphanus*), and lettuce (*Lactuca*), however, there are introduced weedy relatives in the U.S. If these weeds grow with the related crops, they may acquire, for example, herbicide resistance from them. In Europe, the acquisition of herbicide resistance by weedy beets (*Beta vulgaris*) within fields of sugar beets, a specialized strain of the wild species, is a matter of concern because of the added difficulty in controlling the herbicide-resistant weeds with the crop fields. Clearly, every situation must be dealt with by appropriate agronomic practices, as would be the case even if GE traits were not involved.

Transfer of genes between GE and non-GE crops of the same species

A second area of concern has to do with the transfer of genes from GE crops of a given species and other non-GE crops of that species. The problem here arises to a large extent because of the classification of GE crops as 'non-organic' by the U.S. Department of Agriculture, which in turn drives a concern about their 'purity', a strange notion given the ways in which plants actually evolve. We see no logic in this designation, which basically puts an additional obstacle in the way of attempts to achieve sustainable agriculture, and I particularly would like to endorse the suggestion made here by M.S. Swaminathan that these two approaches to agriculture be brought together to accelerate the improvement of desirable characteristics of crops. As I emphasized earlier, agriculture itself is unnatural and all cultivated plants and domesticated animals have characteristics that they have acquired over the years as a result of genetic manipulation. In the context of a world that so badly needs increased food production, it seems unwise in the extreme to rule out modern, precise methods of crop improvement on ideological grounds.

In general, there will be transfer between different kinds of crops of any given species, provided that the plants are outcrossing. The distance over which such transfers will occur depends on the way that pollen is transferred in the individual crop species. For plants in which the pollen is transported by the wind, such as walnuts, poplars, pines or grasses, the distances the pollen may move may be relatively great. In outcrossing grasses such as maize and sorghum, for example, the wind may, as we have seen for *A. stolonifera*, carry pollen over tens of kilometers to a receptive stigma under certain circumstances and result in the appearance of GE or other traits far from the place where crops with those traits are grown. In some crop plants, such as rice, wheat, barley and soybeans, self-pollination is the rule and only a very small proportion of the pollen is shed and dispersed by the wind. For many other crops, such as apples, potatoes, canola, squashes, alfalfa,

lettuce, sunflower, fruit trees and berry crops, the pollen is transferred by insects and the distances the pollen regularly travels will depend on the nature, abundance and habits of the individual pollinating insects and the characteristics of the flowers they visit.

As in the previous discussion, and leaving aside the legal designation of GE crops as 'non-organic', the effects of such transfer will depend on the nature of the genes involved, and the persistence of these genes will in turn depend on the selective pressures to which the plants with the new genes are subjected. Given the genes that are now used on a wide scale in producing GE crops, the recipient crops may be resistant to particular herbicides, less vulnerable to attack by pests, or resistant to plant diseases. One can easily see the ways in which the genes associated with these characteristics would increase or decrease under various selective regimes. In general, it is not obvious why any of the possible outcomes should be a matter of concern regardless of the degree of gene transfer that may occur in particular situations.

Production of new weeds

Some 20,000 plants are regarded as weeds, spreading in natural or artificial situations somewhere in the world. Those that grow among crops negatively affect their yields. The great majority of weed species were originally introduced by people from one place to another, often deliberately, and in connection with agriculture or horticulture. Other weeds have moved accidentally, contaminating or adhering to some product or object that is itself transported. One of the arguments used against planting GE crops is that in some way they might give rise to new, particularly aggressive weeds that would otherwise not occur. There are in fact a few examples of the origin of important new weeds involving crops, notably Johnson grass (*Sorghum halepense*) and weedy red rice, which originated as a hybrid between cultivated rice, *Oryza sativa*, and its progenitor species, *O. rufipogon*. Both of these weeds pose serious agronomic problems because they have characteristics similar to those of the crops from which they were derived and thus are particularly difficult to control. Neither of these cases, however, involves GE technology.

By contrast, the movement of genes for resistance to pests or herbicides from the crops into particular weeds, which I discussed earlier, certainly adds to the difficulty of controlling these weeds in the cultivated fields. Thus, wild beets (*Beta vulgaris*) that have acquired herbicide resistance are important weeds in the fields where a domesticated strain of the same species, the sugar beet, is grown; a modest number of similar examples are known. One should, however, view this problem in the context of the thousands of known aggressive weeds and deal with it on a case-by-case basis. As many have pointed out, the characteristics of weeds are very different from those of most cultivated plants, and many crops – maize and soybeans being good examples – never establish themselves in nature and rarely even re-seed in cultivation, so that their possible contribution to the formation of new weeds is particularly difficult to imagine.

Effects on non-target species

Particularly with respect to those GE plants that manufacture Bt toxin, it has at times been claimed that non-target species could be endangered. The case of the monarch butterfly (*Danais plexippus*) in North America provides an illustrative example. It was claimed, on the basis of laboratory experiments, that Bt toxin engineered into maize was expressed in such large quantities in the maize pollen that it could, when shed, coat milkweed plants (Asclepiadaceae), the food plants of monarch caterpillars, so thickly that it would poison them. In fact, such a thick coating of pollen virtually never occurs in nature and all maize strains used currently have been engineered so that Bt toxin is not produced in the pollen; so that there is actually no problem. In another case, it was claimed, on the basis of faulty laboratory data, that Bt toxin from residual plant material was poisoning caddis fly larvae (Trichoptera) in streams near the maize fields; such effects simply do not hold for the concentrations of the toxin that could occur in such streams.

All such effects need to be weighed against the effects on the environment of alternative agricultural practices not involving GE plants. In Europe, for example, where applications of pesticides and herbicides are much higher than those used in the U.S., human and environmental health are clearly compromised to a degree that would not be true if GE crops were grown widely, avoiding the use of such large amounts of chemicals in the environment. When Bt toxin is produced by bacteria grown in vats, killed and ground up, it can by the rules of 'organic' agriculture be spread in vast quantities over fields and forests, with the resulting death of a large proportion of all species of moths, butterflies and caddis flies in the environment. In contrast, when Bt toxin is produced internally by GE plants, only those herbivores that actually feed on these plants are affected. The former situation would be ruled 'organic', the latter 'non-organic', which we consider to be a strange application of logic. It must however be added that for herbivores feeding on GE plants producing Bt toxin, their exposure to the toxin and therefore their chances of developing resistance to it are presumed higher than in those species periodically subjected to 'blasts' of the pesticide.

In many tests, invertebrates have been found to be much more abundant and diverse in agricultural fields where GE crops were being grown than in those subjected to the continual application of pesticides, not a surprising outcome. On cotton fields in the Southeastern U.S., for example, more than 20 applications of pesticides per crop have conventionally been applied, with obvious and directly traceable environmental effects. Other crops are even more highly doused in poisons, especially in Europe, where the chemical industry sells much higher amounts of pesticides and herbicides than in the U.S. In view of these considerations, it is understandable why such a high proportion of the cotton cultivated throughout the world has been engineered to produce Bt toxin, with higher yields and improved human health a characteristic outcome. Why many Europeans should have chosen to live in unhealthy, highly polluted environments rather than use the new, much cleaner technologies remains a mystery to me.

Legalities

Having been involved personally in the formation of the Convention on Biological Diversity in the 1980s, I am truly saddened by the fact that it has become so preoccupied with GE crops. The so-called principle of 'biosafety' is not based on any valid scientific principles, and working it up through the Cartagena Protocol and by other means has given license to those who for personal

reasons, presumably of a political nature, wish to vent their spleen. This unwise and wasteful procedure has consumed thousands of hours of time by hundreds of diplomats and idealists, and not produced any result of the slightest use for the preservation of the world's biodiversity, which we all hoped would be the outcome of activities under the mantle of CBD. As I have explained in these remarks, there is no valid scientific basis to assume that 'biosafety' principles concerning GE organisms would have any effect whatever on the survival of biodiversity, which is so threatened throughout the world. In that sense, it seems to me to be a good thing that the CBD is now moving on to issues connected with the purpose for which it was formed, namely, the preservation of biodiversity.

Conclusions

There appear to be few situations in which limiting the planting of GE crops with the genes currently available would pose particular threats to biodiversity or to the environment generally. Indeed, the environmental damage caused by traditional farming systems, involving the application of large amounts of chemicals to the crops, would normally be much greater. It is proper to consider additional genes proposed for inclusion in commercial crops individually in terms of their effects, however. In that sense, the close consideration given to the new transgenic crops should also be applied to the extent considered desirable to other new strains of crops regardless of the ways in which they were produced.

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Food safety risks and consumer health

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The major food safety risks are not eating a healthy diet, and failure to avoid foodborne illness. Over one billion people in the world suffer from food insecurity and malnutrition. Nutritionally enhanced transgenic crops such as Golden Rice are one potential strategy for reducing malnutrition in the world. Transgenic crops are subjected to a rigorous pre-market safety assessment. The safety of novel proteins and other products is established, and through compositional analysis and animal studies, the safety of any observed changes is evaluated. These studies provide evidence that the new product is as safe as, or safer than, comparable varieties. It must be asked, however, if this rigorous analysis is necessary, because unregulated crops produced by other breeding methods also undergo genetic changes and contain unintended effects. Golden Rice poses infinitesimally small, if any, risk to consumers whilst it has the potential to spare millions of lives each year. However, because it is a transgenic crop, it cannot be deployed without years of expensive pre-market safety review. Paradoxically, if Golden Rice had been produced by less precise conventional methods of breeding, it would already be in the hands of poor farmers. It is concluded that the hyper-precautionary regulatory process applied to transgenic crops works to the extreme disadvantage of the hungry and the poor.

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Introduction

The need for an adequate and safe supply of food has been a driving force for innovation in agriculture and the food industry [1]. In developed countries, consumers have come to expect that supermarkets will be amply stocked with safe and nutritious food. Affluent consumers hear food safety scares through the media almost daily and are bombarded with messages that question if government and industry are taking all possible measures to ensure food safety. Food safety regulatory agencies such as FDA in the US and EFSA in the EU, and similar agencies in other countries, have been charged with ensuring the safety of the food supply [2].

The situation is far different in developing countries where a significant portion of the population can suffer from under-nutrition or malnutrition, and micronutrient deficiencies are common ([3,4]; see also: http://www.gainhealth.org/about-malnutrition/nutrition-facts). Consumers in developing countries may be more concerned with obtaining adequate food supplies and ensuring food security than they are with food safety, although – paradoxically – their food is frequently contaminated with biological and chemical agents that have adverse effects on health (see: http://www.who.int/mediacentre/factsheets/fs237/en/ [5]).

The development of the modern molecular plant breeding methods that employ rDNA technology and DNA-mediated transformation provided breeders with a powerful tool for crop improvement. Over the past dozen years, transgenic crops that are resistant to insects, viruses and herbicides have increased yields and profitability of agriculture, and reduced the environmental impact of agriculture, in both developed and developing countries [6,7]. These crops have proven especially beneficial to more than 12 million small-holder farmers in developing countries [8]. Plant breeders have also used the technology to improve the nutritional value of crops designed to reduce malnutrition and improve health [9,10]. Progress towards the introduction of nutritionally enhanced crops has been slower than for crops with improved agronomic traits. To date, transgenic high lysine maize and oilseeds with modified oil content are being planted; many nutritionally enhanced crops are undergoing development and testing ([9,10]; see also The Safety Assessment of Golden Rice (GR) below).

Transgenic crops are required to pass a pre-market safety review by food safety regulatory agencies before they can be distributed freely [2,11,12]. Paradoxically, crops produced by 'conventional' breeding technologies are not required to undergo pre-market testing. As will be discussed in this paper, from a purely scientific perspective, transgenic crops pose no new or different safety risks when compared to conventionally bred crops [13–15]. The reasons why nations chose to single out transgenic crops for regulation as novel foods are beyond the scope of the present paper [16]; however, one of the motivations for regulation are consumer concerns – inflamed by activist groups that oppose what they call 'genetically modified' or GM foods – that foods produced using transgenic technology might be unsafe.

This paper will briefly describe: (1) a scientific risk assessment of the most important food safety risks that confront consumers, (2) the process used for a food safety assessment of novel foods, (3) questions about the safety of GR and (4) the damaging consequences of over-regulation of transgenic crops. Throughout the text, differences between the conclusions of scientific risk assessors and consumer perceptions about food-related risks will be highlighted.

Diet and global health

Malnutrition results from under-consumption, over-consumption or consumption of food that provides an inappropriate distribution of nutrients. Malnutrition, poor diet choices and over-nutrition have, or will have, an adverse impact on more than one half of the world's population over the course of each individual's lifetime. This paper will focus briefly on malnutrition and the poor. Suffice it to say here that affluent consumers are more concerned with consuming the right nutrients and avoiding overindulgence than they are with food insecurity.

Food insecurity affects about 1 billion people across the globe (Fig. 1). It is estimated that at least 10 million children die each year from malnutrition, that 150 million children are underweight and that 178 million are stunted ([3,4]; http://www.gainhealth.org/about-malnutrition/nutrition-facts). Morbidity and mortality owing to under- and over-nutrition are but the tip of the iceberg of a global diet that is inadequate to meet the world's health needs. Associated losses include failure to reach full mental and physical development by 100s of millions of children, loss of economic productivity by workers, reduction in national GDPs and a larger and ever-increasing global bill for medical care. Scarcity of food energy and micronutrients takes a staggering toll of the poor, particularly in underdeveloped countries ([3,4]; http://www.gainhealth.org/about-malnutrition/nutrition-facts).

Iron deficiency, iodine deficiency, zinc deficiency, folic acid deficiency and vitamin A deficiency (VAD) are amongst the leading micronutrient deficiencies; one or more of these effects almost half of the world's population ([17], http://www.gainhealth.org/about-malnutrition/nutrition-facts). VAD causes 250,000–500,000 cases of child blindness each year; half of the blinded children will die within 12 months. In 1992, WHO estimated that between 1.5 and 2.3 million deaths per annum can be attributed to VAD ([18]; Fig. 2); however, the exact numbers of deaths caused by VAD are difficult to assess because diarrhoeal disease and/or infection are often the direct causes of death in malnourished individuals with weakened immune systems; VAD also often occurs simultaneously with protein, energy and other micronutrient deficiencies that confound an exact diagnosis [17]. International programmes

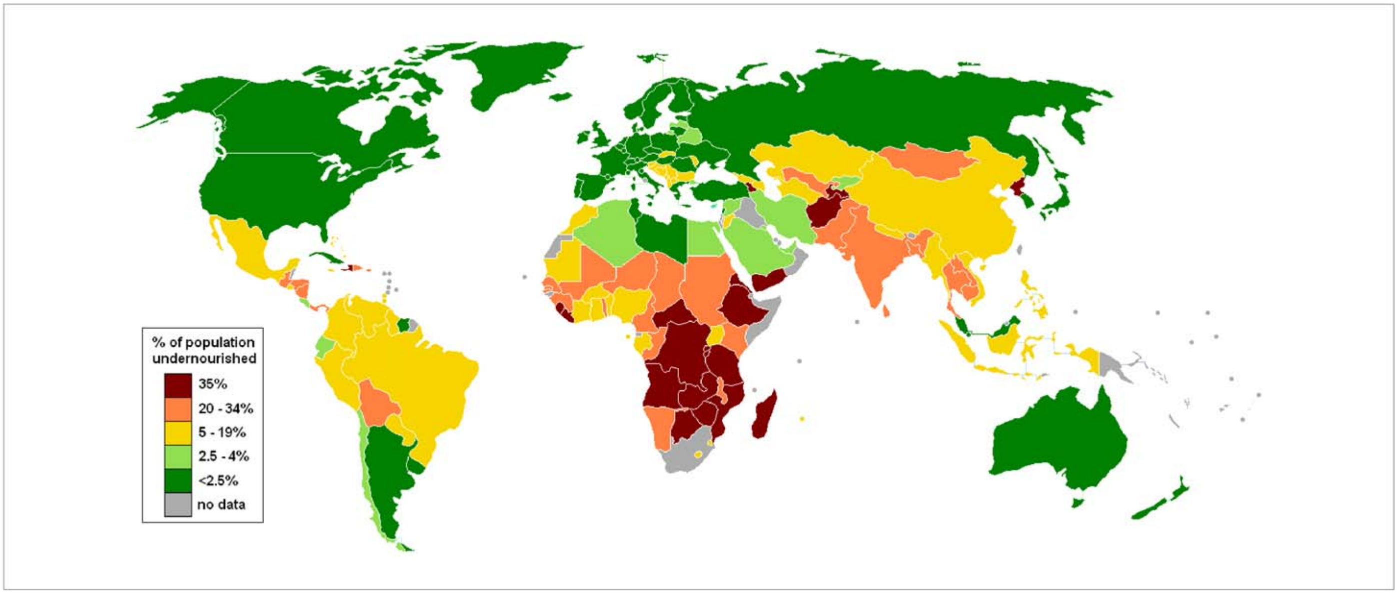

FIGURE 1

The percentage undernourishment of the world population by country (as reported by Lobezón in 2007 (http://en.wikipedia.org/wiki/File:Percentage_population_undernourished_world_map.PNG).

designed to reduce VAD using modalities such as supplementation with capsules or injections have no doubt reduced VAD; however, these programmes are expensive, require recurrent treatment and do not reach the majority of the affected population. Because approximately 70% of the VAD in the world is found in populations that consume rice as a major dietary staple, GR was developed as an adjunct or supplement to other VAD amelioration programmes ([9]; http://www.goldenrice.org/Content3-Why/why1_vad.html). GR is a transgenic plant variety for which a pre-market safety review will be required before it can be distributed to farmers in countries where VAD is prevalent (see The Safety Assessment of Golden Rice).

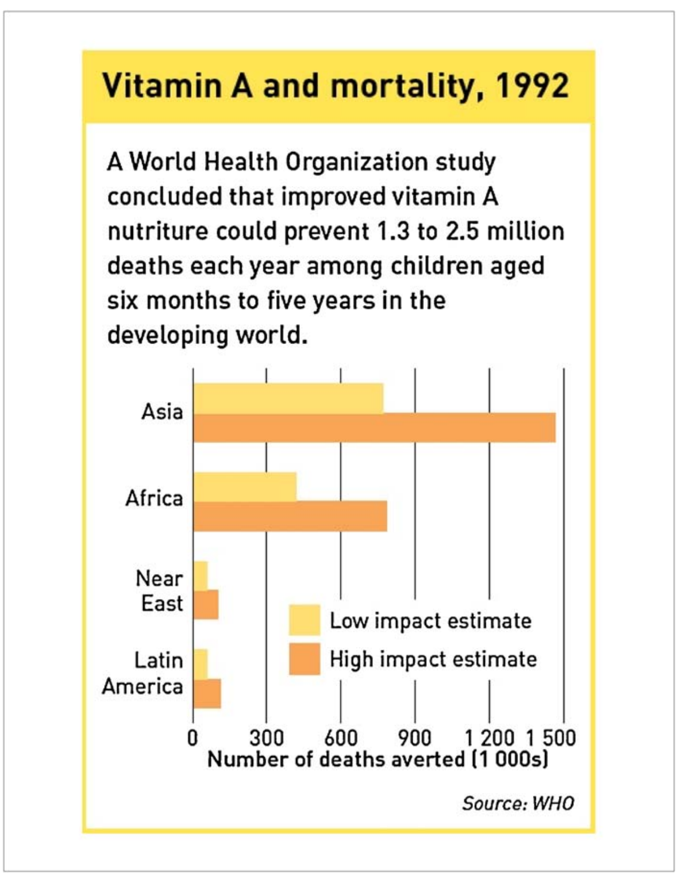

FIGURE 2

VAD mortality in 1992 [18].

Foodborne illness

Bacterial and viral pathogens that are present in consumed food and beverages can infect humans and cause foodborne illnesses. Food is also sometimes contaminated with preformed toxins produced by bacteria before food consumption. Ensuring that the risks of foodborne disease are minimised for the consumer is a major concern for food manufacturers, processors and retailers [19]. Achieving microbial food safety is problematic if proper hygiene and sanitation cannot be maintained. This is often the situation that confronts the very poor and, as a consequence, WHO estimates that 1.8 million people died in the world in 2005 from the effects of foodborne illness (http://www.who.int/mediacentre/factsheets/fs237/en/). WHO also notes that whilst most cases of foodborne disease are isolated and affect only one or a few individuals, widespread outbreaks that affect hundreds of thousands of people have been reported.

As noted previously, although affluent consumers in developed countries expect their food to be completely safe, the total elimination of viruses and bacterial pathogens is virtually impossible. Globally, billions of meals are consumed each day in an environment where potential pathogens are ubiquitous – not only are foods handled by humans, but also the ingredients themselves may be contaminated [19]. It has been estimated that foodborne diseases cause approximately 76 million illnesses, 325,000 hospitalisations and 5000 deaths in the United States each year [20].

Some affluent consumers have turned to organic foods in the belief that they are safer, more nutritious and better for the environment. It is ironic that organic foods may fall short on all the aspirations of consumers. There is no evidence that organic products are more nutritious [21], nor do they appear to be uniformly superior for the environment [22,23]. From a food safety standpoint, organic foods have been observed to have higher bacterial counts than their conventional counterparts and have been associated with foodborne disease outbreaks. The exclusive use of organic fertilisers such as composted manure in their cultivation may be responsible for the higher number of outbreaks and pathogens associated with organic products [21–23]. The objective here is not to attack organic foods *per se*, but simply emphasise the point that ensuring the best possible food safety depends on a science-based understanding of the food system rather than on value preferences and lifestyle choices such as consuming conventional versus organic foods.

Mycotoxins

Mycotoxins are toxic secondary metabolites that are produced by fungi and are found primarily in grains, tree nuts and groundnuts, but which also can be passed through animals into products such as milk [24]. The toxic components of poisonous mushrooms can also be considered mycotoxins because mushrooms are classified as fungi. About a dozen families of mycotoxins cause diseases as varied as liver cancer, kidney cancer, oesophageal cancer, neural tube defects (NTDs), liver and kidney toxicity, gangrene, convulsions, CNS malfunctions and suppression of the immune system [5,24]. Consumption of mycotoxin-contaminated feeds by production animals is estimated to cause billions of dollars in losses to farmers around the world through adverse effects on animal growth and reproduction.

Somewhat surprisingly, the impact of mycotoxins on human health is not well understood because it has not been the subject of extensive investigation. Some countries set safe upper limits for various mycotoxins in foods, raw materials and ingredients, whilst others have no system of assay or control, in spite of the fact that mycotoxins are amongst the most toxic and carcinogenic chemicals known to science [5,24]. For example, hundreds of Kenyans are reported to have died of acute aflatoxin poisoning in 2004 [25]. It has recently been suggested that the adverse health effects of two classes of mycotoxins, fumonisins and aflatoxins, have been seriously underestimated, particularly in many developing countries where products that are prone to mycotoxin contamination make up a large portion of the diet [5]. Often these same countries have no means to test or control for the presence of lethal mycotoxins. The major impacts of these mycotoxins are liver and oesophageal cancers, hepatitis, NTDs and productivity losses in animal agriculture. Fumonisin contamination is typically a pre-harvest event, whilst poor storage conditions often lead to post-harvest aflatoxin contamination. Strategies for prevention and remediation exist but are not widely employed prompting Wild and Gong [5] to conclude:

"Notwithstanding the need for a better evidence-base on mycotoxins and human health, supported by better biomarkers of exposure and effect in epidemiological studies, the existing data are sufficient to prioritize exposure reduction in vulnerable populations. For both toxins there are a number of practical primary and secondary prevention strategies which could be beneficial if the political will and financial investment can be applied to what remains a largely and rather shamefully ignored global health issue."

Biotechnology provides an excellent strategy for the prevention of fumonisin contamination of maize [5,26]. There is clear evidence from the SW US, Guatemala and South Africa that women who eat a diet that is high in fumonisin-contaminated maize content give birth to a higher percentage of NTD-birth defect babies than otherwise matched populations that eat less contaminated maize products. It is known that fumonisin interferes with folic acid uptake by cells and thus mimics folic acid deficiency that is known to give rise to NTDs. It has also been demonstrated that the amount of insect damage to maize kernels has a positive correlation with levels of fumonisin and that Bt-maize (insect-protected transgenic maize) which suffers far less insect damage typically has markedly lower levels of fumonisins [5,26]. The planting of transgenic Bt-maize is therefore an efficacious means to lower exposure to fumonisins and thereby reduce the incidence of birth defects as well as oesophageal and kidney cancers.

As noted previously, affluent consumers in developed countries are enamoured with organic foods that they perceive to be safer than food prepared with ingredients isolated from conventional and transgenic crops. A consequence of the requirement in organic agriculture that no synthetic chemicals be used in cultivation is that control of fungi on organic crops is challenging for the organic farmer and organic crops can at times contain higher levels of mycotoxins than their conventional counterparts [23]. In 2003 the UK Food Standards Agency randomly sampled 30 corn meal (maize meal) products found on the shelves of UK supermarkets [27] and found that 6 out of 6 samples of organic corn meal contained fumonisin levels more than tenfold higher than the maximum safe level set by the FSA (Table 1). By contrast, 20 of 24 samples of corn meal prepared from conventionally cultivated maize were found to have fumonisin levels below the recommended safe maximum; 4 samples of conventional corn meal exceeded the recommended safe level (Table 1). Other studies have shown that Bt-maize protected against stem-boring insects

TABLE 1

Total Fumonisin content of cornmeal brands from UK supermarkets [27]

A. Low fumonisin

Type	# Below[a] 500 μg/kg	Mean (μg/kg)	Range (μg/kg)
Conventional	20	130	10–330
Organic	0	–	–

B. High fumonisin

Type	# Above 500 μg/kg	Mean (μg/kg)	Range (μg/kg)
Conventional	4	3127	1798–4737
Organic	6	8353	3800–16,430

[a] Recommended upper limit of fumonisins is 500 μg/kg.

generally contains far lower levels of fumonisins than conventional maize [5,26]. Thus, whilst many consumers perceive that there may be food safety risks associated with 'GM' maize, there is clear evidence that switching to transgenic maize could lower the incidence of certain cancers and birth defects.

Natural toxicants

Plants produce a variety of toxic molecules as part of their defences against predators and competitors [28]. During the process of crop domestication, the concentration of such toxicants is often reduced. Food processing and preparation methods, as well as consumption patterns, help control any potential adverse effects to humans and animals associated with plant-derived foods. Commonly eaten foods can, however, be toxic to humans [29,30]. Most consumers would be surprised to know that deaths resulting from ingestion of green tomatoes or potatoes containing high levels of glycoalkaloids (e.g. solanine, tomatine and chaconine) have been documented [30–33].

Many consumers buy organic foods because they are concerned about the presence of trace amounts of synthetic pesticide residues in their food. A careful analysis of pesticide intake in 1990 concluded that 99.99% (by weight) of the pesticides in the American diet are chemicals that plants produce to defend themselves [32]. Evidence also indicated that natural pesticides were as likely as synthetic pesticides to be carcinogenic, and that the risk from exposure to dietary synthetic pesticides is insignificant, whilst so-called 'natural pesticides' that are used in organic agriculture, such as pyrethrin, are as likely to be carcinogens as synthetic pesticides [33,34]. Consumers are largely unaware that pesticides are even used in organic agriculture believing them to be 'pesticide free'; they are also unaware that plants manufacture their own *natural* pesticides. Although synthetic pesticide residues pose insignificant risks to consumers, the risks posed by *natural* toxicants in foods remain largely unstudied. Doll and Peto [35], estimated that approximately 35% of cancer deaths are attributable to variation in diet. It may be that over-nutrition and its consequences are the cause of most of these deaths; however, a role for endogenous *naturally occurring carcinogens* on the incidence of cancer cannot be excluded.

In spite of the fact that the safety of approved food ingredients and food additives must be established before their use in foods, and it must be demonstrated that they will pose no risk when used as intended, in recent years consumers have expressed fears that chemicals added to foods will do harm unless they are *natural* chemicals. This completely misses the underlying scientific understanding that any chemical can be toxic and it is only the dose and exposure that determine if a chemical will do harm in a specific situation [36]. To learn that a compound is *natural* does not in any way inform a toxicological food safety assessment. Somewhat paradoxically, the public eagerly consume large quantities of antioxidants and other chemicals whose safety and efficacy have not been tested, in the belief that such compounds will prevent ageing and ensure good health.

There is ample reason to believe that small amounts of some chemicals that are toxic at high doses may in fact stimulate health when consumed in sub-toxic quantities through a phenomenon known as 'hormesis'; a compound that exerts a hormetic effect may have a positive beneficial effect at low levels of intake, whilst at high levels of intake it produces adverse effects and harm [37]. It may be that low levels of exposure to various potential toxicants actually stimulate or induce our natural immunological defences and detoxification systems, rendering the body more resistant to subsequent chemical threats. It cannot simply be assumed that because a chemical is toxic or causes cancer at high doses, that it will not be innocuous, or even beneficial, at lower doses. Toxicologists emphasise that the dose makes the poison.

One example of an unexpected outcome of hormesis was observed by researchers studying the impact of antioxidants on ageing in *Caenorhabditis elegans*, a small worm used as a model system in biology [38]. In *C. elegans*, as in many other species in which the phenomenon has been studied, mild to moderate caloric diet restriction increases life span. Paradoxically, it also produces a syndrome called 'oxidative stress' that has been proposed as one of the factors that leads to ageing. To evaluate the impact of this oxidative stress on the organism, the researchers treated one group with antioxidants that were known to eliminate oxidative stress. The result observed was that the prolongation of life produced by caloric deprivation was eliminated by antioxidants. The researchers speculated that the oxidative stress had a hormetic effect that allowed the organisms to fend off ageing reactions and that by cancelling out the oxidative stress, antioxidants shortened rather than lengthened life. It is noteworthy in this regard that millions of consumers spend billions of US$ annually on antioxidants that could be shortening rather than extending life spans. The important point here is that sound diet choices are based on sound science, not wishful hopes, and scientific understanding of the complexities of slowing the ageing process has not been unravelled.

A food safety perspective on novel foods

As had been previously noted, transgenic crops are subjected to rigorous pre-market safety assessment, in spite of the fact that they can be less genetically modified than crops produced by other modalities of breeding. They pose no new or different risks to humans or animals. Precautionary regulation was triggered because these crops were considered to be novel foods – foods that humans had not previously consumed. This definition is itself debatable because it is fair to ask if an organism into which one or two genes have been added to 20 or 30 thousand genes in the plant genome makes the plant a novel food. From a purely scientific perspective it is simply a crop variety that has one or two novel traits; crop varieties often differ by two or more genes. Most of us expect, however, that some degree of care and safety consideration should be taken before one consumes a food that one has never seen before and which is not commonly eaten. We will return to the issue of the safety of novel traits in the next section and will here explore the history of novel foods.

The great majority of the plant foods that we consume today did not exist before the development of agriculture approximately 10,000 years ago [1]. In 1859, Darwin [39] described the process of domestication of wild plants and their gradual evolution through a process of human-directed selection into crop plants. Domestication is brought about through selection of several genetic modifications that, for example, increase yield, reduce toxic molecules and improve harvest qualities. At the end of the process, the domesticated plant has often lost all resemblance to its wild progenitor and can no longer grow in the wild, but depends on cultivation by humans for survival [15]. Different crops were

TABLE 2

Origins of some common crops ([1]; see also http://www.hort.purdue.edu/newcrop/history/lecture05/lec05.html)

Crop	Origin
Avacado	Central and South America
Beans	Mesoamerica
Cacao	Aztec (xoco-latl)
Corn (maize)	Mesoamerica
Cotton	South America
Gourds	Americas
Papaya	Tropical America
Peanuts	South America
Peppers	Mexico-Mesoamerica
Pineapples	South America
Potatoes	Andes Mountains
Pumpkins	Tropical America
Squash	South America
Strawberries	Americas
Sunflowers	Central and North American
Tomatoes	Mesoamerican

developed in various locales and became part of the local or regional cuisines.

Over thousands of years, some crops such as wheat were widely disseminated across the Eurasian landmass [1]; however, many crops remained restricted in distribution until the era of European exploration and colonisation and the establishment of global trade routes. For example, varieties of crops that were restricted to the Americas were not found elsewhere in the world until Spanish Conquistadores brought them to Spain upon their return from the New World (Table 2). In particular, maize (the world's number one grain crop), tomatoes (a leading vegetable crop) and potatoes

TABLE 3

Incomplete list of toxic and allergenic plants that would not pass the current safety assessment applied to GM crops

Crop	Harmful substance
Celery	Psoralens (furanocourmarins)
Potato, tomato	Glycoalkaloids
Cassava	Cyanogenic alkaloids
Rubarb, spinach	Oxalic acid
Soy, wheat, milk, eggs, mollusks, crustaceans, fish, sesame, nuts, peanuts, kiwi	Food allergy

(the world's 4th most important staple crop) were unknown throughout most of the world until sometime after the 16th century. All of the crops listed in Table 2, and many others from other parts of the world, were introduced as wholly novel foods to humans the world over during the past 300–400 years ([40]; Fig. 3). They appear to have been very readily adopted, and the globalisation process appears to have occurred largely with without adverse health effect.

It is noteworthy that many of the crops that were disseminated around the globe over the past few hundred years contain toxic components and are potentially deadly if not prepared and consumed properly. Cassava, for example, moved from the Americas to Africa and Asia where it was widely adopted in spite of the fact that it contains highly poisonous cyanogenic compounds that can kill if not properly removed through tedious and complex preparation. Potatoes and tomatoes, as noted previously [30,31], contain toxic glycoalkaloids (tomatine, chaconine and solanine) as do all the *Solenaceae* of the Nightshade family. There is in fact a long list of potentially toxic plants that have crossed international frontiers and cultural barriers in spite of apparent hazards (Table 3). Many of these crops would not be approved for distribution if they were subjected to the standards that are applied to GM

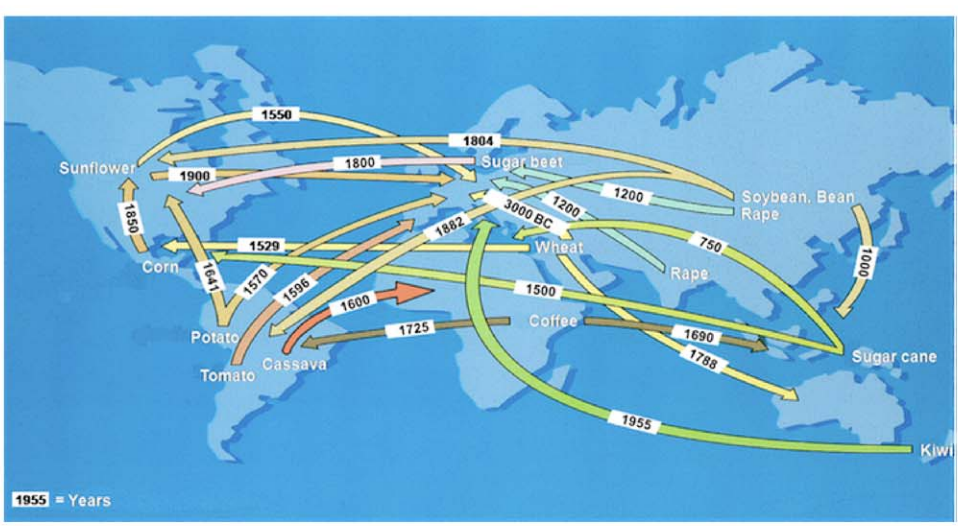

FIGURE 3

Map of history of movement of crops around the globe [40].

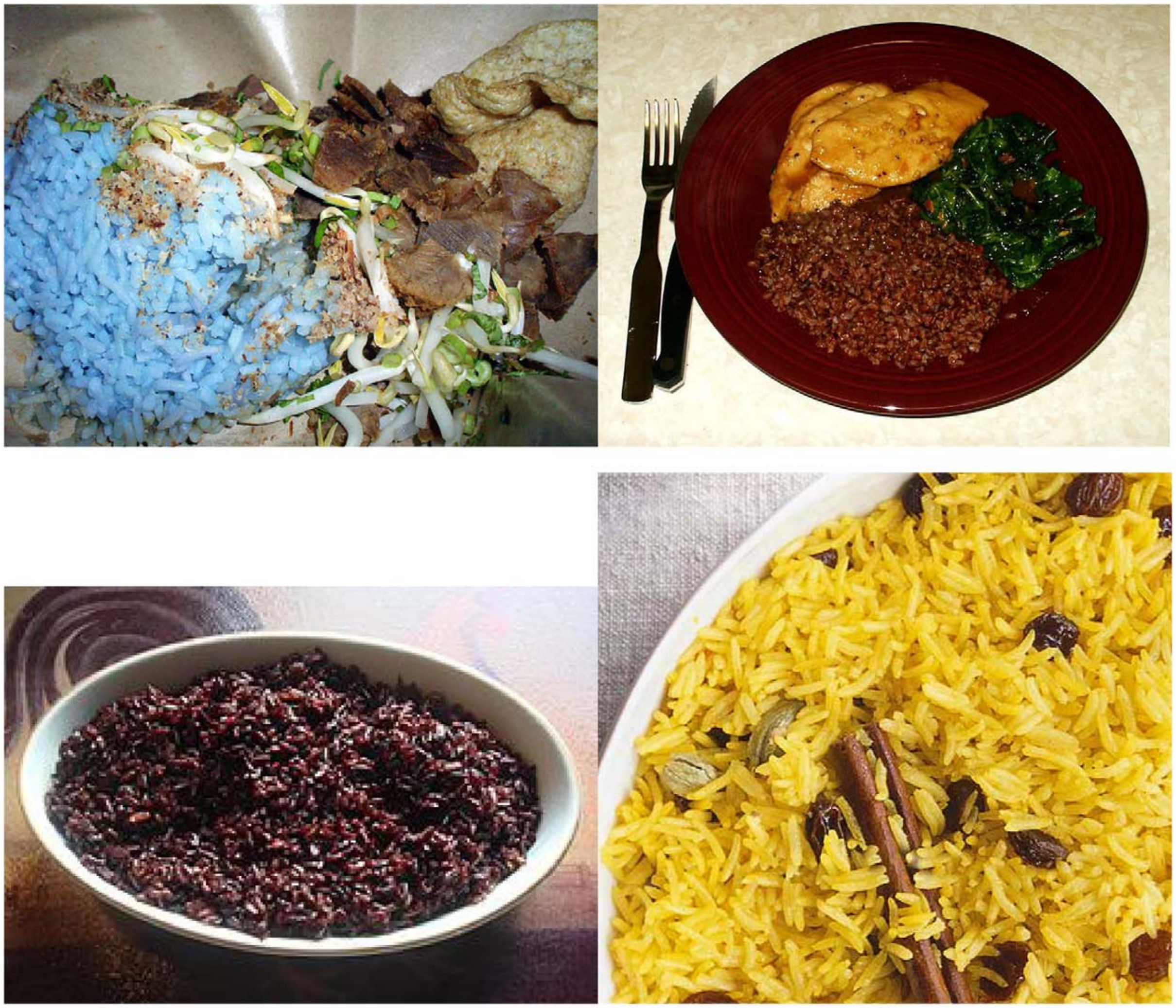

FIGURE 4

Coloured rices. Starting in the upper left-hand corner and moving clockwise the rice dishes are: Malaysian Blue Rice (http://www.haveyoueaten.net/2007/09/28/nasi-kerabu/); Bhutanese Red Rice (Glane23, Flickr; http://upload.wikimedia.org/wikipedia/commons/4/40/Bhutanese_red_rice_with_chicken_and_spinach.jpg); Saffron Rice (http://www.saffronspices.co.uk/wp-content/uploads/2009/02/saffron-rice.jpg); Black Rice (http://www.thenibble.com/reviews/MAIN/rice/images/black-rice-250.jpg, ElinorD).

crops today around the world. If international treaties such as the Cartagena Protocol on Biosafety, that seeks to restrict movement of LMOs (living modified organisms) across borders, had been in place during the era of crop globalisation, the historical transboundary movement of crops depicted in Fig. 4 would not have occurred.

The safety of transgenic crops

It is not an easy matter to ensure that a truly novel food is safe, because foods are composed of hundreds or even thousands of distinct metabolites, some of which may be allergenic or poisonous. The safety assessment process applied to the mycoprotein product Quorn provides a good example of the challenges of assessing the safety of a whole food. Quorn is a single-cell protein product that can be formed into cheese, meat or poultry-like foods [41]. Researchers performed extensive compositional studies, fed the material to animals, rubbed it on their epidermis, injected it under their epidermis, fed it human volunteers and at the end of the day called for approval of the product even though there was no clear test to show the product was safe; what could be demonstrated was that its composition was similar to other high quality protein foods and that it was apparently innocuous to living subjects when consumed by them. Approval was granted in spite of the fact that about 1 in 100,000 people, who consumes the product has an adverse reaction.

The safety assessment process applied to transgenic crops, foods and feeds should be much more straightforward than that described for Quorn because only one, or at most a few genes, are inserted and the changes that are introduced are small, well-defined and usually predictable [2,9,42,43]. Transgenic crops are not wholly novel foods as was the case in the case with Quorn. In the case of transgenic crops, the crop is essentially unchanged, except for the intended additions. When a gene is inserted into a plant, three questions emerge:

1. Is the inserted DNA safe to consume?
2. Is the product(s) of the gene safe to consume?
3. Are the intended, and any unintended changes, safe to consume?

Several recent reviews have discussed the food safety assessment process that is designed to evaluate the above questions [2,9,42,43]. Although regulators set high standards for evidence and require that uncertainties be resolved before approval of a new transgenic crop, several key issues discussed in the recent reviews [2,9,42,43] continue to concern consumers and will be discussed briefly below.

Substantial equivalence

The comparative safety assessment paradigm that is used by regulators to guide the safety assessment process is called the substantial equivalence paradigm. There have been claims that GM crops are never identical to their conventional counterparts, so it is incorrect to call them substantially equivalent and that, because they are not identical, they are not safe. It is important to recognise that developers and regulators do not claim that new transgenic varieties are identical to their conventional counterparts because, as a result of any breeding process, no two varieties of any crop have the same composition [43]. More importantly, what the substantial equivalence paradigm actually asserts is that components that are identical between two crop varieties pose the same risk, and that any differences in risk between two varieties are restricted to components that are present in different amounts. Substantial equivalence does not require that two varieties be identical, indeed, if two varieties of any crop are identical they are not distinct varieties. Safety assessors use the substantial equivalence (or comparative assessment) paradigm as a guide to differences whose safety must be evaluated.

Safety of DNA

There have been several claims that transgenic DNA could become incorporated into human or bacterial cells and give rise to cancer or promote the spread of antibiotic resistance [9,44,45]. Research has demonstrated that transgenic DNA is no more or less likely to be transmitted than other DNA and it is important to note in this regard that humans consume >100 mg DNA per day which is digested and metabolised without ill effect. Careful studies have also demonstrated that antibiotic resistance genes are ubiquitous in the environment and transgenic crops have not added to the spread of antibiotic resistance. The spread of antibiotic resistance is most probably the result of poor stewardship in the use of antibiotics by humans [45].

Safety of transgenic proteins

The vast majority of dietary plant proteins are digested and absorbed without any adverse effect, although a very few proteins can be toxic or have anti-nutrient activity, for example, trypsin inhibitors in soybeans [46]. Similarly, very few proteins are food allergens; most known food allergens affect less than 0.1% of the population [47]. The sequences of virtually all known toxic or allergenic proteins have been determined and using that information it is possible to test if a newly introduced protein resembles in any way proteins that are known to be toxic or allergenic. If a protein resembles an allergen or toxin in any way, further research is discontinued. Tests are also done to determine if a protein is quickly digested, which adds further assurance that the protein is safe to consume [47]. It is important to remember that a transgenic protein is no more likely to be an allergen or toxin than any other, and perhaps less likely since careful pre-market screening is required of transgenic crops but not crops produced by other less precise and more genome disruptive breeding technologies [46,47].

Unintended effects

The critics of GM crops continue to assert that inserting DNA into a plant genome could cause unintended effects that might be harmful. A large body of evidence points to a very different conclusion: transgenic insertion can produce fewer unintended effects than other forms of breeding [13–15]. Unintended effects occur in all forms of breeding; however, compositional and phenotypic analyses, as well as extensive backcrossing, are used by breeders to cull out unintended effects.

The Safety Assessment of Golden Rice

Although vitamin A is retinol, many humans acquire vitamin A by synthesising it from β-carotene derived from plant sources such as carrots and orange-fleshed sweet potatoes in which it is abundant. Unfortunately for the billions of people who depend on rice as the major portion of their diet, white or polished rice contains no β-carotene [9,48]. GR was constructed by inserting a cassette of DNA containing genes for phytoene synthase (ex daffodil; *Narcicssus psuedonarcissus*) and carotene desaturase (ex *Erwinia herbicola*) into rice (*Oryza sativa*) to allow the plant to synthesise β-carotene from its precursor, geranyl-geranyl-diphosphate [48]. A second version of Golden Rice (GR2) was produced by the use of a phytoene synthase gene from maize (*Zea mays*) in lieu of the gene from daffodil used in GR. GR contains about 1.6 μg β-carotene/g rice and GR2 contains about 10–40 μg β-carotene/g rice [49]. The β-carotene content of the rice makes GR a light yellow or golden colour whereas GR2 has more intense amber golden colour. A case study of the key elements for the safety assessment of GR2 has been published [9]; the safety assessment of transgenic rice varieties in general has also been reviewed [42]. In the following paragraphs key points in the safety assessment and adoption of GR will be discussed.

DNA safety

As noted previously, DNA is safe to consume. To address negative perceptions about the safety of antibiotic resistance genes used as markers in transgenic plants, GR2 was constructed using the phospho-mannose-isomerase (PMI) marker system that allows the simple sugar mannose to be used to select transformants. The system has been used in other transgenic crops and has been approved by regulators.

Protein safety

Allergy to rice is uncommon and rice contains no major anti-nutrients or toxins. The sequences of the proteins produced by rice plants containing the GR and GR2 constructions have been compared to all known toxins, anti-nutrients, lectins and food allergens with no similarities detected. The maize phytoene synthase

protein that was incorporated into GR2 is commonly consumed by humans and animals. The PMI marker system has been consumed in other approved transgenic crops and the enzyme itself is ubiquitous in nature, including in bacteria found in the human gut, and has no similarity to any known allergen or toxin; the protein is also digestible. The bacterial carotene desaturase protein is the only protein that will be unique to the human diet, and for this reason, extensive safety analysis of this protein (and perhaps the others mentioned above) will be required. Large quantities of the protein will be required for animal toxicity studies; small amounts will be used for digestibility studies. Other studies will be required to determine the quantity of each of these proteins present in the rice, and that the proteins are identical to the corresponding protein found in the donor of the gene that encodes them. It is worth noting that these rigorous protein safety tests will be required by regulators even though the quantities of proteins present will probably be far lower than would be required for most known toxins to exert a biological effect. That is to say, few potent toxins would have an adverse effect in the quantities these proteins are present in GR. Moreover, because rice is cooked at high temperature for long time periods, the proteins will be thoroughly inactivated and denatured and will thus likely pose no threat to humans and animals. It is worth repeating that proteins with but rare exception are safe to consume. It is difficult to understand the need for extensive protein safety testing on proteins that are present in infinitesimal quantities.

Composition analysis

The composition of transgenic crops is routinely evaluated as part of the process of establishing that there have been no losses in nutritional value and that no unintended changes have occurred. Because GR and GR2 varieties have been crossed with many different varieties that farmers grow in different growing regions in Asia, there will be many distinct compositional profiles collected for GR- or GR2-derived varieties. Particular attention will be paid to the pool of compounds associated with carotenoid biosynthesis and the carotenoids because this is the pool of metabolites targeted by the genetic engineers and most likely to have been affected. Composition testing is not required for rice varieties produced by other modalities of breeding. Additionally, rice is a very poor source of almost all required nutrients; rice mainly supplies carbohydrates for energy and limited quantities of proteins; the micronutrient content of rice is virtually nil. Composition testing is expensive and time-consuming and its value has been questioned [43]. Although it certainly is clear why the developers would need to know the concentration of β-carotene in each variety, because only a few micrograms of β-carotene per gram of rice are being added to the rice, it is far less clear why composition testing is even necessary.

Does GR contain enough β-carotene?

Critics of GR have claimed that GR would not provide the RDA of vitamin A. A careful analysis of this claim demonstrated that GR could indeed make an important contribution to vitamin A intake, although it might not provide 100% of the RDA [9,50]. Zimmerman and Qaim [50] calculated that GR could supply between 11 and 86% of the RDA. It should be noted that GR was intended as a supplement and that 100% of an RDA is not necessary to ameliorate VAD; intake of 25% of the RDA will prevent blindness and death. In addition, most users of GR will have some other sources of vitamin A in their diets. The key issue in debate over the effectiveness of GR centres around assumptions about the bioavailability of GR, with critics arguing that only one molecule of retinol would be produced from 25 molecules of β-carotene (a 1:25 ratio) and researchers countering that 1:6 or 1:12 would be a more likely scenario. The issue was recently resolved when it was reported that the conversion ratio in human subjects was close to 1:4 [51]. It is now clear that GR can make a significant contribution to vitamin A intake. GR2 is capable of providing an RDA of vitamin A in a single bowl of rice [9]. Any continuing claims to the contrary are not rooted in science or evidence.

Is the β-carotene in GR toxic?

Critics have claimed that adding β-carotene to rice may give rise to toxic degradation products and they point out that retinoids can exert toxic effects – which is correct. Their logic is, however, flawed. Carotenoids are not retinoids and they are not converted to toxic levels of retinoids *in vivo* at levels of exposure that occur in foods [52–54]. The conversion of β-carotene to retinol is a highly regulated and compartmentalised process that ensures that excesses of potentially toxic retinoids will not be generated. This controlled biological regulation might have in part evolved to cope with the fact many foods we eat contain β-carotene and other carotenoids and it would not be undesirable to convert them to toxic retinoids. It is noteworthy as well that GR contains less β-carotene than carrots, orange-fleshed sweet potatoes, papayas and several other commonly eaten plant foods. β-Carotene has also been consumed safely in even higher quantities by consumers for its anti-oxidant properties with no adverse reactions reported. It is thus uninformed or deliberately misleading to claim that the β-carotene in GR could be toxic. Parenthetically, arguing that GR has too little β-carotene to be of any nutritional value and also that it has so much β-carotene that it could be toxic is mutually inconsistent.

Will consumers accept Golden Rice?

Critics of transgenic crops rushed to claim that people will not accept any colour of rice but white. They based their claim on the well-known fact that people who consume polished white rice will often refuse to eat brown unpolished rice. This is an imperfect analogy because white and brown rice are very different foods with respect not only to appearance but also to flavour and texture. It should also be added that brown rice is also a better source of some nutrients than white rice. Brown rice does not keep well in tropical and semi-tropical climates where the great majority of rice is consumed. The real problem with the claim that people will not accept coloured rice is that the critics are also simply ignoring the fact that coloured rice foods are widely consumed around the world (Fig. 4). Yellow coloured or GR is the leading choice of discerning rice consumers. Saffron, annatto or achiote and tumeric are all extensively used in various countries to produce golden yellow rice dishes. Black rice was considered so desirable in ancient China that only the Emperor was allowed to consume it. The Bhutanese prepare red rice and blue rice is a specialty in Malaysia. Any objective reading of consumers' rice colour preferences suggests that rice colour *per se* is not necessarily a barrier to acceptance and can in fact be a desirable property. It should be noted that

research subjects that have tasted GR state that it tastes the same and has the same mouth feel as conventional rice. Perhaps the best way to test if GR is acceptable to consumers is to allow consumers the choice of deciding whether they want to plant it and/or grow it for themselves and their children.

The silent holocaust

As noted previously, VAD kills approximately 2 million people a year – most of them rice-eating children. If GR had been bred by conventional means, two or three years might have been required to propagate and distribute the seeds, and – assuming a reasonable adoption rate – perhaps the lives of a half a million or a million people a year might have been saved until now. GR was not, however, in any way conventional, it was a paradigm-shifting innovation. GR has instead been confronted with critics who have delivered a long list of ill-founded claims about safety and efficacy. GR has also confronted an intransigent regulatory system that requires millions of US$ and many years to navigate for each new product. At ten years after the first development of GR, the world's VAD sufferers may still be two to five years away from receiving the seeds that could save their lives. Considering the minimal safety concerns associated with GR and the staggering annual toll of VAD, would it not have been a better choice to distribute the seeds just as would have been done if they were conventionally bred? The moral calculus is surprisingly simple: if GR had been distributed in 2002 or 2003, millions of lives might have been saved. Not to have disseminated the seeds of GR until now has allowed as many people to die silently as were killed in the holocaust.

Damage by distraction

Science-based risk assessment of the food system reveals that the adequacy and quality of the diet has more influence on morbidity and mortality, as well as quality of life, than any other food risk. Dietary choices affect all of us; however, the billion humans that do not have enough food, or a sufficient variety of nutritious foods to eat, are in extreme peril. Foodborne illness kills and sickens hundreds of millions of people each year, many of whom do not have access to sanitary supplies of food and water. Mycotoxins cause a significant portion of liver, kidney and oesophageal cancer in the world as well as birth defects, reproductive failure and a host of other ills most likely affecting hundreds of millions of consumers, including affluent consumers living in industrialised countries. Plants can synthesise a wide variety of toxicants, anti-nutrients and allergens that can also adversely affect health. Although their impact on health has not been quantified, a considerable number of the chemicals that are naturally occurring plant secondary metabolites are carcinogens. These are the major food safety risks that need to be understood, avoided and/or managed.

By contrast, some consumers are more concerned about pesticide residues and chemicals in their food that pose little if any risk. Consumers perceive human-made chemicals to be inherently toxic and respond to each new claim that a chemical is a carcinogen, or – more recently – a pseudo-hormone or a hormone blocker. In some cases, it may be that the compound the public seeks to avoid might even be beneficial through a hometic mechanism of action. Every year brings a new scare to television and newspapers. The consequence of these misperceptions about real risks is that consumers' buying choices are manipulated, as for example rushing to buy more costly organic food that is no more nutritious or safe than conventional foods, and which may arguably less safe in certain circumstances. Public pressure, as well as economic and political agendas, leads to attention being paid to relatively minor safety issues at the expense of investment of resources into control of safety issues that do real harm. Public concern about perceived risks is also often translated into stringent regulations that are not only costly, but which inhibit innovation and distract government, industry and consumer attention away from real risks. Ames and Gold [36] have coined the phrase 'damage by distraction' to describe this phenomenon.

Nowhere is 'damage by distraction' more apparent than in the way transgenic crops are regulated in the world today. In spite of scientific analysis that indicates that transgenic crops are as safe as, or safer than, crops produced by other breeding modalities, transgenic plants are treated as if they were toxic chemicals or nuclear waste. In the case of GR, negative perceptions and unscientifically stringent regulations have inhibited the introduction of a potentially lifesaving crop innovation. It is hard to imagine any food safety risk arising from transgenic rice that could rival the global impact of VAD. Precautionary fears have caused regulators and consumers to forego real benefits and not erase harms caused by current practices and products. One must ask in the final analysis if it is not *immoral* not to use a technology that can save lives.

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Genetically modified myths and realities

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Myths abound when it comes to GE crops. At their worst, myths play an active role in discouraging the use of GE to solve problems that afflict humankind, such as malnutrition and birth defects. Of all the various myths, two have been particularly important in preventing the use of GE maize in its areas of origin. The first is that transgenic maize will contaminate and destroy land races, thus destroying biodiversity and its associated cultural traditions. This myth totally ignores the fact that the gene flow that has taken place between maize and its progenitor, between the land races, and between land races and modern hybrids, has not led to any dire consequences. The second myth is that crops are natural and have not been modified by humans, or if they have, that plant breeding does not alter DNA. This myth ignores the fact that for the most part, it is impossible to alter the appearance of crops without changing the DNA. In fact, DNA movement within the crop genome is normal and its movement leads to double-strand DNA repair, with results like those found around transgene insertion sites. In addition, plants have ways to create novel genes. These changes help plants adapt to evolution and to human selection. The net result is that changes similar to what happens during the production of engineered plants takes place anyway in plant genomes.

Contents

Introduction

> ***"And all who told it added something new, and all who heard it made enlargements, too". (Alexander Pope).***

As noted above by Alexander Pope, certain topics are particularly prone to distortions as they are repeated. The topic of genetic engineering in agriculture is probably the one topic that has most lent itself to misinformation over the past decade. The following excerpts from websites illustrate the extent and nature of the myths surrounding GE (genetically engineered) crops:

> ***"The Microbial Ecology in Health and Disease journal reported in 1998 that gene technology may be implicated in the resurgence of infectious diseases."***
>
> (http://www.raw-wisdom.com/50harmful, 8 Dec 2009)

> ***"A number of studies over the past decade have revealed that genetically engineered foods can pose serious risks to humans, domesticated animals, wildlife and the environment."***

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1871-6784/$ - see front matter doi:10.1016/j.nbt.2010.05.016

(http://truefoodnow.org/campaigns/genetically-engineered-foods/, 16 Dec 2009)

"The introduction of genetically modified organisms (GMOs) by choice or by accident grossly undermines sustainable agriculture and in so doing, severely limits the choice of food we can eat."

(http://www.greenpeace.org/international/campaigns/genetic-engineering/hands-off-our-rice, 16 Dec 2009)

"Our country's children are fed inadequately tested and unlabeled genetically engineered foods in their school meal programs"

(http://www.sierraclub.org/biotech/school_lunch.asp, 17 Dec 2009)

"Latest GMO Research: Decreased Fertility, Immunological Alterations and Allergies"

(http://www.naturalnews.com/025001.html, 17 Dec 2009)

"The proof is obvious that one of the major reasons of the bees' decline is by the ingestion of GMO proteins."

(http://www.infowars.com/death-of-the-bees-gmo-crops-and-the-decline-of-bee-colonies-in-north-america/, 17 Dec 2009)

"If the corn gene that creates Bt-toxin were to transfer into gut bacteria . . ., it might turn our intestinal flora into living pesticide factories."

(http://www.seedsofdeception.com/Public/GeneticRoulette/ExcerptfromIntroduction/index.cfm). See rebuttal to this particular point at http://academicsreview.org/reviewed-content/genetic-roulette/section-5/5-7-bt-genes-and-gut-survival/.

The existing GE myths are numerous and widespread, and they cover the gamut of topics from health and safety to various aspects of environmental safety. In as much as there are time and space limitations, only two myths will be covered in detail. These two myths are particularly pernicious, as they prevent the deployment of GE crops in areas where they are most needed. They therefore serve to perpetuate conditions that may lead to chronic malnutrition and extraordinary rates of birth defects among the population.

The great maize myth: transgenic maize in its center of origin will destroy it via contamination

As background information, maize originated in southern Mexico [1]. Today, 11 million maize farmers plant 6 million ha of maize and support a population of 77 million. The average farm size is 3.5 ha, of which 1.50 ha are planted with maize [2]. The central Andean region of South America is a secondary center of maize diversification. This region has about 7 million farmers on 3 million ha that support 16 million inhabitants. Maize yields average about a ton per ha [2].

Agroecologically, traditional maize production in Mesoamerica was very effective when the population was low. Today, the system is not meeting the food needs of the population. The population has tripled in the past 50 years, forcing the land to be subdivided into ever-smaller parcels with each generation. In 1964, there were 321,000 parcels in the Guatemalan highlands. By 1996, the number had increased to 667,000 in the same land area [2]. A yield of ~1500 kg/ha is considered good; yet such a yield is barely ~1/6 of maize yields in the USA. More worrisome is the fact that ~50% of children under 5 are malnourished [3], in part owing to the chronic food insufficiency derived from low yields and small parcel sizes.

The second limitation associated with maize production in Mesoamerica is the prevalence of growth of *Fusarium* spp. and subsequent fumonisin production [4,5] on corn cobs, which follows feeding damage by caterpillars [6–8]. Fumonisin is a carcinogen which is also associated with neural tube birth defects (NTDs) owing to its ability to interfere with sphingolipid metabolism, and hence, folic acid [9–12]. Fumonisin is almost ubiquitous in corn products in the region [4,13–15]. It is therefore not surprising that the region manifests some of the highest rates of NTDs in the world [16], surpassing 115 cases of anencephaly, spina bifida, or encephalocele per 10,000 births, as compared to the world average of about 15 cases per 10,000 (Fig. 1) (Dr Julio Cabrera, Guatemala City, pers. comm.).

The bottom line is that there is a real cost in terms of human health that is associated with the current maize production system. Yet, both yield loss, and particularly, fumonisin production, could be attenuated through the use of insect-resistant maize. Maize transgenic for the Bt gene has been known to lower fumonisin production under several, although not all, circumstances [7,17–20]. Thus, the use of Bt maize would be a simple solution to help address some of the most pressing issues associated with maize production.

Despite the obvious advantages of deploying Bt maize from a humanitarian point of view, there is fierce opposition to the release of GE maize in its center of origin. The arguments are that GE would at best 'contaminate' or at worst, displace, the existing genetic diversity of maize. In addition, there are claims that GE maize would have cultural consequences:

FIGURE 1

Examples of suspected fumonisin-associated birth defects: anencephaly, spina bifida and encephalocele. All are from one summer in one hospital in Guatemala. Photos courtesy of Dr Julio Cabrera.

"There are over 59 known races and thousands of varieties, which will be inevitably contaminated."

(http://endefensadelmaiz.org/No-to-transgenic-maize.html, 17 Dec 2009)

"Scientists worry that the genes could spread through the region's corn population reducing its genetic diversity."

(http://www.historycommons.org/timeline.jsp?seeds_crops=-seeds_cropsCorn&timeline=seeds_tmln, 20 Dec 2009)

"The introduction of genetically engineered varieties also threatens the indigenous cultures and the very knowledge that indigenous peoples have developed for millennia. Genetic contamination of maize threatens the food sovereignty for hundreds of millions of people that rely on maize as their primary source of food."

(http://www.globalexchange.org/countries/americas/mexico/news/gmo100101.html, 17 Dec 2009)

"transgenes might threaten the character or continuance of the Mexican maize landraces. They might thus alter the Mexican diet and the global fate of corn itself"

(http://www.theotherjournal.com/print.php?id=874, 21 Dec 2009)

Reports of transgenes in Mexican maize are routinely made [21,22] and rebutted [23,24]. It is probably fair to say that if transgenes are not yet in maize, it is just a matter of time before they are. Regardless of whether or not transgenes have been introgressed into native maize varieties, there is no question that genes flow between maize varieties and landraces. Thus, the issue is not about whether there will be gene flow, but rather about the consequences of such flow.

It is possible to examine the consequences of gene flow by studying maize production in its historical context. First, maize and its progenitor, teosinte, have grown sympatrically for millennia. In some regions, maize has evolved a gene to limit crosses between maize and teosinte; in others, there are no crossing barriers [25], so a low level of gene flow between the two does occur [26] (Fig. 2). The point is that despite the gene flow with each other, neither maize nor teosinte have been damaged or have lost their identities.

The same is true of the various land races. Historically, they have been planted contiguously (Fig. 3), and they readily cross pollinate (Fig. 4). The point again is that these varieties have coexisted for centuries, and despite their intercrossing, have not lost their identity.

Finally, improved maize cultivars and hybrids have been grown in the region for decades now. There is evidence that genes from modern hybrids have been introgressed into the traditional land races [27], *but again, the land races have not perished, nor have there been cultural consequences*. In fact, the greatest threat to the maintenance of land races does not come from introgression of genes, but rather from migration of farmers from the field to the city [28], or economic diversification that lessens farmers' dependence on maize [29].

On the basis of the fact that there has been gene flow between teosinte, traditional varieties and modern hybrids, it becomes possible to predict the consequences of transgene flow. The topic has been considered previously. The following conclusion is from the findings of the Commission for Environmental Cooperation [30]:

FIGURE 2
A maize–teosinte hybrid growing in a Mexican maize field. Photo courtesy of Raúl Coronado.

"16. There is no reason to expect that a transgene would have any greater or lesser effect on the genetic diversity of landraces or teosinte than other genes from similarly used modern cultivars. The scientific definition of genetic diversity is the sum of all of the variants of each gene in the gene pool of a given population, variety, or species. The maize gene pool represents tens of thousands of genes, many of which vary within and among popula-

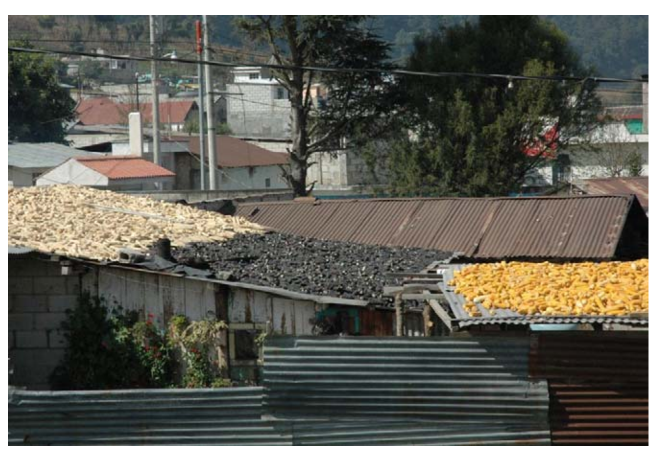

FIGURE 3
White, black and yellow maize drying on a Guatemalan rooftop after harvest.

FIGURE 4
Maize from the Guatemalan highlands, showing that cross pollination takes place naturally between the landraces. Photos courtesy of Eduardo Roesch.

tions. Transgenes are unlikely to displace more than a tiny fraction of the native gene pool, if any, because maize is an outcrossing plant with very high rates of genetic recombination. Instead, transgenes would be added to the dynamic mix of genes that are already present in landraces, including conventional genes from modern cultivars. Thus, the introgression of a few individual transgenes is unlikely to have any major biological effect on genetic diversity in maize landraces."

In summary, there is sufficient experience to state that, by itself, gene flow from transgenic maize will not have the destructive effect predicted by those who oppose GE maize. Any claims to the contrary are not consistent with the available evidence and thus must be considered in the realm of myths.

What is the origin of the great maize myth? There are undoubtedly numerous motivations, combined with a general lack of knowledge on maize genetics and cultivation. First, implicit in the concept that a novel gene introgressed into a land race constitutes 'contamination' implies that land races are somehow genetically defined, static entities. They are not. Whereas land races have recognizable phenotypes, they are genetically dynamic. As mentioned previously, there is gene flow among land races planted adjacently, and farmers exchange seed among themselves, further contributing to gene flow. However, gene flow is countered by selection – farmers participate actively in selecting for the desired phenotypes [29,31,32]. Thus land races are the product of continuous crossing and selection that maintains the phenotype while continuously selecting for the most adapted types for each region. New traits that are considered desirable by the farmers will be maintained; the rest are discarded.

The starting misconception: the myth of natural food

The second concept that is implied by the use of the term 'contamination' is that today's food crops are natural. The perception is that our crops' ancestors were found in the wild, and brought into cultivation. Other than the fact they are now cultivated, they have remained in their original, pristine state. Transgenes thus contaminate them; much like industrial effluent can contaminate and ruin a natural lake.

Few people realize the extent to which today's crops have been modified during the domestication process. It was Charles Darwin who pointed out in his *Origin of the Species* that our domesticated crops have been so altered by breeding and selection, that at times it can be difficult to recognize their wild progenitors. Maize is an extreme example of Darwin's observation, as cobs of teosinte bear little resemblance to those of modern maize (Fig. 5). Thus, there is very little that is natural about our current crops.

However, what makes Darwin's observation so relevant to GE is that, barring a few cases that involve epigenetics, *it is impossible to change the appearance of a plant without changing its DNA*. Yet, the perception remains that breeding does not alter DNA [33]:

"Insertion of DNA can cause deletions and rearrangements of the original DNA at the insertion site. This information helps us understand that GE is significantly different from conventional breeding techniques."

To really evaluate the differences between conventional breeding and GE, it is necessary to evaluate the changes at the DNA level that take place during breeding and selection.

FIGURE 5
A teosinte cob, showing the extent of changes that had to take place during domestication to produce modern maize. Photo courtesy of Raúl Coronado.

Mutation breeding is the most obvious example of a methodology known to alter DNA. There are 2543 known crop varieties developed from mutation breeding (FAO/IAEA database http://www-infocris.iaea.org/MVD/). Yet very few of these have been studied to determine the change at the DNA level.

However, mutations from ionizing radiation have been studied most extensively in *Arabidopsis*, and these probably represent the type of changes that take place in crop plants. Deletions ranging from 300 bp to 8 kb are probably the most common result [34]. Small inversions are also possible from mutagenesis. Null alleles have been characterized for chalcone flavanone isomerase and dihydroflavonol 4-reductase. The first contained a loss of 4 bp along with a 1.5-kb inversion within the gene, and an insertion of 272 bp that were originally 38 cM away. The second also has an inversion of the genomic region, with 52 bp deleted at one end and 7.4 kb at the other [35]. *Thus, it is clear that changes brought about by ionizing-radiation-mutagenesis exhibit the same features as do transgene insertions*. The latter can result in deletions that range from 1 to 825 bp, along with larger duplications and insertions [36].

Naturally occurring DNA segments also get inserted into crop genomes. It is a feature of plant genomes that they are rife with DNA insertions of various types. Plant genomes are primarily composed of retrotransposons [37]. These are DNA elements that get transcribed into messenger RNA which gets reverse-transcribed into DNA copies which get inserted elsewhere in the genome. It can be inferred that retrotransposons are actively moving in crops, as their RNA appears in EST libraries. However, it is only now that genomic technologies are advancing to a point where genomes can be evaluated for active retrotransposition. Although the data are still very limited, an example has already been found in rice variety 'Nipponbare,' which contains a retrotransposon that still moves in the genome [38].

In addition, plant genomes have transposable elements. Unlike retrotransposons, transposable elements excise from the genome and reinsert themselves elsewhere in the genome, without going through an RNA intermediate. Transposable elements were first discovered in some experimental maize inbreds, but active elements were thought to be absent from varieties of maize and other crops used in agriculture. As detection methodologies have improved, and more transposable elements have been discovered, that view has changed. For example, active Ping elements and their derivatives have been found in 'Gimbozu,' a rice variety that is ancestral to many modern rice cultivars. The transposition rate in Gimbozu is 49–63 new insertions per plant per generation, a rate that is representative of what historically took place in farmers' fields. By contrast, the rate of new insertions in its derivative cultivar, 'Nipponbare,' is only about one new insertion per three plants per generation [39], perhaps because breeders have selected for greater phenotypic stability.

Over time, other types of DNA move between cell organelles as well. Lough *et al.* [40] used *in situ* hybridization to illustrate that mitochondrial sequences have inserted themselves into different chromosomes in different maize hybrids over time. Likewise, Huang *et al.* [41] developed transplastomic tobacco, with chloroplasts transgenic for a gene for kanamycin resistance, driven by a nuclear promoter. Thus, the frequency of transfer to the nucleus could be monitored by the presence of kanamycin-resistant progeny, which is 1 per 11,231 gametes. Huang *et al.* [42] had previously determined that the DNA fragments that move from the chloroplast to the nucleus range in size from 6 to 22 kb.

Biologically, the excisions of transposons and the integration of DNA segments all lead to double-stranded DNA breaks that must be repaired. For example, spontaneous 60–880-bp deletions in the waxy locus of maize acquired from 1 to 131 bp of filler DNA, with the filler sequences frequently being homologous to sequences near the deletion endpoint [43]. In all cases, the filler DNA is derived from the normal double-stranded break repair mechanisms of plants [44,45]. Therefore, the filler DNA that is added during the repair of spontaneous double-stranded DNA breaks is identical in origin to that which is found many times in the T-DNA/plant DNA junctions. Filler DNA, up to 51 bp in length, is homologous to sequences near the T-DNA border or the plant DNA border [46,47]. *In the end, the repair of double-stranded DNA breaks does not discriminate between inserts of DNA and movement of endogenous DNA elements* [48]. Such double-stranded DNA break repairs, and their associated deletions and additions of DNA, are so common that they may even contribute to changes in plant genome size [46,49].

To summarize up to this point, any changes other than insertions that take place at the DNA level are due to the same repair mechanisms that normally mediate DNA double-strand break repair, and thus are in no way unique to transgenic plants. Nevertheless, the fact remains that GE crops do have exogenous DNA, and this DNA is operating in a novel background. To properly evaluate the significance of a novel gene, it is first important to consider that there is a core set of about 13,300 genes necessary for angiosperms. From there, different genes are either amplified in copy number or created in different plant families as these evolve and adapt to their environments and growth habits [50].

The process of gene duplication and creation continues to this day. For example, glyphosate-resistant amaranth arose over the past decade. Resistant plants can have up to 160 more copies of the EPSPS enzyme gene compared to susceptible types, and these genes have moved to all its chromosomes [51]. Alternatively, retrotransposons can capture exons from other genes, and assemble them into novel combinations never before seen. For example, the *Wp* mutation in soybean appeared in Illinois in 1987. It was noticed because the seed were 22% larger and had 4% more protein, while the flower color changed to a very pale pink. The mutation is due to retrotransposon that inserted itself into one of the chalcone synthase genes. This particular retrotransposon has captured five exons from four different genes, and these are transcribed into a novel mRNA [52,53].

The above is an example of a retrogene. Of 898 retrogenes identified in rice, 55% appear to be functional, and about 35% are chimeric in nature, in that they have components from different genes in novel combinations [54]. *The point is that there is little difference, if any, between an entirely novel retrogene being created in a crop, or a transgene being inserted into it*. In contrast to a transgene, a retrogene is almost impossible to detect in the absence of advanced genomic technologies.

All these examples illustrate that DNA in crop plants is dynamic; it changes in response to human selection and other evolutionary forces, such that novel variability is created along the way. The realization that DNA is so changeable does not come as a surprise.

Previously, Rasmusson and Philips [55] realized that modern barley cultivars had more genetic variability than their ancestors, and surmised that new variation must have been created during the past century of breeding efforts. Likewise, McClintock had predicted that plant genomes were particularly prone to change during periods of stress [56]. However, these early visionaries lacked the necessary tools to test their hypotheses.

Today, a wealth of information is starting to come in from genomics projects, and it is becoming evident that, if anything, plant genomes are even more dynamic than originally envisioned. Maize, more than any other crop, has turned out to have more genetic variability than any other eukaryotic species that has been studied to date. A comparison between 'B73' and 'Mo17,' the two inbreds most commonly used to produce hybrids revealed several hundred examples of genes that are present in different numbers in the two inbreds, along with several thousand DNA sequences that are present in one inbred but not in the other, and which contain hundreds of genes [57]! A comparison between B73 and 'Palomero Toluqueño,' a Mexican landrace, revealed that the genome of the latter is 22% smaller than that of B73 [58]. These examples serve to illustrate the amount of variability that maize can tolerate and still be maize.

It is not surprising then, that gene expression profiles are consistent with the expectations derived from highly variable plant genomes, namely that the use of transgenics yields less variability than the use of other breeding technologies. Gene expression profiles from mutagenized rice plants showed more differences than transgenic plants did when each was compared to its parental variety [59]. The same results were obtained when expression profiles were compared for transgenic wheat and their conventionally bred, non-transgenic counterparts [60,61].

To summarize, the current model that is emerging depicts plant genomes as dynamic entities that respond to environmental stimuli. Under this model, change is the norm, not the exception. Thus, the assertion that the plant breeding process is not like the transformation process must also be considered a myth. The only difference between the two is the time scale.

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Benefits of genetically modified crops for the poor: household income, nutrition, and health

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The potential impacts of genetically modified (GM) crops on income, poverty and nutrition in developing countries continue to be the subject of public controversy. Here, a review of the evidence is given. As an example of a first-generation GM technology, the effects of insect-resistant Bt cotton are analysed. Bt cotton has already been adopted by millions of small-scale farmers, in India, China, and South Africa among others. On average, farmers benefit from insecticide savings, higher effective yields and sizeable income gains. Insights from India suggest that Bt cotton is employment generating and poverty reducing. As an example of a second-generation technology, the likely impacts of beta-carotene-rich Golden Rice are analysed from an *ex ante* perspective. Vitamin A deficiency is a serious nutritional problem, causing multiple adverse health outcomes. Simulations for India show that Golden Rice could reduce related health problems significantly, preventing up to 40,000 child deaths every year. These examples clearly demonstrate that GM crops can contribute to poverty reduction and food security in developing countries. To realise such social benefits on a larger scale requires more public support for research targeted to the poor, as well as more efficient regulatory and technology delivery systems.

Contents

Introduction

The global area under genetically modified (GM) crops grew from 1.7 million hectares in 1996 to 134 million hectares in 2009. Today, 14 million farmers worldwide grow GM crops in 25 countries, including 16 developing countries [1]. So far, most of the commercial applications involve herbicide tolerance and insect resistance, but other GM traits are in the research pipeline and are likely to be commercialised in the short-term to medium-term future. The rapid global spread of GM crops has been accompanied by an intense public debate. Supporters see great potential in the technology to raise agricultural productivity and reduce seasonal variations in food supply due to biotic and abiotic stresses. Against

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the background of increasing demand for agricultural products, natural resource scarcities and additional challenges posed by climate change, productivity increases are a necessary precondition for achieving long-term food security. Second-generation GM crops, such as crops with higher micronutrient contents, could also help reduce specific nutritional deficiencies among the poor. Furthermore, GM crops could contribute to rural income increases, which is particularly relevant for poverty reduction in developing countries. And finally, supporters argue that reductions in the use of chemical pesticides through GM crops could alleviate environmental and health problems associated with intensive agricultural production systems.

By contrast, biotechnology opponents emphasise the environmental and health risks associated with GM crops. Moreover, doubts have been raised with respect to the socioeconomic implications in developing countries. Some consider high-tech applications *per se* as inappropriate for smallholder farmers and disruptive for traditional cultivation systems. Also, it is feared that the dominance of multinational companies in biotechnology and the international proliferation of intellectual property rights (IPRs) would lead to the exploitation of agricultural producers. In this view, GM crops are rather counterproductive for food security and development.

Although public controversies continue, there is a growing body of literature providing empirical evidence on impacts of GM crops. This article reviews the pertinent literature, focusing especially on GM crop effects for poor agricultural producers and consumers in developing countries. Two concrete examples are chosen. The first example is insect-resistant *Bacillus thuringiensis* (Bt) cotton. Bt cotton is currently the first-generation GM technology with the widest distribution among smallholder farmers. Hence, solid data about the socioeconomic effects are available for different countries. The second example is Golden Rice. This is a second-generation GM technology that promises to reduce nutritional deficiencies and health problems among the poor through improving the vitamin A status of rice consumers. Golden Rice is not yet available in the market, so that related impact studies are *ex ante* in nature. Although Bt cotton and Golden Rice certainly do not cover the whole range of current and future GM crop applications, they can nonetheless provide some useful insights into the type of effects to be expected from the first-generation and second-generation technologies.

Impacts of Bt cotton

Bt cotton, which is resistant to different lepidopteran and coleopteran insect pests, was among the first GM crops to be commercialised in the mid-1990s. In the US, Bt cotton was commercially approved in 1995. One year later, cotton farmers in Australia started using the technology and in subsequent years it was commercialised in China, Mexico, Argentina, South Africa and India and to a limited extent also in Indonesia. Very recently, Burkina Faso has approved Bt cotton as the first low-income country in Sub-Saharan Africa. In 2009, Bt cotton was grown on 16 million hectares (ha), which is over 45% of the total worldwide cotton area. India is now the country with the biggest Bt cotton area (8.4 million ha in 2009), followed by China (3.7 million ha), and the US (2 million ha) [1]. Most of these areas are cultivated with Monsanto's Bollgard I technology, involving the Cry1Ac Bt gene, but Bollgard II – with stacked Cry1Ac and Cry2Ab genes and a broader spectrum of target pests – has also been released in several countries. In addition to the Monsanto technology, in China – and recently also in India – the public sector has developed and commercialised Bt cotton varieties. The widespread and rapid adoption of Bt cotton over the last 15 years suggests that farmers are satisfied with this technology from an economic point of view. Indeed, numerous studies that have been carried out in different countries confirm that the socioeconomic benefits are sizeable [2].

Profit gains in India

In India, over 5 million farmers have already adopted Bt cotton, which is now grown on almost 90% of the country's total cotton

TABLE 1

Crop enterprise budgets for Bt and conventional cotton in India.

	2002		2004		2006	
	Bt	Conventional	Bt	Conventional	Bt	Conventional
Number of insecticide sprays	4.2***	6.8	4.6***	7.2	3.3*	3.8
Insecticide use (kg/ha)	5.1***	10.3	5.2***	10.4	3.0*	3.8
Yield of raw cotton (kg/ha)	1,628***	1,213	1,836***	1,362	2,080***	1,458
Production cost (US$/ha)						
Seed	81.0***	25.2	83.6***	27.1	41.3***	24.7
Insecticides	64.8***	109.5	81.0***	124.2	60.4	58.6
Fertilizer	96.9***	85.4	96.9**	85.7	100.5	75.5
Labour	150.3***	116.0	178.1	151.2	236.9	209.4
Other cost	41.5	35.7	19.6	19.6	58.1**	34.5
Total cost (US$/ha)	434.5***	371.9	459.2***	407.8	497.2***	402.7
Revenue (US$/ha)	707.1***	533.2	712.5***	518.8	864.0***	617.9
Profit (US$/ha)	272.5***	161.3	253.3***	111.0	366.7***	215.2

Sources: [3,5].

* Mean values are significantly different from those on conventional plots at the 10% level.

** Mean values are significantly different from those on conventional plots at the 5% level.

*** Mean values are significantly different from those on conventional plots at the 1% level.

TABLE 2

Comparative advantage of Bt over conventional cotton in India.

	2002	2004	2006	Average
Insecticide use	−50%	−51%	−21%	−41%
Yield	+34%	+35%	+43%	+37%
Seed cost	+221%	+208%	+68%	+166%
Total cost	+17%	+11%	+24%	+17%
Gross revenue	+33%	+37%	+40%	+37%
Profit	+69%	+129%	+70%	+89%
Profit gain in US$/ha	+111$	+142$	+152$	+135$

Source: [5].

area. Most of the cotton farms are small-scale, especially in central and southern India. The average size of Bt-adopting farms is less than 5 ha, with an average cotton area of about 1.5 ha. Therefore, a closer look at the impacts in India is particularly interesting.

Table 1 shows cotton enterprise budgets in India with and without Bt technology for three growing seasons between 2002 and 2006. The data were collected from randomly sampled farms in four states and are representative of India's smallholder-dominated cotton production systems [3]. The results are summarised in Table 2. In all three seasons, the number of insecticide sprays and insecticide amounts used were significantly lower on Bt than on conventional plots. The exact reductions vary from year to year, which is partly due to seasonal variations in pest pressure. Moreover, owing to increasing adoption of Bt over time, target pest populations declined, so that even conventional cotton growers could reduce their insecticide sprays considerably in recent years. Average reductions in insecticide use through Bt technology were 41% over the three growing seasons. These reductions occur mostly in highly toxic chemicals, so that Bt cotton is also associated with significant benefits for the environment and farmers' health.

In addition to insecticide reductions, a major effect of Bt cotton in India is a sizeable yield advantage due to lower crop losses, as previously predicted by Qaim and Zilberman [4]. Over the years, average yields were 30–40% higher on Bt than on conventional plots, which is due to more effective pest control and thus a reduction in crop damage. Again, differences over the years are largely due to variability in pest pressure. Regression analyses confirm the gains in effective yields through Bt even after controlling for differences in input use and other factors [3,5]. Higher yields and crop revenues are also the main reasons for the significant gains in cotton profits, in spite of higher seed prices. Profit differences between Bt and conventional cotton even increased over time, which is partly due to seed price caps that state governments have introduced since 2006. Over the three seasons observed, mean profit gains were in a magnitude of 89%, or 135 US$ per ha. These are large benefits for cotton-producing households in India, many of whom live near or below the poverty line. Extrapolating these profit gains to the total area under Bt cotton in India (8.4 million ha) implies an additional 1.13 billion US$ per year in the hands of smallholder farmers.

In spite of this evidence, which is also confirmed in other studies [6,7], there are widespread public concerns that smallholder farmers would not benefit from Bt and that the technology would rather cause economic and social problems among the poor [8]. What the mean values discussed above (Tables 1 and 2) mask is that there was considerable impact variability in the early years of Bt cotton adoption. Especially in 2002, there were some farmers in certain regions who did not profit, due to insufficient information on how to use the technology successfully. Moreover, only a small number of Bt varieties were available, which were not suitable for all agroecological conditions [3,9]. These initial problems were overcome, however, as is reflected in the rapid and widespread aggregate adoption.

Income distribution and poverty in India

Beyond the direct effects on crop profits for adopting farmers, new technologies such as Bt cotton also entail indirect effects through backward and forward linkages to other markets. For instance, higher cotton yields through Bt provide more employment opportunities for agricultural labourers and a boost to rural transport and trading businesses. Income gains among farmers and farm workers entail higher demand for food and non-food items, inducing growth and household income increases also in other local sectors. Such indirect effects were positive and large for Green Revolution technologies in the 1970s and 1980s [10]. Related studies for GM crops have hardly been carried out. One exception is Bt cotton in India, for which wider rural development effects have been analyzed by Qaim *et al*. [11] and Subramanian and Qaim [12]. The results of this research are summarised in the following.

Using detailed census data from a typical cotton-growing village in central India and building on a social accounting matrix (SAM) multiplier model, the total income effects of Bt cotton were estimated. These effects not only incorporate the direct benefits for cotton farmers in terms of higher profits, but also include the indirect effects that occur in other markets and sectors. Overall, each ha of Bt cotton creates aggregate incomes that are 246 US$ higher than those of conventional cotton (Figure 1). For the total Bt cotton area in India, this translates into an annual rural income

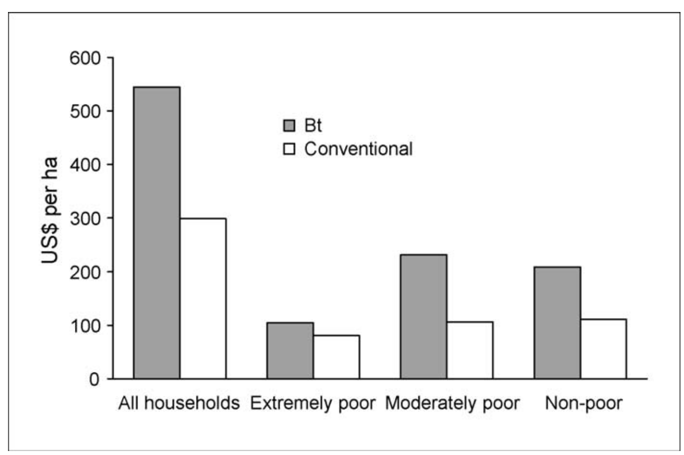

FIGURE 1

Income effects of Bt cotton in comparison to conventional cotton in rural India.

Note: The results shown include direct benefits among cotton farmers as well as indirect effects through backward and forward linkages with other rural markets and sectors. For the evaluation of income distribution effects, households were disaggregated using local poverty lines, which are very near to the World Bank's thresholds of 1 and 2 US$ a day (purchasing power parity) for extreme and moderate poverty, respectively. *Source*: [11].

gain of 2.07 billion US$. Considering that the direct profit gains for Bt cotton farmers are in a magnitude of 1.13 billion US$ (see previous subsection), it can be concluded that each dollar of direct benefits is associated with about 83 cents of additional indirect benefits in the local economy.

In terms of income distribution, all types of households benefit, including those below the poverty line (Figure 1). 60% of the gains accrue to the extremely and moderately poor. Bt cotton is also net employment generating, with interesting gender implications: compared to conventional cotton, Bt increases aggregate returns to labour by 42%, while the returns for hired female agricultural workers increase by 55%. This is largely due to additional labour employed for picking cotton, which is primarily a female activity in India [12]. As is known, women's income has a particularly positive effect for child nutrition and welfare [13].

These results on income distribution cannot be simply extrapolated to other regions and other GM technologies, as impacts always depend on the conditions in a particular setting. Nonetheless, the fact that a first-generation GM crop such as Bt cotton already contributes to poverty reduction and rural welfare growth has not been widely recognised up till now. Income gains among the rural poor can also have positive food security effects, as 50% of the worldwide hungry are smallholder farmers and another 20% are landless rural workers [14]. For these people, rising incomes mean better access to food, even when the income gain itself is due to a new technology in a non-food crop such as cotton. Needless to say, positive food security effects could be higher still when GM food crops – adapted to smallholder conditions – become available in the future.

Evidence from other countries

As mentioned above, Bt cotton has also been widely adopted in several other countries, for most of which studies on the direct impacts are available in the literature. Table 3 gives an international overview. Although the concrete effects vary, the overall trends observed in India – namely that the technology reduces insecticides, increases effective yields, and allows significant gains in cotton profits – are confirmed in the other countries as well. Strikingly, the gains are predominantly higher in developing countries than they are in the US or Australia. This is partly due to more pronounced yield effects of Bt as a result of higher uncontrolled crop losses among smallholder farmers in the tropics [4,15]. Moreover, Bt seeds are mostly cheaper in developing countries due to weaker IPR protection. An exception is Argentina, where Bt cotton is patented and seed prices are relatively high [16].

As in India, cotton is often also cultivated by small-scale farmers in other developing countries. Especially in China and South Africa, Bt cotton is often grown by farms with less than 3 ha of land. Several studies show that small-scale farmers benefit to a similar extent from Bt adoption as larger-scale producers. In some cases, the advantages for smallholders are even significantly greater [17,18]. However, distributional effects do depend not only on the characteristics of a technology, but also on the institutional setting at national and local levels. For instance, information, credit, and infrastructure constraints can hinder proper access of poor farmers to GM seeds, especially in countries where rural markets do not function well. Therefore, beyond introducing new technologies, policies that strengthen institutions and reduce market failures are required, to achieve pro-poor outcomes on a larger scale. This is particularly important when GM crops are commercialised in the least-developed countries.

TABLE 3

Effects of Bt cotton in different countries.

Country	Insecticide reduction (%)	Increase in effective yield (%)	Increase in profit (US$/ha)
Argentina	47	33	23
Australia	48	0	66
China	65	24	470
India	41	37	135
Mexico	77	9	295
South Africa	33	22	91
USA	36	10	58

Source: [2].

Expected impacts of Golden Rice

Golden Rice (GR), which has been genetically modified to produce β-carotene in the grain, has been proposed as a possible intervention to control vitamin A deficiency (VAD) [19,20]. VAD is a considerable public health problem in many developing countries: it affects 140 million pre-school children and 7 million pregnant women world wide. Of these, up to 3 million children die every year [21]. Apart from increasing child mortality, VAD can lead to visual problems, including blindness, and also increases the incidence of infectious diseases. The deficiency is most widespread in poverty households, where diets are dominated by staple foods with relatively low nutritional value. Food supplementation and industrial fortification programs can be effective in reducing VAD, but they often do not reach the target populations in rural areas [22]. Widespread consumption of Golden Rice promises to improve the situation in rice-eating populations. However, this technology is not yet available in the market, so that concrete outcomes can only be predicted. Golden Rice will probably be commercialised in selected Asian countries starting from 2012.

Nutrition and health benefits

Stein *et al*. [23] developed a methodology for comprehensive *ex ante* evaluation of Golden Rice, focusing on nutrition and health effects as well as on socioeconomic aspects. This methodology was used for an empirical study in India [24]. India is one of the target countries for Golden Rice, because mean levels of rice consumption are relatively high, and VAD is widespread. Of the 140 million pre-school children suffering from VAD worldwide, more than 35 million live in India [21].

Adverse health outcomes of VAD include increased mortality, night blindness, corneal scarring, blindness and measles among children, as well as night blindness among pregnant and lactating women. Stein *et al*. [24] calculated the disease burden associated with VAD-attributable fractions of these outcomes, building on a disability-adjusted life year (DALY) approach. The combined annual mortality and morbidity burden is expressed in terms of the number of DALYs lost. The present burden, calculated based on available health statistics, is the situation without Golden Rice.

In a next step, present β-carotene intakes from nationally representative food consumption data were derived and the likely shift in the intake distribution through future consumption of Golden Rice was established. This required assumptions which were based on experimental data and expert estimates about the technology's efficacy and future coverage. Higher β-carotene intakes will improve the vitamin A status of individuals, thus reducing the incidence of adverse health outcomes. These new incidence rates were derived and used to re-calculate the expected remaining burden with Golden Rice. The difference in the disease burden with and without Golden Rice is the expected impact of the technology expressed in terms of the number of DALYs saved.

According to these calculations, the current annual disease burden of VAD in India amounts to a loss of 2.3 million DALYs, of which 2.0 million is lost due to child mortality alone. In terms of incidence numbers, more than 70,000 Indian children under the age of six die each year due to VAD. In this context, widespread consumption of Golden Rice could reduce the burden of VAD by 59%, which includes the saving of almost 40,000 lives each year (Table 4). Because the severity of VAD is negatively correlated with income, the positive effects are most pronounced in the poorest income groups.

While these results suggest that Golden Rice alone is unlikely to eliminate the problems of VAD, the projected improvements in public health and nutrition are huge. Similar effects can also be expected in other rice-eating countries with a high prevalence of VAD. Beyond the reduction in health costs and individual suffering, nutritional improvements are associated with positive impacts on labour productivity. Anderson *et al*. [25] used a macroeconomic model to simulate the benefits of Golden Rice at the global level. Modelling consumer nutrition and health effects among the poor as an increase in the productivity of unskilled labourers, they estimated worldwide welfare gains of over 15 billion US$ per year, with most of the benefits accruing in Asia.

TABLE 4

Burden of vitamin A deficiency in India and potential impact of Golden Rice.

Current burden of vitamin A deficiency	
Number of DALYs lost each year (thousands)	2,328
Number of lives lost each year (thousands)	71.6
Potential impact of Golden Rice	
Number of DALYs saved each year (thousands)	1382
Reduction of the DALYs burden (%)	59.4
Number of lives saved each year (thousands)	39.7
Cost-effectiveness of Golden Rice and other vitamin A interventions	
Cost per DALY saved through Golden Rice (US$)	3.1
World Bank cost-effectiveness standard for DALYs saved (US$)	200
Cost per DALY saved through supplementation (US$)	134
Cost per DALY saved through industrial fortification (US$)	84

Note: The impact estimates reported here build on the 'high impact scenario' in [24]. Given recent evidence about the high efficacy of Golden Rice [27] the assumptions in that scenario appear realistic when the technology receives public support for social marketing efforts. *Source*: [24].

In China, for instance, Golden Rice is projected to entail a 2% growth in national income [25].

Cost-effectiveness

The high expected effectiveness of Golden Rice in reducing the problems of VAD was shown in the previous subsection. This certainly is a cause for optimism. However, from an economic perspective it needs to be asked at what cost a certain effect is achieved. The major costs of Golden Rice are the investments in research as well as in developing, testing and disseminating the GM technology. Dividing these costs by the number of DALYs saved, and taking into account the time when costs and benefits occur through discounting, results in the average cost per DALY saved, which is a common measure for the cost-effectiveness of health interventions. This was done by Stein *et al*. [24] in their analysis for Golden Rice in India. According to their projections, the cost per DALY saved through Golden Rice is in a magnitude of 3 US$ (Table 4), which is very low. A sensitivity analysis showed that, even with much more pessimistic assumptions, the cost would not rise to more than 20 US$ per DALY saved.

These results should be compared with suitable benchmarks. The World Bank classifies health interventions as very cost-effective when their cost is less than 200 US$. This underlines that Golden Rice could be extremely cost-effective. But how does Golden Rice compare with conventional vitamin A interventions? Scaling up food supplementation or industrial fortification programs for vitamin A in India would cost between 84 and 134 US$ per DALY saved (Table 4). The major cost of these conventional interventions is not to produce the vitamin pills or food fortificants, but to reach the target population in remote rural areas, which requires large investments and monitoring on a regular basis. This is different for Golden Rice: even though the initial investment is high, recurrent costs will be low, because Golden Rice seeds will spread through existing formal and informal distribution channels and can be reproduced by farmers themselves. Nonetheless, possible issues of consumer acceptance must be considered, and suitable strategies to convince farmers to adopt Golden Rice varieties have to be developed. A combination of β-carotene with interesting agronomic traits in rice might be a practicable avenue.

In spite of the high projected cost-effectiveness, Golden Rice should not be seen as a substitute for existing vitamin A interventions, but as a complementary strategy. No single approach will eliminate the problem of VAD and all interventions have their strengths and weaknesses in particular situations. While supplementation and industrial fortification might be more suitable for urban areas and feeding programs for well-defined target groups, Golden Rice is likely to achieve a wider coverage, for example in remote rural areas. It is only in the long run that poverty reduction and economic growth may be expected to contribute to dietary diversification, which might then reduce the urgency for more specific micronutrient interventions.

Conclusion

GM crops are not a magic bullet against all problems in developing countries, but they hold significant potential to contribute to poverty reduction, better nutrition and health, and sustainable development. Some of these potentials have already materialised. Yet it should be stressed that GM technologies can be very diverse,

so instead of talking about the impacts of GM crops in general, concrete statements have to be differentiated. For instance, the impacts of herbicide tolerance are different from the impacts of insect resistance or of nutritionally enhanced crops. Moreover, impacts depend on the agronomic and institutional conditions, such as pest pressure, intellectual property rights, and the functioning of seed and other rural markets.

This article has reviewed the outcomes of Bt cotton in different contexts, highlighting that this technology can be very suitable for smallholder farmers. In particular, the example from India showed that Bt cotton not only reduces insecticide use and increases yield, but also contributes to employment generation and income gains among the rural poor. Preliminary evidence suggests that similar effects are also likely for other Bt crops that are already available in some developing countries (like Bt maize and Bt rice) or may be commercialised soon (like Bt eggplant) [26]. The benefits of future GM crop applications, including those that involve tolerance against abiotic stress, could be much greater than the ones already observed [2].

As a promising second-generation GM technology, this article has analysed the expected impacts of Golden Rice, building on available *ex ante* research. It was shown that Golden Rice has the potential to reduce the burden of vitamin A deficiency substantially and at low average costs, even when accounting for sizeable outlays that might be necessary for future social marketing. Therefore, Golden Rice promises to be an effective, efficient and sustainable pro-poor nutrition intervention. Its inclusion into strategies that aim at the elimination of vitamin A deficiency in rice-eating populations should be promoted.

In spite of these encouraging examples, more public support is needed in biotechnology development, to ensure that other promising technologies for the poor are being developed, and in technology delivery, to ensure that they are widely accessible. In this respect, the negative public attitudes towards GM crops, especially in Europe, which are largely the result of biased information, are a fundamental obstacle. Not only do they limit public investments into GM crop research, but they also contribute to an overly complex regulatory framework. Some regulation is necessary to avoid risks, but over-regulation unnecessarily increases the cost of technologies, thus introducing a bias against small crops, small countries and small research organisations, which also implies a bias against the poor. This situation needs to be rectified through better and more science-based information flows.

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Review

Economic impacts of policies affecting crop biotechnology and trade

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Agricultural biotechnologies, and especially transgenic crops, have the potential to boost food security in developing countries by offering higher incomes for farmers and lower priced and better quality food for consumers. That potential is being heavily compromised, however, because the European Union and some other countries have implemented strict regulatory systems to govern their production and consumption of genetically modified (GM) food and feed crops, and to prevent imports of foods and feedstuffs that do not meet these strict standards. This paper analyses empirically the potential economic effects of adopting transgenic crops in Asia and Sub-Saharan Africa. It does so using a multi-country, multi-product model of the global economy. The results suggest the economic welfare gains from crop biotechnology adoption are potentially very large, and that those benefits are diminished only very slightly by the presence of the European Union's restriction on imports of GM foods. That is, if developing countries retain bans on GM crop production in an attempt to maintain access to EU markets for non-GM products, the loss to their food consumers as well as to farmers in those developing countries is huge relative to the slight loss that could be incurred from not retaining EU market access.

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Introduction

Up until the 19th century, the pace of improving the productive efficiency and quality of the world's food crops had been slow [1]. Then, following a century of wheat improvements [2], hybrid varieties dramatically increased average corn yields from the 1940s [3], and dwarf varieties of high-yielding wheat and rice caused what became known as the green revolution in Asia and elsewhere from the 1960s [4,5]. Those technological developments

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of the past six decades contributed to an acceleration of the long-term decline in real international food prices so that, by the late 1980s, they were below 1930s' levels,[1] which in turn led to complacency about the need for further agricultural research. As a result, growth in public funding for such research fell substantially in both rich and poor countries [6] – despite overwhelming evidence that this is a very high payoff investment area [7]. In particular, the aid agencies and foundations reduced their support for the Consultative Group on International Agricultural Research (CGIAR) and for complementary national agricultural research systems in developing countries – which quickly led to fears that food crop productivity growth would slow [8].

The emergence in the 1990s of new agricultural biotechnologies, and in particular transgenic crop varieties, seemed to offer new hope that the private sector might fill this lacuna. But to those early hopes were added three other concerns. One was that a small number of huge biotech firms would capture most of the gains from the new agricultural biotechnology. This ignores the fact that competition among those firms forces down the selling price of new seeds, and that farmers will only adopt the new technology if they perceive a net benefit to themselves.

A second concern was that those firms would not invest in poor countries where profits would be slim because of poor protection of intellectual property rights, the high cost of getting over national regulatory barriers, and small commercial seed markets [9]. In so far as these characteristics prevail, the solution lies in improving property rights, streamlining the regulatory processes and opening up the seed market to more competition.

The third concern was that Europeans and others would reject the technology because of environmental and food safety concerns, thereby thwarting export market prospects for adopters of the transgenic crops [10–12]. That third concern was vindicated by the European Union's imposition, in late 1998, of a *de facto* moratorium on the production and importation of food products that might contain genetically modified organisms (GMOs), which helped to constrain widespread adoption to just three GM food/feed crops (maize, soybean and canola) in three countries where production had already taken off by 1998, namely the United States, Argentina and Canada. Even when the other important GM crop is added (cotton), those three countries continue to dominate [13].

In May 2004 the European Union (EU) replaced its moratorium with new regulatory arrangements, but they involve such onerous and laborious segregation, identity preservation and labelling requirements as to be almost as restrictive of exports of GM products as was the moratorium. With several other countries also imposing strict labelling regulations on GM foods [14], and even private importing firms seeking GM-free foods [15], biotech firms are diverting more of their R&D investments away from food. At the same time, the public agricultural research system has been shy about investing heavily in this technology – including the CGIAR which depends heavily on rich-country grants from EU member states.

How are these events affecting food security in developing countries, where food security can be thought of as everyone having access to the minimum amount of basic food that is necessary for survival, that is, having the wherewithal to grow or to purchase a minimum basket of food? Transgenic crops can boost food security in either of two ways: by improving a farm household's net real earnings (including not only the implicit value of subsistence food production but also earnings from cash crops such as cotton), or by lowering the price or improving the quality of the food brought by a non-farm household. The real price of food in international markets would be lowered because of farm productivity growth in any trading countries that adopt the new technology, and that would reduce food prices in the domestic market of all countries that are at least somewhat open to trade.

What has been the impact on developing country welfare of the limited adoption of GM varieties so far and of the EU's reaction to that, and what would be the impacts of wider adoption of GM crops? This question is addressed in this paper by considering first-generation corn and oilseed GM crops, then the prospective adoption of 1st or 2nd generation (nutritionally enhanced) rice and wheat, and finally the adoption of GM cotton. This is done by drawing on empirical data and some simulation results from a multi-country, multi-product model of the global economy. The paper concludes with some policy implications that follow from the results of this analysis.

China and India are the most significant developing countries to consider, in the sense that they house the majority of the world's poor [16], they comprise almost one-third of the world's production and consumption of grain (and even more of cotton), and they (especially China) have the potential to rapidly apply and disseminate this new biotechnology. But Sub-Saharan Africa is also of crucial concern, given its extreme poverty and strong dependence still on agriculture for employment and export earnings and, in some cases, on food aid imports (which can be problematic if food provided as aid is not GM-free, as was the case for US shipments to southern Africa in 2002).

How has national welfare been affected to date in GM-adopting countries, in the EU, and in non-adopting developing countries?

To estimate the welfare consequences of policies affecting GM crop adoption, we have employed a model of the world economy known as GTAP (see [17]) and report several sets of simulation results.[2] We begin with GM adoption for just coarse grains and oilseeds but then add rice and wheat, and then cotton, to get a feel for the relative economic importance to different regions and the world as a whole of current versus prospective GM crop technologies. The impacts of GM food crop adoption by just the United States, Canada and Argentina are considered first, without and then with policy reactions by the EU. The simulation is then re-run with the EU added to the list of adopters, to explore the tradeoffs for the EU between productivity growth via GM adoption and the benefits of remaining GM-free given the prior move to adopt in the Americas. A change of heart in the EU would reduce the reticence of the rest of the world to adopt GM food crop varieties, so the effects of all other countries then adopting is explored as well.

Specifically, the base case in the GTAP model, which is calibrated to 1997 just before the EU moratorium being imposed, is compared with an alternative set of simulations whereby the

[1] The other key contributor was the post-war growth of agricultural protectionism in developed and newly industrialising countries [29,30].

[2] This section draws on results presented in [31], which in turn has been inspired by earlier global modelling analysts including [32–34].

TABLE 1

Estimated economic welfare effects of GM coarse grain and oilseed adoption by various countries (equivalent variation in income, 1997 US$ million per year)Source: [31].

	US, CAN and ARG adopt		All countries adopt	
	Without policy response	With EU moratorium	Without policy response	
	Sim 1a	Sim 1b	Sim 1c	EV as % of GDP (sim 1c)
Argentina	312	247	287	0.11
Canada	72	7	65	0.01
US	939	628	897	0.01
EU-15	267	−3145	595	0.01
Southern African Customs Union	3	7	9	0.01
Rest of Sub-Saharan Africa	−2	14	60	0.03
Rest of the world	700	1027	2204	0.02
World	2290	−1243	4047	0.013

effects of adoption of currently available GM varieties of maize, soybean and canola by the first adopters (Argentina, Canada and the US) is explored without and then with the EU *de facto* moratorium on GMOs in place.[3] Plausible assumptions about the farm productivity effects of these new varieties and the probable percentage of each crop area that converts to GM varieties are taken from the available literature including [18–20].[4]

The estimated national economic welfare effects of the first set of these shocks are summarized in Table 1. Assuming no adverse reaction by consumers or trade policy responses by governments, the first column shows that the adoption of GM varieties of coarse grains and oilseeds by the US, Canada and Argentina would have benefited the world by almost US$2.3 billion per year, of which $1.3 billion is reaped in the adopting countries while Asia and the EU enjoy most of the rest (through an improvement in their terms of trade, as net importers of those two sets of farm products). The only losers in that scenario are countries that export those or related competing products. Australia and New Zealand lose slightly (not shown in Table 1) because their exports of grass-fed livestock products are less competitive with now-cheaper grain-fed livestock products in GM-adopting countries. But so too do the non-SACU countries of Sub-Saharan Africa (SSA) as a group, although again only slightly. South Africa gains slightly as a net importer of coarse grains and oilseeds, while the net welfare effect on the rest of SADC is negligible.

Column 2 of Table 1 shows the effects when the EU's moratorium is taken into account. The gains to the adopting countries are one-third less, the EU loses instead of gains (not accounting for the value EU consumers place on being certain they are not consuming food containing GMOs), and the world as a whole would be worse off (by $1.2 billion per year, instead of better off by $2.3 billion, a difference of $3.5 billion) because the gains from the new technology would be more than offset by the massive increase in agricultural protectionism in the EU because of its import restrictions on those crops from GM-adopting American countries. For SSA other than SACU, however, welfare would be $46 million p.a. greater than in Sim 1b because in Sim 1c African farmers are able to sell into the EU with less competition from the Western Hemisphere. As a proportion of GDP, those economies gain three times as much as SACU (see final column of Table 1).

However, if by adopting the technology in the EU the rest of the world also became uninhibited about adopting GM varieties of these crops, global welfare would be increased by nearly twice as much as it would when just North America and Argentina adopt, and almost all of the extra global gains would be enjoyed by developing countries. If one believes the EU's policy stance is determining the rest of the world's reluctance to adopt GM varieties of these crops, then the cost of the EU's moratorium to people outside the EU15 has been up to $0.4 billion per year for the three GM-adopting countries (compare columns 2 and 3 of Table 1) and $1.1 billion per year for other developing countries.

Those estimates understate the global welfare cost of the EU's policy in at least four respects, however. First, the fact that the EU's stance has induced some other countries to also impose similar moratoria on GM food crops (if not cotton) has not been taken into account. Sri Lanka was perhaps the first developing country to ban the production and importation of GM foods. In 2001 China did the same (with some relaxation in 2002), having been denied access to the EU for some soy sauce exports because they might

[3] This has to be done in a slightly inflating way in that the GTAP model is not disaggregated below 'coarse grains' and 'oilseeds'. However, in the current adopting countries (Argentina, Canada and the US), maize, soybean and canola *are* the dominant coarse grains and oilseed crops.

[4] We assume 45% of US and Canadian coarse grain production is GM and, when they adopt, all Latin American countries and Australia are assumed to adopt GM coarse grains at two-thirds the level of the US while all other countries are assumed to adopt GM coarse grains at one-third the level of US adoption. For oilseeds, we assume that 75% of oilseed production in the US, Canada and Argentina (and Brazil when we allow it) is GM. Again Other Latin American countries and Australia are assumed to adopt at two-thirds the extent of the major adopters and the remaining regions adopt at one-third the extent of the major adopters. For the prospective rice scenarios, major assumed adopters, including the US, Canada, China, India, and all other Asian countries are assumed to produce 45% of their crop using GM varieties. All other regions adopt at two-thirds this rate. Prospective GM wheat adoption is assumed to occur to the same extent as coarse grain adoption for all regions. The GM varieties are assumed to enjoy higher total factor productivity than conventional varieties to the extent of 7.5% for coarse grains, 6% for oilseeds and 5% for wheat and rice. The simulations are able to estimate the equivalent variations in income, measured in 1997 US dollars, that would result from these assumed degrees of adoption and productivity growth for the GM potion of each crop and its consequence effect on markets.

TABLE 2

Estimated economic welfare effects of GM coarse grain, oilseed, rice and wheat adoption by various countries (equivalent variation in income, 1997 US$ million per year)Source: [31].

	US, CAN, ARG, CHN and IND adopt		All countries adopt	
	Without policy response	With EU moratorium	Without policy response	
	Sim 2a	Sim 2b	Sim 2c	EV as % of GDP (sim 2c)
Argentina	350	285	312	0.12
Canada	83	−23	63	0.01
US	1045	754	1041	0.01
China	841	833	899	0.25
India	669	654	669	0.14
EU-15	355	−4717	810	0.01
Southern African Customs Union	7	11	15	0.01
Rest of Sub-Saharan Africa	5	27	187	0.11
Rest of the world	964	1322	3509	0.03
World	4308	−892	7506	0.024

have been produced using GM soybeans imported by China from the US. Second, these are comparative static simulations that ignore that fact that GM food R&D is on-going and that investment in this area has been reduced considerably because of the EU's extreme policy stance as biotech firms redirect their investments towards pharmaceuticals and industrial crops instead of food crops. Third, the gains to the biotech firms that produce GM seeds are ignored in these results (and all subsequent simulations reported below). And fourth, the above results refer to GM adoption just of coarse grains and oilseeds. The world's other two major food crops are rice and wheat, for which GM varieties have been developed and are close to being ready for commercial release.

How might GM rice and wheat adoption affect developing countries?

The above numbers refer to adoption only of GM foodcrop varieties currently in production. If 1st generation (i.e. farm productivity enhancing) GM rice and wheat adoption also were to be allowed at the rates assumed in footnote 4 above, global welfare would be increased by nearly twice as much (compare bottom row of column 3 of Tables 1 and 2: $7.5 versus $4.0 billion), because the market for those two crops is even larger than for coarse grains and oilseeds. Again, though, SSA economies would gain little if they do not participate, with the benefit in terms of enhanced competitiveness from abstaining in the presence of the EU moratorium being very minor relative to the foregone productivity benefits from adopting the new technology. Comparing columns 2 and 3 of Table 2, these results suggest SSA would be better off by more than $130 million per year if the world were to embrace 1st generation GM technology for all four groups of foodcrops rather than for just coarse grains and oilseeds.

While 2nd generation (nutritionally enhanced) GM rice and wheat has not yet been commercialised, several varieties have been approved for field trials and environmental release in various parts of the world. An early study found that, even under conservative adoption and consumption assumptions, introducing Golden Rice in the Philippines could decrease the number of disability-adjusted life years (DALYs) lost because of Vitamin A deficiency by between 6 and 47% [21]. That is equivalent to an increase in unskilled labour productivity of up to 0.53%. On the basis of those findings, Anderson *et al.* [22] represent these health impacts with an assumed 0.5% improvement in unskilled labour productivity in all sectors of golden rice-adopting Asian developing economies. Given the low nutrition levels of poor workers in Africa, and the fact that if golden rice were to be adopted in Asia and Africa then nutritionally enhanced GM varieties of wheat and other foods would soon follow, we assume the productivity of unskilled labour would rise by 2% following adoption of 2nd generation GM crops. We also assume no direct impact on the productivity of skilled labourers, who are rich enough to already enjoy a nutritious diet.[5] And to continue to err on the conservative side, we assume 2nd generation GM crop varieties are no more productive in the use of factors and inputs than traditional varieties net of segregation and identity preservation costs, even though there is evidence to suggest they might indeed be input-saving.[6]

Table 3 suggests this 2nd generation GM technology could have a major impact on poor people's welfare: if it were to be adopted in SSA, for example, its estimated gain is 18 times as great as it would be if the GM varieties were just farm productivity enhancing (compare Sims 2c and 3a). And again, this startling result is independent of whether the EU maintains its current moratorium (compare Sims 3a and 3b). Needless to say, adopting these 2nd generation GM varieties in the developing countries of Asia would add far more, given the large population of rice and wheat consumers in Asia. Anderson *et al.* [22] show that even Golden Rice on its own could add $3.2 billion per year to developing country economic welfare.

[5] There would also be non-pecuniary benefits of people feeling healthier, and less expenditure on health care, but these too are ignored so as to continue to err on the conservative side.

[6] Bouis [35,36] and Welch [37] suggest nutritionally enhanced rice and wheat cultivars are more resistant to disease, their roots extend more deeply into the soil so they require less irrigation and are more drought resistant, they release chemical compounds that unbind trace elements in the soil and thus require less chemical inputs, and their seeds have higher survival rates.

TABLE 3

Estimated economic welfare effects of GM crop adoption with Sub-Saharan Africa's being 2nd generation, nutritionally enhanced rice and wheat (equivalent variation in income, 1997 US$ million per year)Source: [31].

	US, CAN, ARG, CHN, and IND adopt first-generation GM coarse grains, oilseeds, rice and wheat and SSA adopts 2nd generation rice and wheat	
	Without EU moratorium Sim 3a	With EU moratorium Sim 3b
Southern African Customs Union	1786	1789
Rest of Sub-Saharan Africa	1824	1846
All Sub-Saharan Africa	3610	3635

What difference can GM cotton make to developing country welfare?

The spread of GM cotton to developing countries is beginning to pick up speed. As of 2009, it accounted for one-eighth of the world's total area of GM crops, and GM varieties accounted for 49% of all land sown to cotton [13]. The United States and China account for much of that. The only other countries with high GM adoption rates as of 2004 were Australia and South Africa, both with slightly more than four-fifths of their cotton areas under GM varieties, but in barely half a decade India has gone from zero to five-sixths of its cotton crop being GM.

What impact has that adoption by those first four countries had on global welfare, and how much greater would be that impact if India is added and other producing countries were to promote widespread adoption of GM cotton varieties? To answer that question, results are drawn from global simulation modelling in Anderson *et al.* [23]. They suggest that world cotton output had hardly changed up to 2001. This is because the output gains in the first four GM-adopting countries were offset by output losses in the non-adopting countries, which were driven by the downward pressure on the average price of cotton in international markets (which fell by 2.5% as a result of this initial adoption, according to that study).[7] Globally, both value added by cotton farmers and the value of cotton exports were reduced by about 1% and by more than that in most non-adopting regions. The largest regional changes in value added in cotton production are in Sub-Saharan Africa, with a rise in South Africa of 3.5% and a fall in the rest of Sub-Saharan Africa of 4.4% by 2001. Among the GM cotton adopters, estimated value added in cotton production fell in both the United States and China, in part because of the decline in export prices. This is not to say individual farmers in those countries were irrational in adopting GM cotton, because had they not they would have still suffered from the product price fall, following adoption by other farmers, but would not have had a productivity improvement to partly offset it.

The net economic welfare effects of this initial adoption of GM cotton are summarized in Table 4. For all four adopting countries this was positive despite the loss because of their terms of trade deterioration, while welfare improved in all non-adopting regions but one. This is because they are net importers of cotton and so enjoy an improvement in their terms of trade and a greater flow of imports. The exceptional non-adopting region is Sub-Saharan Africa (excluding South Africa) which as a net exporter of cotton faces lower cotton export prices and also has resources move to sectors in which it had a lesser comparative advantage. Globally, annual economic welfare is estimated to have been enhanced by more than $0.7 billion from GM cotton adoption as of 2001, plus whatever net profits accrued to the biotech and seed firms (which are not explicitly modelled).

In the next scenario, in which all other countries then adopt GM cotton, cotton output in the early-adopting countries falls in response to the output expansion in newly adopting regions. If Sub-Saharan Africa continues to procrastinate, its cotton output, value added and exports would fall even further; but if it also were to embrace this technology, its cotton industry would expand more than any other region's and would more than make up its losses to 2001 from adoption by the first four adopters. Global welfare is boosted very much more with greater adoption by developing countries. Even without Sub-Saharan Africa adopting, it would jump to $2.0 billion per year. But adoption by Sub-Saharan Africa would raise that global benefit to $2.3 billion, with two-thirds of that extra $0.3 billion being enjoyed by Africa (more than offsetting its earlier loss because of adoption by others up to 2001), and the rest by cotton-importing regions. Asia's developing countries that are net importers of cotton gain even if they grow little or no cotton, not only because of greater imports but also because the international price of that crucial input into their textile industry would be lowered further, by an average of 4.1% when Sub-Saharan Africa also adopts, as compared with 2.5% from GM adoption by just the first four adopting countries. With complete catch-up as in this third scenario, the gains to Central Asia, Sub-Saharan Africa and South Asia are 10, 13 and 23 times greater than the global gains when expressed as a percentage of regional GDP (last column of Table 4). South Asia's are especially large because it is a large producer of both cotton and textiles.

Caveats

As with all CGE modelling results, the above are subject to several qualifications. One has to do with the way consumer preferences are handled. The estimated market and welfare effects vary with the elasticities of substitution assumed between GM and non-GM varieties of a product. Anderson *et al.* [24] examine this issue and show that this is unlikely to be an important issue because results do not vary much as those elasticities (which are set very low for Europe and Northeast Asia and at moderate levels elsewhere) are altered.

Of more importance is that we have no satisfactory way of valuing any loss of welfare for consumers who would like to avoid consuming foods containing GMOs but cannot if such foods are introduced into their marketplace without credible labelling. Since we have assumed that loss to be zero (following [25]), we are overstating the gains from adopting this technology to that extent. An alternative way to cope with this issue is to introduce a cost of segregation and identity preservation. We did that implicitly by choosing conservative cost savings because of the new technology, saying they were net of any fees charged for segregation and

[7] That estimated price fall would have been somewhat less had we also included GM corn and soybean adoption at the same time, since that would have reduced the extent of diversion of resources to cotton.

TABLE 4

Effects of GM cotton adoption on national economic welfare as of 2001 (equivalent variation in income, 2001 US$ million)Source: [23].

	4 countries adopt		All but SSA adopt		All including SSA adopt		
	TFP Shock (%)[a]	Welfare change ($m)	TFP Shock (%)	Welfare change ($m)	TFP Shock (%)	Welfare change ($m)	Welfare change (% of GDP)
Adopters as of 2001							
United States	−5	324	0	61	0	57	0.001
China	−2.5	162	2.5	113	2.5	100	0.009
Australia	−5	26	0	−14	0	−28	−0.008
South Africa	−5	2	0	5	0	12	0.010
Non-adopters as of 2001							
Other high-income countries	0	147	5	271	5	337	0.003
Eastern Europe and Central Asia	0	5	5	325	5	317	0.048
Southeast Asia (ex China)	0	36	5	31	5	63	0.009
South Asia	0	14	5[b]	964	5[b]	970	0.158
Middle East and North Africa	0	14	5	157	5	175	0.020
Sub-Saharan Africa (excluding S. Africa)	0	−17	0	−18	15	187	0.091
Latin America and Carib.	0	29	5	124	5	135	0.007
World		742		2018		2323	0.007

[a] By applying a negative TFP shock to cotton production we examine how the world would have been had that productivity gain from cotton GM adoption not taken place in these countries (but for comparative purposes we express the welfare results with the opposite signs).
[b] Except for India, where the TFP is 15%.

identity preservation. If such fees were a high share of the farm gate price, it would be unprofitable to market many GM varieties if that was a required condition of sale. But some suggest those costs could be miniscule – at least in developed economies – on the grounds that such segregation is increasingly being demanded by consumers of many conventional foods anyway (e.g. different grades or varieties or attributes of each crop) so the marginal cost of expanding such systems to handle GM-ness would not be great, at least in countries that have already shown a willingness to pay for product differentiation.

The version of the GTAP database used in the above modelling does not include tariff preferences enjoyed by Africans exporting to the EU. In so far as they enjoy preferences on the products considered above, then African exporters are currently receiving the domestic EU price minus trading costs (including the share of the tariff rent enjoyed by the importing firms). That price would be raised by the EU moratorium on GM products, but whether that rise would be greater or less than the rise in the international price of GM-free varieties sold to the EU under non-preferential conditions is unclear. In practice this issue is probably to be of minor importance though, for two reasons. One is that the EU's MFN tariffs on coarse grains and oilseeds are low and hence so is the margin of preference. The other is that many exporters find the rules of origin so complicated that it is cheaper for them just to pay the regular import duty rather than try to take advantage of tariff preferences.

In all these simulations we assume for simplicity that there are no negative environmental risks net of positive environmental benefits associated with producing GM crops, and that there is no discounting and/or loss of market access abroad for other food products because of what GM adoption does for a country's generic reputation as a producer of 'clean, green, safe food'. In fact some GM crops (e.g. cotton) will reduce not only negative environmental externalities but also farmers' health risks associated with spraying pesticides (see [26]).

It is difficult to know how close to the mark is our assumed boost to unskilled labour productivity following adoption of 2nd generation GM varieties (see [27]). But even if it is a gross exaggeration, discounting heavily the massive magnitude of the estimated welfare gain from adopting such varieties would still leave a large benefit – particularly bearing in mind that developing countries are being offered this technology at no cost by its private sector developers, and that we have included no valuation of the non-pecuniary gain in well-being for sufferers of malnutrition. The cost of adapting the off-the-shelf technology to local conditions in Africa might well be non-trivial, however, and might require a better-functioning agricultural research system than has operated in the past four decades (as evidenced by Africa's relatively poor take-up of the previous green revolution – see [4]).

Finally, and perhaps most importantly, the above comparative static modelling assumes 1st generation GM technology delivers just a one-off increase in total factor productivity for that portion of a crop's area planted to the GM varieties. But what is more probable is that, if/when the principle of GM crop production is accepted, there would be an increase in the *rate* of agricultural factor productivity growth into the future. Similarly, 2nd generation GM varieties with additional health attributes such as those associated with Golden Rice would be quicker in coming on stream the more countries embraced the technology. And biotech firms would be encouraged to invest more in non-food GM crop varieties too (adding to the success already achieved with GM cotton) if there was an embracing of currently developed GM crop varieties by Sub-Saharan African and other developing countries. Hence the present value of future returns from GM adoption might be many times the numbers shown above. For that reason, care is needed in interpreting cases where our results suggest that when rich countries introduce trade barriers against GM products, food-importing developing countries benefit. This is because our analysis does not take into account that moratoria have slowed the investment in agricultural biotechnology and so reduced future market and technological spillovers to developing countries from that prospective R&D.

Conclusions

From the above results it is clear that the new agricultural biotechnologies promise much to the countries willing to adopt GM

crop varieties. Moreover, the gains from farm-productivity enhancing GM varieties could be multiplied – perhaps many fold – if 2nd generation biofortified GM varieties such as Golden Rice were also to be embraced. The estimated gains to developing countries are only slightly lower if the EU's policies continue to effectively restrict imports of affected crop products from adopting countries. Importantly, developing countries would not gain if they imposed bans on GM crop imports even in the presence of policies restricting imports from GM-adopting countries: the consumer loss net of that protectionism boost to Asian and Sub-Saharan African farmers is far more than the small gain in terms of greater market access to the EU.[8]

The stakes in this issue are thus very high, with welfare gains that could alleviate poverty directly and substantially in those countries willing and able to adopt this new biotechnology. Developing countries need to assess whether they share the food safety and environmental concerns of Europeans regarding GMOs. If not, their citizens in general, and their poor in particular, have much to gain from adopting GM crop varieties – and those gains will increase as climate change proceeds and requires adaptation by farmers to changes in weather patterns and in particular to increased weather volatility and higher costs of water for irrigation. Unlike for North America and Argentina, who are heavily dependent on exports of maize and oilseeds, the welfare gains from GM crop adoption by Asian and Sub-Saharan African countries would not be greatly jeopardised by rich countries banning imports of those crop products from the adopting countries.

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[8] This is consistent with the finding [38] that African exports of food crops in general to the EU that might be affected adversely by GM adoption represent a very small share of the region's exports. See also [39].

Support for international agricultural research: current status and future challenges

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The success of the first Green Revolution in the form of abundant food supplies and low prices over the past two decades has diverted the world's attention from agriculture to other pressing issues. This has resulted in lower support for the agricultural research work primarily undertaken by the 15 research centers of the Consultative Group on International Agricultural Research (CGIAR). The total support in real dollars for most of the last three decades has been more or less flat although the number of centers increased from 4 to 15. However, since 2000, the funding situation has improved for the CGIAR centers, with almost all the increase coming from grants earmarked for specific research projects. Even for some centers such as the International Rice Research Institute (IRRI), the downward trend continued as late as 2006 with the budget in real dollars reaching the 1978 level of support.The recent food crisis has renewed the call for a second Green Revolution by revitalizing yield growth to feed the world in the face of growing population and a shrinking land base for agricultural use. The slowdown in yield growth because of decades of neglect in agricultural research and infrastructure development has been identified as the underlying reason for the recent food crisis. For the second Green Revolution to be successful, the CGIAR centers will have to play a complex role by expanding productivity in a sustainable manner with fewer resources. Thus, it is crucial to examine the current structure of support for the CGIAR centers and identify the challenges ahead in terms of source and end use of funds for the success of the second Green Revolution. The objective of this paper is to provide a historical perspective on the support to the CGIAR centers and to examine the current status of funding, in particular, the role of project-specific grants in rebuilding capacity of these centers. The paper will also discuss the nature of the support (unrestricted vs. project-specific grants) that will be needed for a much-desired second Green Revolution.

Contents

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Introduction

The beginning of organized, post-colonial international agricultural research programs can be traced back to the early 1940s when the Rockefeller Foundation collaborated with the Mexican government to increase the production of wheat, maize and beans. In the mid-1940s, Mexico imported nearly half of its wheat for consumption. Within a short span of ten years, the pilot program led by Dr. Norman Borlaug developed high-yielding semi-dwarf wheat varieties that enabled Mexico to achieve self-sufficiency. This marked the beginning of the so-called ''Green Revolution''. By 1963, 95% of Mexican wheat area was under the new semi-dwarf varieties, with yield six times higher than in 1944. Eventually, the Mexican wheat program grew into the International Maize and Wheat Improvement Center (CIMMYT) in 1963, with the support of the government of Mexico and the Rockefeller Foundation to extend this program to other countries.

Despite this rousing success in Mexico, most of Asia and Africa in the 1950s and 1960s faced acute food shortages and struggled to feed its rapidly expanding population because of frequent famine and drought. According to the FAOSTAT database, per capita grain production in Asia was 194 kg in 1961 compared with 868 kg for the U.S. This is reflected in the nutritional status of the population, with per capita calorie intake of 1891 kcal per day for Asia compared with 2882 kcal for the U.S. During this period, life expectancy in most Asian countries was less than 50 years and infant mortality was unbelievably high, at 125–150 deaths per 1000 births. The situation in Africa then was better than in Asia, where per capita calorie intake was 2089 kcal per day and infant mortality was 100–300 deaths per 1000 births.

Faced with an uncertain food situation, the Indian government invited Dr. Borlaug in the early 1960s to repeat the success with Mexican wheat. Soon after, the government introduced high-yielding wheat varieties in the northwestern state of Punjab with the help of Dr. Borlaug and the Ford Foundation. From India, Dr. Borlaug introduced semi-dwarf wheat varieties into Pakistan. Attempting to replicate the success of wheat in rice, the Ford and Rockefeller Foundations established the International Rice Research Institute (IRRI) in the Philippines in 1960 with the objective of developing high-yielding rice seeds for Asia.

The release of high-yielding semi-dwarf variety IR8 by IRRI in the late 1960s and the dissemination of high-yielding wheat varieties in India and Pakistan marked the beginning of the Green Revolution in Asia. This modern high-yielding variety was developed with the objective of increasing yield in response to applications of fertilizers, and reliable irrigation. By 1980, high-yielding wheat and rice varieties covered large area on the Indian subcontinent. Such rapid adoption was possible because of active support from the government in the form of guaranteed support prices, free irrigation, and heavily subsidized inputs.

The grand success of modern wheat and rice varieties in Latin America and Asia in the 1960s led to the creation of the CGIAR (Consultative Group on International Agricultural Research) in 1971 to coordinate and spread the benefits of agricultural research globally. The World Bank led the efforts to create the CGIAR with active sponsorship of the FAO (Food and Agriculture Organization) and UNDP (United Nations Development Program). Apart from IRRI and CIMMYT, the group also included two additional centers, established by the foundations in the 1960s, CIAT (International Center for Tropical Agriculture in Colombia) and IITA (International Institute of Tropical Agriculture in Nigeria). Over the years, the group expanded to include 11 additional centers to widen the scope of international agricultural research to cover other food crops, livestock, fish, water management, agroforestry, and policy research. The establishment of these centers led to the development of high-yielding varieties of sorghum, millet, maize, root crops, and pulses.

The Green Revolution and its impacts

Before the beginning of the Green Revolution in the late 1960s, Indian paddy yield was static at 1.5–1.6 tons per hectare. Since then, more than 1000 modern varieties have been released to farmers, resulting in a rapid increase in global rice production, with half of these varieties developed at IRRI and by its partners (IRRI 2004) [1]. By 1980, Indian paddy yield reached 2 t/ha (FAOSTAT) [2]. Yield increased further by another 30% to 2.6 t/ha by 1990. By 2000, paddy yield was hovering around 3 t/ha. Shorter duration of the high-yielding varieties also allowed farmers to harvest a second crop. For example, IR36, developed by crossing IR8 with other varieties, matured in 105 days compared with 130 days for IR8 and 170 days for traditional varieties.

With the expansion of both area and yield, Indian rice production during these three decades more than doubled from 60 million tons in 1970 to around 135 million tons in 2000 (FAOSTAT). The modern high-yielding rice varieties were also adopted across other Asian rice-producing countries in the 1970s. In the Philippines, rice production nearly doubled two decades after the introduction of IR8. The Green Revolution also had a similar impact in other Southeast Asian countries, with the doubling of paddy production from 63 million tons in 1970 to 126 million tons in 1994 (FAOSTAT). Indonesia changed from a food-deficit country in the 1960s to a food self-sufficient country in 1984. Similarly, Vietnam became a food-surplus country in the mid-1980s from being a food-deficit country in the 1960s.

The introduction of semi-dwarf varieties also increased South Asian wheat production, with Indian production rising from 12 million tons in 1965 to 66 million tons in 1995, more than a fivefold increase in three decades (FAOSTAT). Over the four decades, more than 3000 modern wheat varieties have been released to farmers to sustain the production growth that began in the early 1960s [3].

Overall, cereal production in Asia during the last four decades of the Green Revolution era increased from 385 million tons in 1965 to more than a billion ton in 2005 (FAOSTAT). This has been possible due to the rapid adoption of high-yielding varieties in developing countries from 20% for wheat and 30% for rice in 1970 to about 70% for both crops in 1990 (IFPRI, 2002). Even with more than doubling of the Asian population during this period, the increase in cereal production has been able to more than offset population growth, with *per capita* cereal production rising from 207 kg in 1965 to 275 kg in 2005. In line with rising cereal consumption, *per capita* calorie intake also increased by more than 40% from 1891 in 1960 to 2695 in 2003. Similarly, life expectancy and infant mortality also witnessed significant improvements during the post-Green Revolution era. The undernourished population also declined all across Asian regions with East and Southeast Asia witnessing the maximum drop from 43% in 1969–1971 to

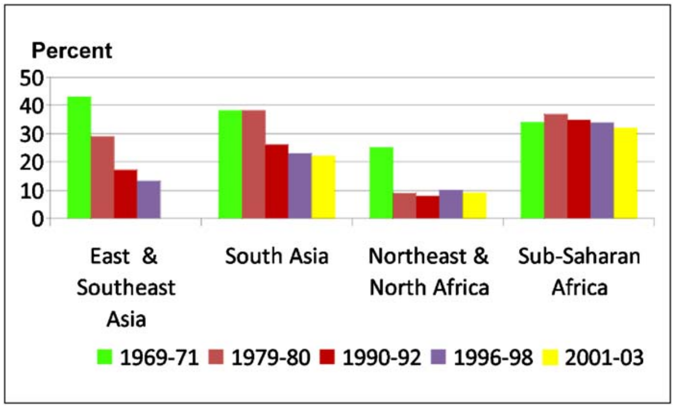

FIGURE 1

Percentage of people undernourished in developing regions.*Source*: Food and Agriculture Organization.

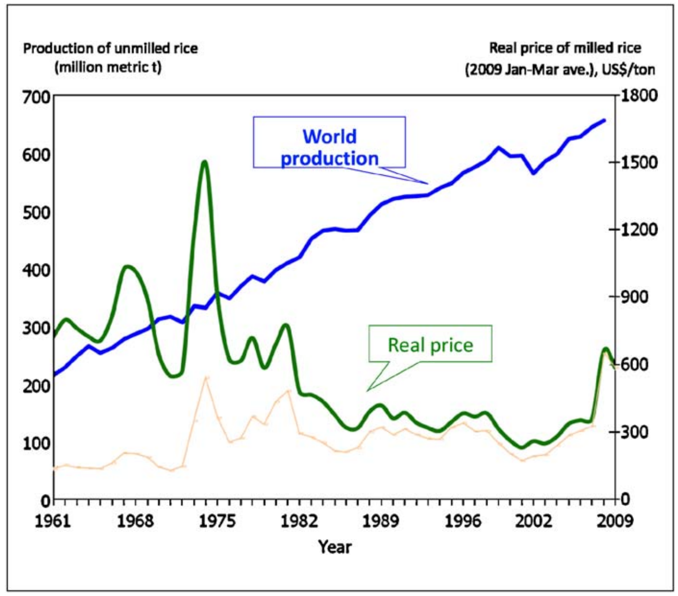

FIGURE 2

Trends in world rice production and price, 1961–2009.*Source*: Production: USDA, Mar 2009. Rice price: Relate to Thai rice 5%-broken deflated by G-5 MUV Index deflator (adjusted based on 28 January 2009 data update). Source of raw data: www.worldbank.org.

13% in 1996–1998 and South Asia from 38% to 23% during the same period (Fig. 1). Unlike Asia, sub-Saharan Africa during this period hardly witnessed any decline in undernourished population.

In a recent study conducted by the Special Project on Impact Assessment (SPIA) of the CGIAR's Technical Advisory Committee, the impact of the Green Revolution was estimated using the International Food Policy Research Institute's multi-market commodity model (IMPACT). The simulations suggested that crop yields in developing countries would have been 19.5–23% lower without the Green Revolution and crop prices would have been constant in real terms rather than a 40% decline between 1965 and 2000 [4]. Lower production would have resulted in higher crop prices, with 30–65% higher than the actual prices. Lower food consumption would have reduced *per capita* calorie intake by 13.3–14.4% and would have increased malnourished children by 6.1–7.9%. In addition, infant mortality would have been much higher in developing countries without the Green Revolution.

Contributions to overall economic growth

The increase in per capita cereal production resulted in a decline in cereal prices during the Green Revolution era. As shown in Fig. 2, a steady increase in *per capita* rice production in the 1970s, 1980s, and the first half of the 1990s resulted in a steady decline in real rice prices. A similar trend is seen for wheat and maize. During this period, lower food prices kept the wage rate low, contributing to faster overall growth of the Asian economy. The transformation of Asian countries from food deficit to self-sufficiency enabled them to use foreign exchange for infrastructure and other development activities rather than using it for food imports. Apart from the direct contribution to overall economic growth, agricultural development also played an important role in augmenting development in the rest of the economy [5,6].

A study by Hazell and Ramasamy [7] surveyed 11 villages in Tamil Nadu in the beginning of the Green Revolution and again in the early 1980s. The study concluded that every rupee generated in increased sales of agricultural output created 1.87 rupees of activities in the non-agricultural sector, with about half in demand for inputs, marketing, and processing of crops, and half in meeting consumer demand. In addition, growth in the agricultural sector during the Green Revolution has been instrumental in freeing millions from poverty over the past 40 years. The absolute numbers of poor people fell from 1.15 billion in 1975 to 825 million in 1995 despite a 60% increase in population, and most of the decline was attributable to agricultural growth and the corresponding decline in food prices [8]. The number of undernourished in Asian countries also declined significantly in the last four decades.

Not so good effects of the Green Revolution

Despite resounding success in expanding food production and improving the lives of billions of poor people, the Green Revolution has been criticized on several grounds. The first and foremost is the environmental and land degradation caused by the excessive use of fertilizers, pesticides, and irrigation water. This contributed to the pollution of groundwater and other waterways, weakened the natural protection system by killing beneficial insects and other wildlife, and affected the health of farmers [8]. The critics of the Green Revolution have also mentioned genetic erosion because of the wide-scale cultivation of fewer varieties of high-yielding crops.

Fertilizer use in Asian countries increased markedly in the last four decades. It is noteworthy to point out that IRRI survey data estimate Chinese per hectare NPK use on irrigated rice farms in China at 256 kg in 2004 compared with 173 kg in Vietnam, 167 kg in Indonesia, and 95 kg for India. Although 95 kg of NPK in India sounds low, the variations among Indian states are still very large. The problem is much more severe in the frontline Green Revolution states of Punjab and Haryana, where per hectare NPK use is 200 kg/ha compared with 50 kg/ha for Orissa and 10 kg/ha for Arunachal Pradesh, the states mostly left behind by the Green Revolution. Similarly, irrigation water use has also increased in many Asian countries, more notably in India, where water withdrawal for agriculture increased by more than 70% in the last three decades (Fig. 3). In a recent study published in *Nature*, Rodell *et al*. [9] concluded that

Review

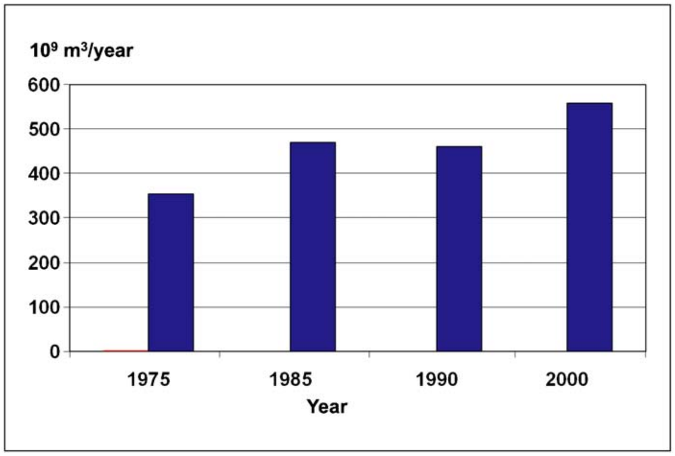

FIGURE 3

Indian agricultural water withdrawal.*Source*: FAO AQUASTAT database.

groundwater use for irrigation in northwestern India is not sustainable. According to this study, the water table over this part of India is declining by 4 cm per year.

On the socioeconomic front, it has also been argued that the Green Revolution catered to resource-abundant regions and left behind resource-scarce regions that needed the most support. Sub-Saharan Africa and eastern India are some of the regions where the Green Revolution did not have much impact although poverty density in these regions is probably one of the highest in the world. Paddy yield in eastern India and sub-Saharan Africa throughout the Green Revolution era from the 1960s to late 1980s was stagnant at around 1.5 t/ha (Fig. 4). Yield growth in eastern India revived in the last two decades with renewed attempts by the government to have a reliable supply of quality seeds, fertilizer, pesticide, plant protection equipment, and some improvement in irrigation. But the yield growth in sub-Saharan Africa remains extremely low even in recent decades. Over the years, many attempts have been made to introduce improved varieties but none has been very effective so far. Even NERICA rice, which was initially thought to be a miracle rice for Africa, is yet to have a significant impact 15 years after its development. The failure of the Green Revolution in resource-scarce regions has made some even go to the extent of pointing out that the Green Revolution was custom-made for wealthy farmers and widened the gap between rich and poor farmers by making the rich richer. However, these farmers were poor before the Green Revolution.

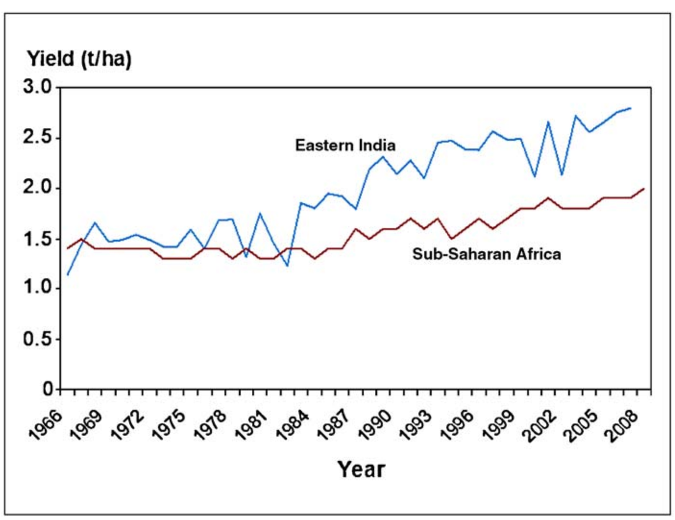

FIGURE 4

Paddy yields in sub-Saharan Africa and eastern India.*Source of basic data*: World Rice Statistics and USDA 2009.

Making the Green Revolution sustainable

After achieving much-needed food production growth by introducing high-yielding varieties, agricultural scientists have been working tirelessly to provide solutions to problems that have come to the forefront since the onset of the Green Revolution. Some examples are improved crop management practices such as integrated pest management (IPM), site-specific nutrient management, and water-saving irrigation technologies to sustain productivity growth. The focus has also shifted to improving productivity in unfavorable environments by developing stress-tolerant varieties.

The rice varieties developed for salt tolerance through collaborative research at IRRI and in other national rice research centers are already increasing the productivity of salt-affected areas. Similarly, the recent introduction of Sub1 or flood-tolerant modern varieties in India and Bangladesh, where around 7 million hectares of rice land are prone to flash flooding, allows the rice plant to survive up to 2 weeks under water. This is long enough to completely destroy traditional non-submergence-tolerant modern varieties. According to IRRI estimates, these Sub1 varieties have the potential to increase production by up to 4 million tons in India and Bangladesh. These varieties are being introduced in many Southeast Asian countries this year for field trials. In total, these Sub1 varieties can work as protection against flash flood for up to 2 weeks on 20 million hectares of flood-prone rice area in South and Southeast Asia.

In 2002, severe drought in rainfed rice-growing regions in India lowered rice production by 21 million tons, accounting for 80% of the world decline in rice production. IRRI recently developed the first drought-tolerant variety (IR74371-70-1-1) and a few other drought-tolerant varieties are in the pipeline at different stages of development and field trials. According to Dr. A. Kumar from IRRI, the recommended line maintains the same yield as that of current varieties in normal rainfall years and provides a yield advantage of 0.8–1.0 t/ha under severe drought stress. If successfully disseminated, the drought-tolerant varieties could have an even bigger impact on production than the submergence- or salt-tolerant varieties. Drought is also a major stumbling block in expanding maize production in Africa, a staple food for a majority of the people on that continent. On average, maize yield declines by at least 15% because of drought [10]. IITA, CIMMYT and various national partners have worked together over the years in developing drought-tolerant varieties for sub-Saharan Africa. More than 50 drought-tolerant maize varieties have been released for dissemination to the private sector and national partners and other non-government organizations in recent years. These varieties are expected to produce 20–50% more than other traditional varieties under drought.

Apart from expanding production in both favorable and unfavorable growing conditions, new research efforts are seeking to

improve the nutritional content of grain to alleviate micronutrient deficiency of millions of poor people around the world. Despite the documented success of the Green Revolution in expanding food production, malnutrition in many parts of the developing world (Fig. 2) remains unexpectedly high, especially in sub-Saharan Africa (SSA) and South Asia (SA). To alleviate malnutrition, scientists have developed vitamin A-rich rice called ''Golden Rice'' to help overcome vitamin A deficiency in 3 million children in developing countries. Golden Rice is a genetically modified variety of rice that contains beta-carotene, a vitamin A precursor. A recent study conducted by Tang *et al*. [11] found that four units of beta-carotene from Golden Rice contain 35 μg of beta-carotene per gm, which converts to one unit of vitamin A in humans. Scientists at IRRI are also working to develop rice with high iron and zinc concentrations. (See article by I. Potrykus, Lessons from the ''Humanitarian Golden Rice'' project, this volume.)

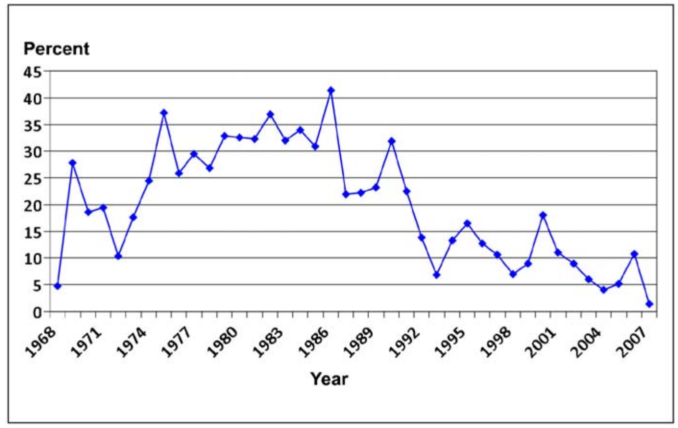

FIGURE 6

Share of agriculture in ADB's total lending.*Source*: ADB Annual Reports and other sources.

Declining support for agricultural research

The great early success of the Green Revolution in the form of abundant food supplies and low prices has also been its worst enemy in turning attention away from agriculture. This developed complacency among policy makers that the war against hunger had been won and this resulted in a diversion of resources from agriculture to other pressing needs in the last two decades. This is clearly evident from the spiralling downward of agricultural research and infrastructure development loans by international financial institutions such as the World Bank and Asian Development Bank (ADB). As Fig. 5 shows, World Bank lending for agriculture steadily declined to close to US$1 billion in 2008 since reaching its peak of $6 billion in 1987. A similar trend is evident in Asian Development Bank (ADB) lending for agriculture, whose share in total lending declined from more than 40% in 1986 to less than 2% in 2007 (Fig. 6). Both ADB and the World Bank have also reduced their lending for agricultural research in recent years. For example, the World Bank's lending for agricultural research declined from its peak of around $400 million in 1998 to less than $100 million in 2007 (Fig. 7).

The growth of investment in public-sector agricultural research and development also declined over time from 6% in the 1970s to 4% in the 1990s for Asia, from 10% to 2% in Latin America, and from 2% to 1% for Africa [12]. For developed countries, public-sector investment in agricultural research and development during the same period declined from slightly above 2% to negative growth in recent years.

The overall decline in support for agricultural research and development has also resulted in lower support for international agricultural research primarily undertaken by the 15 research centers of the CGIAR. Fig. 8 shows the trend in CGIAR funding over the last 50 years. After a steady increase in support for the CGIAR centers in the initial years, the total support in real dollars has been more or less flat for the remaining period although the number of centers increased from 4 to 15. Under this scenario, one would expect a significant decline in support at the center level and this is evident in the funding trend at IRRI (Fig. 9), where the total budget in real dollars declined from $63.7 million in 1993 to $28.7 million in 2006, a decline of more than 50%. A similar trend has been witnessed for most centers in the CGIAR system during the last two decades.

The impact of the decline in support of agricultural research and development has started to show up in a slowdown in productivity

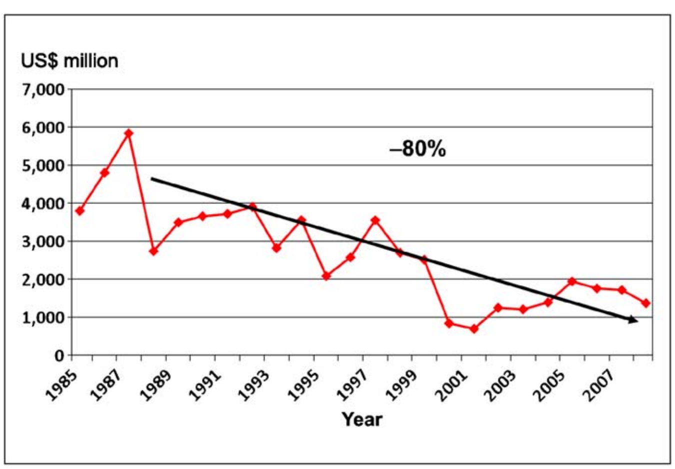

FIGURE 5

World Bank lending for agriculture.*Source*: World Bank Annual Reports and various other online sources.

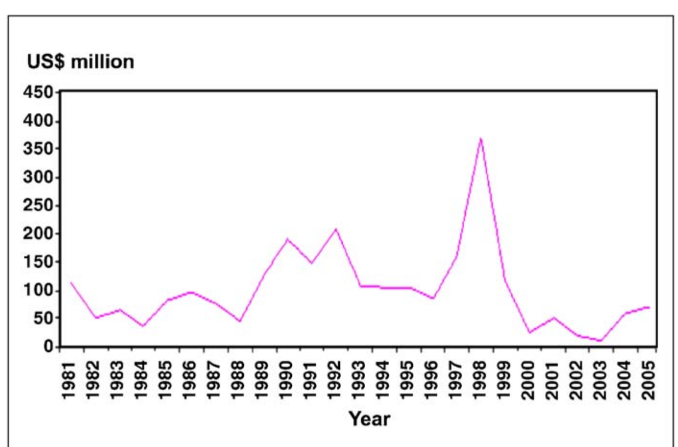

FIGURE 7

World Bank lending for agricultural research.*Source*: The World Bank.

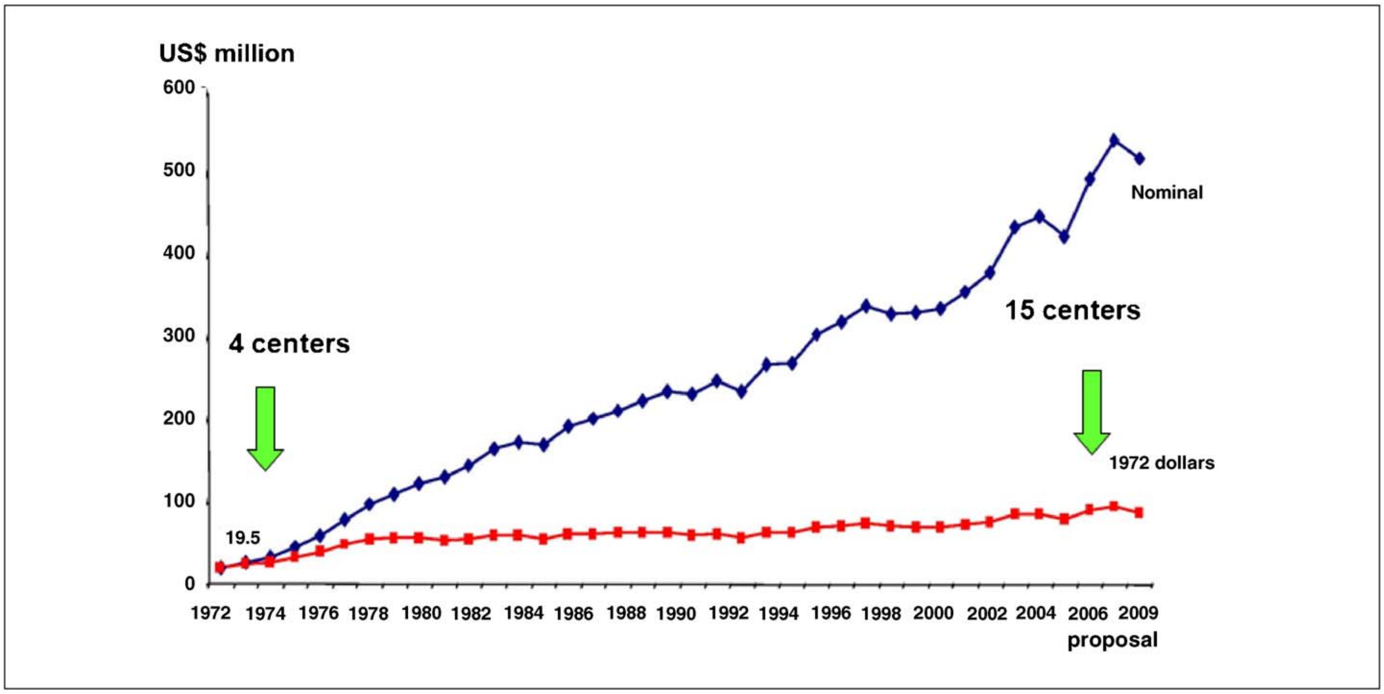

FIGURE 8

CGIAR funding trends in nominal and 1972 dollars. Consultative Group on International Agricultural Research

growth of cereal crops. Yield growth of the two major food crops (rice and wheat) declined to less than 1% in the recent years compared with more than 2% during the first two decades of the Green Revolution period. For maize, the decline in yield growth during the same period does not appear to be that drastic because of the adoption of genetically modified maize in most maize-growing countries, including the United States, Argentina and Brazil. Among the three grains, the slowdown in rice is the highest although production has been increasing at a higher rate because of additional rice area.

The slowdown in productivity growth combined with increasing demand arising out of economic development and population growth in developing countries and biofuel expansion in developed countries has resulted in a drawing down of cereal stocks in the recent years. In the last eight years, global stocks for rice, wheat and maize declined by around 40% from 546 million tons in 2000 to 331 million tons in 2008 [13]. For rice, the drawing down of stocks since 2001 to meet the deficit has resulted in a steady increase in rice prices during this period. From 2001 to 2007, rice prices nearly doubled primarily, because of supply-demand imbalances.

Thus, even before the recent rice price spike, the market was primed for such a mishap with stocks hovering around a level not witnessed in decades. Rising wheat prices due to drought in Australia, and the expansion of biofuel crops put pressure on rice, which led to trade restrictions in many rice-producing countries and unprecedented rises in prices. During a span of six months, from November 2007 to May 2008, rice prices nearly tripled in the international market. As expected, rice prices have declined after reaching an all-time high in May 2008 but they still remain high relative to a few years ago.

Global grain consumption remains strong, driven by both population and economic growth in many Asian and African countries. FAO projects that cereal demand will grow by 50% by 2050 (Fig. 10). Specifically for rice, Mohanty [14] estimates that rice consumption will grow by 60 million tons of milled rice or 90 million tons of rough rice by 2020. The study estimates that overall per capita rice consumption will decline slightly from 64 kg in 2007 to 63.2 kg in 2020, with declining per capita consumption in some countries (China, Thailand, South Korea, Japan, and Taiwan) more or less offset by rising per capita consumption in others. The projected future demand for cereals may even go higher than the projected level depending on the extent of ongoing economic downturns and the price of other food items (livestock products, fruits, and vegetables).

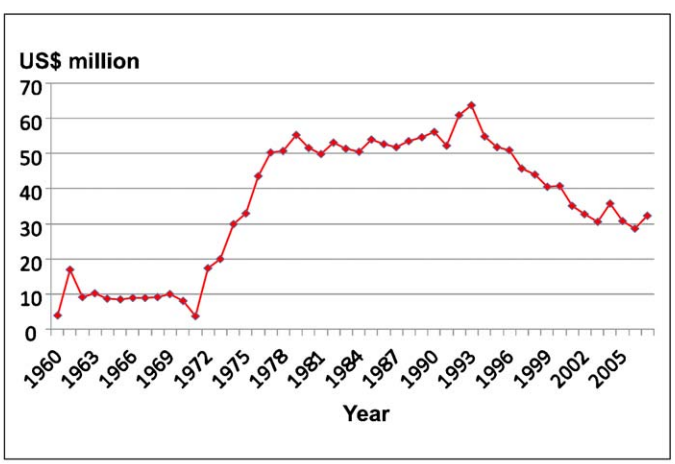

FIGURE 9

IRRI budget, 1960–2007 (US$2007).

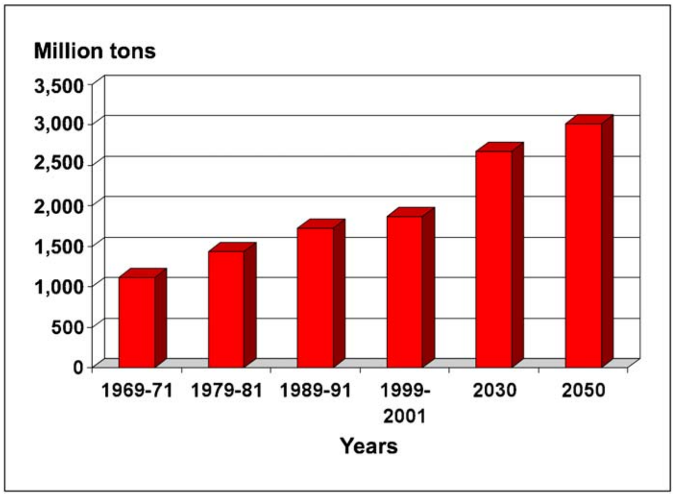

FIGURE 10

2050 world cereal demand projections.*Source*: Food and Agriculture Organization.

Although things have calmed down on the supply side because of record production in many rice- and wheat-growing countries, uncertainties are huge regarding the source of future growth in global grain production. This is particularly true for rice, for which the recent crisis has exposed the fundamental imbalance between supply and demand. Over the past 8 years, nearly half of the production increase has been attributed to area expansion rather than productivity growth [15]. Current rice area is at a historic high and yield growth has fallen below 1%. At the same time, global rice consumption has been rising at a healthy 1.55% annually. As indicated earlier, production growth of 1.2–1.5% will be needed in the medium term to keep rice affordable to millions of poor people [15].

Refocusing on agricultural research and development

Realizing the need for faster production growth, there has been a call from all quarters for a second Green Revolution. Nobody really questions the need to revitalize yield growth for achieving global food security; however, there are differences on how to go about achieving this objective in the face of several 21st-century constraints, including land and water scarcity, environmental degradation, and high input prices and higher incidence of extreme weather. Irrespective of how we go about achieving a second Green Revolution, the international agricultural research centers will have to play a pivotal role in making this a reality, that is, raising productivity with few resources and in a sustainable manner.

Successful realization of another Green Revolution definitely hinges on CGIAR research centers and how quickly they can retool themselves and develop products that can withstand climate change and protect the environment. A recent study by the International Food Policy Research Institute (IFPRI) estimates that rising temperature and increasing weather variability are likely to have their greatest effect in many parts of Asia. South Asia is estimated to bear the brunt of the impact as many areas become unsuitable for crop production and, without any intervention, the region is estimated to be a significant food-deficit region.

As already established by researchers from IFPRI and the University of Minnesota, there is a 10–15-year lag between agricultural research spending and its impact on productivity. What we witness now is an outcome of our action toward agriculture in the last two decades in neglecting agricultural research and development support. If we start reinvesting now, the effects are likely to be evident somewhere around 2025. Before it is too late, the world should start reinvesting in agricultural research and use all tools at its disposal, including using agricultural biotechnology to improve global food security.

However, the infrastructure and core scientific capacity of these centers have been eroded because of declining financial support. The financial situations in most international research centers have begun to reverse in the last few years, primarily through support from non-traditional donors. After years of downward spiralling of research support, these centers are beginning to regroup and rebuild their infrastructure and the scientific capacity they once possessed. But, it is important to realize that most of the increase in funding to these centers is special projects, known as ''restricted support'', and this is expected to be used for achieving objectives and milestones explicitly identified in the projects. This is very different from the early days when the centers were receiving funding without any strings attached, known as ''unrestricted support'', which was spent for achieving the institute's core research activities. In the case of IRRI, unrestricted support accounted for 50% of the total budget in 1997 compared with less than 20% today. Even in absolute terms, restricted support during this period has declined from $18.3 million in 1997 to less than $12 million in 2009. This is happening at a time when IRRI's total support has increased substantially from $36 to $60 million.

Things are definitely better now than a few years ago. The rise in restricted funding has definitely come at an opportune time to keep many international agricultural research centers afloat at least for the time being. But it is important to note that restricted funding may not produce products that have global applicability as is the case with unrestricted funding. In addition, it is becoming increasingly difficult for the centers to focus and implement their strategic plan when attention is diverted toward achieving success with special project grants. In response to the third ICRAF (International Center for Research in Agro-Forestry) External Program and Management Review report, the Science Council of the CGIAR in 2007 [16] advised that the center needed to learn to manage its restricted funding in a way that contributed to its strategic goals. In their recommendations, the Council advised the center to be selective in calling for support. In addition, the Council suggested a strict implementation of full cost recovery of sponsored projects. This is definitely something new for most centers because, during the days of unrestricted funding, special projects accounted for a very small share of total funding and had normally been subsidized. But, in the current environment in which sponsored projects account for the majority of funding, business as usual is no longer an option.

One can argue that the rise in restricted support also increases unrestricted funding through overhead charges and should support the activities for pursing strategic goals. But the truth is that overhead charges of the CG centers, which range from 10% to 20% vis-à-vis 40–50% in most U.S. universities, are not enough to cover all project-related costs, including fixed costs, incurred by a center. One option is to go the U.S. universities' route and raise the overhead to 50%. A second option is to keep the overhead as is

and put in place a system that can recover most of the project-related costs incurred by a center. It appears that donors are more receptive to the second option than the first one, in which they cannot tract 50% of the total funds up front.

Concluding remarks

International agricultural research has definitely played a key role in the last 50 years in expanding food production to offset the ever-expanding population growth in many food-deficit countries around the world. This has improved the nutritional intake of billions and has reduced child mortality and undernourishment of infants around the developing world. The benefits of a vibrant agricultural sector have also supported overall economic growth in many Asian countries over the years. The economic boom witnessed by developing Asia in the last two decades can be easily linked to cheap food during this period. But things are not the same anymore and negligence in this sector is reflected in the slowdown in productivity growth. The recent food crisis is an example of what the future will look like if we do not intervene and reinvest in agricultural research and development. Unlike the first Green Revolution, this will be much more complex because of our dwindling resource base, more severe environmental problems, and climate change.

In this complex world, CGIAR research centers will have to play a key role in making another Green Revolution a reality. Although support for these centers started to turn around in the last few years, the support now is quite different from what it used to be. For CGIAR centers to contribute effectively to a second Green Revolution, two things need to happen. First and foremost, the world should turn its attention to agriculture and support agricultural research and development. Second, the centers should focus on producing global public goods regardless of the restricted/unrestricted funding balance.

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Intellectual property, commercial needs and humanitarian benefits: must there be a conflict?

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'*By far the best proof is experience,*' wrote Francis Bacon. Given the experience of countries – both developing and developed – that have used intellectual property (IP), IP protection and IP management to stimulate innovation, there is ample proof that good IP management has benefited multitudes of people around the world with new technologies, products and services. Innovations in health and agriculture have greatly enriched lives. But does this experience apply to all countries? If the best proof is experience, then what can be said authoritatively about the effects of using IP systems wisely in developing countries?

Contents

Introduction: What is intellectual property (IP) in the context of international development?

First, IP (comprising essentially patents, copyright, trademarks, trade secrets, plant variety protection and geographic indications) is a tool to foster innovation. IP is here, and here to stay, because of its undisputable value as a business asset and an instrument to achieve humanitarian objectives. Because inventions can become property and can therefore be owned and sold, many individuals have been encouraged to invest in innovation, based on the profit potential from resulting technologies. But because IP protections by definition, or by design, exclude competitors and encourage higher pricing, they limit and, in some cases, can altogether prevent access by some individuals and populations. There are many ways, however, for IP to be distributed and utilised and put to work for the public interest. Hence IP should be neither feared, nor blindly embraced; rather, it should be managed to maximise the benefits of innovation for all of society, especially the poor.

Second, IP rights are a compromise and an imperfect solution, representing the search for balance between *public domain* and granting *ownership*. This balance encourages investment, and reinvestment, in innovation, although the innovation too infrequently is directed towards the needs of the poor. Fortunately, as numerous case studies have shown, the public sector can craft effective solutions that can approach or even achieve a suitable

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balance. This can be accomplished by the existing IP system, especially as it addresses situations in which companies agree to donate or otherwise share their IP.

Third, genius can flourish anywhere, and the emerging global systems of innovation in health and agriculture open up new prospects for innovation everywhere. This notion has profound implications for the management of innovation, technology transfer, market competition and economic development in every country. Irrespective of whether inventions are home grown or originate abroad, authoritative IP management will play a crucial role in enabling and preserving access to the resulting technologies.

Fourth, policies to promote the creation and management of IP by public sector institutions should give the first priority to advancing the mission of those institutions. Put differently, technology transfer should support the larger mission and not merely be seen as potential revenues.

Fifth, IP has historically benefited mostly the affluent. This is, in part, because insufficient attention has been paid by the public sector to managing IP. This lack of focused attention must be corrected. Fortunately, there is growing interest, within both the public and private sectors, in putting IP to work for public benefit, although concurrently, there is a lack of knowledge and capacity to use IP appropriately and responsibly.

This chapter is designed to present case studies in health and agriculture that demonstrate how these complex issues have been addressed successfully in practice. It is hoped that they will inspire and encourage others to take greater advantage of the unprecedented opportunity in strategically managing IP to benefit especially those who have been unable to benefit from technology. Seizing this opportunity will lead, in turn, to a healthier and more equitable world.

Experiences from around the world

Developing countries already have a vast amount of experience with IP protection, and this experience proves that they can use IP to their advantage. This chapter reviews how developed and developing countries alike are deploying and adapting IP management to meet their needs. Tapping into the dynamism of product development partnerships (PDPs) and utilising the potential of their universities, public sector institutions and private companies, many developing countries are quickly and creatively building on the experience of their own institutions, of neighbouring countries and of countries around the globe.

India's experience in the pharmaceutical sector during the past 50 years is described by Satyanarayana [1], demonstrating how the country has made great strides in science through a series of policy initiatives promoting high-quality research. But especially since 2005, when India became fully compliant with the agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), big changes have occurred. India's rigorous IP rights regime and professional IP management in both private sector companies and public sector research institutions are driving success. But this is only part of a larger coordinated attempt that includes increased public and private R&D expenditures, new policies governing traditional medicines, overhauled regulatory regimes for new drugs and biotechnologies, initiatives to emphasise and build on already competitive regions or technologies, and newly created governmental, research and educational institutions.

In the pharmaceutical sector, the effects of these policies can be seen in:

- a shift in the Indian pharmaceutical industry from an approach based solely on the low-cost manufacture of generic drugs to research-driven innovation of novel drugs for the global market,
- the emergence of an entrepreneurial biotechnology sector in India,
- the consideration by multinational pharmaceutical companies of investing in R&D and manufacturing operations in India.

In agriculture, these effects are apparent in a rich pipeline of innovations that promise to make India's agricultural sector more competitive and profitable. Besides a substantial allocation of funds for R&D by the government, two new initiatives were started in 2005: the National Agricultural Innovation Project (NAIP) and the Indo-U.S. Agricultural Knowledge Initiative (AKI). India's transition from a protected economy to an open, global economic power has prompted the government to take a series of steps to address the new challenges of globalisation, and the lessons it has learned apply broadly to many developing countries. Strengthening R&D, establishing policies to create and manage IP and fostering PDPs are all important steps for making important health products available for public distribution available in all countries.

Changing contenting, and according to Wolson [2] who writes from South Africa, technology transfer offices (TTOs) are a crucial part of IP management. But several problems challenge nascent TTOs there: a weak flow of invention disclosures, scepticism or a lack of awareness amongst faculty about the TTO's role, low levels of research funding, high patenting costs, few experienced technology transfer practitioners and unrealistic expectations about financial returns. Indeed, many there believe that the main motivation for undertaking technology transfer activities at a university is to generate income. Solutions to these problems are being addressed organisationally by the Southern African Research & Innovation Management Association (SARIMA), legislatively by the Framework for Intellectual Property Rights from Publicly Financed Research (the Framework) and financially through the Innovation Fund. Established in 2002, SARIMA is a stakeholder organisation providing a platform for those from government, academia and industry with an interest in using research and innovation management to foster networking and promote common interests. The Framework is intended to bridge the 'innovation chasm': the gap in South Africa between knowledge generators (in particular, universities and research institutions) and the market. It calls for a consistent approach to protecting IP developed with public financing and draws heavily on the U.S. Bayh-Dole Act. Of course, as other countries have discovered, the Bayh-Dole Act cannot simply be imported. Its principles must be adapted to local frameworks and needs. In South Africa, for example, research funding comes mostly from external sources and requires a different structure for determining the use and ownership of project IP.

TTOs in South Africa have already met with success. Some have been operating for several years and more are being launched. A vibrant stakeholder organisation provides a platform for networking and professional development in the field, and links have been forged that strengthen international research collaborations and technology transfer partnerships. All of this has government support.

For completeness, notable case studies from other countries are published about Brazil [3], Chile [4], China [5], the EU approach by Blaya [6] and Japan [7].

Public sector institutions and universities

Salicrup and Rohrbaugh [8] provide more evidence of the ability of for-profit and nonprofit institutions in developing countries to bring new products to market that meet critical regional public health needs. The authors discuss the technology transfer and licensing approach of the U.S. National Institutes of Health (NIH). The institution's technology transfer experience has shown that many combinations of licensing strategies can be used to segment the world market to meet each region's needs. Even when patent protection is unavailable, unique biological materials (for example, an essential component of a vaccine) can be licensed for commercial use.

Institutions in developing countries have been found to be dependable licensees and partners. With careful review, a capable institution with commercialisation capabilities may be found, and one should keep an open mind because, depending on the country, it may be a for-profit company, a nonprofit or government entity or a semi-privatised company. NIH has several examples of different strategies involving various types of institutions that have reached the early stages of the commercialisation process. Although discussions continue about IP capacity building in developing countries, some leading institutions are simply forging ahead and building their own capacity.

The State University of Campinas, or Unicamp, one of the leading research universities in Brazil, is an example [9]. A large university with a diversity of affiliated research institutes, Unicamp has moved up the patenting league tables in recent years to become the single largest patentor in Brazil. The university's current portfolio includes almost 50 granted and 400 filed patents. Unicamp emphasises chemistry, which accounts for close to half of its portfolio, and engineering, which accounts for a third. In addition, Unicamp conducts significant research in the life sciences (for example, a soy-based phytoestrogen for hormonal therapy licensed to a Brazilian pharmaceutical company).

These major advances in technology transfer at Unicamp are largely because of the efforts of its new TTO, *Inova Unicamp*, founded in 2003. *Inova* began its operations by assessing all of the technologies being researched in Unicamp's many laboratories and institutes. It then aggressively pursued new patent applications and licensing deals for the most promising technologies. In the short space of two and a half years, the office signed 128 technology transfer agreements with both private industry and government agencies. It also saw ten start-up companies in the university's business incubator become self-sustaining.

What lies behind these successes in Brazil? New public policy. In particular, the work of *Inova* is directly informed by two pieces of legislation. A 1996 law gave the university ownership rights to employee inventions. A 2004 law on innovation, however, gives the university the option to either hand over title to the employee inventors, or share 5–33% of any royalties with them. In addition, the government has instituted several sector-specific incentives to support innovation in Brazil, including tax deductions on royalty payments, R&D investments and foreign IP filing fees, as well as subsidies to firms to help pay scientists' salaries.

The 2004 innovation law requires all government universities and R&D institutions to open an IP management or a TTO. One major consequence of these policies will likely be increased patenting and licensing activities at universities throughout Brazil. Currently, Unicamp's rapid establishment of a functioning TTO stands as a sterling example for other institutions in Brazil to emulate. Other case studies that are noteworthy of public sector institutions include Arizona State University [10], Chinese Universities [11], the Donald Danforth Plant Science Center in the United States [12], the National Health Service in England [13], Stanford University's Office of Technology Licensing [14], the University of California System [15] and the University of California Agricultural Experiment Station [16].

Product development partnerships (PDPs)

Banerji and Pecoul [17] describe the Drugs for Neglected Diseases Initiative (DND*i*) that seeks to give patients in developing countries the opportunity to directly benefit from new products of drug R&D for diseases that lack a viable market. Only a tiny fraction (1.3%) of the drugs that came to market from 1975 to 2004 targeted tropical diseases (such as human African trypanosomiasis, Chagas' disease, leishmaniasis, helminthic infections, schistosomiasis, onchocerciasis, malaria and tuberculosis) that together make up 12% of the global disease burden and kill more than 35,000 people a day. The drugs that do exist are either inaccessible to patients or unbearably costly. DND*i* believes that drug research can exist in the public domain, and that patented products do not always benefit those who need them most.

As clearly articulated in its IP policy statement, DND*i* is committed to managing IP to pragmatically and effectively advance its mission of providing the most vulnerable populations in developing countries with equitable access to critically needed medicines. As the preamble of DND*i*'s IP policy states: the DND*i* IP approach will be pragmatic, and decisions regarding the possible acquisition of patents, ownership and licensing terms will be made on a case-by-case basis. DND*i* will put the needs of neglected patients first and will negotiate to obtain the best possible conditions for them. The DND*i*'s decisions regarding IP will contribute to ensuring access and encouraging further innovations.

DND*i* has led two successful campaigns to negotiate terms that allowed them to get important drugs to the world's neediest people at minimal cost. In the first case, DND*i* approached French pharmaceutical giant Sanofi-Aventis in 2003 to develop artesunate–amodiaquine, a fixed-dose combination therapy for chloroquine-resistant malaria. That negotiation process eventually led to a contract with very favorable terms for DND*i*; the drug was made available for production by generic manufacturers with no payment owing to either Sanofi-Aventis or DND*i*, and Sanofi-Aventis agreed to supply the drug at cost to the public sector, NGOs and international organisations. In the second case, DND*i* successfully collaborated with the University of California, San Francisco's (UCSF) business development office to support research leading to treatments for the lethal human African sleeping sickness. Whilst conventional wisdom holds that a university should always seek the largest possible return on research investment, DND*i* was able to convince university officials of the seriousness of its mission, and a compromise was reached that advances the effort to bring new treatments to persons suffering

from this deadly and largely neglected disease. In pursuing its humanitarian mission, DND*i* has learned that it is crucial to thoroughly familiarise all parties with the organisation's aims and guiding principles. By the end of contract negotiations with UCSF, for example, decision makers expressed great personal satisfaction at helping to advance DND*i*'s work. Through similar efforts DND*i* hopes to have developed and made available, by 2014, six to eight field-relevant treatments.

Boadi and Bokanga [18] describe the building of public–private partnerships (PDPs) in Africa by the African Agricultural Technology Foundation (AATF). AATF emerged from a Rockefeller Foundation initiative in the early 2000s following a wide-ranging and unprecedented consultation amongst African, European and North American stakeholders who were, and are, actively seeking to improve food security and reduce poverty in sub-Saharan Africa. AATF recognises that new and unique PDPs are needed to remove many of the barriers that have prevented smallholder farmers in sub-Saharan Africa from gaining access to existing agricultural technologies. Focusing on the creation of these PDPs, it promotes efforts to create sustainable markets and seeks to dramatically improve access to agricultural technologies, materials and know-how. AATF has two unique characteristics: first, it is prepared in license technologies from the private sector, which it then sublicenses to its partners. This is no small issue and requires careful considerations of a range of issues, including liability. Second, AATF strongly focuses on downstream activities or, to put it more broadly, on technology stewardship. This includes facilitating access to local, national and regional markets for products based on transferred technologies. The goals are to create more sustainable technology transfer mechanisms and to allow national institutions to more effectively absorb new technological concepts and adopt them for productive use.

But the fundamental raison d'être of AATF goes much deeper than 'merely' IP management. As Gordon Conway, then president of the Rockefeller Foundation, put it in the AATF annual report of 2005: *We should examine the current system and ask ourselves, 'How can those who care about the fate of the small-scale farmer make technological options more available?' The rise of a sophisticated global IP system covering many building block technologies has meant public researchers [in Africa] have little access to new ideas and tools in their field. Left to its own devices, the gap is likely to grow—with wealthy nations' farmers using techniques that are ever more sophisticated and poor farmers left with the same tools they have used for centuries*.

Other case studies sharing PDP experiences describe PATH [19] and ICIPE, a nonprofit institute that partnered with Africert Ltd. in transferring standards certification know-how, crucial for the introduction of new products [20].

Focus on solutions: accelerating product development and delivery

Numerous partnership efforts are underway to accelerate access and delivery for agricultural and health products in developing countries. For example, in the tropics, where just about everyone eats eggplant, it is commonly infested with eggplant fruit and shoot borer (EFSB), which inflicts a 70% crop loss. Conventional efforts to breed for resistance have been unsuccessful, so farmers rely heavily on pesticides. These chemicals, however, are expensive, and the pest is becoming more and more resistant to them. Moreover, some pesticides damage the environment and/or are illegal. Recently, a new solution to the problem of EFSB was developed in partnership with many organisations [21], including by MAHYCO, a private Indian company. It was the first company in India to develop a transgenic hybrid eggplant genetically engineered with a gene that provides resistance to EFSB. The gene (cry1Ac) is obtained from the bacterium *Bacillus thuringiensis* (Bt). A spore-forming bacterium, Bt produces crystal proteins (Cry proteins) that are toxic to many species of insects, including EFSB. Cultivation of the hybrid eggplant reduces the need for pesticide applications.

This breakthrough was made possible when MAHYCO obtained the rights under license for the use of the Bt cry1Ac gene technology for insect pest management from the Monsanto Company. The license also allows for sublicensing of the technology on a royalty-free basis to a partnership of public institutes and agricultural universities in India, Bangladesh and the Philippines. This consortium is developing a nonhybrid form of Bt eggplant for use by farmers in developing countries. The nonhybrid form will be less expensive, but the yield is higher for the hybrid technology. Therefore, more farmers might choose the hybrid technology.

Commercial release of the first transgenic Bt hybrids developed by MAHYCO is planned for India by the end of 2007, after the fulfilment of all regulatory requirements. The transgenic Bt open-pollinated varieties under development by the PDP are expected to be commercialised about six months later. This approach to EFSB is an excellent example of how biotechnology applications can be concurrently commercialised for the market and subsidised for poorer market segments.

In health, a prominent example of improvement regarding access to innovations in health is the PATH Malaria Vaccine Initiative (MVI), a programme funded by the Rockefeller Foundation that analysed whether consolidating patents in the malaria vaccine field could streamline access by advancing and accelerating the development of vaccines. The project was designed to ensure market access for the malaria vaccine candidates that are most likely to receive regulatory approval and be developed as products. The study assessed the status of the relevant patents, determined their availability for licensing and explored the potential of patent consolidation or technology trust to enhance access to the vaccine [22]. Developing a broad-based technology trust for existing malaria antigen patents was not recommended. Instead, several other steps were recommended for consolidating available rights and improving access with regard to future patent families.

Before this study, MVI had identified some potentially obstructive IP issues for a malaria vaccine for developing-country markets. Public and academic institutions – institutions with missions that in many cases include some form of public benefit – hold many of the patents related to malaria antigens. As the study's findings reveal, with few exceptions the patents held by public and academic institutions have been assigned or exclusively licensed to private companies and, therefore, are currently unavailable for licensing from the original public institution patent holders.

Although it may be possible to sublicense these malarial antigen patents from the current private holders of the technology, it is likely to be more difficult and costly; engaging the patent holders to contribute to a patent pool or clearinghouse also might be challenging. Moreover, a patent pool for a malaria vaccine might generate further obstacles: potential antitrust issues, real

or perceived, might trigger scrutiny by the U.S. Department of Justice and the Federal Trade Commission. Although the concept of a technology trust or patent pool may be useful for patents filed in the future, even some of those would be under option for license by the private companies holding the current patents. Finally, the number of high-priority cases for any malaria antigen is small, as is the number of entities likely to seek access to any given patent family. This makes the expense of a patent pool even less justifiable. Taking all of these things into consideration means fewer missteps and faster progress towards a vaccine for malaria.

Other notable accounts of important case studies relate to the Cohen–Boyer patents at Stanford University [23], IP issues related to molecular pharming, specifically for plant-derived vaccines [24], corn/maize breeding and the impact of biotechnology on the breeding and commercialisation process [25], the University of California's Strawberry Licensing Program being the most successful programme in terms of the generation of licensing revenues of any U.S. university [26], the successful resolution of IP constraints that led to the introduction of virus resistant papayas [27] and a project on the somatic embryogenesis of grapes in Chile [28].

Conclusions

If indeed the best proof is experience, then the case studies described here indeed speak for themselves. The experiences represented by these case studies provide all the evidence needed to spur further efforts to build upon the IP strengths of developing countries. Many forward-thinking people have seen the possibilities, and this section broadly maps out work that is already underway around the globe to make these possibilities into realities. Such experiences offer the most powerful proof of the benefits that can be obtained through creative IP management in developing countries and indeed around the world.

Acknowledgement

Portions of this chapter draw heavily from Krattiger *et al.* [29] which is a summary of Krattiger *et al.* [30].

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Review

The private sector's role in public sector genetically engineered crop projects

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There is widespread interest within academia to work on public good genetically engineered (GE) projects to the benefit of the poor, especially to use GE-technology to contribute to food security. Not a single product from this work has reached the market. The major cause is GE-regulation, which prevents use of the technology for public good beyond proof-of-concept (Potrykus, I. (2010) *Lessons from the Humanitarian Golden Rice project: Regulation prevents development of public good GE-products* (these Proceedings)). There is, however, another key problem responsible for the lack of deployment of public good GE-plants: the public sector is incompetent and disinterested for work beyond proof-of-concept, and has neither capability nor funding to develop GE-plant products and introduce them to growers and consumers. The private sector has the expertise for both and in the right circumstances can be ready to support the public sector in public good enterprises. Public–private-partnerships are the best solution so far, to advance exploitation of GE-technology to the benefit of the poor. Public–private-partnerships are viable, however, only, if there is mutual interest from the private sector and initiative and funding from the public sector.

Contents

Background

The following observations are exclusively based on our experience with our public good project on 'Golden Rice' [1,2]. The conclusions are, however, probably applicable to all public sector GE-projects with an altruistic objective. As the private sector has an important role to play, it is appropriate to present at least one case study of a successful public–private-partnership, to illustrate the key role of the private sector for public good projects, of which neither the public nor the media are aware.

Golden Rice represents an almost unique case in as far as it is the only public good project from the public sector, which has been advanced beyond the proof-of-concept phase, across all hurdles from intellectual property (IP) rights, to product development and GE-regulation, and to a state close to deployment [2]. There is only one precedent of deployment of a public sector GE-product, which is the case of the virus-resistant Papaya [3]. This case is, however, not comparable, because it passed the regulatory hurdles before extreme precautionary regulation was established to block all public good GE-plant deployment.

The Golden Rice project was initiated in 1990 in response to the wish of rice breeders of the International Rice Research Institute

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(IRRI), Philippines, to produce vitamin A-rice (yellow rice), because of the severe problems of vitamin A-malnutrition in rice-dependent poor populations. Because there was no chance to reach this goal with traditional breeding techniques, it became a challenge for genetic engineering technology. Together with my colleague Dr (now Prof.) Peter Beyer, from the University of Freiburg, Germany, the author was motivated to take up this challenge and to use genetic engineering technology, in a public good project, to the benefit of the vitamin A-deficient and rice-dependent poor in developing countries. The author knows of many scientists around the globe which work in the arena of GE-plants with similar motivations.

The task of engineering the biochemical pathway for pro-vitamin A into rice endosperm was (correctly) considered almost impossible by the scientific community at the time. Thanks to longer term funding from public sources and philanthropic foundations, the complementary expertise of our two teams, and good fortune, proof-of-concept results were established in Spring 1999. They were presented to the public on the day of the author's retirement, 31st March 1999, and published, with some delay, in Summer 2000 [4].

Proof-of-concept and publication are normally the endpoints of the engagement of public sector scientists, although much of their work is financed with the argument that it will contribute to the solution of humanitarian problems. However, practical problems are not solved by proof-of-concept and publication. Solutions require subsequent product development, regulatory approval and product deployment for use, tasks generally not considered appropriate for an academic environment and readily left to 'someone else'. For public good GE-plant product development and deregulation there is, however, no one else to take over. The private sector must recover its investment from commercial products. International organisations with a mandate for food security or micro-nutrient malnutrition (e.g. WHO, FAO and UNIDO) stay away from GE-projects.

As we were determined to ensure an impact from our work, we had to develop it ourselves. When proof-of-concept was established, this was also the end of any financial support from the public sector. Financial support in academia is for scientific novelty. There was (and is) no mechanism in the public domain for support in either product development or deregulation, for the simple fact that no scientific novelty can be expected. Fortunately, visionary organisations (The Rockefeller Foundation and USAID) supported some initial work, but all this would not have rescued the transition into the product development phase and the extension into the deregulation phase, as not only were funds a problem, but expertise was absent. The public sector International Rice Research Institute (IRRI), Philippines, volunteered to take responsibility for variety development. But IRRI had no experience with GM-product development and was initially as naive as the inventors in this respect. In that situation 'Golden Rice' was very much in danger of remaining an academic exercise – unless something unusual would happen. The unusual approach we finally took was to search for support for the humanitarian project in the private sector.

How the private sector rescued the public good project

During the ten-year phase of proof-of-concept work, IP rights did not play a restrictive role. On the contrary, patenting enables inventors to publish their discoveries, which in turn enables the scientific community to use this information, which otherwise would remain secret. Appreciating this aspect of patents, we applied for patents on our invention of Golden Rice.

However, this free situation for basic research changes dramatically, when working towards practical application. As common for academic scientists, we had no idea which and how many patented inventions we had been using in the course of our work. A study commissioned by the Rockefeller Foundation revealed that more than 70 patents were involved in Golden Rice [4]. As our concept was to provide Golden Rice to subsistence farmers free of charge, this meant that we would need free licences for those 70 patents. Such a complex problem was beyond the capacity of public scientists and their institutions.

Peter Beyer and I realised that we needed professional help to address this problem. At the time we thought that this was the only problem standing between our invention and our vision of adoption of Golden Rice to contribute to Vitamin A Deficiency alleviation. We decided to approach the private sector for assistance, and entered into discussions with a relevant company, but were finding the attitude of the individual we were dealing with less than helpful.

Shortly after this realisation occurred, Zeneca's head of licensing, Dr Dubock[1] approached us with an interest in commercial rights to our invention. (Zeneca has since 2001 been merged as part of Syngenta, and is so referenced henceforward.) We explained our perceived problem with IP. Dr Dubock realised that we had no commercial interests and understood fully our interest in humanitarian applications. Dr Dubock proposed and negotiated with us a contractual basis for our collaboration. His vision complemented ours, was consistent with Syngenta's needs, and became the basis for a fruitful public–private-partnership which laid the foundations for the progress with our humanitarian project. *Without that public–private-partnership, Golden Rice would probably have remained a scientific curiosity*.

We licensed our rights in our invention to Syngenta which added further technologies and obligations (including donating technology improvements to us) and licensed them back to us for carefully and precisely defined humanitarian applications, including the defined right to sublicense further for the same defined humanitarian purpose. Syngenta retained the commercial exploitation rights.

One of the first tasks of Syngenta was to address the perceived problem of IP for the humanitarian project. The initially worrying analysis had considered only the situation in the USA; it turned out, almost irrelevant to our developing country targets. Thanks to the support from Syngenta's patent lawyers (which reduced the 70 general IPs to a handful of patents which may be important), the bargaining skills of our partner Dr Dubock and the good will of private sector patent holders, this problem was solved within less than half a year. We learned that there is good will in the private sector to grant free licences for public good projects, as long as this does not compete with commercial plans, does not lead to liability problems and the relationships are clearly defined in written form. *Without the cooperation of the private sector we would, probably not have been able to resolve the IP mass and the project would have ended at this stage*.

[1] Dr Adrian Dubock, has fortunately remained strongly associated with the project to this day, even after his retirement from Syngenta.

Dr Dubock proposed how we could develop a network of licensed public sector institutional collaborators (the Golden Rice Network) in countries where vitamin A deficiency (VAD) was a problem, and proposed and helped us set up a novel governance and strategy body, the Golden Rice Humanitarian Board (see http://www.goldenrice.org) providing multidisciplinary expertise, and taking all the strategic decisions which has guided Golden Rice close to its delivery to the target population. As a result of the mutual obligations and rights so created, and the collaborative structures put in place, Syngenta and the inventors had from then on access to all the missing knowhow and in-kind support for product development and deregulation for 'the humanitarian project'. *Without the advice and the experience of the private sector there would be no defined collaborative structure nor Humanitarian Board for the strategic guidance of the project*.

A scientific breakthrough is a necessary first step for a product. Application to the benefit of the poor, however, requires many more to follow. In the area of GE-plants, the public sector is totally unprepared, naïve and incompetent for any further step along those lines. In the philosophical world view of academia, there is no room for any support along those lines, neither with regard to financial support, nor with regard to recognition, motivation, publication or any other reward for scientists motivated to step out of the ivory tower.

The Golden Rice project was rescued because the private sector invested its know-how, its personnel and its laboratory facilities to advance the development of transgenic events along the lines of established regulatory requirements. It also invested hundreds of experiments into the search for events producing so much pro-vitamin A that half a cup full of Golden Rice a day would protect from malnutrition. All this was, of course, not done to advance the humanitarian project, but to promote a commercial project. However, according to the license terms offered by Syngenta and accepted by us, improvements made by Syngenta were to be licensed to the Humanitarian Golden Rice project. When the commercial project was abandoned as being too small, Syngenta donated all their materials and the rights to use their related data to the Humanitarian project. They were even persuaded by Dr Dubock to spend a further $1.0m+ after the commercial project was terminated to bring the research to 'donatable form' and to pay for the first field trials in the USA in 2004. Again, we learned that the private sector could be far more generous than expected if it did not have to concern itself with liability problems and there was no other conflict with its commercial strategies. *Without the contribution from the private sector it would have been difficult to arrive at a product with the present high level of expression*.

Once agronomically optimised Golden Rice varieties are registered for use and authorised for distribution to farmers, this is not yet the end of the story. Effective intervention requires careful preparation of nationally adjusted social marketing for which prior marketing research for a humanitarian project has to be organised. This again is a very complex field of activities requiring a different set of expertises, and into which the project is entering just now to have everything necessary ready, as soon as the varieties have been registered for use and seed material has been multiplied (best done again by the private sector) for distribution. Members from academia, who have not developed and registered a product, nor been involved with product launch for use, have not the slightest idea of how small the academic contribution is to the solution of a practical problem. *Without the advice and the experience of the private sector there would be no marketing research and social marketing and the putative success for Golden Rice would be totally unpredictable*.

These were only a few examples from the history of the Humanitarian Golden Rice project, which demonstrate how much a public sector project, despite the best intentions, might have failed, had not the private sector and visionary funders supported it throughout. Public good projects fall, beyond any doubt, within the responsibility of the public sector. In the case of Golden Rice the public sector completely failed to honour its responsibility. And it turned out that the public sector was totally incompetent for such a task anyway. Without support and expertise from the private sector this altruistic project would probably have failed. If the public sector sometime, hopefully, decides to honour its responsibility for public good GE-projects, the best it can do is to aim at public–private-partnerships, with a clear definition of the respective interests. There is lot of room for clearly defined, mutually respectful partnership, where commercial competition is not a problem – and where liability problems for the private sector can be avoided.

Fortunately there is progress with regard to the public sectors capacity for GMO product development and deregulation. To develop a GMO product, guide it through the regulatory hurdles, and deliver it as seed to the needy require expertise in numerous areas of which members of academia have not the slightest idea. The Golden Rice Network [1] involves numerous scientists in public sector rice institutions in developing countries such as The Philippines, India, Bangladesh, Vietnam, Indonesia and China which play an important role in breeding the Golden Rice trait into locally preferred rice varieties. The International Rice Research Institute (IRRI), Philippines [5], has taken a lead within the CGIAR system [6] and has, with recruitment from the private sector and funding from USAID and subsequently the Rockefeller Foundation, built the capacity to handle GE-variety development, interaction with regulatory authorities, as well as supporting the planning for social marketing, and IP management – again exploiting the capacity and experience of the private sector. We gratefully acknowledge that IRRI now has taken the lead, under the legally defined strategic guidance of the Golden Rice Humanitarian Board – in which key IRRI staff participate – to complete the task. IRRI could teach other CGIAR institutes how to manage GE events beyond the proof-of-concept phase. It should, however, not be overlooked that this is not typical public sector activity. It is dependent on philanthropy and one government – the US – which appreciates the potential of GE crops for development. There is no support from the donor countries of the CGIAR system (mostly European countries) for any GE-related activity – except for superfluous 'biosafety research' (see respective contributions in these proceedings). On the contrary, there is impressive and generous support from these donor countries for anti-GE activities (see A Apel, these proceedings).

Acknowledgement

The author is grateful to Dr A. Dubock for editing the language of this manuscript.

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Review

Ethical arguments relevant to the use of GM crops

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The Nuffield Council on Bioethics (NCOB) has published two reports (1999 and 2004) on the social and ethical issues involved in the use of genetically modified crops. This presentation summarises their core ethical arguments. Five sets of ethical concerns have been raised about GM crops: potential harm to human health; potential damage to the environment; negative impact on traditional farming practice; excessive corporate dominance; and the 'unnaturalness' of the technology. The NCOB examined these claims in the light of the principle of general human welfare, the maintenance of human rights and the principle of justice. It concluded in relation to the issue of 'unnaturalness' that GM modification did not differ to such an extent from conventional breeding that it is in itself morally objectionable. In making an assessment of possible costs, benefits and risks, it was necessary to proceed on a case-by-case basis. However, the potential to bring about significant benefits in developing countries (improved nutrition, enhanced pest resistance, increased yields and new products) meant that there was an ethical obligation to explore these potential benefits responsibly, to contribute to the reduction of poverty, and improve food security and profitable agriculture in developing countries. NCOB held that these conclusions were consistent with any practical precautionary approach. In particular, in applying a precautionary approach the risks associated with the *status quo* need to be considered, as well as any risks inherent in the technology. These ethical requirements have implications for the governance of the technology, in particular mechanisms for enabling small-scale farmers to express their preferences for traits selected by plant breeders and mechanisms for the diffusion of risk-based evaluations.

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Introduction

The Nuffield Council on Bioethics is an independent body established by the Nuffield Foundation and co-funded by the Wellcome Trust and the UK's Medical Research Council. Its terms of reference are:

1. To identify and define ethical questions raised by recent advances in biological and medical research to respond to, and to anticipate, public concern;
2. To make arrangements for examining and reporting on such questions with a view to promoting public understanding and discussion; this may lead, where needed, to the formulation of new guidelines by the appropriate regulatory or other body;
3. In the light of the outcome of its work, to publish reports; and to make representations, as the Council may judge appropriately.

Within these terms of reference, the Council determines its own priorities and topics. In 1999 it published its first report on GM crops, *Genetically Modified Crops: the Ethical and Social Issues* [1]. In 2004 it published a follow-up report, *The Use of Genetically Modified Crops in Developing Countries* [2]. The present paper summarises the relevant arguments from those two reports, noting developments since 2004. Two main conclusions were asserted in both reports. Firstly, policy towards GM crops should rest on a case-by-case analysis, with no general presumption in favour or against. Instead of general assertion, what was required was a sober assessment of the benefits and risks of particular applications against the feasible alternatives. This principle carries several implications, including those related to administrative capacity in developing countries. The second main conclusion was that where there were grounds for a responsible use of GM crops, there was a moral imperative for making such crops readily and economically available to those in developing countries who wanted them. If benefits were available, it would be contrary to the principles of justice and solidarity for those benefits to be hoarded to the detriment of the poor.

In what follows I shall set out the considerations that led the Council to come to these conclusions. The main consideration leading to the view that there was a moral imperative to make modern plant technology available to those in developing countries was that poverty and food insecurity called for action and there was no reason to deny developing countries the benefits of a valuable technology. Obviously this argument depends on denying what some have asserted, namely that there are strong ethical or prudential reasons for resisting the introduction of GM crops. The principal arguments involved in these latter claims relate to naturalness, the risks associated with GM and the justice of property rights. All of the ethical issues have implications for governance.

The moral imperative

The potential benefits of GM crops will be well known to this audience, so I shall simply list the ones that the working party thought were most important. They included:

1. Herbicide tolerance, enabling reduced applications of herbicides.
2. Insect and pest resistance.
3. Bacterial, fungal and viral resistance.
4. Abiotic stress resistance.
5. Micronutrient enrichment.

How might these benefits be especially relevant to developing countries? The relevant argument runs as follows. In the developed world, food production has kept ahead of population growth during the past 60 years. This was also the case for much of Asia and Latin America where the benefits of the Green Revolution were felt. However, Africa and some parts of Asia saw little gain in agricultural productivity, and poverty persisted. Moreover, the initial rates of improvement of the Green Revolution were not sustained between 1985 and 1990. Even in countries like India, where there are ample stores of staple foods, poverty still causes problems of access for large numbers. Moreover, given that 70% of the world's poor live in rural areas and two-thirds of those rely upon agriculture, there is a strong case for focusing upon agricultural development, particularly as improvements in agricultural productivity contribute to the creation of employment, thus raising incomes.

The above argument can be succinctly summarised in Fig. 1. As can be seen, the central thrust of the argument related to the need to raise agricultural productivity as a way of improving food supply and increasing agricultural incomes. However, there are specific potential applications of GM technology, of which the most important is the provision of micronutrient enrichment, that were also an integral part of the working party's thinking.

The argument assumes that GM technology is beneficial and that there is a moral imperative to enable developing countries to take advantage of these technologies. Although not expressed in the same words, the message of both reports is consistent (I believe) with the Social Doctrine of the Catholic Church when it asserts that:

> ***'Modern biotechnologies have powerful social, economic and political impact locally, nationally and internationally. They need to be evaluated according to the ethical criteria that must always guide human activities and relations in the social, economic and political spheres. Above all the criteria of justice and solidarity must be taken into account.' [3]***

There are several points to make about the argument developed by the Nuffield Council.

1. The argument assumes that there is a need to raise agricultural productivity to deal with the problems of poverty and food insecurity. It may be true that there are enough foodstuffs in the world such that if they were more equally distributed existing production levels would be sufficient to feed everyone. However, this would require a politics of redistribution on a global scale that would dwarf any politics of redistribution even in advanced welfare states. As the 2004 Report put it, '[g]iven the limits of redistribution, we consider that there is duty to explore the possible contributions which GM crops can make in relation to reducing world hunger, malnutrition, unemployment and poverty.'
2. It is *not* part of the argument that the only way in which the problems are to be addressed is by the use of technology in general or GM technology in particular. The important point is that a potentially valuable technology should not be ignored. The moral imperative relates to the circumstances in which the technology is valuable, but there is no assumption that GM is

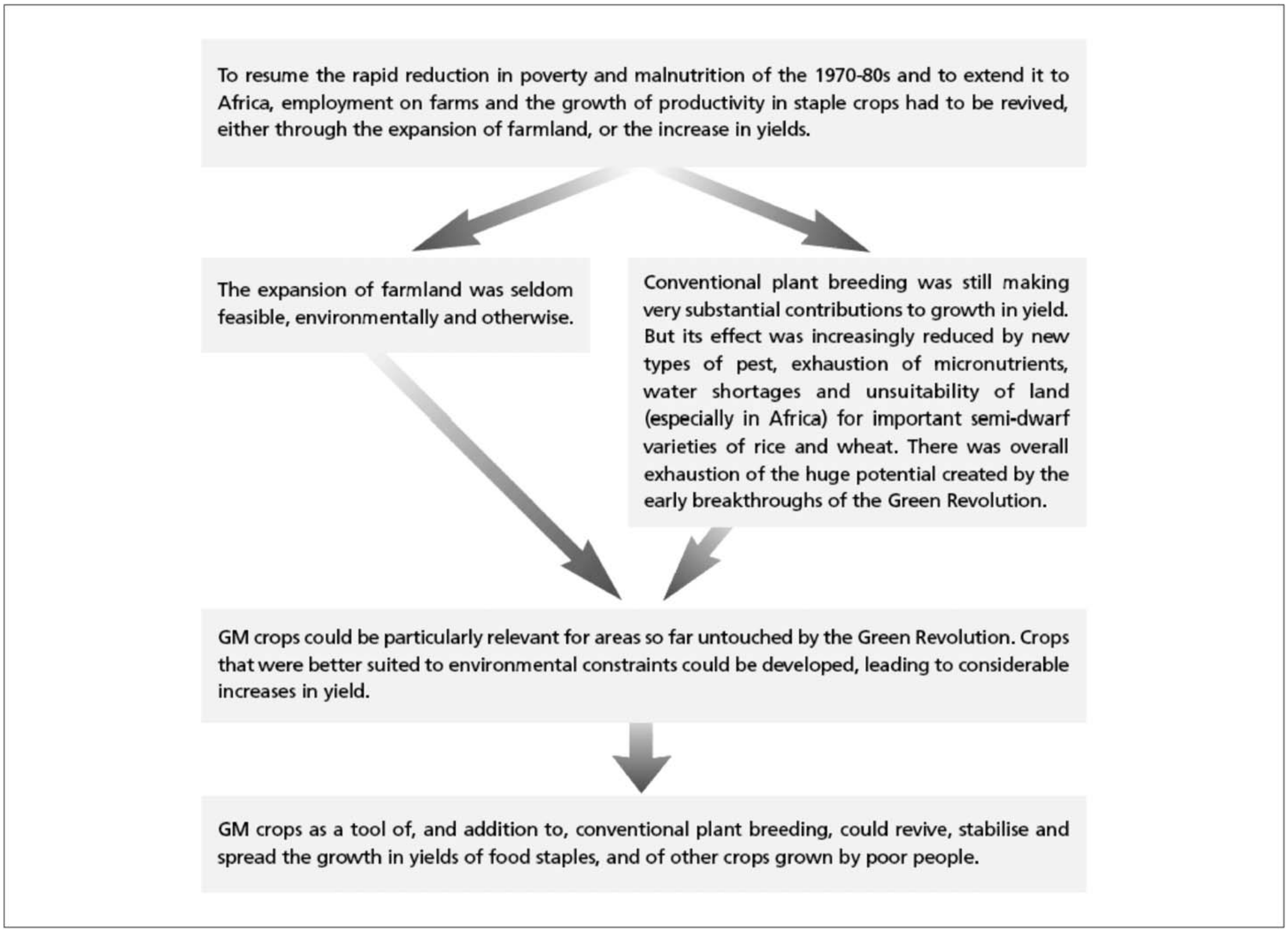

FIGURE 1

Summary of Nuffield Council Argument.

the only, always the best or most appropriate technology, and indeed one needs to accept that promised GM solutions may fail in particular cases.

3. Because the provision of agricultural technology will not on its own solve the problems of poverty and food security, attention needs to be given to administrative and regulatory capacity in developing countries as well as regimes of property rights, if the benefits are to be equitably shared.
4. The reports were written at times when the debate on GM was polarised. From Nuffield's point of view this is unfortunate, because it prevents a case-by-case approach in which the benefits and the risks of the technology are assessed in particular instances.

This then is a summary of the claim for there being a moral imperative to make the responsible use of GM technology available. However, as I have noted, this position involves denying the claims of some critics of the technology. So I now pass to an assessment of these crucial points of view.

Naturalness

One reaction to GM crops is that they are in some sense 'unnatural' and that it is wrong in itself to change the 'essence' of species or to interfere with the natural order. This is a widespread sentiment: many of the respondents to the consultation on our first report for example thought that the breaches involved in genetic modification represented an improper tampering with nature. Such sentiments were probably reinforced in the case of UK citizens by the experience of BSE in cattle, in which the BSE agent was spread to cattle in meat and bone meal, leading many to think that the disease would not have arisen had herbivores not been fed meat.

However, although these sentiments are widespread, both of the working parties involved in the Nuffield reports found it hard to make sense of the claims involved, for the following reasons.

Any form of plant breeding can be regarded as unnatural. To be sure, if plant breeding simply relied upon the selection of individual plants from the variety of naturally occurring plants, then one might say that the practice was natural, in the sense that there was no human intervention beyond the mere selection of desirable specimens. However, since the discovery of Mendel's laws, plant breeding has become scientific, involving such practices as mutation breeding, in which plants and seeds are exposed to radiation or chemicals as with Calrose 76 or Golden Barley, or wide crosses as in the case of Triticale. The difficulty of distinguishing GM as 'unnatural' from conventional forms of plant breeding as 'natural' is enhanced by the fact that GM may be used as a technology to produce traits or characteristics in plants that could have been

produced by conventional plant breeding only more speedily or at less cost.

One form of GM plant breeding that to the layperson may seem unnatural is the introduction of genetic material from non-plant species, for example in the case of *Bt* crops where bacterial gene sequences have been used or the use of genetic material from salmon into strawberries. Clearly these sorts of transformations would not be possible without advanced techniques of genetic modification. However, the mixing of genetic material across very different species occurs in nature without human intervention, as in the mixing of genetic material from humans and animals in viruses.

One concern about the unnaturalness of GM techniques pertains not to their mode of production but to their possible effects, in particular cross-pollination with non-GM crops in the wild. However, this view can only make sense in a general form if non-GM crops are seen as the product of nature and GM crops seen as artificial, but that view ignores the fact that conventionally bred crops are unnatural by the same test as are GM crops. To hold otherwise is to hold that there is an unaltered realm of nature.

However, the concern about effects may be standing proxy for another reason, related to safety. It may be that the order of nature needs to be respected because biological and ecological systems are relatively robust and predictable, and so pose few risks for humans, who have after all evolved with those environments. Horizontal gene transfer does occur in nature, but over a long time scale, whereas with genetic modification the transfer of genetic material is sudden so that if GM plants are released into the environment, biological and ecological systems might not be sufficiently adapted to integrate the plants.

Of course, the introduction of any plant, however produced, can have untoward effects on the environment. The introduction of the rhododendron, which originated in Spain and Portugal, or of Japanese knotweed (*Fallopia japonica*) into the UK has resulted in a significant loss of biodiversity. However, it may be argued that the advantages of GM technology, in particular its speed and power, are precisely the features that should make one sceptical of its use. In other words, although it is hard to see what merit there is in the argument from naturalness, there might be an argument from safety.

Before turning to the arguments on safety, I note one further point about naturalness. The argument that it would be wrong to introduce GM crops because the technology results in what is 'unnatural' relies on the assumption that it is wrong to intervene in nature. If, as the Compendium on the Social Doctrine of the Catholic Church says, nature 'is a gift offered by the Creator to the human community, entrusted to the intelligence and moral responsibility of men and women' (Pontifical Council, §473), then there is no general reason to defer to the genetic stock of the natural order and no reason why nature cannot be improved.

GM and risk analysis

General points. The chief advantage of genetic modification in the breeding of plants is that changes can be introduced more quickly and directly, with a more precise targeting of the traits that is desired. Moreover, a wider range of traits than is possible with conventional breeding can be introduced. However, from the point of view of risk analysis, some of these features of GM look as although they are problematic rather than advantageous. The speedy introduction of a wider range of traits may create untoward effects that are difficult to control. If rhododendrons or Japanese knotweed have had severe environmental effects in the UK, one might think that GM plants will pose a potentially greater threat to whichever environment they are introduced.

In this context, many urge the relevance of the precautionary principle. The precautionary principle has been formulated in very different ways both in law and in civic discourses. To evaluate the relevant arguments, therefore, we need to consider the strength of the claims contained in any precautionary approach.

Viewed in a moderate way, there is nothing exceptional about the precautionary principle at all. It is simply the principle that is followed in all cases of good design or good husbandry. For example, furniture is designed to carry much more weight than will ever be placed upon it, and buildings are designed to withstand shocks. Usually precautionary design of this sort leads to an increase in the cost of the product over a cheaper but less safe alternative, but the protection of human health and life from unnecessary risks is an obvious duty. Interpreted as such, the precautionary principle would not raise special considerations in relation to the development of GM crops. The technology would simply be subject to the usual safety assessments that any comparable technology would be subject to.

However, in recent years, the precautionary principle has sometimes been given some very stringent interpretations, and some of these interpretations have been taken to imply that there should be a moratorium or possibly even outright ban on GM technology. In its strongest form, a precautionary principle would place the complete burden of proof upon someone introducing a new technology to show that it did no harm. In this strong form it would be impossible to satisfy, and indeed it would place scientists and those developing potentially beneficial technologies in a situation that challenged their integrity, because no responsible scientist can promise no risk of harm whatsoever. As the 2004 Nuffield report put it 'an excessively conservative interpretation, demanding evidence of the absence of risk before allowing the pursuit of a new technology is fundamentally at odds with any practical strategy of investigating new technologies' ([2], p. 57). More generally, such a stringent approach would make the mistake of regulating on the technology rather than the traits produced by that technology.

With this general point in mind, we need to consider risk assessment both in relation to the environment and in relation to human health.

Environmental risk assessment. One particular risk that has concerned some people in connection with the planting of GM is that of gene flow from the modified plant to wild plants, particularly in areas of sensitive biodiversity. Gene flow occurs in nature of course, and is responsible for the wide variety of plants that have evolved. That gene flow occurred in the case of GM maize and native Mexican maize landraces in Oaxaca has not been disputed. The question has been over the threat of that gene flow to genetic diversity. There are many factors that help determine the effects of gene flow, but in the view of the Nuffield Council the existence of gene flow does not provide an argument for prohibiting the use of GM although it does suggest that in sensitive areas of biodiversity, GM crops ought not to be used without monitoring and that the

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establishment of comprehensive seed banks to conserve genetic resources of crop plants and their relatives is of crucial importance.

More generally, it would be part of a precautionary approach to develop GM crops first in the laboratory and then in field trials before going to large-scale production, but this sequence is the one that is good practice in plant breeding in any case.

One potentially significant problem arising from an extreme interpretation of the precautionary principle is the potential for environmental regulation to become a disguised form of economic protectionism. Thus, if the stringent EU regulations on GM foods make it impossible for farmers in developing countries to export to the EU, this could be a serious problem.

Health risk analysis. In principle, some evidence of harmful health effects would provide a reason for being cautious about the introduction of GM crops, but such purported evidence as has been offered has not withstood scrutiny.

Against the lack of evidence relating to health risks, the 2004 working party was impressed by the potential of GM technology to enhance micronutrients, and took as one of its case studies the production of Golden Rice. At the time at which the report was being written there was no firm evidence about the bioavailability of β-carotene, but this is now available and would suggest that the moral priority is no less urgent.

There is an important general point about the precautionary principle in this context. The precautionary principle was initially developed in the Federal Republic of Germany before being taken up and developed in the European Union and international agreements. The context in which the early developments took place was in relation to pollution control, where much of the argument turned on the question of whether it was worth paying extra for clean-up costs given the lack of complete scientific evidence about the link between the pollution and the damage being caused. In other words it was a principle of action rather than inaction.

In relation to technological innovation, the precautionary principle is usually interpreted in a conservative way, and is thought to imply a disposition to hold back the introduction of the technology until further evidence comes to light. However, this conservative interpretation only makes sense in the context of a status quo that is satisfactory, such that no damage is done to human values by delay. This is not the case where there is known damage being done to human health and there is good reason to believe that some benefit can be achieved. In this respect, the precautionary principle ought to be an injunction to action rather than inaction.

Justice and solidarity

One reason why the Council returned to the topic of GM crops in its 2004 report was that at the time a renewed heated debate took place in the EU about the use of GM crops which largely ignored the global perspective. In most Western countries, agriculture is a highly efficient process, with a range of means of improving yields through fertilisers and controlling pest and abiotic stressors through pesticides and other means. GM crops improve this system in some cases. But many members of the public remain unconvinced about the technology, especially in view of only marginal improvements. Independently of the justification of these concerns, major issues around justice and solidarity arise from the fact that highly restrictive policies at the EU level affect not only EU citizens, but also small-scale farmers in developing countries. For example, the Food and Feed and Traceability and Labelling regulations may perhaps seem like appropriate and feasible policy instruments for the governance of GM crops in the EU – but the segregation of GM from non-GM crops will generally not be feasible in developing countries. This has implications for the use of GM crops not only for export purposes, but also for domestic purposes. For even non-GM exports may be ''contaminated'' by GM crops used for domestic purposes.

For many commentators, justice issues are also raised by the role of industry in the production and marketing of GM crops. It seems plausible to assume that the GM story would have unfolded in a very different way if the first GM crop had been a GM food crop developed by the public sector (as opposed to 'cash crops' developed by industry). One key element in the public debate about GM crops is therefore the danger arising from monopolistic or oligopolistic control of the technology. The concern is that large private seed producers will put themselves in a position where they are able to exploit small farmers to the disadvantage of the latter. The 2004 report noted that five main companies (Syngenta, Bayer CropSceince, Monsanto, DuPont and Dow AgroSciences) control most of the resources that are needed to undertake commercial research in the area of GM crops. There are large questions about the responsible use of property rights and the administrative capacity to implement adequate biosafety procedures. The Green Revolution was largely funded publicly, and rested on a property rights regime in which it was assumed that the fruits of scientific research should be freely available for all. Current plant breeding is now taking place in a different world, in which much of the lead is by private companies or by universities anxious to take advantage of patent protection. There is an interesting contrast here with other developments in science where 'open source' principles operate, whether in respect of Wellcome funding for the Human Genome Project or some branches of synthetic biology. However, the Nuffield Council does note that there are several specific issues that constantly need addressing both by those involved in the development of research and by the relevant public authorities:

1. Owners of patented technology should be encouraged to license their technology non-exclusively. There are examples where this has applied, but it is a constant area of concern.
2. Material transfer agreements are implicated in the development of GM crops, and where these include such provision as reach through rights, they may inhibit development.
3. Patent offices should be discouraged from granting overly broad patents.
4. The impact of patents on access to germplasm should be monitored.

One criticism of GM technology that is often made by critics is that it poses a threat to informal or traditional seed systems. However, when it considered this matter, the 2004 working party did not think that contemporary plant breeding practice was likely to be such a threat for the obvious reason that no form of high technology plant breeding prevents farmers from retaining and re-sowing their own seed varieties or landraces if that is what they choose to do. Conversely, if new or improved seeds are preferred by farmers, then it is entirely their own concern, provided that

environmental responsibilities are not at issue. The working party noted that farmers were aware that saved seed for open-pollinated crops like maize produced lower yields that F1 hybrids. So, farmers in Zambia, Kenya and South Africa have been buying hybrid seed from local or multinational companies for many years. For self-pollinated crops, there is nothing to prevent farmers from retaining seed from the harvest for many years.

Further evidence on this point comes from the use of *Bt* cotton in China, where the working party noted that, although seed costs were more than four times higher that the non-*Bt* varieties, the overall net revenues from the *Bt* variety were greater because of savings in pesticides and fertilisers. In short, the development of GM crops will confront resource-poor farmers with a wider range of commercial options, but it would be a mistake to focus merely on one element of their costs.

A particular problem might be thought to arise in the use of GURT (Genetic Use Restriction Technologies). One difficulty here is that such technologies have been developed to deal with the objection that GM crops pose an environmental threat, and so there is a trade-off of values that need to be taken into account. There is no obvious easy solution to this problem except insofar as the technology develops we learn more about the environmental risks that may or may not be associated with particular GM crop varieties.

It is worth noting in passing that one factor leading to oligopoly in commercial seed production is strong regulatory requirements, because it is larger companies that have the capacity to manage the obligations in relation to those requirements.

Conclusion

Since 2004, when the second Nuffield report was published, there have been several developments that are worth noting in conclusion:

1. The number of farmers in developing countries using GM crops has more than doubled and there has been a threefold increase in acreage, with the most common crops being soybean, maize and cotton. This is evidence that farmers are finding it advantageous to take advantage of the technology. The moral imperative is to ensure that they are in a position both to have access to the technology and to make a choice about its use in the light of their own circumstances.
2. Not all developments noted in the report have been successful, the most important example being the development of virus-resistant sweet potato in east Africa. This is an illustration of why the case-by-case analysis advocated by Nuffield is important.
3. Concerns about climate change are focusing attention on abiotic resistant crops, where issues about patent rights are likely to be important. Similar concerns are likely to lead to an interest in second-generation biofuels, where the potential of conventional and GM plant breeding looks significant.

It is not the task of an ethical analysis to be the champion for a particular technology. Instead such an analysis leads to laying down the criteria by which any particular technology can be assessed. Above all, we should avoid the fallacy of thinking that an ethical assessment will indicate a brake on technological development, particularly in cases where the technology addresses urgent human needs.

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Review

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Review

Experience from use of GMOs in Argentinian agriculture, economy and environment

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Argentina is the second largest grower of genetically modified (GM) crops. This high level of adoption of this new agricultural technology is the result of a complex combination of circumstances. We can identify four main causes that led to this: political support (from agriculture officials), ability to solve prevalent farmers' needs, economic and environmental factors and an early implementation of effective regulations. The political willingness to study this new technology and crops as well as the recruitment of sound professionals and scientists to perform the task was crucial. These professionals, with very diverse backgrounds, created the necessary regulatory framework to work with these new crops. Farmers played a decisive role, as adopting this new technology solved some of their agronomic problems, helped them perform more sustainable agronomic practices and provided economic benefits. Nonetheless, all these advancements had not been possible without a rational, science-based and flexible regulatory framework that would make sure that the GM crops were safe for food, feed and processing.

Contents

Introduction

This article describes the situation and the conditions that led Argentina to adopt and develop crops modified through genetic engineering. This is mainly, but not exclusively, a historical perspective. However, some of these conditions and situations may shed some light on the present and may contribute to the development of similar processes elsewhere. The main regulatory guidelines that oriented this process are also included, as these may be useful examples when facing the challenge of adopting the use of GM technology [1,2].

It is important to mention that when Argentina started assessing GM material in 1991, there had been several conditions that had favoured this situation. First, the political situation of the

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1871-6784/$ - see front matter doi:10.1016/j.nbt.2010.05.011

country had changed. This was extremely important as the authorities were interested in and willing to give this new technology an opportunity. The former Secretariat of Agriculture promoted the study of these new crops. This in-depth analysis of the new technologies could only have been possible if the necessary human resources were available, the second key element. At that time, sound and committed professionals and scientists with different backgrounds, from the academia and the private sector, became staff of the regulatory body within the (at the time) Secretariat of Agriculture. They faced the challenge before them and created in 1991 the necessary framework to regulate GM crops.

Argentina approved the first GM crop, glyphosate-tolerant soybean (GTS), in 1996, which coincided with the global commercialisation of GM crops. Only six countries were involved in this; Argentina, with the planting of 370,000 ha of GTS, was one of them [3]. The area planted with GM crops has grown since then by more than 50 times (2008/2009 planting data), placing Argentina as the second largest grower of biotech crops in the world, as per 2008/2009 figures. Argentina now grows 21% of the global biotech crop area. Nowadays, areas grown with GM crops, relative to the total planted in the country, are 99% for soybean, 83% for maize, and 94% for cotton. Since 1991, fourteen different GM crops (events) have been approved for commercialisation (Table 1).

Regulators and the regulatory framework

Several factors accompanied the early adoption of GM crops in Argentina. The government was willing to study and implement a regulation for GM crops and the public and the private sectors devoted to studying agricultural biotechnology needed a framework to develop and handle this new technology, which, back then, was at an experimental stage. Consequently, the regulators and the regulations in themselves played a crucial role in this process.

Although the leadership was present in the figure of the Competent Authority (the Secretary of Agriculture at the time), the regulatory capacities were not available yet within the structure of the government. To that end, people from outside the government were recruited. They did not have the typical bureaucratic background, as they were mostly scientists and stakeholders' representatives, who brought a whole range of diverse and solid professional experience. They had the disposition to update their backgrounds according to the new scientific knowledge. Scientists from academia were deeply involved in this process, definitively setting science as the basis of the regulations from the very beginning. The regulatory bodies included government personnel, as well as representatives from the public and the industrial sectors. It was a very productive combination of science, societal interests and field experience. This 'eclectic' background would conform the regulatory bodies (the National Advisory Commission on Agricultural Biotechnology, CONABIA in the Spanish acronym, and the Technical Advisory Committee on GM Organisms Use, CTAUOGM) (http://www.minagri.gob.ar/SAGPyA/areas/biotecnologia/20-CONABIA/creacion_conabia.pdf; http://www.senasa.gov.ar/contenido.php?to=n&in=1079&ino=1079&io=5743).

In a nutshell, the process to approve the trial of a new (in Argentina) GM crop and its eventual commercialisation has remained basically the same since 1991 (http://www.infoleg.gov.ar/infolegInternet/anexos/145000-149999/146801/norma.htm; http://www.minagri.gob.ar/SAGPyA/areas/biotecnologia/60-Solicitudes/Res-39-english.doc). All applications are submitted to the Ministry of Agriculture, as the Minister of Agriculture is the Competent Authority on the matter. The applications are analysed and assessed on a case-by-case basis by the Ministry and its regulatory and advisory bodies and by other areas of the government. At both levels, field trials and commercial approvals, the assessments are science-based and the ultimate aim of the process is to make sure the crop is safe with regard to the agro-ecosystem as well as in all other respects, as food, as feed and processing material. The applications require the applicant to submit information on the engineered crop concerning the phenotypic expression, the description of the agronomic practices, including eventual changes in the geographic zones (if different from the non-GM counterpart), and the molecular genetic characterisation. Up to 2008, a total of 1511 applications for field trials and related regulated activities had been assessed.

Although the processing of the applications has not suffered major changes, the regulations and the regulators have undergone several updates, as more knowledge is available. The early regulations for the biosafety assessment of GM crops in Argentina were similar to those of the European Union and the United States. As time went by, Argentina modified the regulations based on new scientific knowledge and developments and its own understanding of biotechnology and biosafety (http://www.minagri.gob.ar/SAGPyA/areas/biotecnologia/60-Solicitudes/Res-39-english.doc). Argentina was able to do this because its regulatory framework had, and still has, three very important characteristics: it is flexible; it is rational and it is scientific. These key ingredients have helped it 'grow' and adapt to the new technologies, knowledge and resources available. The regulators have had to keep up with it. For example, at the beginning, the number of authorisations for field trials was just a handful whereas at present over two hundred applications are assessed per year.

Applications for field trials may include: (i) several transformed individuals with the same construct but at presumably different genome locations or (ii) transformants obtained with different trait-related constructs, or both. Therefore, the 'development efforts' of the developers, the regulatory framework and the regulators are better depicted by the number of *different events* (not of single applications) tested in field trials. This number has been steadily increasing to reach around two thousands in the past few years. Still a different, qualitative measure of the development efforts in the advance of GM crop technology in Argentina is given by the increasing complexity of the traits, which are currently tested (http://www.minagri.gob.ar/SAGPyA/areas/biotecnologia/50-Evaluaciones/_archivo2/000400-Evaluaciones para liberación experimental.php).

Precommercial tests, that is, extensive sowing, are a good way of seeing the regulations and the regulators in action. These tests, in fact a second phase in the regulatory process after the field trials, are carried out to assess the possible effects on agronomical practices and the environmental impact of GM crops. Also, these precommercial releases are done to perform local-specific tests and to collect material or data for regulatory purposes. In retrospect, an essential criterion for the biosafety review that has helped the further expansion of GM crop technology in Argentina was

that agriculture deals with highly managed agro-ecosystems. This was crucial because it gave to the application of agricultural biotechnology in Argentina an initial impetus even under very strict biosafety guidelines.

These sound and strict biosafety guidelines were 'put under test' in the European Union's moratorium. Argentina was trading some GM crops with it, and the EU withheld the import of these products using the Cartagena Protocol on Biosafety to the Convention on Biological Diversity as one of its main arguments. Argentina, together with Canada and the United States, presented a demand before the World Trade Organisation (WTO), because of this unreasonable delay in the imports – hence the name 'moratorium'. The WTO ruled in favour of Argentina, Canada and the United States, because the products followed all the environmental and food safety standards [4]. The application of the precautionary approach in the assessment of GM crops and in the ultimate granting of a commercialisation permit was crucial in this huge international dispute.

For all these reasons, Argentina and its regulatory framework have gained a good reputation around the world. The underlying principle of the regulations is safety, and with that in mind the assessments only allow for scientific, sound and strict arguments.

The crops and the traits

As stated before, field trials with GM crops started in Argentina in 1991. The first commercial GM crop, GTS, was released in 1996 (http://www.minagri.gob.ar/SAGPyA/areas/biotecnologia/50-Evaluaciones/_archivo2/00http://www.minagri.gob.ar/SAGPyA/areas/biotecnologia/50-Evaluaciones/_archivo2/000200-Eventos con evaluación favorable de la CONABIA y permiso de comercialización.php).

Very favorable combinations of crops and traits were relevant conditions at the beginning of the adoption process. Two cases, linked to the first approved GM crops are analyzed here: GTS and Lepidoteran Resistant maize, which contains an insecticidal toxin from *Bacillus thuringiensis* (Bt).

GT soybean

At the time of the commercial release of GTS, soybean was already an important crop in Argentina. Production was initially pushed by better land use through rotation (with maize), lower production costs [5,6] and by high commodity prices in the mid-1990s. Soybean production came together with glyphosate from the beginning. Pre-sowing application of the herbicide helped to clear the field from weeds (mostly Johnson grass) and cleaned the soil for the further sowing of maize, where these weeds were more difficult to eliminate. Soybean–maize rotation was a very common practice in Argentina. However successful non-GM soybean in Argentine agriculture was, the new GM varieties delivered farmers a significant improvement in the agronomic practices, what stimulated an increased, enthusiastic adoption. Operations were drastically simplified as farmers discontinued the use of complicated mixtures of expensive and more toxic herbicides and switched to a low toxicity, single chemical, friendlier to the environment and to them. Moreover, set-aside land heavily infested with noxious weeds could be brought back to production.

To all these advantages to the farmer, it was also added that the use of GTS has shown a very convenient synergy with no-till farming, which became widely used (Argentina is one of the leading countries in the implementation of low- or no-till farming) [7]. It is well known that low- and no-till farming reduce both soil erosion and emission of greenhouse gases, thereby contributing to agricultural sustainability through a better conservation of soil organic matter and reducing the impact on climate change.

Bt maize

The second important GM crop, also quickly adopted by farmers, was Bt maize (http://www.minagri.gob.ar/SAGPyA/areas/biotecnologia/50-Evaluaciones/_archivo2/00http://www.minagri.gob.ar/SAGPyA/areas/biotecnologia/50-Evaluaciones/_archivo2/000200-Eventos con evaluación favorable de la CONABIA y permiso de comercialización.php). With non-GM maize, insecticide applications were complicated because of the 'asynchronous' occurrence of pest attacks. Several, non-standard 'recipes' were used, according to pest and variable suggestions given to farmers. With Bt maize, farmers could reduce the use of not only toxic insecticides but also of toxic herbicides if rotating with GTS (see above).

Bt maize brought also very important additional benefits:

(i) better grain quality, which increased farmers' competitiveness and a healthier product, as mycotoxin levels were consistently well below mandatory regulations [8,9];
(ii) longer sowing/harvest windows, on account of a longer stand of the plants in the field as plants were not damaged by the tunneling caused by maize borers.
(iii) this latter advantage not only increased yield but also allowed harvesting at a higher grain dry matter weight, thereby reducing drying costs and environmental contamination. Again, a significant contribution to sustainability was achieved.

The following chart (Table 1) describes the 14 events currently approved in Argentina (http://www.minagri.gob.ar/SAGPyA/areas/biotecnologia/50-Evaluaciones/_archivo2/00http://www.minagri.gob.ar/SAGPyA/areas/biotecnologia/50-Evaluaciones/_archivo2/

TABLE 1

Commercial approvals for planting, processing, food and feed

Crop	Event	Trait/s	Year
Soybean	40-3-2	HT	1996
Maize	176	IR	1998
Maize	T25	HT	1998
Cotton	MON531	IR	1998
Maize	MON810	IR	1998
Cotton	MON1445	HT	2001
Maize	Bt11	IR	2001
Maize	NK603	HT	2004
Maize	TC1507	HT, IR	2005
Maize	GA21	HT	2005
Maize	NK603 × MON810	HT, IR	2007
Maize	TC1507 × NK603	2HT, IR	2008
Cotton	MON1445 × MON531	HT, IR	2009
Maize	GA21 × Bt11	HT, IR	2009

HT: Herbicide tolerance; IR: insect resistance.

000200-Eventos con evaluación favorable de la CONABIA y permiso de comercialización.php).

Environmental benefits

The benefits that GM crops have brought to the farmers are also reflected in the significant positive effects on the environment. Nonetheless, it must be said that glyphosate does not perform miracles and when misused, it may produce undesired effects on the environment by, for example, generating herbicide resistant weeds [10–12], as will always occur with conventional crops. It should be understood that agricultural biotechnology does not escape the laws of biology and the rules of good agronomic practice.

GTS has brought many benefits to farmers and the environment. First, farmers could turn massively to no-till agriculture. This practice has spread rapidly in Latin America. Argentina is one of the leading countries in the use of no-till farming with 19 million ha cultivated under this system, almost 20% of the global area [13–15]. Conservation tillage systems offer numerous benefits such as fuel savings, reduced soil erosion, wildlife conservation and reduced release of greenhouse gases. The adoption of GTS has changed the pattern of the use of herbicides. Second, even though the number of applications and the amounts per hectare of glyphosate have increased, this did not inevitably involve a negative environmental impact [16]. Indeed, the intensification in the use of glyphosate has caused a reduction in the use of atrazine, a herbicide with high residual effects and environmentally harmful. By contrast, glyphosate has a low toxicity level, has no residual activity and is rapidly decomposed by soil microorganisms. According to the World Health Organization classification [17], glyphosate belongs to Class IV, the 'less toxic' group. A 2005 survey [16] showed that in Argentina glyphosate has completely replaced other herbicides belonging to the more toxic Classes II and III.

In addition, the adoption of insect-resistant (Bt) cotton has resulted in dramatic reductions in insecticide use. On the basis of farm survey data, it was found [18] that the technology reduced application rates of toxic chemicals by 50%.

Overall, the adoption of GM crops has made a positive contribution to the sustainability of the agricultural production. Cotton yields, for example, have increased by 30% in the case of Bt cotton and by 17% in the case of herbicide tolerant varieties [19]. Maize yields increased between 5.5% and 9% in the case of insect-resistant varieties and from 3% to 22% in the case of herbicide-tolerant hybrids, depending on the year and the region.

These yield increases have allowed for the deployment of lesser amounts of land needed for cultivation (an increasingly limiting factor worldwide) and through better conservation of soil and biodiversity [20], which is one of the major contributions of GM crop technology. In addition, no-till practices have had a major beneficial role as it helps to keep soil moisture and to improve water infiltration, what contributes to the conservation of soil structure.

Economic benefits

As regards the economic benefits, many things should be taken into consideration. There are other issues involved in a rather complex way (e.g. high commodity prices, international markets and local economic growth). For these reasons, the economic measurements have estimated that the total gross benefits derived from the adoption of GM crop technology in the 1996–2006 period were of USD 19.7 billion for GTS (1996–2006), USD 482 million for Bt maize (1998–2005) and USD 19.7 million for insect-resistant cotton (1998–2005), making a total of USD 20.2 billion [19]. In the case of soybean for the same period, the cost of re-stocking soil phosphorous consumed by the crop was estimated at USD 2.3 billion, giving a net gain of USD 17.4 billion [21].

Another important estimation is that of the farmers' profit. It has been calculated that the farmers' share of these benefits was 77% for soybean, 43% for maize and 86% for cotton [21]. Other studies [19] estimated that the farmer's income in the 1996–2006 period increased by USD 6.6 billion, and the revenues for 2006 alone were USD 1.3 billion.

Additionally, it was estimated that that the release of GTS has contributed to the creation of almost a million jobs (whole economy-wide), representing 36% of the total increase in employment over the 1996–2006 period [21].

As explained above, GM crop technology has been beneficial in more than one respect. When analysing the whole range of benefits, for the environment and for the economy, that this technological advancement has brought to Argentina, the reasons why this technology was so well received and had such a rapid adoption rate seem quite clear and straightforward.

Concluding remarks

When analysing the conditions that have determined the high rate of adoption of GM crop technology in Argentina, it can be said that it is the result of a complex combination of circumstances. As a first approximation, it is possible to identify four central issues: political support, the early implementation of an effective regulatory framework, the benefits this technology would bring to farmer's prevailing needs, and the positive economic and ecological impact of the GM crops.

The new products allowed farmers to solve important agronomic problems while providing significant and positive environmental benefits. For example, it was possible to achieve a sharp decrease in the use of insecticides in the case of Bt cotton. For GT soybean, there was a shift from toxic, classes II and III herbicides to environmentally friendlier class IV herbicides. To sum up, all these advantages have led to an overall beneficial contribution to sustainability, by the extensive use of no-till practices, and a consistent increase in yields, what allowed for less land deployment.

It was decisive that the Competent Authority rested on agriculture officers, as production concepts largely dictated the approval criteria. Regulations played also a major role, as their early implementation allowed the developers to work in an environment of certainty. Field trials and commercialisation guidelines were science-based, designed by experts with different backgrounds and experiences, who put biosafety of the product first, without jeopardising, or possibly so that they would not jeopardise, the country's exports, one of the strong sources of Argentina's domestic product.

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Do Russia and Eastern Europe need GM plants?

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Russia, Ukraine and Kazakhstan are the leading agricultural producers, especially for potato, sugar beet and sunflower. The cumulative effect of adverse climatic conditions, high weediness and losses related to viruses and pests (without any insecticide and herbicide treatments) led to losses amounting to 40–80% of potential production in the Russian Federation and other mentioned countries. We have used new biotechnology methods to obtain several crops (potato, sugar beet, sunflower and others) tolerant to abiotic and biotic stresses. For the first time – on the basis of domestic varieties bred by Russian scientists – GM potato varieties have been obtained, resistant to Colorado beetle. These GM potato varieties were recognised as being as safe as traditional ones and have been registered for food use. Using this technology, new biotechnological sugar beet lines tolerant to herbicides were also obtained.

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Russia and two neighbouring Eastern Europe countries – Ukraine and Kazakhstan represent one of the leading regions of the world for the agricultural production, especially for potato, sugar beet and sunflower

According to the Ministry of Agriculture of the Russian Federation, potatoes were grown on an area of approximately 3.3 million hectares at Russian farms of all categories (2008). In 2008 Russia produced an annual potato yield equal to 30.0 million tons (exceeding 10% of world potato production), Ukraine – about 19.5 million tons, and Kazakhstan – 2.4 million tons. Yields and yield stability were influenced by continental weather-related environmental factors in this region: cold winters, and dry and hot weather which is usual for the first half of the vegetation period. The resulting average level of potato productivity in Russia consists of about 9.4–10 tons/ha. The cumulative effect of these adverse growing conditions, high weediness and losses related to viruses and pests, lead to the fact that the total potato losses in the Russian Federation are about 48%.

After 20 years when Colorado beetle was detected in Russia (1949–1969), it has occupied its permanent habitat in the basic zones of agriculture manufacture and was found in many territories of Russia. By 1990 (when the reforming of agriculture of Russia began) the pest was found in 40 areas, 2 territories and 12 Autonomous Socialist Republics (ASSR).

Potato production in Russia is practically everywhere concentrated in the private (individual) farm sector, which has become the main production system: the share of their potato production remains at a level of 95%. Owing to the absence of any insecticide

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and herbicide treatments, the losses amount to 40–80% of potential production and some experts estimate the real annual losses from the Colorado potato beetle alone to be 2–2.5 billion $ US.

It is obvious that development protective measures should be planned on the basis of expansion of existing chemical and biological plant protection methods, and also include the use of new opportunities offered by genetically modified crops.

Biotechnological methods can be seen as the summation of genetic engineering technology and traditional plant breeding. These methods were developed to obtain several crops (potato, sugar beet and other crops [1,2]) tolerant to abiotic and biotic stresses. The technology scheme includes the introduction of original plant lines to *in vitro* culture, the insertion of target gene sequences into the plant cells, the selection of plant lines with the target gene sequences, micropropagation and breeding of modified plant lines.

This advanced technology allows us not only to considerably reduce the time needed for breeding, but also to insert agriculturally important traits which cannot be done in the traditional way. Using this technology, we have obtained biotechnological potato varieties resistant to Colorado beetle and biotechnological sugar beet lines tolerant to herbicides.

The application of the potato varieties and sugar beet lines obtained allows improving reliability, profitability and simplicity of plant cultivation. It will also provide considerable, positive ecological effects and will reduce health risks of both producers and consumers.

Development of the Russian GM potato varieties resistant to Colorado beetle

Scientific work during the past 15 years has led to the creation of GM potato varieties resistant to herbicides, pests, fungal and viral diseases in Russia [3]. For the first time – on the basis of domestic varieties bred by Russian scientists – GM potato varieties have been transformed. Integration of novel trait, resistance to Colorado beetle, was performed with the method essentially new to the Russian selection process, namely, genetic engineering.

Colorado beetle resistant potato varieties have passed all field and biosafety trials (Fig. 1) and were recognised by the Russian state authorities as being as safe as traditional ones and have been registered for food use:

- BT potato 'Elizaveta' Centre 'Bioengineering' RAS, Russia (2005, for an unlimited period).
- BT potato 'Lugovskoy' Centre 'Bioengineering' RAS, Russia (2006, for an unlimited period).

Three GM potato lines have received approvals by the Russian State Seed Committee (the date of priorities November 2004).

Development of Russian sugar beet varieties, resistant to viral infection

Sugar beet (*Beta vulgaris* L.) is another important cultivar of present day Russian agriculture. It is used as raw material, and its gross crop in 2008 was about 29.0 million tons for Russia; about 13.7 million tons for Ukraine, and for Kazakhstan – 0.3 million tons. It is also a traditional and basic domestic source for the production of sugar in the Russian Federation.

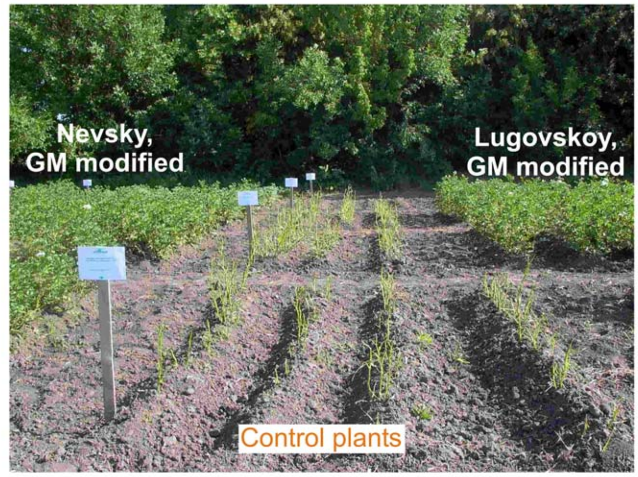

FIGURE 1
Field tests of transgenic potato, resistant to Colorado beetle.

Over half of sugar beet cultivation costs are caused by weed control, but weediness still leads to a 25–30% average yield. In addition, losses of up to 10–11% in sugar beet yield (in Russia) are associated with the infection of beet yellows virus and beet necrotic yellow vein virus. Recently, a group of scientists of the Centre 'Bioengineering' of the Russian Academy of Sciences have created GM sugar beet lines tolerant to herbicides on the basis of phosphinotricine [4] (Fig. 2). Another major research direction is development of new virus resistant sugar beet lines.

These new crops – GM potatoes with their unique border identifiers and all GM sugar beet lines – are protected by 22 patents.

FIGURE 2
Control plants (*on the left*) and transgenic plants (*on the right*) of sugar beet after treatment with herbicide 'Basta'.

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First generation biofuels compete

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Rising petroleum prices during 2005–2008, and passage of the 2007 U.S. Energy Independence and Security Act with a renewable fuel standard of 36 billion gallons of biofuels by 2022, encouraged massive investments in U.S. ethanol plants. Consequently, corn demand increased dramatically and prices tripled. This created a strong positive correlation between petroleum, corn, and food prices resulting in an outcry from U.S. consumers and livestock producers, and food riots in several developing countries.Other factors contributed to higher grain and food prices. Economic growth, especially in Asia, and a weaker U.S. dollar encouraged U.S. grain exports. Investors shifted funds into the commodity's future markets. Higher fuel costs for food processing and transportation put upward pressure on retail food prices.From mid-2008 to mid-2009, petroleum prices fell, the U.S. dollar strengthened, and the world economy entered a serious recession with high unemployment, housing market foreclosures, collapse of the stock market, reduced global trade, and a decline in durable goods and food purchases. Agricultural commodity prices declined about 50%.Biotechnology has had modest impacts on the biofuel sector. Seed corn with traits that help control insects and weeds has been widely adopted by U.S. farmers. Genetically engineered enzymes have reduced ethanol production costs and increased conversion efficiency.

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Introduction

This article analyzes the U.S. corn-based ethanol industry, its impacts on food prices, and the role of biotechnology.

Recent economic history

Rising petroleum prices during 2005–2008 and the passage of the 2007 U.S. Energy Independence and Security Act with a renewable fuel standard of 36 billion gallons of biofuels by 2022, generated incentives for a massive investment in U.S. corn-based ethanol plants. Most of these approximately 200 ethanol plants are located in the Midwestern United States (Fig. 1). Since the early 2000s, ethanol production has increased sixfold from about 2 to 12 billion gallons (Fig. 2).

As petroleum prices increased in early 2008 and more ethanol plants came on-line, corn demand for ethanol increased dramatically and prices increased threefold to nearly $8.00 per bushel. Although this nominal price surpassed the record prices experienced in the early 1970s, adjusted for inflation they were not record high (Fig. 3). The simultaneous occurrence of the increase in world demand for petroleum and U.S. policy incentives to produce corn-based ethanol resulted in a strong positive correlation between petroleum prices, corn prices, and food costs resulting in an outcry from U.S. consumers and livestock producers, food riots in several developing countries, and debate about U.S. energy policy, especially biofuel mandates and subsidies.

Others factors contributed to higher commodity prices. Economic growth, especially in Asia, increased U.S. grain export demand [1]. A weak U.S. dollar encouraged U.S. grain exports, and drove up petroleum prices expressed in dollars. Investors shifted funds from capital markets to commodity future markets causing commodity prices to rise sharply. While the ethanol boom influenced food prices, some of the increase in retail food prices could be attributed to the higher fuel costs for transportation of raw materials to the processing plants and food to the retail outlets.

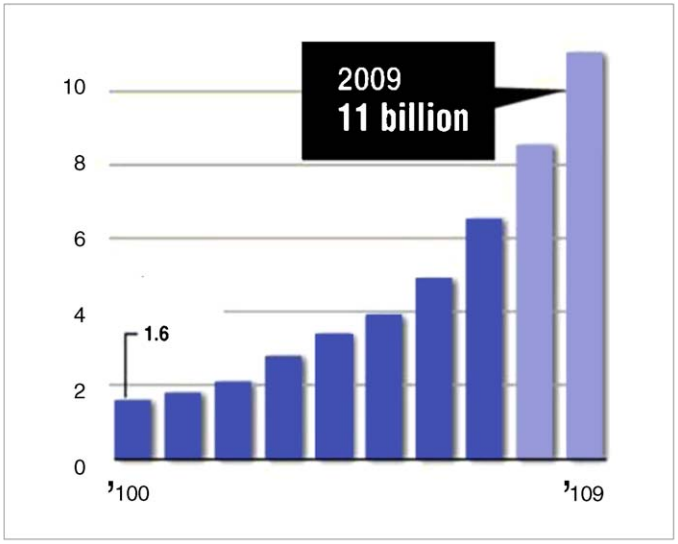

FIGURE 2

U.S. ethanol production (gallons). *Source*: Fastech LLC, March 2009.

From mid-2008 to mid-2009, economic conditions changed dramatically. Petroleum prices fell from $140 to $50 per barrel. The U.S. dollar strengthened, the world economy entered the most serious recession since the 1930s with high unemployment, housing market foreclosures, collapse of the stock market, a reduction in global trade, and a decline in durable goods and food purchases, especially away-from-home food consumption. Agricultural commodity prices declined about 50%. Despite the lower cost of corn for ethanol production, less liquid fuel demand due to the global recession eroded profit margins in the ethanol industry (Fig. 4).

Production of corn-based ethanol

Ethanol is an alcohol produced by yeast from sugars through fermentation [2]. Fuel ethanol is ethanol that has been highly

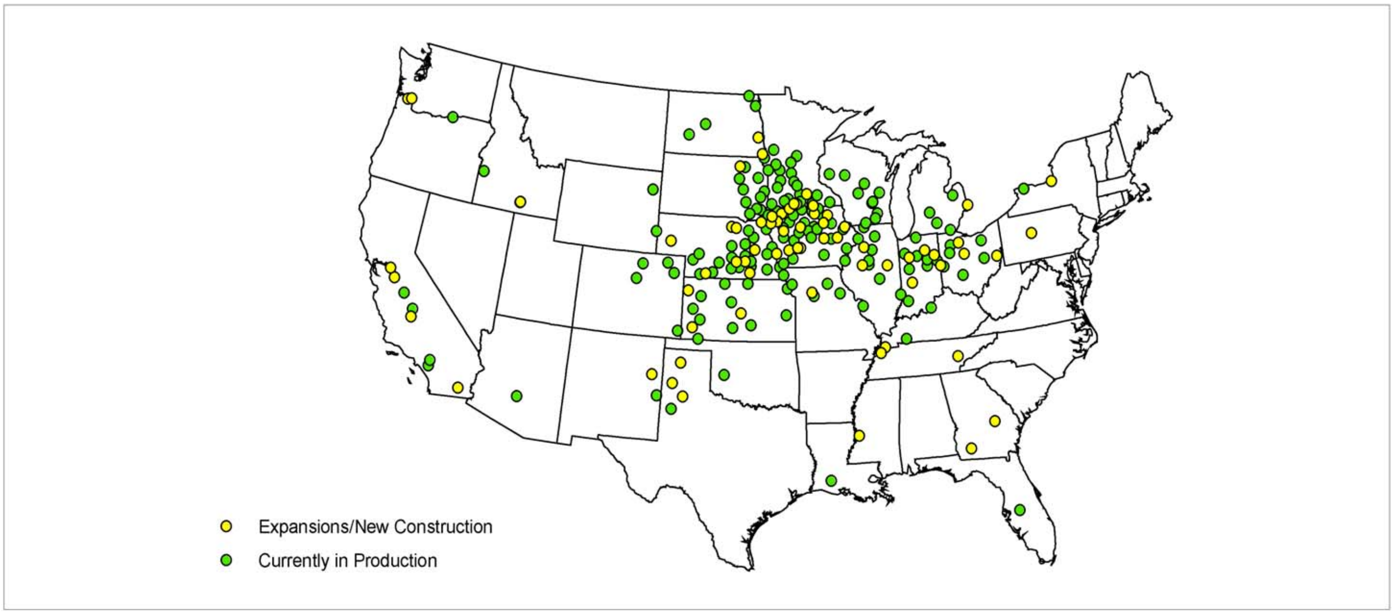

FIGURE 1

U.S. ethanol plant locations. *Source*: www.renewable-ag.com.

Review

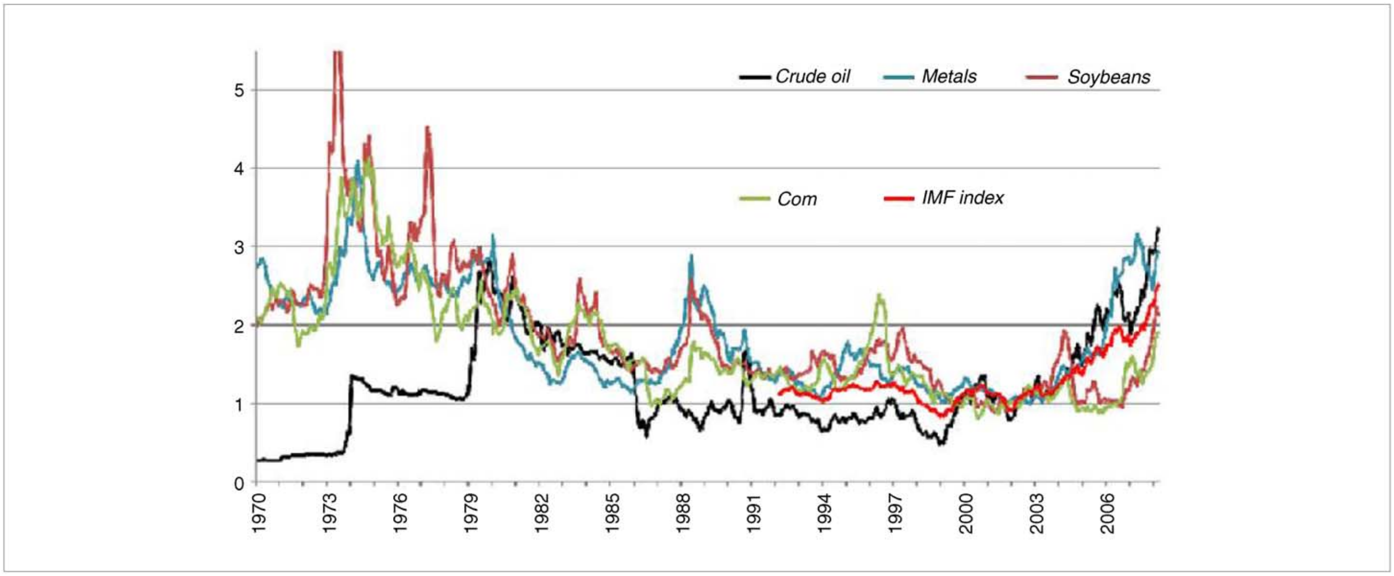

FIGURE 3

Deflated commodity prices and indices, 1970–2008 (2002 = 1). *Source*: Abbott et al., What's Driving Food Prices, Farm Foundation, July 2008.

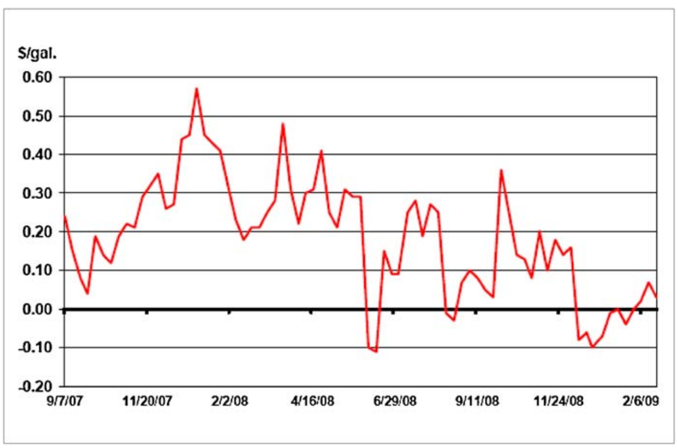

FIGURE 4

Ethanol producer net returns. *Source*: Glauber, USDA Chief Economist, February 2009.

concentrated to remove water and blended with gasoline (Fig. 5). All cars and trucks in the United States with gasoline engines can burn a 10% blend of ethanol with gasoline. Flex-fuel vehicles can burn up to an 85% blend of ethanol.

Corn is a valuable feedstock for ethanol because it contains a large amount of carbohydrates. A modern ethanol plant can produce approximately 2.7 gallons of ethanol from one bushel of corn plus about 17 pounds per bushel of distillers dried grain with soluble DDGs. (Note: There are 56 pounds per bushel of corn grain.) DDGs are a primary co-product of ethanol production which can be fed to livestock. Over 70% of the ethanol plants in the United States use a dry-grind process. Wet milling is primarily used to produce high fructose corn syrup for food uses such as sweeteners for soft drinks and baked goods. In a dry mill, the corn is ground, and a heat-stable enzyme and water are added. This slurry is cooked, converted to corn mash and another enzyme is added. Then the fermentation process begins.

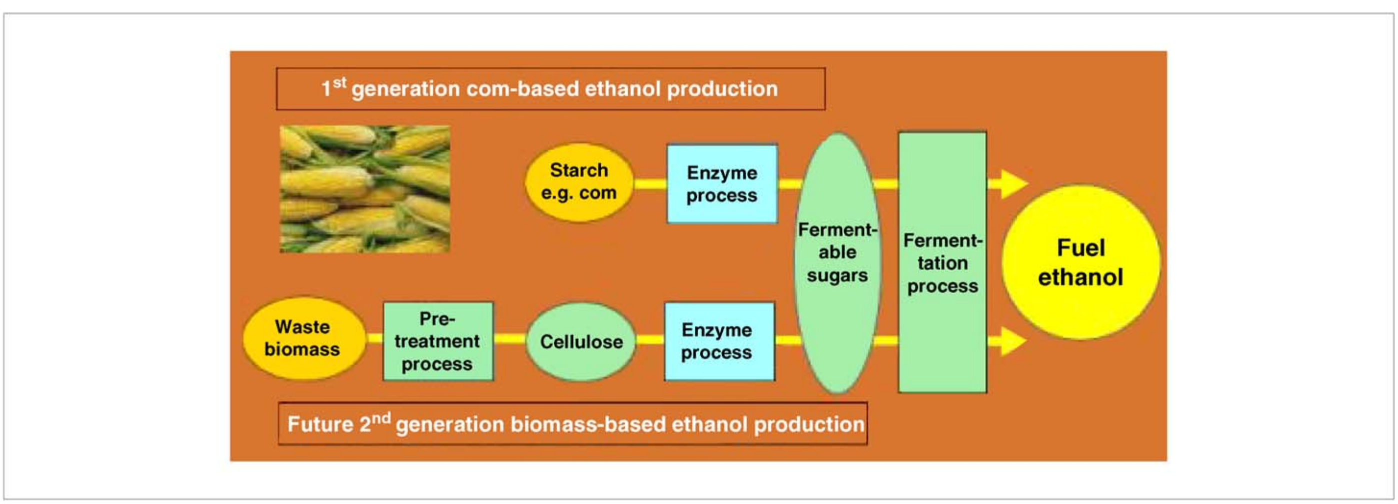

FIGURE 5

Ethanol production process. *Source*: Enzyme Use for Corn Fuel Ethanol Production, Novozymes, July 2007.

TABLE 1

Renewable fuels standards

Year	Renewable biofuel	Advanced biofuel	Cellulosic biofuel	Biomass-based diesel	Undifferentiated advanced biofuel	Total RFS
2008	9					9
2009	10.5	0.6		0.5	0.1	11.1
2010	12	0.95	0.1	0.65	0.2	12.95
2011	12.6	1.35	0.25	0.8	0.3	13.95
2012	13.2	2	0.5	1	0.5	15.2
2013	13.8	2.75	1		1.75	16.55
2014	14.4	3.75	1.75		2	18.15
2015	15	5.5	3		2.5	20.5
2016	15	7.25	4.25		3	22.5
2017	15	9	5.5		3.5	24
2018	15	11	7		4	26
2019	15	13	8.5		4.5	28
2020	15	15	10.5		4.5	30
2021	15	18	13.5		4.5	33
2022	15	21	16		5	36

Source: Renewable Fuels Association.

After fermentation the liquid portion is distilled producing ethanol of 92–95% purity. The remaining water and solids is centrifuged to separate the liquid from the solid. The solid material is the DDGs. The residual water is recycled into the beginning of the dry-grind process.

Government mandates

The U.S. Energy Independence and Security Act of 2007 contains a renewable fuel standard with a target of 36 billion gallons by 2022 (Fig. 6). The conventional biofuel category encompassing ethanol from corn grain is mandated to increase to 15 billion gallons by 2015 and remain at that level. Except for modest amounts of biodiesel from vegetable oils such as soybean oil, most of the rest of the mandated renewable fuels must come from biomass or cellulosic feedstocks (Table 1).

The food vs. fuel debate

Factors driving food prices are complex. Some are related to long term trends while others are caused by recent market events and policy decisions [3].

Rapid economic growth in developing countries such as India and China over the past decade has increased demand for raw materials ranging from petroleum and steel to agricultural commodities. When *per capita* income rises, countries experience a dietary transition with increased demand for animal protein which requires livestock feed such as corn and soybeans.

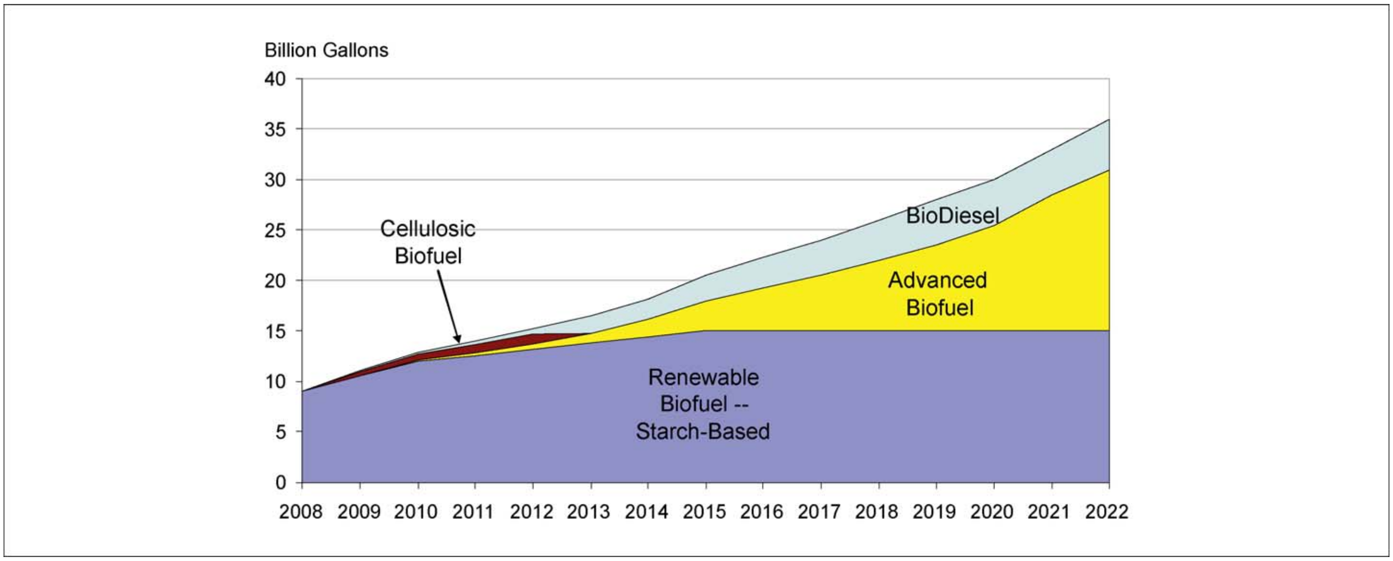

FIGURE 6

U.S. renewable fuel standard. *Source*: Steve Meyer, Paragon Economics Inc., March 2009.

Lack of investments in agricultural research, especially public research, in recent years has contributed to a slower rate of global agricultural productivity growth at a time when global agricultural commodity demand has been increasing. This has put upward pressure on food prices.

Since 2001, world grain stocks have declined due to world demand growing faster than production [1]. With tight stocks (see Fig. 7), commodity prices have become more inelastic and risen even more rapidly as consumer concerns about future food supplies increased. Weather concerns such as a drought in Australia and a late, wet spring and flooding in the U.S. Midwest in 2008 added to the price increases. By mid-2008 grain supplies reached minimal 'pipeline' levels, and prices rose to ration the short-run use of the limited supplies until the 2008 harvest occurred. The last time the 'stocks-to-use' ratio for grains, including corn, was as tight as in 2008 was in 1972–1973 when the United States sold large volumes of grain to the former Soviet Union and the Nixon Administration put in place wage and price controls because of inflation and food shortage concerns. In 2008, the combined food/bioenergy/feed demands heightened the inelasticity of the grain stocks–price relationship resulting in higher and more volatile commodity prices.

Exchange rates influence commodity prices. Most commodities, including petroleum and grains, are priced in U.S. dollars, but are purchased in local currencies. When the value of the U.S. dollar depreciates relative to other currencies, as occurred during the past several years, commodity prices increase. A decline in the value of the U.S. dollar is linked to greater demand for U.S. agricultural commodity exports, as well as higher petroleum prices (Fig. 8).

In 2008, higher petroleum prices increased production costs for farmers, especially nitrogen fertilizer and diesel fuel. Higher petroleum prices also increased the cost of transportation of inputs to the farms, commodities from the farms to processing plants, and finished foods to the retail outlets.

Recent commodity and food price behavior

From mid-2008 to mid-2009, commodity prices collapsed 50% from record high in nominal dollars [4]. World food prices fell nearly 40% in the last half of 2008 after increasing nearly 60% during the previous 12 months (Fig. 9). The recent world recession, driven initially by collapse of the U.S. housing and stock markets, resulted in high unemployment, loss of family income, a sharp decline in the value of pension and other investment funds, and an unwillingness of many to spend on goods and services. Lower demand for petroleum resulted in a sharp decline in fuel prices. Lower commodity prices and transportation costs have contributed to the decline in food prices relative to a year ago. A slightly stronger dollar also has contributed to a decline in export sales.

U.S. consumer food prices increased sharply in 2007–2008 (Fig. 10). In the United States in 2005 and 2006, food prices increased by an average rate of only 2.4% (Table 2). In 2007 and 2008 they increased 4.0% and 5.5%, respectively [5]. Perrin [6] estimated that in 2007–2008 the increased demand for corn for ethanol contributed to about a 1% increase in food prices. The direct impact of higher corn prices on foods is relatively small because the value of the corn in breakfast cereals or similar food products is a relatively small proportion of the price of the final good. However, grain prices do impact livestock feed costs and

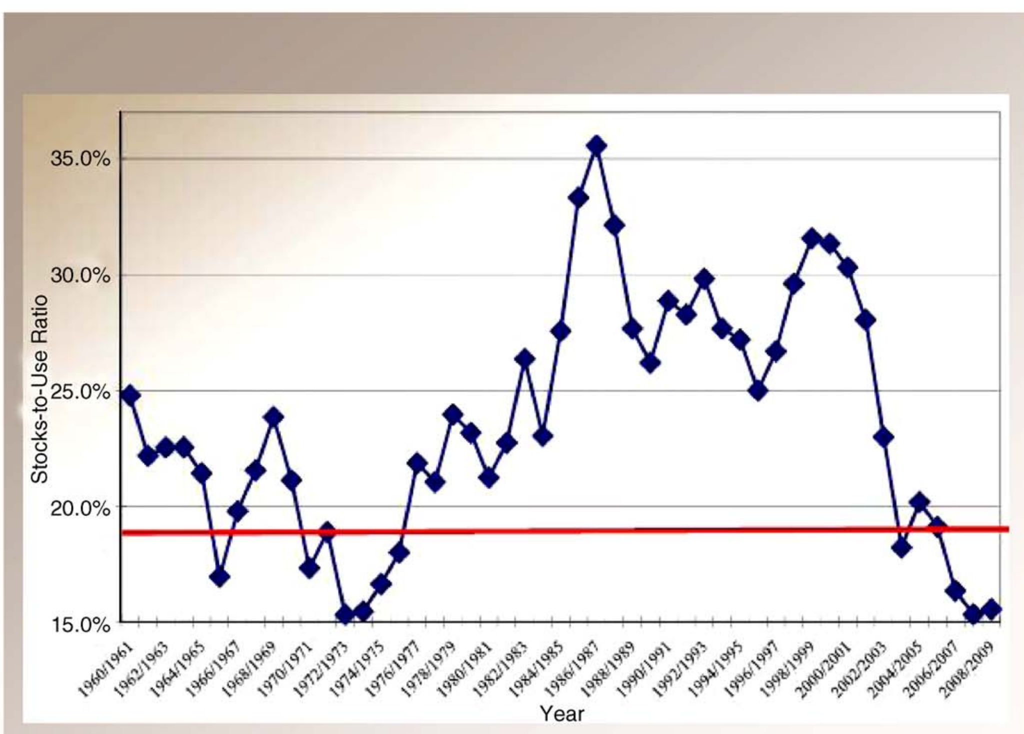

FIGURE 7

Stocks-to-use ratio for total grains in the world (1960–2009). *Source*: Chris Hurt, Indiana Ag Outlook 2009.

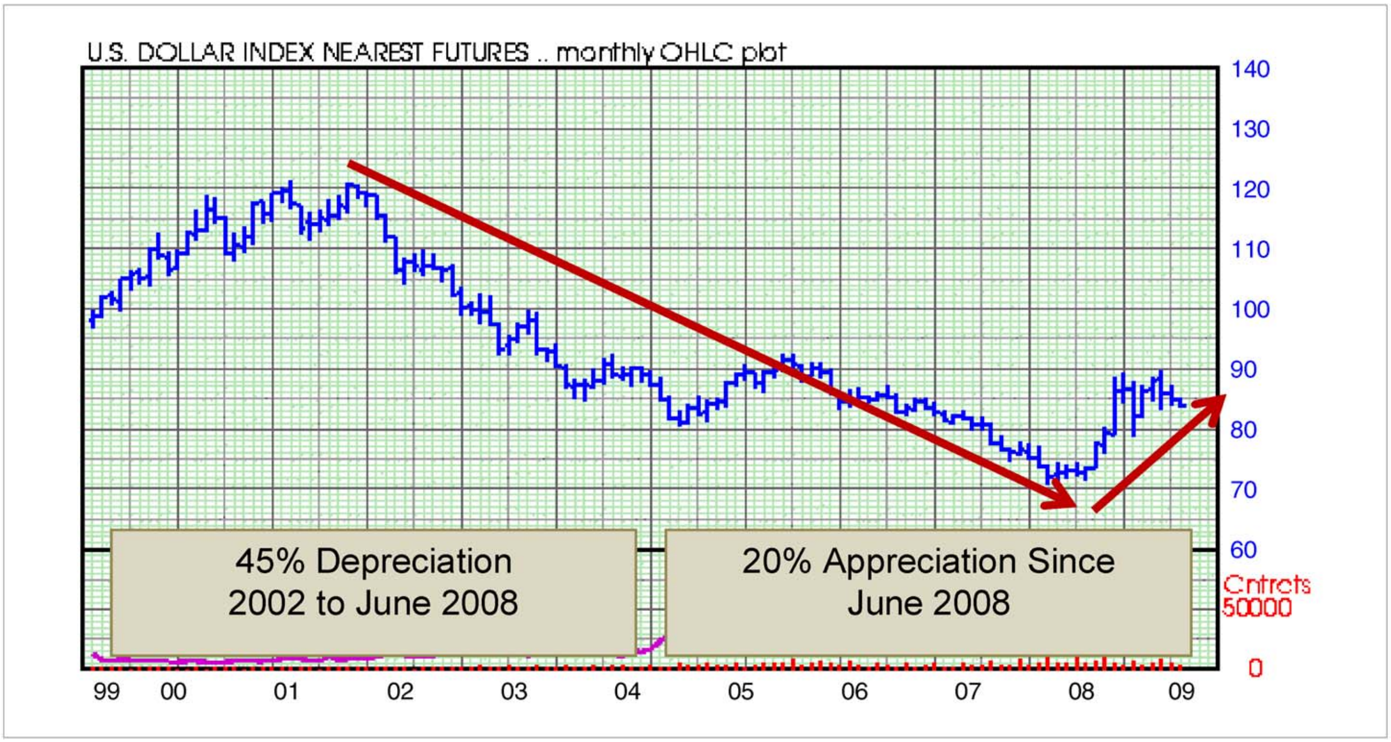

FIGURE 8

U.S. dollar exchange rate. *Source*: Barchart.com, May 2009.

eventually the consumer price of meat and other livestock products. Because broilers and eggs involve a relatively short production cycle, increases in grain prices in 2007–2008 impacted broiler and egg prices rather quickly (Table 2). Increases in retail beef and pork prices were more modest and delayed due to the longer production cycle.

Commodity prices are highly correlated. For example, the increase in planted corn acres in the United States in the 2007–2008 marketing year was in response to the increased demand for corn for ethanol, but given a relatively stable total crop area, concurrently there was a reduction in the acreage planted to other crops in the United States such as wheat and soybeans. Thus, less production of these substitute crops caused their prices to rise also, contributing to upward pressure on food prices for products such as breakfast cereals, bakery goods, and cooking oils.

In 2009, food prices are expected to increase in the 3.0–4.0% range due to lower agricultural commodity and energy costs combined with a weaker economy. Livestock prices are expected to increase less in 2009 than in 2008.

The fierce food/biofuel price debate of 2008 subsided in 2009. But it is important to realize that these price increases were the result of a complex set of inter-related economic and policy events.

The livestock vs. fuel debate

The U.S. livestock sector was adversely impacted by the sharp increase in feed costs in 2008. However, the higher price of corn grain was partially offset by the increased availability of DDGs from the ethanol industry. DDGs can be readily used (up to 40%) in cattle rations because ruminants can more easily digest this feed source. The amount of DDGs used in swine and poultry rations is more limited (typically 5–10% of the ration).

These increases in grain prices in 2007–2008 occurred at a time when livestock prices, especially pork, were already declining. The U.S. swine sector has faced negative profit margins as a result of low pork prices and higher feed costs for nearly two years (Fig. 11). Pork profit margins continued to erode in 2009 because some countries refused to import pork as a result of the ''swine flu'' scare (H1N1).

In 2008, several livestock organizations called for a reduction in the blend subsidy, a reduction or removal of the ethanol import tariff, and/or a modification in the renewable fuel standard. To date, no such actions have been taken by the U.S. government.

Subsidies

Currently, there is a $.54 per gallon import duty on ethanol and a $.45 per gallon subsidy for domestic blenders of ethanol with gasoline. The import tariff is primarily directed at preventing the importation of Brazilian sugarcane-based ethanol. The 2008 U.S. Food, Conservation, and Energy Act (U.S. Farm Bill) reduced the ethanol blend subsidy from $.51 to $.45 per gallon. Tyner [7] provides an excellent summary of biofuels legislation and policy analysis. Thompson *et al.* [8] analyze potential ethanol policy changes to ease the pressures on corn prices. Their analysis looks at renewable fuel standard mandates, world oil price levels, and import tariff effects on ethanol production and the demand for corn grain.

If the import tariff and/or blend subsidy were reduced, profit margins would be even lower for the ethanol industry (see Fig. 4). One legislative proposal suggests replacing the fixed $0.45/gallon subsidy with a variable rate subsidy that reflects changes in petroleum and corn prices, i.e., the corn ethanol blend subsidy would increase when corn prices increase and/or petroleum prices decrease [7].

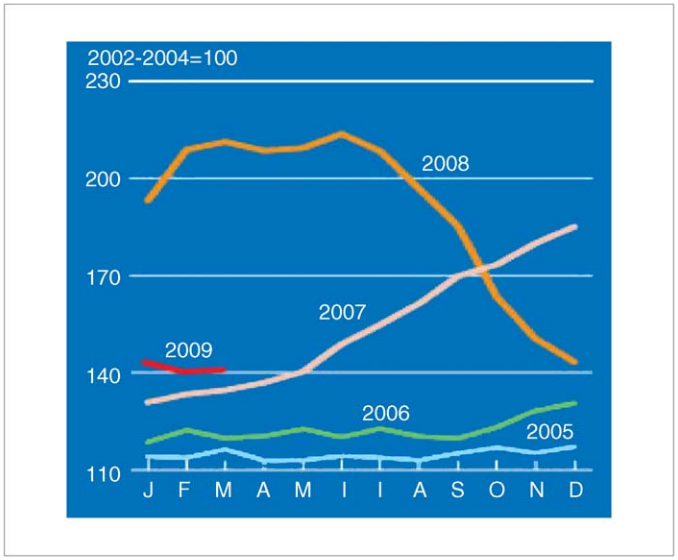

FIGURE 9

FAO food price index. *Source*: Brian Wright, University of California Berkley. Snyder Lecture, Purdue University, April 17, 2009 .

There has been some expansion of U.S. biodiesel processing capacity, especially from soybean oil, in response to the renewable fuel standard mandate [9]. When diesel prices exceeded \$4.00 per gallon and soybeans approached \$16 per bushel in early 2008, even with the \$1.00 per gallon tax credit, the profit margins were relatively modest for biodiesel producers. The decline in petroleum prices in early 2009, despite concurrent declines in soybean prices, significantly tightened the biodiesel processor profit margins. Under current price relationships, vegetable oil based biodiesel is not economically viable without government subsidies. Also vegetable oils compete for various food uses.

The blending wall

In 2008, higher petroleum prices reduced gasoline consumption. In 2009, despite lower petroleum prices, the U.S. recession has further reduced gasoline consumption (Fig. 12). Gasoline use declined from 143 billion gallons in early 2008 to 137 billion gallons in early 2009 [9].

Ethanol production capacity in mid-2009 was estimated at 12.4 billion gallons, but the industry was operating 16% below capacity. Lower petroleum prices, the relatively high price paid by some ethanol plant managers for corn in 2008, and the reduction in the blend subsidy substantially reduced profit margins for the ethanol industry. In fact, in 2009 several firms, such as VeraSun, filed bankruptcy and sold several of their plants. Construction stopped on a few plants and some were idled.

If petroleum prices continue to increase in 2010, and the world economy has not recovered significantly from the current recession, and given the renewable fuel standard of 12 billion gallons of ethanol in 2010, the U.S. ethanol industry will approach the blend wall, i.e., with a 10% blend of ethanol in each gallon of gasoline there would be almost enough ethanol to blend with every gallon of gasoline consumed in the United States [10]. The U.S. Environmental Protection Agency is considering increasing the current 10% blend ratio to 15%. The automotive sector argues that despite the increased sales of flex-fuel cars, the majority of the cars in the

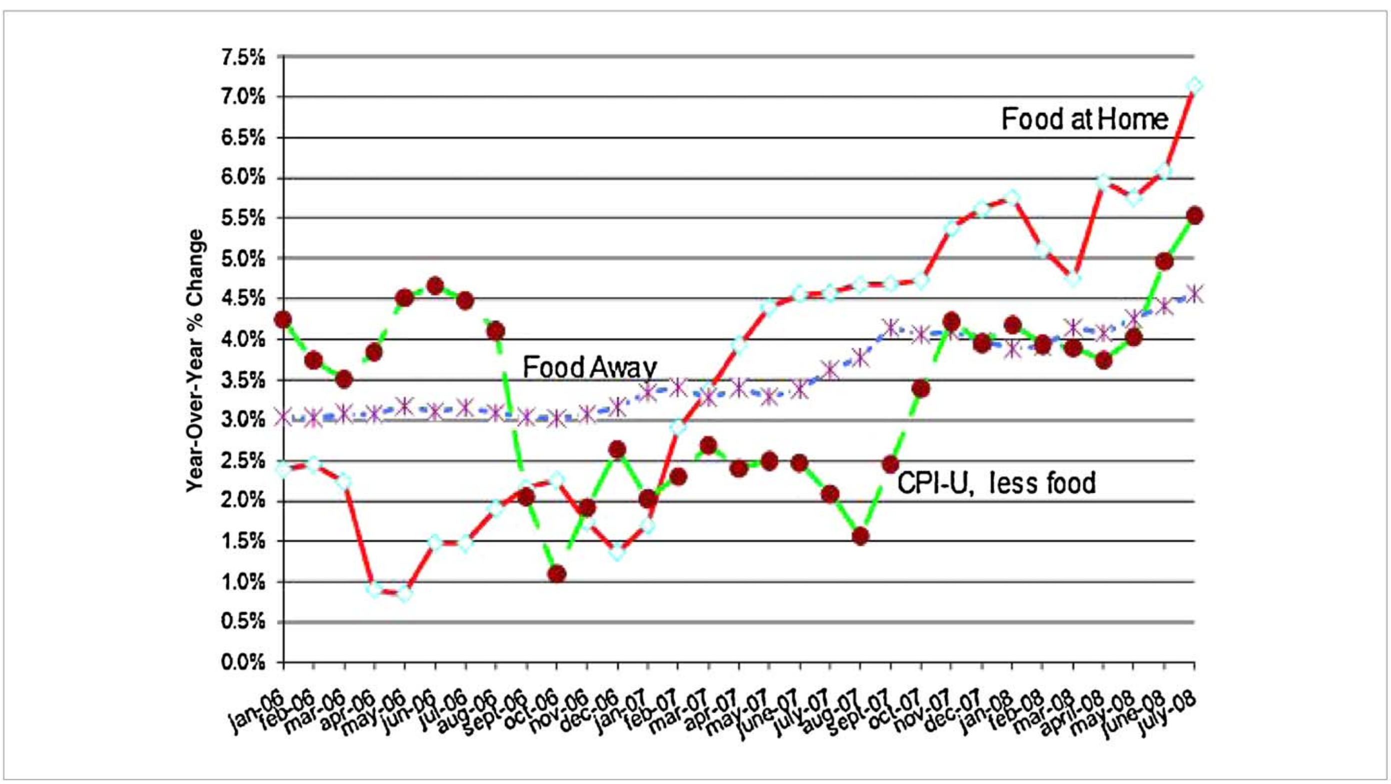

FIGURE 10

Retail food price changes, year-over-year annual rates, by months, 2006–July 2008. *Source*: Corinne Alexander, Department of Agricultural Economics, Purdue University, August 2008.

TABLE 2

U.S. food price changes

Consumer price indexes	Relative importance[a]	Final 2005	Final 2006	Final 2007	Final 2008	Forecast 2009[b]
	Percent	Percent change				
All food	100.0	2.4	2.4	4.0	5.5	3.0–4.0
Food away from home	44.3	3.1	3.1	3.6	4.4	3.5–4.5
Food at home	55.7	1.9	1.7	4.2	6.4	2.5–3.5
Meats, poultry, and fish	12.2	2.4	0.8	3.8	4.2	2.0–3.0
Meats	7.9	2.3	0.7	3.3	3.5	1.5–2.5
Beef and veal	3.8	2.6	0.8	4.4	4.5	1.5–2.5
Pork	2.4	2.0	−0.2	2.0	2.3	1.5–2.5
Other meats	1.7	2.4	1.8	2.3	3.1	0.0–1.0
Poultry	2.3	2.0	−1.8	5.2	5.0	2.0–3.0
Fish and seafood	2.1	3.0	4.7	4.6	6.0	4.0–5.0
Eggs	0.7	−13.7	4.9	29.2	14.0	−5.0 to −4.0
Dairy products	6.2	1.2	−0.6	7.4	8.0	−4.0 to −3.0
Fats and oils	1.6	−0.1	0.2	2.9	13.8	3.0–4.0
Fruits and vegetables	8.2	3.7	4.8	3.8	6.2	3.5–4.5
Fresh fruits and vegetables	6.2	3.9	5.3	3.9	5.2	4.0–5.0
Fresh fruits	3.1	3.7	6.0	4.5	4.8	4.0–5.0
Fresh vegetables	3.1	4.0	4.6	3.2	5.6	3.5–4.5
Processed fruits and vegetables	1.9	3.3	2.9	3.6	9.5	3.0–4.0
Sugar and sweets	2.1	1.2	3.8	3.1	5.5	3.0–4.0
Cereals and bakery products	7.9	1.5	1.8	4.4	10.2	2.5–3.5
Nonalcoholic beverages	6.7	2.9	2.0	4.1	4.3	3.0–4.0
Other foods	10.1	1.6	1.4	1.8	5.2	3.0–4.0
Market basket of farm foods:						
Farm value	N.A.	−0.4	−3.1	18.3	3.8	N.A.
Farm to retail price spread	N.A.	5.2	0.4	0.9	7.5	N.A.
Retail price	N.A.	3.9	−0.3	4.5	6.7	N.A.

Source: USDA-ERS, Briefing Room, March 25, 2009.

[a] BLS estimated expenditure shares, December 2008.

[b] Forecasts updated by the 25th of each month. *Source of historical data*: Bureau of Labor Statistics Forecasts by Economic Research Service.*Source:* USDA-ERS, Briefing Room, March 25, 2009.

national fleet were not designed for an ethanol blend greater than 10%. However, in countries such as Brazil cars are designed to operate on more than a 10% blend, and in fact many run on a 100% ethanol fuel. The other limiting factor for the sales of E85 cars in the United States is the lack of infrastructure, i.e., relatively few service stations have pumps dedicated to E85. In recent months, given the lower miles per gallon with E85 compared to regular gasoline and the very small price differential between E85 and regular gasoline, there has been no economic incentive for drivers to purchase E85 cars or fuel.

Environmental concerns

The debate continues on the benefits of ethanol blends with gasoline. Some critics argue that with the fertilizer and diesel fuel required to produce corn, plus the energy required to operate the ethanol plants, there is a relatively modest net energy gain. Plus some worry that with increased corn acreage and higher input use there will be greater potential for environmental damage from soil erosion, and chemicals and fertilizers entering the surface and ground water.

Others suggest, however, that with improved corn hybrids that yield more per unit of fertilizer applied, plus conservation and no-till farming systems, there is no significant adverse environmental impact from increased corn production. Also ethanol/gasoline blends enhance air quality, especially in larger cities where smog has been a problem. Ethanol is more environmentally friendly than methyl tertiary butyl ether (MTBE)—a fuel additive or oxygenate that improves the burning of hydrocarbons and reduces air pollution. MTBE is a carcinogen and was found in ground water from leaking fuel tanks in states such as California. Its use has been restricted by U.S. Environmental Protection Agency regulations and ethanol has become the preferred substitute in gasoline as an oxygenate.

Robertson *et al.* [11] provide an insightful comparative analysis of the potential environmental harm of both grain-based and biomass/cellulosic-based ethanol production. They point out that without proper management, corn-based ethanol can increase the carbon debt, increase soil erosion, and additional use of agricultural chemicals and fertilizer can pollute ground and surface water. But these potential environmental hazards can be mitigated with

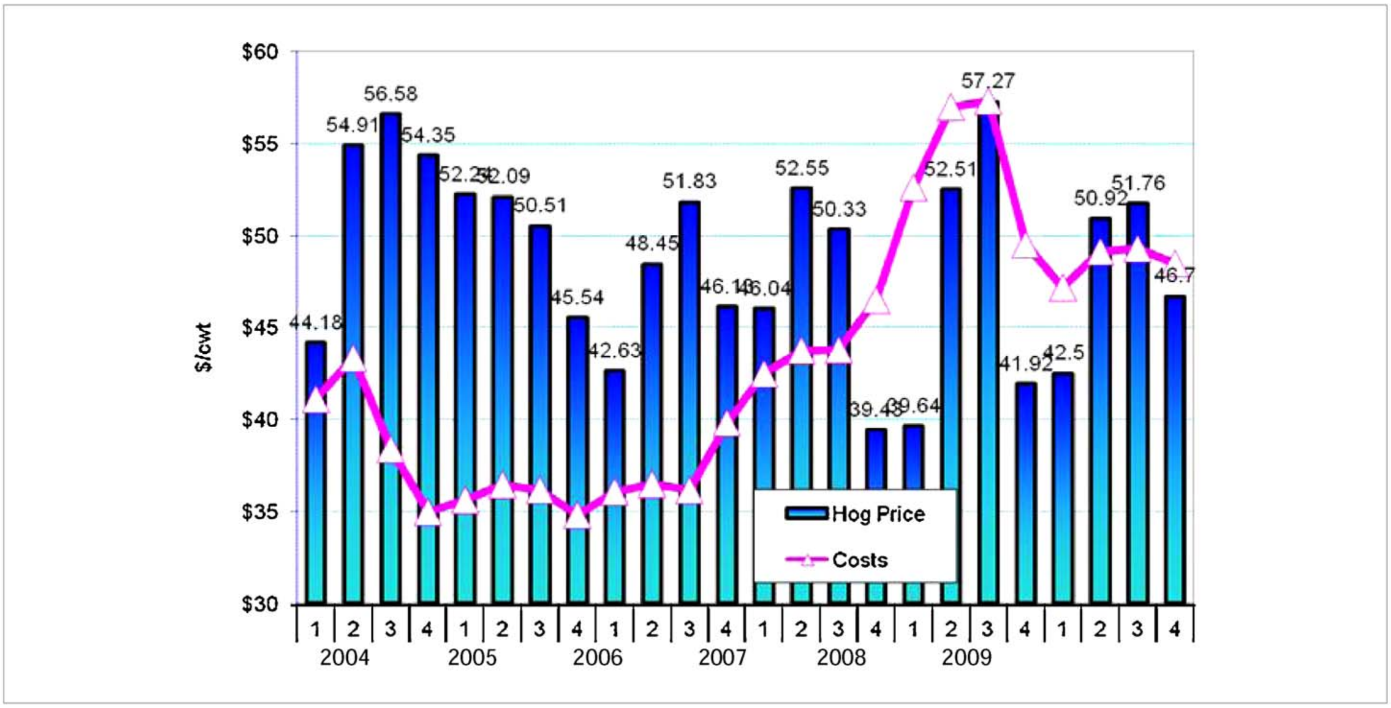

FIGURE 11

Estimated hog prices and costs per live hundredweight. *Source*: Chris Hurt, Department of Agricultural Economics, Purdue University, April 2009.

no-till farming systems, adoption of precision-farming methods that foster fertilizer applications according to the nutrient uptake of the plants, planting of cover crops plus riparian strips along rivers and bodies of water that can sequester soil carbon and intercept nitrate leakage and phosphorus runoff, and adoption of transgenic crops that can reduce the need for pesticides and/or increase drought stress-tolerant varieties which can increase water and nutrient efficiency.

Babcock *et al.* [12] report that once all corn and ethanol direct and indirect impacts are calculated, corn-based ethanol can reduce carbon emissions. But the results depend on whether (1) natural gas or coal is used to power the ethanol plant, (2) distillers grain is dried or sold wet, and (3) expansion in corn production comes mainly from a reduction in acreage of lower valued crops or if idled conservation or forest land is brought into production. In the Western U.S. Corn Belt where many of the ethanol plants are located, cattle feedlots are close by and wet distillers grain can be more readily utilized. Also in the United States most of the expansion in corn production has been the result of rotational changes, i.e., rather than a two-year corn/soybean rotation farmers have shifted to a three-year corn/corn/soybean rotation. Corn acreage increased dramatically in 2007 in response to the demand for corn. By 2008, higher corn production costs (especially for fertilizer and diesel fuel) and relatively higher soybean prices resulted in a shift back towards more soybean acres (see Fig. 13).

World perspective

Approximately two-thirds of the world ethanol production is in two countries—United States (corn grain based) and Brazil (sugarcane based) (see Fig. 14). The volume of ethanol produced per acre is much greater for sugarcane than for corn. Hence, the cost of production per gallon of ethanol is less for sugarcane.

Hertel *et al.* [13] using the GTAP model, provide useful insights into the global land use and potential environmental impacts of U.S., EU and Brazilian biofuel policies. It is important to analyze the combined impacts and not just individual country impacts of these biofuel policies, due to the relative price responses and international ramifications for land use for corn, soybeans and sugar cane production. It is also relevant to estimate whether the increased biofuel production comes from adjustments among crop land, pasture land or forest land. Greenhouse gas emissions can be much greater if forest land is cleared directly or indirectly as a result of these biofuel policies, in contrast to shifts in land use among existing crop and pasture land.

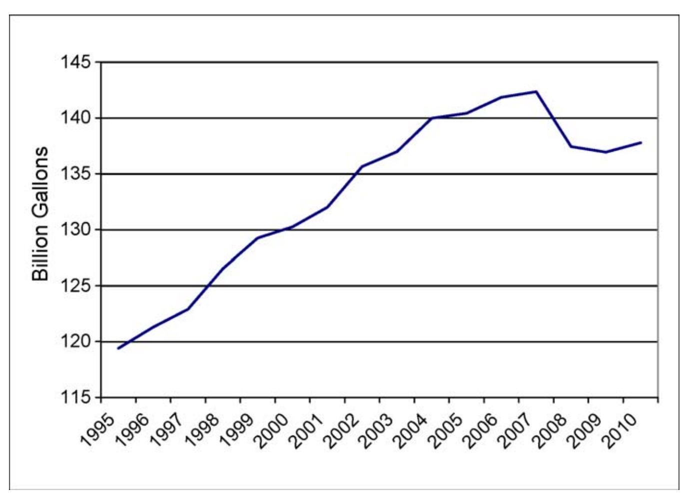

FIGURE 12

U.S. blended gasoline consumption. *Source*: Energy Information Administration.

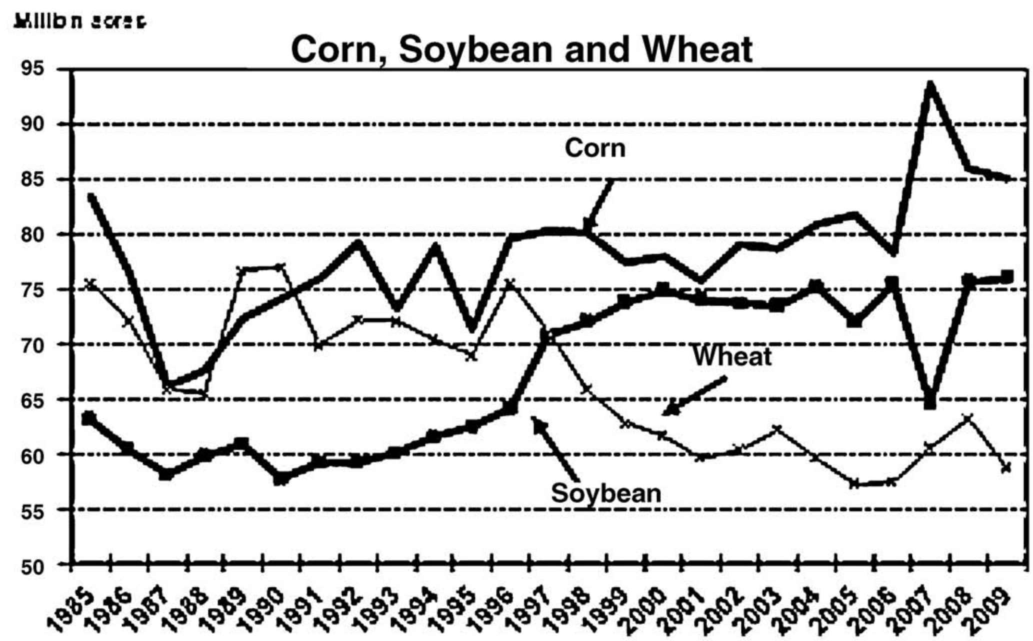

FIGURE 13

U.S. corn, soybean, wheat and cotton planted acreage. *Source*: Glauber, Chief Economist, USDA, February 2009.

Developing country perspective

The sharp rise in commodity prices in global markets in 2008 was a double-edged sword for developing countries. For market-oriented farmers, in contrast to subsistence farmers, this increased their income. However, for low-income consumers, especially in urban areas, who are dependent on the market for their food, increases in food prices had a negative impact. The impacts of higher food prices are especially severe for low-income consumers because they often spend from 25% to 50% of their disposable income on food. Although higher food prices do adversely impact high-income consumers, those who spend 15% or less of their income on food experience a much less severe impact from food price increases than those who spend 25–50%. Expenditures on food consumed at home in 2007 in the United States were only 5.7% compared to 8.6% in the United Kingdom, 11.4% in Germany, 13.7% in France, 14.5% in Italy, 14.6% in Japan, 24.6% in Brazil, 28.7% in Russia, 32.4% in India, 34.9% in China, 38.8% in Egypt and 45.7% in Pakistan [5]. Hence, even though the impact of the increased

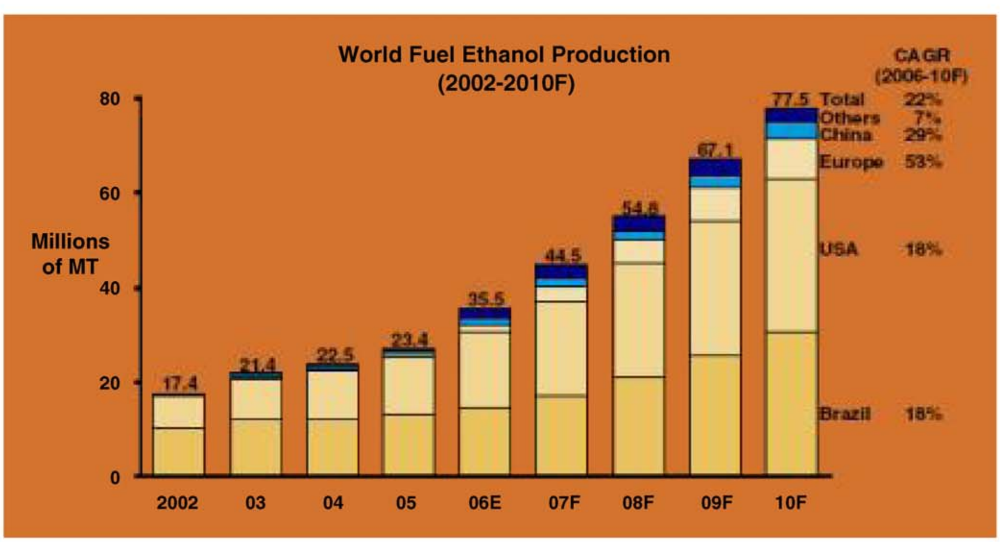

FIGURE 14

World fuel ethanol production. *Source*: Enzyme Use for Corn Fuel Ethanol Production, Novozyme, July 2007.

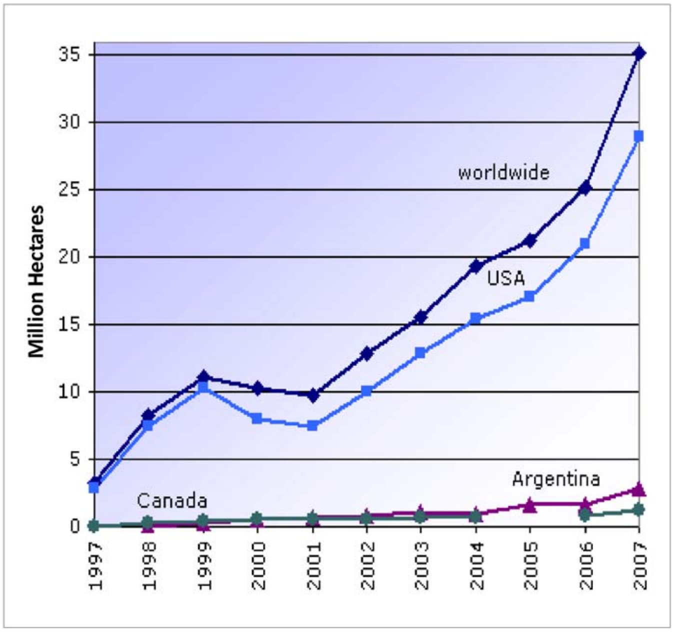

FIGURE 15

Adoption of transgenic corn. *Source*: GMO Compass, October 9, 2008. www.gmo-compass.org.

demand for corn for ethanol had a relatively modest impact on food prices in the United States, any food price increases, from whatever source, can have a much greater adverse impact on low-income consumers in developing countries.

Von Braun [14] provides a perspective on the impacts of food price increases on developing countries. Higher food prices cause the poor to limit food consumption. This can result in undernutrition and adverse health impacts, especially for children who are already at risk. Ivanic and Martin [15] further note that food price increases in 2008 probably increased overall poverty in low-income countries.

As indicated previously, many factors contributed to food price increases in 2008–2009. Although biofuels have been blamed for higher food costs to low-income people, especially in the developing world, it was only one factor, and probably not the primary contributing factor.

Role of biotechnology

Biotechnology has had rather modest impacts on the biofuel sector to date. The adoption of transgenic crops has grown rapidly in many countries during the past decade. According to James [16], in 2008, 13.3 million farmers in 25 countries planted 125 million hectares of transgenic crops. Herbicide tolerant soybean adoption predominates in the three major producing countries (United States: 92%, Argentina: 98%, and Brazil: 64%). Adoption of transgenic corn represents 80% of the area in the United States, 84% in Canada, and 84% in Argentina (Fig. 15).

In the United States, while transgenic corn has minimized yield losses by reducing insect and weed pressure, other techniques such as marker-assisted selection have helped breeders develop hybrids with more desirable agronomic traits and higher starch content. As these varieties with higher starch content are adopted, provided there are price incentives for growers, the ethanol industry will be able to further increase the per acre yield of ethanol. Also as cellulosic fermentation techniques are improved, corn cobs and corn stalks can be harvested and fermented to produce ethanol. Consequently, corn will be a source of ethanol from both the grain and cellulosic components. However, the total biomass furnished by corn will still remain less on a per ace basis than sugarcane. On average, corn grain generates 354 gallons of ethanol per acre in the United States versus 662 gallons per acre from sugarcane in Brazil [17].

Increases in area planted and yields have contributed to the availability of corn for ethanol production in the United States. To satisfy this surge in demand for corn for ethanol, the proportion of corn destined for export and domestic livestock feed has declined.

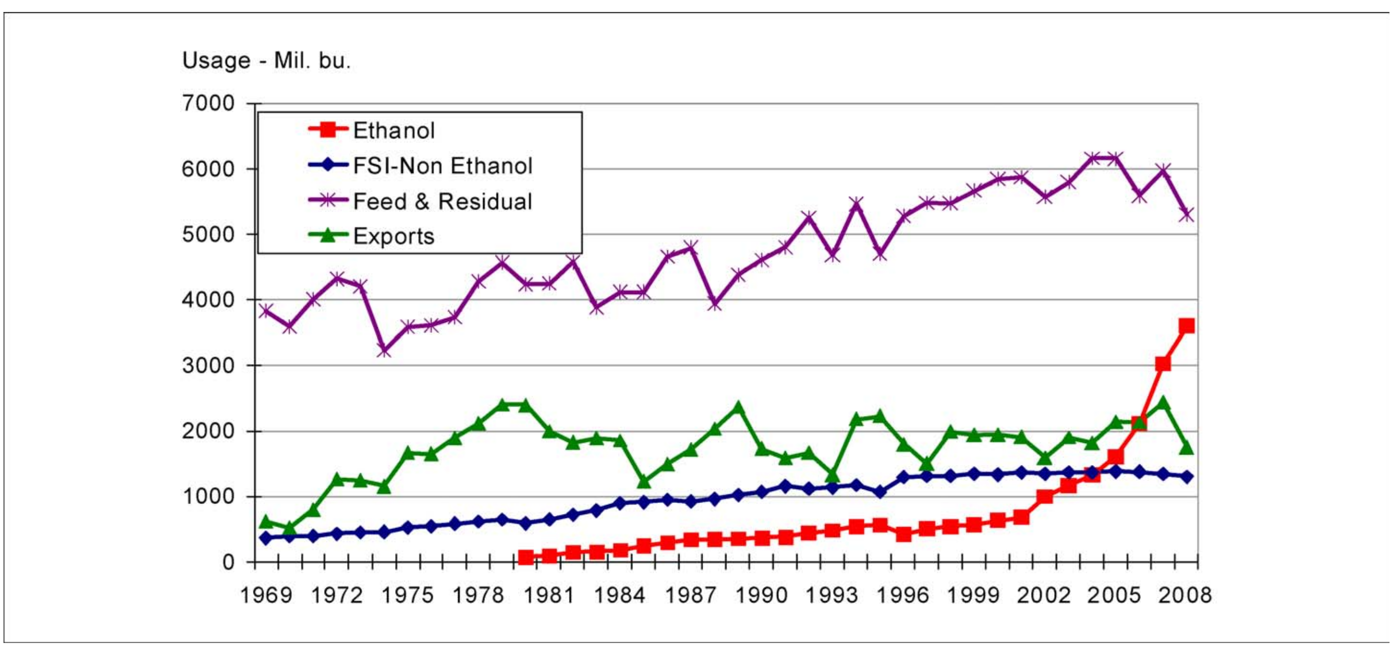

FIGURE 16

U.S. corn production and usage by category. *Source*: Steve Meyer, Paragon Economics, Inc., March 2009.

For example, in the 2008–2009 marketing year, 37% of the total corn supply was used to produce ethanol in contrast to 12% for exports and 39% for livestock feed use. As recently as 2005–2006, only 12% of the corn supply was used for ethanol, 16% for exports, and 46% for livestock feed (Fig. 16).

With continued genetic improvements in corn through marker-assisted conventional breeding as well as transgenic approaches, over the next five to ten years it should be feasible to continue to increase corn yields and meet the 15 billion gallon renewable fuel standard for corn-based ethanol and increase the quantities of corn required for export and domestic livestock feed markets. Drought-tolerant varieties may soon be available which could result in more stable yields and a potential expansion of corn production into more drought-prone regions. However, if petroleum prices return to the record high levels of 2008, this would make ethanol production more profitable and increase corn prices again, but petroleum-based input costs would also increase. This would imply price volatility and uncertain profit margins for corn producers as they attempt to balance higher corn yields and prices against higher fuel and fertilizer production costs.

According to the Biotechnology Industry Organization [18], ethanol yields have increased 20% from 2.5 gallons per bushel in 2000 to almost 3.0 gallons per bushel. New 'no cook' enzymes have been developed to extract sugars from corn at room temperatures, greatly reducing the energy inputs, reducing costs, and improving the environmental profile of ethanol from corn starch. Further scientific breakthroughs are expected that will facilitate the use of corn stover, cobs, and other biomass to generate ethanol.

Conclusions

In 2007–2008, a series of several concurrent worldwide events resulted in a sharp increase in commodity and food prices. Among the most important were: long-term trends towards the dietary transition to more grain-fed livestock products in several developing nations, the low stocks-to-use ratio for grains in the early 2000s, the weak U.S. dollar, high petroleum prices largely driven by economic development in several Asian countries, and government policies (e.g. U.S. renewable fuel standard mandates and subsidies) that provided incentives for the biofuel sector to build ethanol plants.

Since mid-2008, a major world recession has resulted in a dramatic decrease in world petroleum prices, commodity prices have fallen sharply, and there has been substantial moderation in food price inflation. U.S. government biofuel policies remain in place—a long-term renewable fuel standard coupled with an import tariff on ethanol and a domestic blender's subsidy. Consequently, the use of corn for ethanol will continue to increase, albeit at a slower pace than in the recent past as the 15 billion gallon mandate is reached in 2012. In 2009, some ethanol companies filed bankruptcy, construction was halted on others, and there was excess capacity in the U.S. ethanol industry.

Long term trends suggest, however, that higher petroleum prices will probably occur in the years ahead given the world's finite supply of petroleum. There will be continued economic and government policy pressures for energy independence, coupled with governmental policies to encourage environmentally friendly sources of energy. Corn grain as a feedstock for ethanol will probably plateau in the next few years as the mandate of 15 billion gallons of ethanol from corn grain is achieved. At that point, cellulosic sources will become increasingly important if the mandate of 36 billion gallons of biofuels is to be achieved in 2022. The key to success with cellulosic feedstocks will be scientific and technological discoveries that drive down production costs in the field and the processing plants, so that cellulosic ethanol is price competitive with gasoline and the current corn-grain based ethanol sources. Discoveries in biotechnology will be crucial to increase effectively the yield of biomass crops as well as efficiency of fermenting the biomass material in the ethanol plants.

Increased investment in improved plant genetics and farming practices should facilitate growth in grain yields and the ability to satisfy food, feed and biofuel demands at reasonable prices. The world population is projected to reach 9 billion by 2050, and once the world recovers from the current recession and per capita incomes increase, the dietary transition is likely to accelerate, with growth in the demand for animal protein which will require more feed grains and oilseeds. This suggests a tight supply-demand balance for grains, with price volatility which could result from adverse weather, significant climate change and/or political decisions that generate food scares and food price inflation in future years. Thus, the recent food/biofuel debate may be revisited in future years.

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GMO foods and crops: Africa's choice

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There is a scientific consensus, even in Europe, that the GMO foods and crops currently on the market have brought no documented new risks either to human health or to the environment. Europe has decided to stifle the use of this new technology, not because of the presence of risks, but because of the absence so far of direct benefits to most Europeans. Farmers in Europe are few in number, and they are highly productive even without GMOs. In Africa, by contrast, 60% of all citizens are still farmers and they are not yet highly productive. For Africa, the choice to stifle new technology with European-style regulations carries a much higher cost.

The future of genetically engineered foods and crops in Africa will depend heavily on choices African governments make regarding the regulation of this technology. There are essentially two different regulatory approaches available: the approach used by the European Union and the approach used by the United States. There are four key differences between these approaches:

- The regulatory approach used in Europe requires new and separate laws that are specific to genetically engineered ('GMO') foods and crops. By contrast, the United States regulates GMOs for food safety and for environmental safety using the laws that were already in place to govern non-GMO foods and crops.
- The European approach also requires the creation of new institutions (for example, national biosafety committees) and a separate screening and approval process for GMOs. In the United States the institutions that screen and approve GMOs (the Food and Drug Administration, the Animal and Plant Health Inspection Service, and the Environmental Protection Agency) are the same institutions that screen and approve non-GMO foods and crops.
- The European approach also differs because it can decline to approve a new technology on grounds of 'uncertainty' alone, without any evidence of risk. A hypothetical risk that has not yet been tested for is sufficient reason for blockage. This is known as the precautionary approach. In the United States, if standard tests for known risks such as toxicity, allergenicity and digestivity have been passed successfully, there is usually no regulatory barrier to commercial release.
- Finally, in Europe all products in the marketplace with some GMO content must carry identifying labels, while in the United States the FDA does not require labels on any approved GMO foods.

Which of these two approaches is better? In the abstract, the best regulatory approach will be one that allows new technologies to be used while preventing new risks to human health or the environment. Using this standard, the U.S. approach has done a better job because it has allowed many more useful new technologies to be employed by farmers, without any documented new risks so far. By contrast, the European approach has blocked the planting of GMO crops in most countries in Europe, to the frustration of most European farmers who want to share in the productivity gains these crops provide.

There has not yet been any documented evidence that approved GMOs have posed new risks either to human health or the environment. This finding of 'no new risks' is the official view of scientific authorities in Europe itself. European science academies took several years to study the impacts of GMO crops on human health and the environment following the first commercializations in 1995, but by 2001–2004 a consensus had

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emerged that no new risks from these seeds had been documented.

In 2001, the Research Directorate General of the EU released a summary of 81 separate scientific studies conducted over a 15-year period (all financed by the EU rather than private industry) aimed at determining whether GM products were unsafe, insufficiently tested, or under-regulated [1]. The EU Research Directorate concluded from this study, 'Research on GM plants and derived products so far developed and marketed, following usual risk assessment procedures, has not shown any new risks on human health or the environment...' [2].

National academies of science in Europe began drawing this same conclusion one year later. In December 2002, the French Academy of Sciences stated that 'all the criticisms against GMOs can be set aside based for the most part on strictly scientific criteria.' [3]. At the same time the French Academy of Medicine announced it had found no evidence of health problems in the countries where GMOs had been widely eaten for several years [4]. In the UK in May 2003, the Royal Society presented to a government-sponsored review two submissions that found no credible evidence GM foods were more harmful than non-GM foods [5], and the Vice-President and Biological Secretary of the Royal Society, Professor Patrick Bateson, expressed irritation at the undocumented assertions of risk that continued to come from anti-GMO advocates: 'We conducted a major review of the evidence about GM plants and human health last year, and we have not seen any evidence since then that changes our original conclusions. If credible evidence does exist that GM foods are more harmful to people than non-GM foods, we should like to know why it has not been made public.' In March 2004, the British Medical Association (BMA) that had earlier withheld judgment endorsed these Royal Society conclusions [6]. In September 2004, the Union of the German Academies of Science and Humanities produced a report that concluded, '...according to present scientific knowledge it is most unlikely that the consumption of the well characterized transgenic DNA from approved GMO food harbours any recognizable health risk.' [7]. This report added that food from insect resistant GMO maize was probably healthier than from non-GMO maize due to lower average levels of the fungal toxins that insect damage can cause.

A consensus also emerged at the global scientific level of no new risks linked to any of the GMO crops and foods to have reached the market so far. In March 2000, the Organization for Economic Cooperation and Development (OECD) in Paris organized a conference with 400 expert participants from a variety of backgrounds. These experts announced their agreement that 'No peer-reviewed scientific article has yet appeared which reports adverse effects on human health as a consequence of eating GM food.' [8]. In August 2002, the Director-General of the World Health Organization (WHO) endorsed consumption of GMO foods, saying, 'WHO is not aware of scientifically documented cases in which the consumption of these foods has negative human health effects. These foods may therefore be eaten.' [9].

Some accept that GMO foods are probably safe to eat, yet they still question their safety for other living things in the biological environment (their 'biosafety'). Because all farming disturbs and changes nature, it is difficult to agree on exactly what level of disturbance should be considered dangerous or unacceptable. Studies have shown, for example, that planting a GMO variety of beet or rapeseed can help farmers control weeds in the field (compared to conventional beet or rapeseed), but as a result there might also be fewer insects in the farm field (using the weeds for food and shelter) and hence fewer weed seeds for some farmland birds to eat. Are these weedless farm fields to be considered a damaging disturbance of nature? Some ecologists might say yes, but most conventional environmental advocates would say no.

By most conventional definitions of biosafety, the GMO crops currently on the market have not disturbed nature (beyond farm fields) any more than conventional crops. A 2003 study conducted by scientists from New Zealand and the Netherlands [10] examined data collected worldwide up to that time, and the authors concluded from this data that the GMO crops approved so far had been no more likely to worsen weed problems than conventional crops, no more invasive or persistent, and no more likely to lead to gene transfer. There was no evidence that GMO crops had transferred to other organisms (including weeds) new advantages such as resistance to pests or diseases or tolerance to environmental stress.

Later in 2003 the International Council for Science (ICSU) examined the findings of roughly 50 different scientific studies that had been published in 2002–2003 and concluded, '[T]here is no evidence of any deleterious environmental effects having occurred from the trait/species combinations currently available.' [11]. In May 2004, the United Nations Food and Agriculture Organization (FAO) issued a 106 page report summarizing evidence that, 'to date, no verifiable untoward toxic or nutritionally deleterious effects resulting from the consumption of foods derived from genetically modified foods have been discovered anywhere in the world.' [12]. On the matter of environmental safety, this FAO report found the environmental effects of the GM crops approved so far, including effects such as gene transfer to other crops and wild relatives, weediness and unintended adverse effects on nontarget species (such as butterflies), had been similar to those that already exist from conventional agricultural crops. Finally, in 2007, a study done for the journal *Advanced Biochemical Engineering/Biotechnology* surveyed ten years of research published in peer-reviewed scientific journals, scientific books, reports from regions with extensive GM cultivation, and reports from international governmental organizations and found that, 'The data available so far provide no scientific evidence that the cultivation of the presently commercialized GM crops has caused environmental harm.' [13].

Sceptics who remain fearful sometimes respond that 'absence of evidence is not the same thing as evidence of absence.' Yet if you look for something for 15 years and fail to find it, that must surely be accepted as *evidence* of absence. It is not *proof* that risks are absent, but proving that something is absent (proving a negative) is always logically impossible.

The explanation for Europe's highly precautionary regulatory approach toward GMOs goes beyond risks. It is a policy posture that reflects not a presence of new risks for Europeans, but instead an absence of new benefits for most Europeans. The first generation of GMO crops has provided significant benefits to some farmers, but for ordinary food consumers in rich countries there have so far been few benefits so far.

The first generation of GMO crops that came to the market in 1995–1996 provided benefits mostly to farmers growing cotton, maize, and soybean, in the form of lower costs for the control of insects and weeds. Yet Europe does not have many cotton, maize,

and soybean farmers, so the new technology had few champions. For the 99% of Europeans who were not maize, cotton, or soybean farmers, the new technology offered almost no direct benefit. For consumers, the new GMO products did not taste any better, look any better, smell any better, prepare any better or deliver any improved nutrition. Because the vast majority of Europeans saw little or no direct benefit from the technology, they felt they had nothing to lose by keeping it out of farm fields and out of their food supply. They welcomed a highly precautionary regulatory approach as one way to ensure that outcome.

To demonstrate that it was a benefit calculation rather than a risk calculation that mattered most to Europeans in this case, look at the quite different way Europe regulates GMOs in medicine, versus GMOs in agriculture. In the case of medical drugs, Europe does not hesitate to permit the commercial sale of medicines developed with genetic engineering. By 2006, the European Medicines Agency had actually approved 87 recombinant drugs derived from genetically engineered bacteria or from the ovary cells of genetically engineered Chinese hamsters. These drugs were not free from new risks; clinical trials had shown that many actually increased risks of heart disease, malignancy, and gastric illness, but European regulators approved them just the same because of the benefits the drugs could deliver to so many Europeans. While fewer than 1% of Europeans stood to benefit directly from GMO agricultural crops, 100% were vulnerable to the diseases these GMO drugs could help treat, so the regulator treatment of the GMO drugs was far less precautionary. There were both known risks from clinical trials and plenty of uncertainties surrounding long-term exposures, yet the 'precautionary principle' was not allowed to block the commercial release of a technology that could bring significant benefits to Europeans.

Consider now the very different circumstances of Africa. In Africa, the percentage of the population that might benefit directly from agricultural GMOs is much higher than in Euorope, because 60% or more of all Africans are still farmers who depend directly on agriculture for income and subsistence. Some GMO crop traits now widely commercialized outside of Africa, such as *Bt* crops (e.g. for maize and cotton) that resist insect damage with fewer chemical sprays, could have wide benefits if planted in Africa today. Other GMO traits soon to come out of the research pipeline, including abiotic stress tolerance traits such as drought resistance, could provide even wider benefits in the future.

Drought tolerant maize is only one of the new GMO crop technologies now emerging from the research pipeline. Maize is a staple food for more than 300 million people in Sub-Saharan Africa, many of whom are themselves growers of maize. These Africans remain poor and food insecure because the productivity of their labor in farming is so low. Population growth has been pushing maize production into marginal areas with little and unreliable rainfall (only 4% of cropland in Sub-Saharan Africa is irrigated). These factors, combined with human-induced climate change, are expected to increase drought risks to maize growers in Africa in the years ahead. The development of maize varieties better able to tolerate drought is one important response to this growing challenge.

Not all drought tolerant maize varieties will be GMOs. CIMMYT's Drought Tolerant Maize for Africa (DTMA) initiative, funded in 2007 by the Bill and Melinda Gates Foundation and the Howard G. Buffet Foundation, is designed to accelerate the breeding of non-GMO drought tolerant varieties of maize, both hybrids and open pollinated varieties (OPVs) in 13 countries in Sub-Saharan Africa. This initiative will use conventional and marker-assisted selection breeding but no transgenic techniques. Other initiatives, however, use GMO techniques. One example is the Water Efficient Maize for Africa (WEMA) project, funded in 2008 by the Bill and Melinda Gates Foundation and operated in Africa by the African Agricultural Technology Foundation (AATF). CIMMYT is a partner in this project, as is the Monsanto Company. This initiative will use transgenic techniques in addition to conventional and marker-assisted selection.

Regulatory requirements in Africa for GMOs are emerging as a crucial consideration here. WEMA's genetically engineered (GE) varieties of drought tolerant (DT) maize will deliver benefits to African farmers only if African regulators first allow the technology to be tested in open field trials in Africa and then approve the technology for commercial release to farmers. The regulatory gauntlet for this technology will be long and difficult because in Africa, just as in Europe, transgenic technologies are screened using separate and much higher regulatory standards. In each separate African country, technology developers such as AATF will not be allowed to conduct research on a WEMA variety (e.g. conduct a field trial) without explicit prior approval from a national biosafety committee (NBC). Giving or selling the seed to farmers will not be permitted in any country until the NBC has granted a formal commercial release.

Before they grant a commercial release, NBCs typically require technology developers to compile and submit a substantial dossier of data – including the molecular characterization of the variety, the results of lab tests for food safety and the results of field trials for efficacy and biosafety. Once these data are in hand, the NBC can either grant a commercial release promptly, or refuse to approve, or ask for more data, or do nothing at all, in which case the technology cannot be legally sold or distributed to farmers. In the hands of highly precautionary regulators, this system tends to keep new technologies out of the fields indefinitely. So far, 15 years after GMO crops were first planted commercially in the United States, only two governments in Sub-Saharan Africa have given a commercial release to any GMO crops, the Republic of South Africa (for maize, soybean, and cotton) and Burkina Faso (only for cotton).

Why have so many governments in Africa chosen to follow this highly precautionary European approach toward regulating GMO foods and crops, despite the technology blockages and extended delays nearly certain to result? Five separate channels of external influence on Africa have led to this choice of Europe's regulatory approach over the approach of the United States.

Bilateral foreign assistance is the first channel of external influence on Africa. Governments in Africa are still significantly dependent on foreign assistance. On average, they are four times as aid-dependent relative to GDP as the rest of the developing world. For this reason, much that takes place in Africa today remains 'donor driven'. Since Africa's official development assistance from Europe is three times as large as ODA from the United States, the voice of European donors in Africa tends to be louder than any American voice. Governments in Europe have used their ODA to encourage African governments to draft and implement highly precautionary European-style regulatory systems for agricultural GMOs.

A second channel of external influence has been multilateral technical assistance through the UNEP/GEF Global Project for Development of National Biosafety Frameworks (NBFs). Of 23 African governments that had completed a NBF under this UNEP program by October 2006, all but the Republic of South Africa had no previous regulations in place for agricultural GMOs, so UNEP was in effect writing on a blank slate. In the end, 21 of these 23 countries embraced the strongest possible approach (the 'Level One' approach), requiring regulations through binding legal instruments approved by the legislative branch of government (parliament), parallel to the European approach. Europe had greater influence than the United States over this UNEP/GEF program because European governments contribute roughly three times as much to the GEF trust fund as does the United States.

A third channel of external influence has been advocacy campaigns against GMOs from international non-governmental organizations (INGOs), the most active of which are headquartered in Europe. Greenpeace International and Friends of the Earth International, both based in Amsterdam, have campaigned heavily in Africa against agricultural GMOs. Zambian officials were told by Greenpeace that if GMOs were let into their country, organic produce sales to Europe would collapse. An organization named Genetic Food Alert warned Zambia in 2002 of the 'unknown and unassessed implications' of eating GM foods, and a British group named Farming and Livestock Concern warned them that GM corn could form a retrovirus similar to HIV. These assertions were not backed by any evidence, but they frightened the Zambians into banning GMOs completely.

A group of mostly European NGOs continued this campaign against GMOs at the 2002 World Summit on Sustainable Development in Johannesburg. Led by Friends of the Earth International, they coached their African partners into signing an open letter warning that GMOs might cause allergies, chronic toxic effects and cancers, despite the absence of any scientific evidence for these risks. At this same meeting in 2002, two Dutch organizations, HIVOS and NOVIB, joined with partner groups from Belgium, Germany and the UK to finance a 'small farmers march' on Johannesburg (led by a non-farmer) that ended with a pronouncement that Africans 'say NO to genetically modified foods.'

A fourth channel of external influence has been commercial agricultural trade. Africa's farm exports to Europe are six times as large as exports to the Untied States, so it is European consumer tastes and European regulatory systems that Africans most often must adjust to. In 2000, private European buyers stopped importing beef from Namibia because it had been fed on GMO maize from the Republic of South Africa, and then in 2002, Zambia rejected GMO maize as food aid in part because an export company (Agriflora Ltd.) and the export-oriented national farmers union (ZNFU) were anxious that exports of organic baby corn to Europe not be compromised. The risks of export rejections from African countries that plant GMOs are actually quite small, as evidenced by the continued growth of food sales to Europe from the Republic of South Africa, yet anxieties surrounding export loss continues to play a political role.

The final channel of external influence is cultural. Most policy-making elites in Africa have much closer cultural ties to Europe than to the United States, so they are naturally inclined to view European practices as the best practices. For example, the Kenyan author of a 2004 article (published by a European-financed NGO, PELUM) that was titled 'Twelve Reasons for Africa to Reject GM Crops,' http://www.grain.org/seedling/?id=294 later explained to a newspaper reporter, 'Europe has more knowledge, education. So why are they refusing [GMO foods]? That is the question everybody is asking.' Policy-making elites in Africa have often been educated in Europe, they send their children to European schools, and they travel to Europe frequently both on official and unofficial business. It is not surprising that they would be inclined to adopt European-style regulations for GMOs, despite the fact that Africa's needs and circumstances are so different from those of Europe.

External influence of this kind is not unique to Africa, of course. In Latin America, which lies within the traditional sphere of influence of the United States, government policies toward GMO crops have usually been closer to the American approach than to the European approach. As of 2008, seven out of the top ten countries around the world with significant plantings of GMOs were Western Hemisphere countries. It is also telling that the only Asian country to have approved GMO maize, the Philippines, is a former American colony.

Political leaders in Africa pay a price for simply 'doing what Europeans do.' Europe imposes stifling regulations on GMO foods and crops because Europeans have little need for this new technology. European farmers are already highly productive without it and European consumers are already well-fed. Indeed, like consumers in the United States Europeans are increasingly over-fed. In Africa, however, where farmers are not yet productive and where so many consumers are not yet well fed, the potential gains GMO crops can provide are more costly to do without.

Rather than deferring to outsiders, either Europeans or Americans, Africans might usefully look for ways to make independent judgments of their own regarding how to regulate GMO crops. Other countries in the developing world have managed to operate relatively free from external influence – for example, the People's Republic of China. The PRC has seen a strong value in this new technology, and has invested significant public budget resources to develop the technology for Chinese use. Africa has a choice to make independent decisions regarding GMO foods and crops as well.

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Review

Epistemic brokerage in the bio-property narrative: contributions to explaining opposition to transgenic technologies in agriculture

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Unlike some global contentions – abolition of slavery, or universal franchise, for example – the rift over rDNA crops is not about ultimate values. Improvement of farmer welfare and enhanced sustainability of agriculture are universally valued goals. However, means to those ends are politically disputed; that dispute depends on alternative empirical stories about biotechnology, sometimes even alternative epistemologies. Opposition revolves around two fundamental dimensions: bio-safety and bio-property. There is convergence of these dimensions around exceptional risk and vulnerability to corporate control of farmers, but these are analytically separable questions of fact. This paper concentrates on bio-property. Epistemic brokers have successfully established knowledge claims that simultaneously undermine the case for rDNA technologies as potential contributors to development and motivate opposition. Epistemic brokers command authority from their positions at junctures of networks, enabling the screening, weighting, theorizing and diffusion of contentious empirical accounts. In contentions of low information, high information costs and diffuse anxiety, these claims provide cognitive support for opposition to 'GMOs'. Specifically, claims of patents, monopoly corporate control and terminator technology have diffused to and from India in global networks. Though effective in transnational advocacy networks, these claims have proved either false or inconsistent with dynamics on the ground.

Contents

Global rifts and rival networks: the 'GMO'

Transgenic cultivars have spread widely, rapidly but unevenly around the globe [1]. Simultaneously, and reciprocally, networks opposing biotechnology have succeeded in much of the world in limiting or blocking transgenic crops. Much of this success has come from diffusion of powerful knowledge claims around bio-safety and bio-property. These two strands are linked in global resistance to a special construction of agricultural biotechnology: the 'GMO'. The GMO is political shorthand for any agricultural product involving recombinant DNA (rDNA) techniques; its success as a cognitive frame is such that even proponents of genetic engineering in agriculture accept this political terminology. The frame does not apply to rDNA techniques in pharmaceuticals,

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medicine or industry, where transgenics have been globally accepted [2]. Unlike control of international air traffic or infectious diseases, no authoritative knowledge provides consensual norms for products of genetic engineering [3], nor is there any consistent property regime across nations. In this unsettled policy space, intermediaries of knowledge or what I will call epistemic brokers, played a significant role in creating, energizing and sustaining opposition to transgenic crops. Within networks and between networks, intermediaries translate information into terms conducive to political action.[1]

A primary function of epistemic brokers in oppositional networks is to find, ratify and diffuse information that evokes anxiety in mass publics and among public authorities. On the bio-safety strand of this construction are issues such as deaths of livestock from consumption of transgenic crop refuse. For example, reports from NGOs in South India indicated that sheep, then cattle, were dying from ingestion of cotton leaves containing the cry1Ac protein [5–7]. Other stories involve allergenicity, sterility, cancer and a wide range of calamities linked causally to transgenic cultivars. On the bio-property strand, a prominent story has been that of mass suicides of farmers growing Bt cotton in India. This widely distributed and credited narrative posits crushing debt incurred by purchase of expensive and dysfunctional transgenic cotton hybrids from a Monsanto monopoly. Such stories understandably evoke outrage from much of the world [8]. The Bt cotton story from India exhibits common features of the global bio-property narrative: patent control of seeds, monopoly pricing, dependency, debt and agrarian crisis exacerbated by agronomic failure of the technology. Claims of 'bio-serfdom' and 'bio-feudalism' mark the subjugation of the peasant to intellectual property regimes. This bio-property narrative is logically separable from but functionally related to critiques invoking bio-safety: if transgenic ss are novel enough to claim patent protection in some countries, are they not novel enough to be especially risky, to require special regulation and segregation? The single most politically efficacious culmination of this merger is the positing of Terminator Technology, or 'Monsanto's Terminator gene,' that renders second-generation transgenic seeds sterile. The terminator in theory would marry commercial control of bio-property by a multi-national corporation profiting from un-natural processes. Anxiety and outrage together drive a politics that has divided the world into GMO-accepting and GMO-free nations, counties, departments and farms.

Rival networks counter the claims of biotech opponents, typically offering science-based, peer-reviewed studies and wide farmer acceptance of transgenics as counter-weights [8]. Each network claims success. Some nations have approved [25 officially][2] or promoted biotech crops through the logic of the developmental state: China first and most vigorously. Many others prohibit these crops or regulate so heavily as to effectively ban agricultural biotechnology [9,10]. From initiatives in civil society, 'GMO-free zones' have been created around the world. Europe after 1998 has been the epicenter of opposition to agricultural biotechnology, but moratoria are contested globally – from India to California, Poland to Japan – often through diffusion of this spatial tactic. Table 1 indicates the growth of 'GMO-free zones' in Europe between 2007 and 2009.

TABLE 1

GMO-Free resolution signed by European Regions[a] by political unit: 2007 and 2009.

	2007	2009	% Change
Region	167	196	14.8
Provinces, Prefectures & Departments	53	93	43.0
Local Governments	4,278	4,567	6.3
Individuals	27,100	30,370	10.8

Source: www.gmo-free-regions.org. Accessed April 2009.
[a] The EU has specific designations of regions defined by the Assembly of European Regions (AER).

The remainder of this paper will seek to understand the contribution of the bio-property narrative to expansion of political forces for GMO-free space, resolutions, moratoria, laws and direct action. The burden of the argument is that the narrative offers empirical support for the notion that many innocent and powerless people are victims of biotechnology; stopping its spread then becomes a moral imperative. Given those facts, opposition follows naturally among other-regarding citizens at great distance from farmers' fields. There is no need to posit Luddism, or anti-science ideology; opponents are typically quite comfortable embracing new technologies and evoking the authority of science.

Market, developmentalist and catastrophic modes of bio-property

Political opposition to the GMO merged threat narratives of bio-property and bio-safety: threats to nature, in the form of 'biological pollution' (gene flow); threats to human health, in the form of allergens; threats to farmers, in the form of bondage to monopoly seed corporations ('bio-serfs', 'bio-feudalism') and threats to national independence, in the form of dominance of agriculture by multi-national corporations [11–17]. Intellectuals in the ex-colonial world made crucial contributions to theorizing genetic engineering as especially catastrophic for the universal valent of development [18]. These anxieties resonated with fears of neo-colonialism. Diffusion of this intellectual work was facilitated by international non-governmental organizations [INGOs] such as Greenpeace International and Friends of the Earth International. These INGOs carry considerable authority; their imprimatur ratifies authoritative knowledge, particularly in fields where complexity and distance from everyday experience limit access to information. They lead networks built on solidarity around widely accepted normative claims such as sustainability or justice.

What do these abstractions have to do with rDNA cultivars? It is the theoretical work of epistemic brokers to link GMOs to these universal values. Their success in making that linkage negative rather than positive was enabled by the high information costs surrounding molecular biology and the existence of an established cognitive path to anxiety. The bio-safety strand of opposition is

[1] See Mosse and Lewis [4] on theoretical origins and usefulness of the concepts 'brokerage' and 'translation.'

[2] The usual authoritative source is James 2008 and his ISAAA updates. James' data are criticized by opponents for reflecting pro-GMO bias. My critique is that the official data seriously understate diffusion of agricultural biotechnology for reasons of evasion – stealth seeds – discussed in the text. The number 25 does not, for example, include several countries where transgenics are known to be in use – Mexico, Vietnam, Thailand, Pakistan, Ukraine for example.

exemplified by evocation of un-natural acts and unknown consequences: 'Frankenfoods' summarize the narrative, but a wide range of risks is posited, from gene flow to allergenicity. Bio-safety brokers have been successful in diffusing alarming empirical accounts of biotechnology as risky business. Many of these accounts claim the authority of science [8,19].

The 'GMO' came to India, as to many countries, as a multifaceted threat. Reciprocally, international brokers found that reports from the field in India confirmed their larger narrative of threat. A prominent example is biological catastrophe in the form of dead sheep – and then cattle – in Andhra Pradesh [5–7]. In parallel to bio-safety threats, claims about bio-property posed specific threats to an undifferentiated 'peasantry' in the poor world; much of this narrative was theorized to exclude GMOs from the frame of development, particularly for poor farmers. In India, accounts of farmer suicides caused by Bt cotton were presented to brokers in global networks for dissemination in support of international mobilization against agricultural biotechnology.

Bio-property entered the global rift in three modes: market, developmental and catastrophic. The market mode constructed transgenic plants as technological progress that comes with a cost, but a cost that is fundamentally open to free choice. Farmers can and will pay more for seeds if they believe that marginal revenue exceeds marginal cost. The analogy is Microsoft Word: you can choose alternatives, from pencil and paper to open-source processors – but Word costs money if you choose it. That is the normative structure; the reality is more complicated. For many years, enforcement of intellectual property claims in software in the US was lax, and in much of the world remains extremely lax. Few academics of my generation have not had 'pirated' software on their machines. The parallel in agriculture is clear: in market logic, farmers can buy or reject more expensive seeds just as businesses and individuals can buy or reject Microsoft software; their experience will lead to subsequent dis-adoption or re-purchase. And there will be unauthorized usage of the technology. Seed firms believe that enhanced utility will convince farmers to pay extra for transgenic seeds, just as they pay more for hybrid seeds: the financial bottom line will determine farmer choices. The mechanism is farmer experience in the field. Empirically, the market model receives some confirmation: benefits are in fact shared out across firms and farmers [20]. Were this not the case, it would be very hard to explain the diffusion of transgenic plantings in countries with strong property rights such as the US and Canada. The role of the state in this mode is to enforce contracts freely chosen among economic agents.

The developmental mode adopted by international institutions and academics qualifies the market version and assumes a more active state [21]. In the developmentalist understanding, transgenic seeds in poor countries might prove problematic because of unequal access. Poor farmers and nations might need special institutional support and resources to participate in the 'gene revolution'. In this logic, technology fees and intellectual property matter greatly. Moreover, as in all developmentalist logic, intervention might become necessary because market failure is common; market forces are unlikely to drive the kind of research on the kind of crops that are of importance to vulnerable farmers. In the worst-case scenario, poor farmers might be disadvantaged by aggregate market forces generated by new technology, but have no voice in the matter. Poor farmers would lose if technology fees were prohibitive – and enforceable – and costs of production were subsequently reduced for farmers who could afford to pay fees. 'Farmers' as a class could still benefit, but poor farmers would be caught in a backwash of lower output prices because of increased yields on adopter-farms, but with no reduction in input costs or increased yields on their own farms [22]. Enforcement of intellectual property claims of multi-national firms would in this scenario accelerate concentration of land and the decline of small farmers. In the developmentalist version, then, intellectual property that raises costs or restricts access might redound to the disadvantage of the poor, whatever the success of the technology in the aggregate. The normative conclusion is that development policies and institutional change must anticipate these potentially negative outcomes; the public sector is likely to have an important role to play [23–26].

The assumption of both market and developmentalist narratives is that at least some biotechnology is agro-economically favorable for at least some farmers. The catastrophic mode rejects this proposition fundamentally. This logic escalates the cautions posited by developmentalists from inequality to disaster. In this line of reasoning, rDNA seeds are not valuable for agriculturalists of any size class or of any crop, but rather represent a path toward new forms of subjugation and agrarian crisis. There should be no institutional change to facilitate access to biotechnology, nor public investment in the technology. India was cited as powerful confirmation of the catastrophic logic: the 'failure of Bt cotton' on agronomic and economic grounds was widely accepted as established fact and decisive case in networks opposing globalization [7,13]. The primary epistemic broker in this development was Vandana Shiva, whose account illustrates the oppositional property argument in pure – and widely influential – form:

> ***'Pushed into deepening debt and penury by Monsanto-Mahyco and other genetic-engineering multinationals, the introduction of Bt cotton heralds the death of thousands of farmers. High costs of cultivation and low returns have trapped Indian peasants in a debt trap from which they have no other escape but to take their lives. More than 40,000 farmers have committed suicide over the past decade in India—although the more accurate term would be homicide, or genocide.'***
>
> ***'These seeds kill biodiversity, farmers, and people's freedom—for example, Monsanto's Bt cotton, which has already pushed thousands of Indian farmers into debt, despair, and death. Bt cotton is based on what has been dubbed 'Terminator Technology,' which makes genetically engineered plants produce sterile seeds.' [27, p. 86]***

In this narrative, there are no choices, no experimentation in the fields, no farmer choices, no institutional mediation, only compulsion and traps. Vandana Shiva's Biopiracy: The Plunder of Nature and Knowledge was published in 1997, before there was any legal transgenic in India; its themes provided the main frames for the connection between transgenics and bio-property critiques. Chapter One posits the mechanism: Piracy Through

Patents. Chapter Two throws down the rhetorical ethical gauntlet: Can Life Be Made? Can Life Be Owned? Dr. Shiva's over-riding concern with biotechnology is that it enables 'the control of agriculture by multi-national corporations [18, p. 91].' In the movement against transgenic crops in India, concern with intellectual property rights and corporate power was married to nationalist and cultural themes of self-reliance, nonviolence, local knowledge and biodiversity [28]. This narrative was accepted within a section of the Indian middle classes and intelligentsia; the resonance is powerful. But Dr. Shiva's accounts are important to the argument of this essay because of their empirical claims, which diffused though global networks opposing biotechnology.

The mechanisms in this argument are important. The bio-property catastrophe story – debt-driven pandemic suicides – depends on several strong claims. First, there is the claim that the technology does not work economically (high costs and low returns). Second, dependency is generated by the act of purchasing transgenic seeds (loss of freedom). This dependency is more than financial or contractual; property rights are enforced biologically via terminator technology. This claim is diagnostic: it contradicts two facts that would be largely unknown among citizens supporting anti-biotechnology networks. First, patents on plants are by no means universal; in the Indian case Dr Shiva analyzed, there were no patents on any plants, including Bt cotton. Second, the Indian case illustrated precisely why such property claims, even if they were to exist, would be very hard to enforce. By what mechanism would farmers be prevented from sharing, saving, back-crossing or producing transgenic seeds?

India's first transgenic cultivar: Bt cotton

The Government of India approved three Bt cotton hybrids with one genetic event (cry1Ac (MON 531 Event)), developed by Mahyco-Monsanto Biotech (MMB) for cultivation on March 26, 2002. This was the day after a rally of the Kisan (farmer) Coordinating Committee demanding de-regulation of Bt cotton. National civil disobedience was threatened by affiliated farmer groups if the Government did not approve transgenic cotton hybrids. In reality, approval was largely a fait accompli, as two large state governments with a large percentage of India's cotton area had already agreed to farmer demands and permitted Bt cotton cultivation – Gujarat and Maharashtra [28]. Stealth seeds had been growing for three years by the time of official approval. Bt cotton was not officially for sale until the cropping season of 2002–2003; by 2004 the area under official Bt hybrids came to 1,213,359 acres and increased to 3,212,300 acres by 2005; current [2009] estimates top 19 million acres. The area under illegal 'stealth' seeds was and is unknown precisely, but was in the early years of rapid adoption a high percentage of all transgenic plantings and remains a substantial presence in cotton fields [29].

Illegal variants of cry1Ac hybrids bred by farmers and legal seeds from MMB and its licensees dominated acreage in the early years [30]. By 2007 there were four genetic events[3] approved for insertion into hybrids, from three companies, one of which used the Chinese public-sector genetic material (Nath Biogene), one of which was developed by an indigenous firm in India (J.K. Agri Genetics Pvt. Ltd). This process continued with more firms, more hybrids and stacked-gene implementation. The number of approved hybrids increased to 281 by 2009. Beginning in 2009, a public-sector Bt cotton variety was legally being grown on small areas. This OPV was developed in the public sector precisely because of the interest of some farmers in saving seeds; saving and replanting hybrid Bt cottons was possible, and practiced in early years, but at the loss of hybrid vigor [31]. Estimates of coverage of transgenic cotton are necessarily imprecise because of the stealth-seed phenomenon, but Bt cultivars covered roughly 19 million acres or 80% of the total cotton area in India in 2008–2009. The single-gene [cry1Ac] version from Mahyco-Monsanto, implemented by numerous licensees, accounted for 12.7 million acres; another 4.5 million acres were under the newer stacked-gene technology [cry1Ac and cry2ab genes]. Implementations of Bt technology from JK Agri Genetic Ltd's alternate cry1Ac and Nath Biogene's 'fusion' gene technologies covered under a half million acres together. Harish Damodaran estimates that the remaining area – something like two million acres – was planted to illegal Bt hybrids [29], though no one knows real numbers.

These technological and property dynamics certainly undermine one leg of the bio-property narrative of monopoly and control. Intervention by state governments altered the other – market prices of Bt hybrids. An administered price reduced the cost of first-generation Bt seeds by 40–50% in 2007 [30]. The transgenic seed system has thus been quite dynamic: new genetic events, new firms, new licensees developing new hybrids, public-sector intervention in breeding and public regulation of the 'trait value' portion of seed prices. It is difficult to imagine how this process could be portrayed as one of monopoly and control. Nevertheless, for a time, something like a monopoly was conferred on Mahyco-Monsanto's Bt cotton hybrids, but not by terminators or property law. To the extent a temporary monopoly in transgenic cotton was operative in India, it was a function of the bio-safety regime, not bio-property.

In the early years of diffusion in India, the most successful cultivars were illegal implementations of Monsanto's cry1Ac transgene for insect resistance in cotton [31]. The rapid diffusion of Bt cotton in India began with these stealth seeds that neither the government nor Monsanto – nor the suicide seed coalition that Dr Shiva led rhetorically – discovered until a massive bollworm incursion in 2001 devastated the non-transgenic cotton in Gujarat state. This particular stealth seed – Navbharat 151 – was produced by Dr D.B. Desai's Navbharat Seeds of Ahmedabad. Dr Desai was subsequently dubbed 'Robin Hood' in the press for his act of undetected appropriation of Monsanto technology. The discovery of these stealth seeds was made not by the state, nor civil society in surveillance mode, but by Mahyco-Monsanto (MMB) trying to recoup their investment in cotton seeds and testing procedures. No property rights adhered to the Navbharat Seeds, but Robin Hood could be and was quashed for violation of the bio-safety regime – specifically the Environment (Protection) Act, l986, and Rules (1989) that

[3] The genetic events are (1) cry1Ac gene (MON 531 Event) by Maharashtra Hybrid Seeds Company Ltd; (2) cry1Ab-Ac gene (GFM cry1A Event) by Nath Seeds Ltd; (3) cry1Ac gene (JK Event 1) by J.K. Agri Genetics Pvt. Ltd; (4) cry1Ac genes (MON 15985 Event) by Maharashtra Hybrid Seeds Company Ltd.

regulate transgenic organisms [32]. The only transgenic cotton undergoing bio-safety testing to become legal was that of MMB. Banning NB 151 on bio-safety grounds left the field open to MMB to license their technology to other seed firms at high prices after farmers demanded and several state governments effected de-regulation of the cry1Ac hybrids. MMB was in effect empowered by bio-safety regulatory authority to operate as a monopoly in a nation with no patents on seeds. But the ban on Navbharat 151 simultaneously prompted emergence of a vigorous cottage industry in illegal Bt hybrids using the NB 151 germplasm in new combinations with new names: Agni, Luxmi, Rakshak, 151, Sunny, Kavach, etc. Had bio-safety institutions worked better, this underground market would have been suppressed, farmers would have had fewer and less attractive choices and MMB's de facto monopoly would have been strengthened.

Forcing Navbharat Seeds out of the cotton business for failing to comply with bio-safety regulations eliminated one (very effective) competitor to MMB. A cottage industry of transgenic Bt cotton was born, mostly in Gujarat [33–36], whereas the legal Bt seed market was left to Mahyco-Monsanto and its licensees from 2002 to 2006. The vigorous development of an underground Bt seed industry decisively refuted the terminator-technology narrative in the fields, but not in advocacy networks.

Bio-property in extremis: terminator technology

'Monsanto's terminator gene' provides an archetype of the political deployment of powerful intellectual property claims by epistemic brokers in networks. The claim was that a patented gene incorporated into Bt cotton had been brought into India through collusion of the Indian state (obtained with bribes) with Monsanto specifically and with a global neo-liberal regime more generally [26,32]. The terminator summarized in one construct the multiple threats of GMOs: the bio-cultural abomination of seeds that could not reproduce resonated with a narrative of corporate greed and acts against nature [37]. Though rhetorically robust, the story was untrue. How, then, could it become so widely believed and globally disseminated? I think the answer lies in the authority of epistemic brokers in networks of solidarity on topics with high information costs and potential anxiety. Network solidarity is built not on the truth value of factual claims, but on normative consensus around universal values.

The story of 'Monsanto's terminator gene' came to India through international networks, most proximately a Canadian NGO (Rural Foundation International, now ETC) through web communications. It was promulgated within India by networks centered on Vandana Shiva and the NGO Navdanya [28,38]. The terminator would in theory force farmers to return each season to buy new seeds – generating a biological dependence of farmers on firms unmatched by customary arrangements. More important symbolically, the venerable cycle of 'self-organizing' agriculture would be replaced by dependency and cash nexus dominated by patents. That India had no patents on plants would be largely unknown in networks where the patented terminator gene story about Bt cotton was promulgated. That the concept patent itself had not led to a completion of a biological invention, and is in some sense a public-sector technology – since it is jointly owned by the United States Government – is little known as well.[4] Moreover, few people would have known that the original Bt cotton germplasm had been crossed into Indian cultivars numerous times since the mid-1990s to produce viable seeds for field trials; presumably such crosses were not terminated – otherwise there could have been no field trials to protest. The narrative of Monsanto as alleged creator and owner of terminator technology provided a powerful condensation symbol: multinational, American, wielding an un-natural and exploitative technology. Real attributes of the firm's record were combined with a false attribution of property rights in genetically engineered sterile seeds. Together with Dow Chemicals, which 'brought us Bhopal and Vietnam,' Monsanto was accused of planning to 'unleash genetic catastrophes.'[5] In an arena of low information and high anxiety, symbolic appeals have extra-ordinary power [39].

Monsanto's representative in India rebutted charges of suicide seeds: 'Since the so-called terminator gene does not exist today in any plant in any country in the world, the question of its involvement in the field trials currently on in India does not arise.' Mahyco-Monsanto Seeds chairman BR Barwale noted publically that the seeds being tested had been approved by the Government of India's Department of Biotechnology for field trials and had 'nothing to do with the so-called terminator genes.'[6] Nevertheless, the notion of suicide seeds was deployed politically to link technology to intellectual property and ultimately to neo-colonial threats to the nation. Vandana Shiva and colleagues [16, p. 98] wrote:

> ***'Freedom from the first cotton colonisation was based on liberation through the spinning wheel... Freedom from the second cotton colonisation needs to be based on liberation through the seed... The freedom of the seeds and freedom of organic farming are simultaneously a resistance against monopolies... like Monsanto and a regeneration of agriculture... The seeds of suicide need to be replaced by the seeds of prosperity.'***

Terminator seeds were specifically banned by the Government of India in response to this movement, as announced in assurances in the Lok Sabha and Rajya Sabha, and via Office Memorandum No. 82-1/98 PQD, dated May 25, l998. None of these assurances stopped the campaign against terminator technology.

The campaign targeting terminator seeds proved cognitively powerful. Even today, people all over the world firmly believe that

[4] The original patent was granted Delta and Pine Land Company, in collaboration with the United States Department of Agriculture's Agricultural Research Service – U.S. Patent 5,723,765 entitled 'Control of Plant Gene Expression,' on March 3, 1998 for a 'Technology Protection System (TPS).' Further USDA collaboration produced two more patents. Monsanto bought Delta and Pine Land in 2007 (United States Securities and Exchange Commission Form 8-K Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934, dated June 1, 2007). Despite its political prominence, terminator technology was not commercialized, due in large part to vigorous international protests. There have to my knowledge been no applications for field testing of this technology, nor has it been deployed it in any crop anywhere in the world.

[5] Press Release, Asian Social Forum [Hyderabad] Seminar, 2003, 'Beyond Bhopal and Bt.: Taking on the Biotech Giants.' Research Foundation for Science, Technology and Ecology. Delhi. January 4.

[6] Quoted in Dow Jones Agnet November 20, 1998; Sharad Mistry, *Indian Express*, 1998, 'Terminator Gene a Figment of Imagination: Monsanto Chief,' December 4.

farmers cannot save and replant 'GMO seeds', despite extensive evidence to the contrary [30]. The original import of Bt cotton seeds into India was one-hundred grams; there were by 2006 millions of acres under dozens of unauthorized transgenic cottons in the field.[7] Fallout from the decidedly unterminated cry1Ac transgene continues to reverberate through India's cotton sector. Though officially approved Bt hybrids increased from 3 in 2002 to 137 in 2007 to 281 in 2009, deshi (indigenous) Bt hybrids or Navbharat variants continued to circulate.[8] The extent of illicit seed diffusion is unknown; as prices of official seeds have come down dramatically, one would expect the stealth-seed market to recede, and anecdotal accounts indicate that this is happening. Underground seeds are less expensive, but entail greater risk, not of prosecution, but of adulteration. Dr K.R. Kranthi, a scientist with India's Central Cotton Research Institute made a hard estimate based on admittedly limited sampling:[9] 'On average, 28% of the illegal seed brands are non-Bt... Among samples collected and tested by CICR, only 26% of the Bt cotton was true first-generation hybrid, while 46% was contaminated with non-Bt cotton.'

These counterfeit seeds might account for some reports of Bt cotton failure: some farmers purchased seeds of dubious parentage labeled as Bt but did not get the insect protection of the transgene [30]. Not surprisingly, among the first demands of farmers is some system of reliable seed certification.

The terminator hoax so decisively disconfirmed on the ground in India continues to circulate in other countries on the authority of reports from India, largely through the international campaigning of Indian opponents of agricultural biotechnology. This persistence is important because the narrative of a global tyranny of monopoly and patent-controlled GMOs has proved inconsistent with facts on the ground, institutional evolution, farmer ingenuity and state institutional capacity.

First, property claims are not self-enforcing; states will be involved, one way or the other, by intervention or failure to intervene. Monsanto has expended great energies trying to collect technology fees from farmers in Latin America, with spotty results, having failed to obtain a patent from Argentina for glyphosate-resistant soy in 1995.[10] High prices of Monsanto's Bt cotton in India, enabled by government regulatory restrictions, spurred development of the stealth alternatives and eventual emergence of legal competition. Globally, some transgenes have spread so widely underground that they resemble open-access or open-source technology, more Linux than Microsoft.[11] Politics also modifies what corporations can do in markets. Collective action in India demanded a ban on Mahyco-Monsanto's three legal hybrids, and succeeded in one state (Andhra Pradesh); compensation for crop failure unrelated to the transgene was paid by MMB at the insistence of the state government. Continuing resistance to high prices in Andhra Pradesh compelled the state government to pursue a case before the Restrictive Practices Commission (MRTPC) in 2006 [30]. The state government eventually won its case and fixed a price ceiling on transgenic cotton seeds (Rs. 750 per 450 g packet) and ordered all seed companies to abide by its administered price for a 'trait value'. Other state governments then fixed prices at the same level, a reduction of some 40–50% of the purchase price at seed shops. Even in strong property regimes such as the United States, Monsanto is forced into admittedly undesirable publicity to collect technology fees.[12] Strong manifestations of intellectual property have not proved practicable in many countries for reasons of transactions costs, politics and law [41]. Global monopoly power of multi-national property in biota is difficult to find on the ground.

Though enforceable bio-property seems elusive, bio-safety regimes have to some extent provided an alternative route to corporate power in agriculture. Strict control and testing regimes raise costs of seed development beyond what is affordable by small firms, enhancing the power of deep-pocket corporations. Indian farmer and seed organizations have charged that bio-safety officials colluded with Monsanto to give its seeds alone the status of approved hybrids, forcing everyone else to license the technology from Monsanto or give up a rapidly expanding transgenic market. There were demands for regularization of illegal transgenics, especially Navbharat 151 – the original stealth seed – and especially in Gujarat state, where it was first produced. Nevertheless, most seed firms with serious cotton markets chose to license technology from Mahyco-Monsanto, even at prices they considered extortionate.[13] Nor is there evidence of a super-profit gold-mine in biotech dominance. Private firms have been decreasing their investments in agricultural biotechnology, whereas public-sector institutions in low-income countries are increasing investment [42]. Pray and Naseem [20] concluded from their analysis that the

[7] No one knows precise numbers. Data from Navbharat Seeds, progenitor of the first and most successful of the underground *Bt* lines, and parent to most, puts sales at 52.45 *lakh* packets of illegal *Bt* cotton for *kharif* 2005, enough seed cotton to plant 5.245 million acres, or roughly 25% of India's cotton acreage (pers. comm.). Legal *Bt* sales were simultaneously increasing rapidly as well. Conversations with seed producers in Gujarat suggest more stealth seeds than figures from Delhi, but the precise acreage remained unknown, since farmers produced *Bt* hybrids on their own farms and some still used transgenic F2 seeds [31,32,34,36,40].

[8] The highest yield report I found – by accident – in Warangal district in 2006 was 15 quintals/acre from an unmarked package of loose seeds known only as 'Gujarat Bt,' almost certainly a descendent of the Navbharat 151 line so popular with farmers [41].

[9] On 'duplicates' and counterfeits, as opposed to genuine Bt stealth seeds, see Herring and Kandlikar [30]. For Kranti's perspective, http://www.scidev.net/en/features/gm-in-india-the-battle-over-bt-cotton retrieved April 3 2008.

[10] I recently received a communication from Argentina stating that 80% of the soy is illegal. This is significant because Argentina denied Monsanto a patent for glyphostate-resistant soy in 1995, resulting in the spread of stealth transgenic soy all over South America, most egregiously Brazil [41].

[11] Pray and Naseem [20] note that descriptions of many proprietary laboratory technologies have been published. Moreover, '[S]ome genes are in commercial use and can be obtained through reverse engineering, and some techniques have made their way to developing countries by way of unauthorised routes'. Patents either cannot or have not been obtained in many – perhaps most – low-income countries, and are unenforceable in others.

[12] Monsanto states: 'Since 1997, we have only filed suit against farmers 138 times in the United States. This may sound like a lot, but when you consider that we sell seed to about 250,000 American farmers a year, it's really a small number. Of these, we've proceeded through trial with only nine farmers. All nine cases were found in Monsanto's favor.' http://www.monsanto.com/monsanto_today/for_the_record/monsanto_farmer_lawsuits_followup.asp accessed 10.26.09.

[13] Interviews with seed company officials in Gujarat in 2005 first laid out this logic for me.

primary beneficiaries of increased farm revenues to date are not multi-nationals, but farmers and consumers, even in countries that enforce strong intellectual property rights.

Monsanto had no patent in India for the Bt seeds but, with its partner Mahyco, it did have the only technology legally approved by the national bio-safety authority, the Genetic Engineering Approval Committee. Approval came only after lengthy and complex testing procedures. These facts are largely unknown outside specialized knowledge communities. Therefore, reports of epistemic brokers in media-connected networks substituted for knowledge that otherwise incurs high information costs. It is difficult, and time-consuming, to track patent law in numerous countries. More difficult is to assess claims about terminator technology without first some reading in molecular biology. Contrary to the easy assumption of monopoly and control, intellectual property in seeds has generally proved difficult to claim or enforce in much of the poor world, for understandable reasons [41]. Farmers seem not to differ fundamentally from other citizens; opportunistic appropriation of technology has been common in films, pharmaceuticals, music and software [43]. Moreover, there are alternatives to private ownership of biotechnologies. In some countries – most notably China – public-sector research and firms have been important [42]. Public-sector universities have produced important breakthroughs – for example, the ring-spot-virus-resistant papaya [44,45]. Humanitarian use transfers offer an institutional alternative to private property, as developed in pro-vitamin A 'golden rice' [9,46]. Epistemic brokerage within networks shields partisans from these contradictions in the narrative of monopoly and control, just as cognitive and physical distance shields them from questioning reports of biological disasters such as dead sheep in remote villages of South India [6,7].

Transnational opponents of genetic engineering built their critique in part on the presumed monopoly power of multinational corporations, with a parallel critique of bio-piracy enabled by the genomics revolution in biology [18]. When the BBC characterized the small Indian firm Navbharat Seeds' appropriation of Monsanto's Bt cotton gene as 'bio-piracy,' the tables were turned. The assumption that genetic flow can move only from South to North proved problematic. Moreover, the episode of Navbharat Seeds and subsequent pocket breeding in Gujarat illustrated concretely that only a deep urban cultural bias can construct farmers as incapable of agency. Why should farmers be incapable of the kind of agency that makes the illicit sector in non-agricultural technologies so pervasive a global phenomenon? Business software and pharmaceuticals are widely appropriated against standing rules, but agricultural biotechnology is presumed to exert power beyond the agency of its users. Terminator technology offered in theory a plausible explanation for this otherwise condescending portrait of rural people: the 'monopoly' and 'patent' construction of corporate power presupposed an esoteric biological mechanism engineered into seeds. Genetic engineering could, in this view, enforce property claims that were politically and legally unavailable in most countries. How else could patents on seeds have power? But the terminator remains curiously on the shelf. Its political framing outran the technology; there is today no parallel in seeds to copyright protection built into DVDs, music and software.

The so-called T-GURT form of what has been called terminator technology would allow farmers to save seeds minus the transgenic trait [48], and would thus incur less opposition, while reducing the risk of gene flow. But the bio-cultural abomination of the terminator remains, evidently, politically untouchable. Though mass publics have (grudgingly) come to accept terminator-like controls in software, videos and music – with much resistance among the young – the biological expression of termination seems to cross some threshold of hubris and abomination. It could be that this evocation of the unacceptably un-natural exhibits decisive threshold effects, defining what Prince Charles called 'realms that belong to God and God alone.' But I doubt it. It might be that the real explanation is less culturally driven and more biological: perhaps the terminator, despite its international notoriety, simply would not work in the field.

Conclusion: why brokers have power

This paper has asked: what makes the threat narrative of GMOs so powerful internationally? It has argued that despite widespread consensus on fundamental values – farmer welfare and sustainable agriculture – knowledge claims in networks built on trust and solidarity have reinforced a global cognitive rift on biotechnology. It is not normative dissensus, as in the historic contentions over abolition of slavery or female suffrage, but rather contention around knowledge claims integral to those normative positions. These knowledge claims in turn fit into receptors in rival networks contesting genetic engineering in agriculture along two global rifts.

The primal global rift around genetic engineering is between agricultural crops and all other uses – such as pharmaceuticals and medicine. Agricultural crops alone have been segregated into an object of politics and governance termed 'GMOs'. This framing is ensconced in contentious politics, law and trade, whether or not the cultivars are used in food. A second, and logically derivative, global rift divides rival advocacy networks supporting and opposing GMOs – that is agricultural biotechnology. This rift is politically charged and administratively consequential; it hinges on two inter-related dimensions: bio-property and bio-safety. Global opposition forms around critiques of genetically engineered crops on both dimensions. New claims of intellectual property in seeds enabled by the genomics revolution in biology created conflicts over what can be owned, by whom, under what conditions, in which nation. Claims of novelty by firms seeking intellectual property reinforce a second dimension of contention: if novel, might products of genetic engineering raise special risks in comparison with cultivars bred by different techniques? Transnational advocacy politics succeeded in framing 'GMOs' as uniquely risky plants, with corresponding global soft law for special regulation. Farmers have responded to restrictions of both regulation and property claims with stealth strategies [41]. The widespread adoption of Bt cotton in India illustrates why and how evasion of both bio-property and bio-safety regimes is pervasive. Such grass-roots challenges to formal institutions embarrass both sides of the global rift; neither bio-property nor bio-regulations prove so robust as antagonists in advocacy networks contend. The Indian experience also uncovers a fundamental contradiction in mobilization to halt diffusion of agricultural biotechnology. Successful demands for stronger regulation of transgenics strengthen property-like rights

of multi-national firms that find it difficult to enforce their property claims in any other way. Bio-safety regulation can function as bio-property.

If this summary is roughly accurate, it identifies hypotheses for the conditions of politically powerful brokerage of knowledge. Testing these hypotheses would require much more than the case-study briefly sketched above. What the Indian experience suggests as conditions are: (1) networks for diffusion of empirical claims, (2) professionalization of cadres speaking on behalf of the silent, (3) spheres of cognitive distance from both participants and consumers, (4) high information costs, (5) solidarity based on normative consensus.

To illustrate these conditions, consider the narrative of livestock deaths in India. Americans found in 2006 an article entitled 'More on Mass Death of Sheep in India After Grazing in Genetically Engineered Cotton Fields' published by the Organic Consumers Association of Finland, Minnesota.[14] This organization campaigns for 'Health, Justice, Sustainability, Peace and Democracy.' Their source was the Centre for Sustainable Agriculture in Andhra Pradesh, as relayed via Mae-Wan Ho – a self-identified scientist – of the Institute of Science in Society in London. In her disclosure of this catastrophe, she linked dead sheep in Andhra Pradesh to allergenicity of Bt cotton in other parts of India and to deaths of humans from Bt maize in the Philippines.[15]

If this grisly account is accurate, remediation has a moral claim. No one can legitimately oppose 'health, justice, sustainability, peace and democracy,' nor can most people countenance the tragedy of poisoned sheep owned by very poor shepherds, much less deaths of humans in the Philippines. That the association is composed of 'organic consumers' conjures a realm of virtue and purity difficult to fault. Nor can one easily oppose the notion of 'science in society' promoted by Mae-Wan Ho's organization. The idea of embedding science in social processes and values of transparency, of commitment to public awareness and public goods, all seem unexceptional goals. The valence issues on which oppositional networks are based are universal; the empirical claims link specific technology to outcomes contrary to those values. This threat to universal values is what makes action against transgenics justifiable, indeed imperative. Moreover, the claims in this specific case have face plausibility. Their claim to authoritative knowledge is derived from two sources: indigeneity (reports of local villagers and civil society organizations) and science. Additionally, the cognitive distance is great: toxic leaves? allergens in Bt cotton? Remote villages of the 'third world'? But more daunting than cognitive distance are the information costs that would be incurred by trying to make a rational assessment: who are these civil society organizations? Who do they represent? Where does one find authoritative knowledge about the Warangal district? Does the cry1Ac protein have mammalian activity or not? The normative solidarity – being associated with like-minded people – around 'health, justice, sustainability, peace and democracy' is unexceptional; it forms the basis for trust. The empirical claims are contrary to these values, but cognitively inaccessible. As a consequence, trust selects for belief to maintain cognitive consonance: one seeks to keep values and knowledge compatible.

Granted, all citizens are aware of political interests in promulgation of propaganda. But GMO brokerage does differ from that in other advocacy networks. Human Rights Watch and Amnesty International, for example, rest their credibility on factual accounts that face intense scrutiny and refutation by interested authoritative sources: national governments. INGOs in this sphere strongly resist diffusion of erroneous claims, even to the distress of their supporters. INGOs involved with biotechnology work in a field in which cognitive distance of supporters from science and from agriculture is significant, and the possibility of decisive refutation of claims is remote. New technologies are especially susceptible to both framing and epistemic brokerage for valence and evaluation. Torture is inter-subjectively understood; how insecticidal proteins kill sheep is not. Because genetic engineering is cognitively distal, it requires interpretation, mediation by expertise: people who understand gene networks, gene flow, gene-use restriction technology (aka the terminator).

What citizens learn from epistemic brokers has political consequences. If local activists stand for poor farmers and sustainable development, and GMOs destroy farmers, their animals and their environment, campaigns against GMOs are imperative. Funders of NGOs likewise find action imperative when faced with compelling reports of livestock deaths, crushing patents, GMO-driven mass suicides. These outcomes violate universal values embedded in numerous global agreements – sustainability, development, equity – and thus motivate global collective action. The urgency generated by adverse reports from the field quite reasonably motivates remedial actions: mandatory labeling, moratoria, GMO-free zones and financial contributions to NGOs furthering these objectives. Contrary reports are treated skeptically as corporate propaganda, regardless of source – a link back to the bio-property dominance of corporations in the threat narrative.

Opposition to transgenic crops on grounds of bio-property thus finds resonance in mass publics, in parallel to opposition on grounds of bio-safety. Together these strands produce a coherent narrative for mobilization. But there is a deep irony in this theorization of GMOs. Intellectual property claims of commercial firms raise prices of official, approved transgenic seeds; costs of testing raise seed prices; bio-safety regulations restrict competition and options, weeding out small firms and less-experienced firms, as well as public-sector scientists with possible applications based on research findings [9]. Strong bio-property rights and demanding bio-safety regimes therefore together drive high prices of official transgenics and thus invigorate underground markets [30,41]. Both regimes drive farmers to seek illicit seeds whenever these provide agronomic advantages but are too expensive to buy or prohibited by law.[16] Bio-safety regulation sought by oppositional movements thus contributes to de facto bio-property monopolies, to which activists are opposed and to evasion of bio-safety rules by farmers, which activists see as imperative.

[14] The opposition 'organic' and 'GMO,' implying radically alternative approaches to valuation and knowledge, is itself useful for political mobilization, but lacking in sound logic; see Ammann [47].

[15] http://www.i-sis.org.uk/MDSGBTC.php accessed November 12, 2009.

[16] In nations where farmers have some political power, access to expensive seeds may eventually produce pressure on governments for administered prices, as in the case of Bt cotton in India.

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Trade and commerce in improved crops and food: an essay on food security☆

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Agricultural trade between nations is a significant proportion of total international trade. Agricultural trade in transgenic crops faces extra complications due to the existence of domestic and international regimes that focus specifically on agricultural biotechnology. These specialized regimes create legal and commercial challenges for trade in transgenic crops that have significant implications for the food security of the nations of the world. By food security, one should understand not just the available supply of food, but also the quality of the food and the environmental impact of agricultural production systems. These specialized regimes for transgenic crops can either encourage or hinder the adoption of agricultural biotechnology as a sustainable intensive agriculture. Sustainable intensive agriculture offers hope for agronomic improvements for agricultural production, socio-economic betterment for farmers and environmental benefits for societies. Sustainable intensive agriculture offers particular hope for the poorest farmers of the world because agricultural biotechnology is a technology in the seed.

Contents

Introduction

The Royal Society recently issued a report titled ''Reaping the benefits: science and the sustainable intensification of global agriculture'' [1]. In Chapter 1 to the report, the Royal Society describes the 'urgent challenge' facing global agriculture to produce the food needed this 21st century in light of increasing population, changes in food demands and anticipated climate change. Population, food demand and climate explain the words 'sustainable intensification' in the title. As for the title's use of the word 'science', the Royal Society succinctly stated its view, ''Science must play a vital role in this response'' [2]. If science plays a vital role in promoting sustainable intensive global agriculture, then the Royal Society is guardedly optimistic that the urgent challenge will be met and that the world society will reap the benefits – adequate amounts of nutritious, safe food raised by economically, socially, politically and environmentally acceptable agricultural techniques, among which genetically modified crops will have an important place.

☆ Professor Kershen presented this topic at the Pontifical Academy of Sciences Study Week on Transgenic Plants for Food Security in the Context of Development (15–19 May 2009). This essay originated in the PAS presentation, updated with sources through December 2009.

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Scientists and developers

Scientists have been genetically modifying plants for 25 years, since the early 1980s; developers have commercialized genetically modified crops for 15 years, since the mid-1990s. Thousands of scientific projects and field trials and a vast literature of scientific publications provide the scientific evidence that genetically modified plants and crops are efficacious and safe for humans, animals and the environment. Hundreds of millions of hectares planted and harvested with transgenic crops provide the agronomic evidence that genetically modified crops are simply new crop varieties that present no unique or different risks than crops raised through conventional or organic means.

Building upon this substantial scientific and agronomic experience, reliable studies have shown that these genetically modified crops have created positive farm income effects, nonpecuniary benefits for farmers in terms of their labor, safety and resources, important yield increases, improved environmental agricultural footprints and marked reductions in green-house gas emissions [3]. Genetically modified crops – primarily canola, cotton, maize and soybeans modified for insect-resistance and herbicide-tolerance – presently widely used have earned the label of sustainable intensification in global agriculture through the vital role of science [4].

While widely used genetically modified crops have already earned the label of sustainable intensive agriculture, the future for genetically modified crops is brighter than the past. Scientists and developers are working in the laboratories, field trials and the regulatory systems of various nations to create, test and release crops that can address the nutritional needs of the poor-crops described as Golden crops (e.g. Golden Rice) [5] or as nutritionally complete crops (e.g. cassava) [6]. Scientists and developers are similarly working to create and release safer foods (e.g. Bt-maize with fewer mycotoxins) [7] and healthier foods (e.g. high-oleic soybeans) [8] that will benefit consumers directly in both developed and developing nations. Addressing climate issues, scientists and developers plan to create and release drought-tolerant, salt-tolerant, aluminum-tolerant and nitrogen-efficient crops, so that crops can be grown on lands subject to environmental stresses [9]. Finally, biological science will not be stagnant and new techniques, procedures, knowledge and discoveries will flow forth [10]. These new genetically modified crops and these scientific advances, if wisely used, also can earn the label of sustainable intensive global agriculture.

Farmers

Farmers know their fields and know their self-interest in increased income and productivity, better allocation of labor, time and resources, and safer practices and products for themselves and the environment. Consequently, farmers around the world have adopted genetically modified crops at an unprecedented rate [11] and in the face of fierce opposition that has tried to frighten and mislead them about biotechnology [12]. Notably, 13.3 million farmers (over 90% poor resource farmers) in 25 countries (on all continents, except Antarctica) planted 125 million hectares of genetically modified crops in the year 2008 [13].

Farmers plant genetically modified crops depending upon three key factors. First, farmers must have access to seeds that are suitable for the agro-ecological conditions of their particular fields. Seeds bred for particular soils, particular temperature and rainfall zones do not perform to the optimum in other soils and zones. Second, farmers must be able to coexist with their neighbors in neighborly ways so that each farmer can choose what is appropriate for his field. Farmers must not face discriminatory rules and regulations that limit their choices and inappropriately impose liability upon them simply because they desire to grow genetically modified crops. Third, and most importantly, farmers must not be denied access to genetically modified seeds because laws prohibit the growing of genetically modified crops. When laws allow farmers the choice, farmers have chosen quickly and broadly to grow genetically modified crops in their fields.

Two countries can serve as examples of this third point. In Romania, farmers grew vast expanses of genetically modified soybeans until Romania joined the European Union where the law has yet to authorize their planting. By force of law, Romanian farmers were forced to stop growing a crop that they had grown willingly and enthusiastically [14]. By contrast in Pakistan, despite a legal prohibition, farmers have been so anxious to grow this improved crop that they are defying the law [15]. In this regard, Pakistani farmers are doing what farmers in India and Brazil had done previously – ignore the law to improve their lives and their farms [16].

Consumers

If we think of trade and commerce in crops and foods as a chain from production to consumption, scientists/developers and farmers are the first two links of that chain. Consumers are the last link. Consumers assuredly want safe, nutritious foods at a reasonable price. Focusing on genetically modified crops, consumers have additional preferences, that when considered nonideologically, do not constitute an entrenched public opinion against genetically modified foods. Indeed, the majority of consumers are willing to purchase genetically modified foods [17].

Consumers want accurate information communicated by trustworthy sources about genetically modified foods. Consumers may not be especially knowledgeable about the science of genetic modification and plant breeding, or about the realities of farming, but they desire to learn more. At the same time, most consumers do not consider genetically modified crops or foods a crucial issue. On their list of preferences related to food, most consumers consistently rank appearance, familiarity, freshness, price and taste as their primary preferences related to their food purchases. In flush economic times, price is less important; in lean economic times, price becomes the predominate consideration. With respect to safety concerns about food, consumers rank genetically modified foods as a low priority concern. Consumers are much more concerned about other issues related to food safety.

Taking into account the consumer preferences listed above, many consumers are willing to purchase genetically modified whole foods or foods produced with or from genetically modified ingredients. Consumers express even a greater willingness to purchase genetically modified foods if they perceive direct benefits for themselves and their families from the food [18].

A small percentage of consumers actively seek to avoid the purchase and consumption of genetically modified foods. They do so for many different reasons, but they have a strongly expressed preference for avoidance. These consumers can protect

their preference by purchasing food in niche markets that supply their preference – primarily the organic food sector where the intentional use of genetically modified seeds, crops or ingredients is expressly prohibited. Consumer preferences for organic food can be satisfied without prohibiting or stifling other consumers access to genetically modified foods.

Activist groups opposed to agricultural biotechnology consistently focus upon consumers who prefer avoidance and greatly exaggerate their numbers. In addition, activists spend considerable time and resources in attempts to frighten all consumers with false and misleading claims about the safety and nutritiousness of genetically modified foods [19]. Yet, despite the extended and colorfully bizarre campaigns against genetically modified foods, the percentage of consumers who seek avoidance remains small. Activists get media attention but have not successfully moved most consumers to a preference of avoidance of genetically modified foods.

Hundreds of millions of consumers eat genetically modified foods every day and have done so for more than a decade without a single instance of consumer harm that is unique or different in any way from conventional and organic foods. For consumers, genetically modified foods are, in fact and in truth, substantially equivalent to conventional and organic foods. Despite proclaimed perceptions, most consumers are not a blockage in the chain of commerce in genetically modified crops coming from scientists and developers and grown in farmers' fields.

Retailers: food processors and food stores

While in low-income and rural-dominated societies' consumers grow their own foods or purchase from local vendors, in the middle/higher income countries consumers purchase by far the largest percentage of their food from supermarkets [20]. The supermarket revolution of fresh foods, processed foods and baked goods has affected all countries and, indeed, the spending on processed foods is increasing fastest in developing countries [21]. Consequently, retailers are the gatekeepers to consumer choice. If retailers do not offer a particular food to consumers, consumers have no choice to buy that particular food.

Understandably, retailers are sensitive to protecting their brand names, their market share, their reputation and their profitability. But this sensitivity to protecting their legitimate self-interest means that retailers are also subject to activist groups threatening to disrupt retail operations with demonstrations, boycotts and consumer scares based on misinformation, ideologically driven advertising and media distortions. Retailers can thus become quite risk-averse to a new food or a new food technology relatively quickly and easily. As Sir Terry Leahy, chief executive of the UK retail food chain, Tesco, stated in the London City Food Lecture in February 2009,

> ***"It may have been a failure of us all to stand by the science. Maybe there is an opportunity to discuss again these issues and a growing appreciation by people that GM could play a vital role in feeding the world's growing population." [22]***

If retailers had stood with the science of genetically modified plants for food, retailers would have linked scientists/developers and farmers to consumers. Genetically modified foods would be products in trade and commerce no different than other foods in trade and commerce. Genetically modified foods would trade and retail in domestic and international markets like their equivalent foods. While equivalency between genetically modified foods and other foods was not the issue before the World Trade Organization (WTO) in the dispute between Argentina, Canada and the United States versus the European Union, relating to the EU *de facto* moratorium on approving imports of genetically modified foods and crops, the WTO ruled in favor of Argentina *et al.* on the basis that the EU was acting without a scientific basis for its moratorium. The WTO ruling stood with science [23].

As everyone knows, genetically modified crops and foods have not been treated like equivalent crops and foods from conventional and organic agriculture. Specifically from the retailers' perspective, genetically modified foods in many countries must carry labels that impose costs upon retailers while exposing the retailers to targeted campaigns by activists against retailers' ingredient and stocking policies. In light of retailers' sensitivities and risk aversion, mandatory labeling has meant that, in many situations, retailers have attempted to source nongenetically modified ingredients and have tried to avoid stocking genetically modified foods. While activists have touted labels as providing consumer choice, proclaiming the consumer right-to-know, the consumer reality is just the opposite – the denial of consumer choice – because retailers have often refused to offer consumers choices [24].

Leaving aside the legal question as to whether mandatory label laws for genetically modified foods violate the World Trade Agreements [25], mandatory label laws have factually reduced consumer choice and commercially pressured retailers into avoiding genetically modified foods. By so doing, retailers, as the gatekeepers to consumer choice, have blocked consumers from purchasing products that have already shown huge agronomic, environmental, health and economic benefits for sustainable intensive global agriculture and for food security for societies around the world. Even worse, unless retailers change their policies, possibly by influencing public policy to change the mandatory label laws, retailers have forgone for themselves and their customers the scientific and technological advances in agricultural biotechnology that are immediately on the horizon and reasonably expected in future years. By shunning genetically improved crops, retailers could limit their consumers to foods that are less healthy and less safe.

Food and feed traders: exporters and importers

Food and feed traders are the link in the chain of commerce connecting farmers to retailers and on to consumers. While information about available products compared to requested products, and about general market specifications compared to niche market specifications, constantly travels back and forth through the chain of commerce, information mismatches can and do occur. In a basic sense, exporters can only ship products that farmers produce while importers can only sell products that retailers demand. In addition to the demands of the market, food and feed traders must also comply with international and domestic laws that govern trade in food and feed. In attempting to satisfy both market and legal demands, food and feed traders become important

gatekeepers to the cost of food/feed and the availability of food/feed through the international trade in agricultural commodities.

In some countries, responding to retailers asking for nongenetically modified crops and foods, importers have requested that exporters segregate crops and foods between conventional/organic and transgenic. If importers do not find the requested nongenetically modified crops and foods in the exports from a particular country, the importers seek alternative suppliers in other countries. Importers who request these segregated goods assuredly pay for the increased costs associated with segregation. Exporters assuredly are willing to engage in segregation to satisfy the importer's demand so long as the importer pays an appropriate price premium. Markets and contractual obligations usually are adequate to meet this demand for segregation among crops and foods [26]. Moreover, these segregated markets and contractual obligations can function easily and efficiently in accordance with ordinary trade rules established under the WTO Agreements.[1]

However, genetically modified crops and foods/feeds are subject to the Cartagena Protocol on Biosafety (CPB) and to various national legal regimes that focus specifically on agricultural biotechnology. Thus, exporters and importers of genetically modified crops and foods/feeds must comply with these additional legal requirements. These additional legal requirements can create trade disruptions, thereby undermining the smooth flow of agricultural products in international trade that is needed for food/feed availability and food/feed security in developed and developing nations [27]. (This essay focuses on possible trade disruptions and does not focus on international legal issues, i.e. whether the WTO agreements, the CPB, and these specialized domestic legal regimes are compatible or incompatible. Concerning these international legal issues, read [28].)

Simply by their existence, the CPB and special domestic regimes focusing on agricultural biotechnology create disincentives for countries to adopt or to trade in genetically modified crops and foods/feeds. These specialized regimes express, either implicitly or explicitly, the scientifically incorrect message that agricultural biotechnology creates risks that are unique and different from conventional/organic agricultural products. Thus, countries in food crises may deny their citizens access to genetically modified foods even though those same foods are consumed by hundreds of millions of citizens in developed countries on a daily basis [29].

More specifically, the CPB contains two provisions especially applicable to food traders: Article 18 on Handling, Transport, Packaging and Identification and Article 27 on Liability and Redress. Both articles address topics purposefully left unresolved when the CPB text came into final form in Montreal in 2000 because the Parties to the Protocol could not reach agreement. In 2009, the Parties are still not in agreement about these topics, though they have promised to reach agreement in 2012 and 2010, respectively.

With respect to Article 18, those opposed to agricultural biotechnology demand that Parties to the Protocol make it legally binding that food/feed traders specifically identify every possible transgenic trait that might be contained in a shipment of bulk grains or oil seeds and quantify the percentage of each trait in each shipment. Of course, the greater the demands for identification and quantification, the greater the cost becomes for testing, handling, cleaning, segregation, etc. The costs rise very quickly and, at some point, prohibitively for engaging in trade in genetically modified crops – as shown in a careful study from Brazil [30]. By contrast, Article 18(2)(a) would also allow, if the Parties so agree, that agricultural shipments need only state on the shipping documents that the shipment ''may contain'' genetically modified products and that these are not intended for introduction into the environment of the importing nation, but rather are only for processing into food and feed products. If this ''may contain'' option were the ultimate agreement in 2012, this statement on the shipping documents imposes no measurable additional costs upon food/feed traders and creates no significant trade barriers for genetically modified agricultural commodities.

With respect to Article 27 on liability and redress, those opposed to agricultural biotechnology urge the Parties to adopt a civil legal liability regime using strict liability for damages expansively defined (e.g. alleged social, ethical and cultural damages) backed by mandatory insurance or compensation funds. Under such a regime, the liability risks for developers and food/feed traders in genetically modified crops would be enormous and an international liability regime would become a significant hindrance to trade in genetically modified agricultural commodities. By contrast, Article 27 also allows Parties to agree to an administrative system of liability limited to significant adverse or negative environmental harms while focusing on environmental remediation, not monetary damages. As of December 2009, the Parties appear most favorably inclined toward an administrative system as the appropriate legal regime under Article 27 [31]. If Parties agree to an administrative system, the impact on trade in genetically modified crops would probably be minimal because agricultural trade for ten years has involved great quantities of genetically modified crops without a single instance of significant adverse or negative environmental impact.

In contrast to the CPB, the European legal regime for the importation of genetically modified agricultural commodities has had a disruptive impact on agricultural trade. The European system has been very slow to approve transgenic traits for food or feed and has a 'zero tolerance' for unapproved traits. As a consequence of these two European attributes, food/feed traders have become hesitant to engage in agricultural trade with European nations. Feed prices, particularly, have escalated sharply in Europe [32]. Moreover, the European situation is likely to get significantly worse in the coming years as more countries grow several transgenic traits on their agricultural lands [33]. Until Europe quickens the pace for approval and develops a tolerance level for unapproved traits, the European legal regime will continue to have a disruptive impact on agricultural trade [34].

Conclusion

Science in agriculture is essential to feed, clothe and nourish the health and well-being of human beings. Scientists and developers can deliver the benefits of science in agriculture to farmers who will readily adopt these agricultural improvements. But scientists, developers and farmers cannot bring these benefits to consumers unless food traders can export and import genetically modified

[1] The relevant World Trade Organization Agreements are the General Agreement on Tariffs and Trade (GATT 1994), the Sanitary-Phytosanitary Agreement (SPS), and the Technical Barriers to Trade Agreement (TBT). There is another WTO agreement on Trade-Related Intellectual Property Rights (TRIPs) that is not directly pertinent to this essay.

crops free from debilitating legal regimes and unless retailers offer consumers product choices using ingredients from improved crops. Consumers can benefit themselves with safer, more nutritious, environmentally friendly and (probably) less expensive food, if they avoid believing ideologically motivated misinformation and food scares about genetically modified foods and feeds. Poor farmers and poor consumers especially are likely to be the principal beneficiaries of agricultural development flowing from genetically improved crops [35]. But the past 30 years clearly shows that society will not benefit from genetically modified crops without great effort and difficulty.

In the early 1500s, Raphael painted representations of the cardinal virtues – prudence, justice, fortitude and temperance [36] – on the walls of the Vatican Palace. Scientists, developers, farmers, food traders, retailers and consumers will need to exercise these cardinal virtues for scientific rationality lest we let our fears and our passions deny humanity the benefits of genetically improved crops. We must have a habitual and firm disposition to pursue the good in science and to choose concrete actions for the good of humanity through transgenic plants for food security in the context of development [37].

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Review

The regulation of agricultural biotechnology: science shows a better way

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National and international regulation of recombinant DNA-modified, or 'genetically engineered' (also referred to as 'genetically modified' or GM), organisms is unscientific and illogical, a lamentable illustration of the maxim that bad science makes bad law. Instead of regulatory scrutiny that is proportional to risk, the degree of oversight is actually *inversely* proportional to risk. The current approach to regulation, which captures for case-by-case review organisms to be field tested or commercialized according to the techniques used to construct them rather than their properties, flies in the face of scientific consensus. This approach has been costly in terms of economic losses and human suffering. The poorest of the poor have suffered the most because of hugely inflated development costs of genetically engineered plants and food. A model for regulation of field trials known as the 'Stanford Model' is designed to assess risks of new agricultural introductions – whether or not the organisms are genetically engineered, and independent of the genetic modification techniques employed. It offers a scientific, rational, risk-based basis for field trial regulations. Using this sort of model for regulatory review would not only better protect human health and the environment, but would also permit more expeditious development and more widespread use of new plants and seeds.

Contents

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'Genetic engineering' is not new

Over many millennia, there has been a virtually seamless continuum of genetic improvement of crops with increasingly sophisticated techniques [1]. Recombinant DNA modification, a term I will use interchangeably with 'genetic engineering', was introduced as part of this progression of technologies during the 1970s. Thus, because genetic modification, or improvement, has been with us for centuries, 'genetically modified organism' and its abbreviation 'GMO' – commonly used nomenclature – are unfortunate choices of terminology. Defined arbitrarily as organisms containing genes transferred across species lines – but only when accomplished by recombinant DNA techniques – it ignores that genetic modification is achieved using many technologies and that recombinant organisms are not a meaningful 'category'.

Millions of new genetic variants of plants field tested each year are derived from 'wide-cross hybridizations', in which genes have been moved across species or genus barriers. Wide crosses have been performed for almost a century and thousands of such 'non-molecular transgenic varieties' (as they might be called) are in commerce around the world. Examples include:

- *Triticum agropyrotriticum*, a man-made 'species' that resulted from combining genes from bread wheat and a grass called quackgrass or couchgrass, that contains all the chromosomes of wheat and one extra whole genome from the quackgrass.
- Triticale, also a man-made grain, a wheat–rye hybrid.
- Pluots and apriums, plum–apricot hybrids.

T. agropyrotriticum is a particularly apt example. Throughout development, from field-testing through scaling up and commercialization to being fed to animals and humans, neither regulators nor activists were concerned with whether the tens of thousands of genes from quackgrass would make *T. agropyrotriticum* more weedy or whether any of the expression products were toxigenic or allergenic. Nor has the pluot, commonly found at summer farmers' markets, elicited any resistance from activists or scrutiny from regulators.

By contrast, if someone were to move a single gene from quackgrass into Triticum or from plum to apricot using recombinant DNA techniques, the new constructions would be subject to expansive, extensive, lengthy, and debilitating regulatory regimes.

Most agricultural crops are the products of hundreds, if not thousands, of years of genetic improvement. Maize, for example, has undergone drastic, gradual modification, from the original grass-like plant with primitive, meager kernels, into modern maize, with regularly arranged kernels replete with carbohydrate, oil, and protein [2].

A more recent example of the irrationality of current conceptions of 'natural' versus 'genetically engineered' is Golden Rice, several varieties biofortified with beta-carotene, the precursor of vitamin A. Ref [3] shows the entire 'pedigree' of the immediate precursor of Golden Rice, IR64 – a strain of rice widely used in many parts of the world – as well as the addition of two genes that convert IR64 into Golden Rice. What is astonishing about this construction is that for regulatory purposes, all of the complex genetic changes, including mutations, recombinations, deletions, and translocations leading to IR64 are somehow considered 'natural' – and therefore elicit no concern or review – while the insertion into exactly known sites of two well-characterized genes that enable the plant to synthesize beta-carotene (which is converted to vitamin A *in vivo*) precipitates a monumental burden of regulatory costs and delays. Although 'GMOs' (or variations on the theme) are not a genuine, meaningful category, in most regulatory regimes around the world, merely the use of recombinant DNA techniques is the trigger for draconian, dilatory, and expensive regulatory regimes.

Benefits and obstacles

Genetically engineered plants have persuasively demonstrated extraordinary benefits:

- Increased yield, which permits conservation of cultivated land and avoidance of upslope farming.
- Decreased use of chemical pesticides, which leads to less runoff and fewer poisonings. For example in China, the use of Bt cotton has substantially reduced poisoning incidents by pesticides among farmers and their families [4].
- Reduced water requirements with drought resistant or saline tolerant varieties may be among the most important applications worldwide. With recurrent droughts over southern Europe, Australia, parts of the United States, and much of sub-Saharan Africa, small improvements in water requirements for agriculture can make a large difference in the yields and cost-effectiveness of farming.
- Shifts in herbicide usage lead to the use of more environmentally friendly herbicides and increased no-till farming, resulting in lower soil erosion, less runoff, and less carbon dioxide released to the atmosphere.
- Decreased content of fungal toxins in food and feed, and correspondingly reduced incidence of illness in animals and humans.

In spite of these benefits and the absence of any unanticipated or unique negative effects, the technology has encountered various policy and public relations obstacles. A number of 'pseudo-crises' – high-profile incidents that falsely implied significant risks of genetic engineering, fomented by fear-mongering non-governmental organizations, one-sided journalism, and the expansionist tendencies of bureaucrats – have led to flawed public policy and over-regulation of genetic engineering techniques and their products.

The scientific basis of regulation

There exists a decades-old scientific consensus about the need for a more rational, risk-based approach to the regulation of both field trials and commercialization of genetically engineered plants. In 1987, the U.S. National Academy of Sciences (NAS) published a white paper on the planned introduction of genetically engineered organisms into the environment [5]. It noted that recombinant DNA techniques provide a powerful and safe means for modifying organisms, and it predicted that the technology would contribute substantially to improved health care, agricultural efficiency, and the amelioration of many pressing environmental problems. The paper had wide-ranging impacts in the United States and internationally. Its most significant conclusions and recommendations include:

- There is no evidence of the existence of unique hazards either in the use of recombinant DNA techniques or in the movement of genes between unrelated organisms.

- The risks associated with the introduction of recombinant DNA-modified organisms are the same in kind as those associated with the introduction of unmodified organisms and organisms modified by other methods.
- Assessment of the risks of introducing recombinant DNA-modified organisms into the environment should be based on the nature of the organism and of the environment into which the organism is to be introduced, and independent of the method of engineering *per se*.

In a 1989 follow-up to this white paper, the National Research Council (NRC), the research arm of the NAS, concluded that 'no conceptual distinction exists between genetic modification of plants and microorganisms by classical methods or by molecular techniques that modify DNA and transfer genes,' whether in the laboratory, in the field, or in large-scale environmental introductions [6]. The NRC report supported this statement with extensive discussions of experience with plant breeding and the cultivation of these pre-recombinant DNA genetically modified plants and microorganisms:

- 'Crops modified by molecular and cellular methods should pose risks no different from those modified by classical genetic methods for similar traits. As the molecular methods are more specific, users of these methods will be more certain about the traits they introduce into the plants.'
- 'Recombinant DNA methodology makes it possible to introduce pieces of DNA, consisting of either single or multiple genes, that can be defined in function and even in nucleotide sequence. With classical techniques of gene transfer, a variable number of genes can be transferred, the number depending on the mechanism of transfer; but predicting the precise number or the traits that have been transferred is difficult, and we cannot always predict the phenotypic expression that will result. With organisms modified by molecular methods, we are in a better, if not perfect, position to predict the phenotypic expression.'
- 'Information about the process used to produce a genetically modified organism is important in understanding the characteristics of the product. However, the nature of the process is not a useful criterion for determining whether the product requires less or more oversight.'
- As a consequence, 'the *product* of genetic modification and selection should be the primary focus for making decisions about the environmental introduction of a plant or microorganism and not the *process* by which the products were obtained.'

Thus, the NRC articulated some of the principles that should underlie the regulatory oversight field trials of plants, and subsequently these principles have been reiterated repeatedly by countless scientific bodies. The essence is that the mere fact that an organism has been modified by genetic engineering techniques should not determine how the organism is regulated. This was emphasized yet again in the comprehensive report from the U.S. National Biotechnology Policy Board (on which I served as a charter member), which was established by the U.S. Congress with representation from the public and private sectors. The report concluded: 'The risks associated with biotechnology are not unique, and tend to be associated with particular products and their applications, not with the production process or the technology *per se*. In fact, biotechnology processes tend to reduce risks because they are more precise and predictable' [7]. The report went even further, concluding, 'The health and environmental risks of not pursuing biotechnology-based solutions to the nation's problems are likely to be greater than the risks of going forward.' This is true in general for this technology and its products, particularly for parts of the world where subsistence farming predominates.

Various other national and international groups, including the American Medical Association, the United Kingdom's Royal Society, and the UN's Food and Agriculture Organization and World Health Organization, have repeatedly echoed or extended these conclusions. For example, a joint statement from the International Council of Scientific Unions' (ICSU) Scientific Committee on Problems of the Environment (SCOPE) and the Committee on Genetic Experimentation (COGENE) concluded 'The properties of the introduced organisms and its target environment are the key features in the assessment of risk. Such factors as the demographic characterization of the introduced organisms; genetic stability, including the potential for horizontal transfer or outcrossing with weedy species; and the fit of the species to the physical and biological environment ... apply equally to both modified or unmodified organisms; and, in the case of modified organisms, they apply independently of the techniques used to achieve modification' [8]. That is, it is the characteristics of organism itself, and not how it was constructed, that is important.

Similarly, the report of a NATO Advanced Research Workshop concluded, 'In principle, the outcomes associated with the introduction into the environment of organisms modified by recombinant DNA techniques are likely to be the same in kind as those associated with introduction of organisms modified by other methods. Therefore, identification and assessment of the risk of possible adverse outcomes should be based on the nature of the organism and of the environment into which it is introduced, and not on the method (if any) of genetic modification' [9].

Other analyses have focused specifically on the food safety aspects of gene-spliced organisms and their derivatives. For example, in a 1993 report the Paris-based Organization for Economic Cooperation and Development (OECD) described several concepts related to food safety that are wholly consistent with, and expand upon, the consensus discussed above [10]:

- 'Modern biotechnology broadens the scope of the genetic changes that can be made in food organisms and broadens the scope of possible sources of foods. This does not inherently lead to foods that are less safe than those developed by conventional techniques.'
- 'Evaluation of foods and food components obtained from organisms developed by the application of the newer techniques does not necessitate a fundamental change in established principles, nor does it require a different standard of safety.'

Finally, a comprehensive analysis of food safety published in 2000 by the Institute of Food Technologists addressed both the scientific and regulatory implications of foods derived from genetically engineered organisms and specifically took current regulatory policies to task. The report concluded that the evaluation of genetically engineered organisms and the food derived from them 'does not require a fundamental change in established principles

of food safety; nor does it require a different standard of safety, even though, in fact, more information and a higher standard of safety are being required' [11]. The report went on to state unequivocally that theoretical considerations and empirical data do 'not support more stringent safety standards than those that apply to conventional foods.'

What could be clearer than this consensus about the appropriate basis for the oversight of genetically engineered plants in the field and in the food supply?

Principles of regulation

In addition to the consensus described above specifically for the products of genetic engineering, there are certain general principles of regulation that should inform any regulatory scheme:

- The degree of regulatory scrutiny should be commensurate with the perceived level of risk.
- Similar things should be regulated in a similar way.
- If the scope of regulation – i.e. the regulatory net or the trigger that captures field trials or the finished product for review – is unscientific, then the entire approach is unscientific.

Consequences of flawed regulation

All of the principles of regulation described above have been largely ignored. Current regulatory regimes are unscientific, process-based, and require case-by-case review for virtually all genetically engineered plants and microorganisms, no matter how obviously trivial the modification or benign the product might be. This flawed approach, which categorically ignores fundamental principles of regulation and the dictates of common sense, results in enormously inflated costs, lack of agricultural progress, and human suffering.

Increased research and development costs

The compliance costs of regulation for the development of an insect-resistant and a herbicide-resistant maize have been calculated to be between USD 6 and 15 million respectively, not including labeling. This is several times more costly than for similar constructions made with conventional breeding, in spite of the latter being less precise and predictable.

Fewer products in the pipeline with reduced benefits for farmers and consumers

The costs and uncertainty created by the regulatory milieu have inhibited agricultural innovation and product development, decreased commercialization of already-developed genetically engineered crops and decreased the potential for new, improved varieties of fruits and vegetables, tree fruits and nuts, and nursery and landscape crops. That is to say, development is economically viable primarily for commodity crops, which are grown at vast scale.

In 2009, the total area of biotech crops was around *134 million hectares, making it the most rapidly adopted crop technology in history, an 80-fold increase from 1996 to 2009*. Nobody has yet been able to calculate the economic losses from excessive, gratuitous regulation, but it unquestionably imposes a huge punitive tax on a superior technology; with more rational, science-based regulation there would be a far greater shift to genetically engineered crops, with additional traits and species developed and commercialized. Putting it another way, the opportunity costs of flawed, unscientific public policy have been enormous, and as usual, most of those costs have been imposed on the poor.

Pseudo-crises and litigation

Pseudo-crises have led to public relations debacles, flawed public policy, endless debate over inconsequential issues like, coexistence, of genetically engineered and conventional crops, acceptable tolerances for 'contamination', and labeling, as well as costly court trials. One well-known example is the StarLink case where the US Environment Protection Agency gave split approval of maize, sanctioning it for animal but not human consumption. After it was subsequently detected in human foodstuffs [12], the regulatory and civil penalties to the company that developed the StarLink for this inconsequential 'transgression' were substantial (even though not a single person suffered any adverse effects). Other pseudo-crises include the (false) alarms over killing of Monarch butterflies and the contamination of land races from horizontal gene transfer in Mexico. All of these are based on inaccurate or fraudulent reports, or results taken out of proper context.

Vandalism and intimidation of academics

Field trials are constantly being vandalized because in many places the regulatory requirements, which are specific to and discriminate against recombinant DNA-modified products, dictate that the sites of trials become publically known. Researchers have been injured, research destroyed, and in Germany two universities responded to the threats of activists by banning the testing of recombinant DNA-modified plants, an appalling example of cowardice and abdication of academic freedom.

Malnourishment, illness, and deaths

Malnutrition claims thousands of lives per day, many of which could be saved if governments and international organizations would change their hostile attitudes and policies toward genetic engineering. The resulting greater availability of improved crop varieties would enhance food security for poor farmers.

The 'Stanford Model' for risk-based regulation

It is easy to complain about unscientific, non-risk-based regulatory regimes. But there are better proven alternatives, and science shows the way. One is the 'Stanford Model' for risk-based regulation, which was developed in the 1990s [13]. The Stanford Model stratifies organisms according to their risk in field trials. This universe can be divided in two ways (Fig. 1):

- Horizontally, according to risk categories, with higher risk as one goes toward the top of the pyramid.
- By the oblique lines, dividing the universe of field trials according to technology: the green area is all field trials performed with organisms created by conventional breeding or tissue culture, for example, while the area to the far right corresponds to field trials with recombinant DNA-modified organisms.

Conceptually, it should be clear that there is no particular enrichment of risk depending on technology. There can be high-risk organisms – for example foot and mouth disease virus, African killer bees, rusts that infect grains, or highly invasive weeds

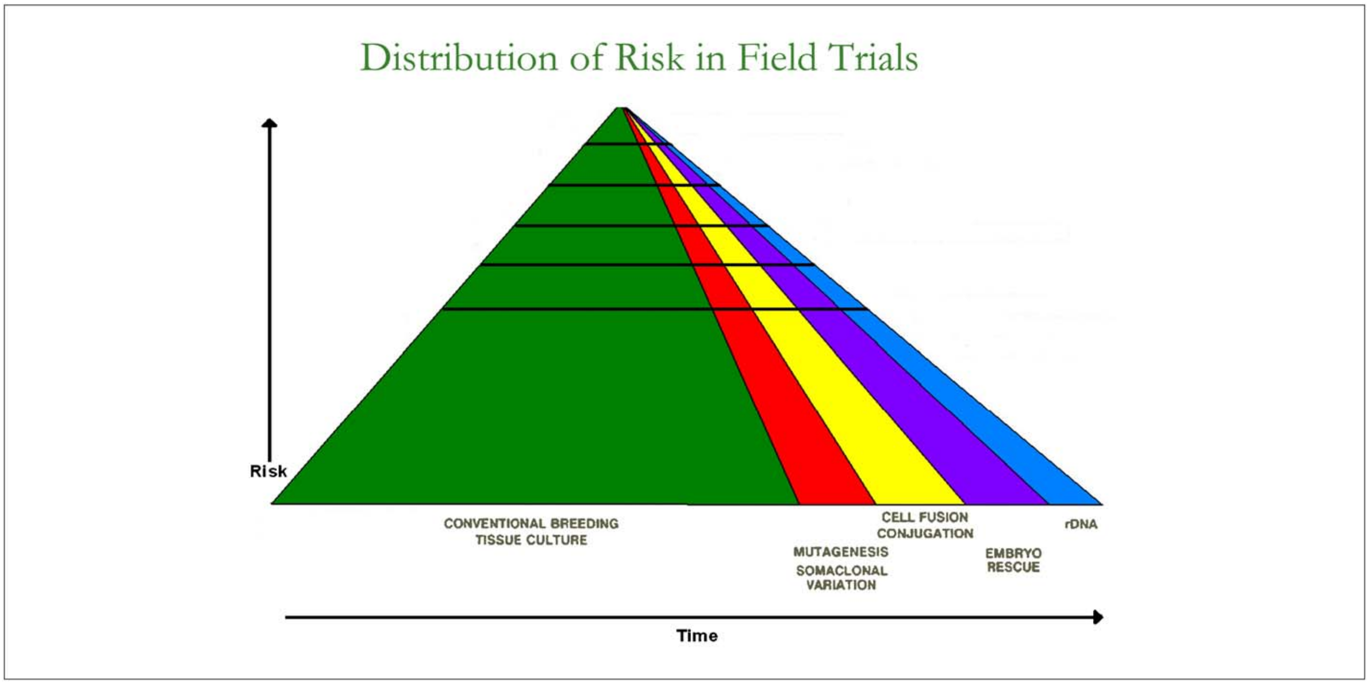

FIGURE 1
Distribution of risk in field trials.

such as kudzu – that require more caution in field tests whether or not they have been genetically modified in any way. Plants may be invasive, produce potent toxins, etc., but in general they are of negligible or low risk. Recombinant DNA technology affords no particular monopoly on safety, but on average, it is far more precise and more predictable than the other techniques.

More than a decade ago, the Stanford University Project on Regulation of Agricultural Introductions developed a widely applicable regulatory model for the field-testing of any organism, whatever the method or methods employed in its construction. The approach is patterned after quarantine systems such as the USDA's Plant Pest Act regulations, which are essentially binary; a plant that a researcher might wish to introduce into the field is either on the proscribed list of plants pests – and therefore requires a permit – or it is exempt. The more quantitative and nuanced 'Stanford Model', which stratifies organisms into several risk categories, more closely resembles the approach that was taken in the National Institutes of Health/Centers for Disease Control (NIH/CDC) handbook *Biosafety in Microbiological and Biomedical Laboratories*, now in its 5th edition, which specifies the procedures and physical containment that are appropriate for research with microorganisms, including the most dangerous pathogens known [14]. These microorganisms were stratified into risk categories by panels of scientists. Interestingly, unlike regulators' approach to recombinant DNA-modified organisms, the NIH/CDC approach – even for the most dangerous pathogens – is only to offer guidance to researchers but not to make adherence compulsory.

The Stanford Model – applied to plants in its first demonstration project – can be readily applied to accommodate different kinds of organisms, geographical regions, and preferences for more or less stringent regulation. In January 1997, the project assembled a group of approximately 20 agricultural scientists from 5 nations at a workshop held at the International Rice Research Institute (IRRI), in Los Baños, The Philippines. The purpose of the workshop was to develop a broad, science-based approach that would evaluate all biological introductions, not just those that involve genetically engineered organisms. The need for such a broad approach was self-evident – there was already abundant evidence that severe ecological risks can be associated with plant pests and 'exotics', or non-coevolved organisms. As part of the pilot project, the IRRI conference participants evaluated and then stratified a variety of crops based on certain risk-related characteristics, or traits, to be considered in order to estimate overall risk. Consensus was reached without serious difficulty – suggesting that it would be similarly possible to categorize other organisms as well.

The participants agreed at the outset that the following risk-based factors would be integral to a model algorithm for field-testing and commercial approval of all introductions:

- Ability to colonize.
- Ecological relationships.
- Human effects.
- Potential for genetic change.
- Ease or difficulty of risk management.

Each of the organisms evaluated during the conference was assessed for all 5 factors, which enabled the group to come to a global judgement about the organism's risk category. Most of the common crop plants addressed were found to belong in Category 1 (negligible risk), while a few were ranked in Category 2 (low but non-negligible risk). One plant (cotton) was judged to be in Category 1 if it were field-tested outside its center of origin, and Category 2 if tested in the vicinity of its center of origin.

It cannot be over-emphasized that in the evolution of this Stanford Model, the factors taken into account were indifferent to either the nature of the genetic modification techniques employed, if any, or to the source(s) of the introduced genetic material. The participants agreed that the use of conventional breeding techniques or recombinant DNA methods to modify an organism was irrelevant to risk. They also agreed that combining DNAs from phylogenetically distant organisms – i.e. organisms from different genera, families, orders, classes, phyla, or kingdoms – was irrelevant to the risk of an organism.

In other words, the group's analysis supported the view that the risks associated with field-testing a genetically altered organism are independent of the process by which it was modified and of the movement of genetic material between 'unrelated' organisms. The Stanford Model suggests the utility and practicality of an approach in which the degree of regulatory scrutiny over field trials is commensurate with the risks – independent of whether the organisms introduced are 'natural', non-coevolved or have been genetically improved by conventional methods or gene-splicing techniques. Variations and refinements of this approach are possible, of course; Professor Wayne Parrott has suggested that the risk category could be adjusted depending on the trait introduced – a gene that enhances weediness or that expresses a potent toxin or allergen, for example, might bump the organism into a higher risk category (Parrott, personal communication).

What, then, are the practical implications of an organism being assigned to a 'risk category'? The level of oversight faced by an investigator who intends to perform a field trial with an organism in one or another of the categories could include: complete exemption, a simple 'postcard notification' to a regulatory authority (without affirmative prior approval required), premarket review of only the first product in a given category, case-by-case review of all products in the category, or even prohibition (as is the case currently for experiments with foot-and-mouth disease virus in the United States).

A key feature of the Stanford Model is that it is sufficiently flexible to accommodate differences in regulatory authorities' preferences for greater or lesser regulatory stringency. Putting it another way, different national regulatory authorities could choose their preferred degree of risk aversion, some leaning more toward exemption and notification, others toward case-by-case review. However, as long as regulatory requirements are commensurate with the relative risk of each category and do not discriminate by treating organisms of equivalent risk differently, the regulatory methodology will remain within a scientifically defensible framework.

Under such a system, some currently unregulated introductions of traditionally bred cultivars and so-called 'exotic', or non-coevolved, organisms considered to be of moderate or greater risk would probably become subject to regulatory review, whereas many recombinant DNA-modified organisms that now require case-by-case review would probably be regulated less stringently. The introduction of such a risk-based system would rationalize significantly the regulation of field trials and it would reduce the regulatory and other disincentives to the use of molecular techniques for genetic modification.

By making possible accurate, scientific determinations of the risks posed by the introduction of an organism into the field, this regulatory model fosters enhanced agricultural productivity and innovation, while it protects valuable ecosystems. It offers regulatory bodies a highly adaptable, scientific paradigm for the oversight of plants, microorganisms, and other organisms, whether they are 'naturally occurring' or non-coevolved organisms, or have been genetically improved by either old or new techniques. The outlook for the new biotechnology applied to agriculture, especially environmentally friendly innovations of particular benefit to the developing world, would be far rosier if governments and international organizations expended effort on perfecting such a model instead of on introducing and maintaining unscientific, palpably flawed, debilitating regulatory regimes.

Advantages of the Stanford Model

- It stratifies all organisms according to risk and is indifferent to the technique (if any) of genetic alteration.
- It is flexible.
- It is scientifically defensible.
- It permits various degrees of risk-aversion depending on the need.
- It permits discretion – in a scientific context.
- It exempts field trials that should be exempt and captures field trials that should be reviewed.

One great advantage is that it is analogous to existing regulatory regimes, such as those for quarantine regulations for plant or animal pests, and also to the U.S. government's approach to handling dangerous pathogens or other microorganisms in the laboratory. In other words, the approach is not fundamentally new and has worked well in practice for decades.

Summary

Compared to its potential, the stunted growth of agricultural biotechnology worldwide stands as one of the great societal tragedies of the past quarter century. Unscientific, excessive, stultifying regulation, nationally and internationally, is a major reason for the failure of agricultural biotechnology to achieve its potential to benefit the poor. Scientists, regulators, and politicians must find more rational and efficient ways to guarantee public health and environmental safety while encouraging new discoveries. Science shows the path, and society's leaders – secular and religious – must take us there.

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The costly benefits of opposing agricultural biotechnology

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Rigorous application of a simple definition of what constitutes opposition to agricultural biotechnology readily encompasses a wide array of key players in national and international systems of food production, distribution and governance. Even though the sum of political and financial benefits of opposing agricultural biotechnology appears vastly to outweigh the benefits which accrue to providers of agricultural biotechnology, technology providers actually benefit from this opposition. If these barriers to biotechnology were removed, subsistence farmers still would not represent a lucrative market for improved seed. The sum of all interests involved ensures that subsistence farmers are systematically denied access to agricultural biotechnology.

Contents

Definitions

For purposes of this discussion, the phrase, 'opponent of agricultural biotechnology' is defined as any individual, group or organization that uses financial or political power to advocate, impose or assist in imposing, severe restrictions or bans on genetically

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modified (GM, transgenic, modified, engineered, biotech) crops or foods made from them. In this context, the term, 'severe' is defined as impeding or preventing the use of GM crops 'for food security in the context of development.'

This definition readily encompasses a large number of opponents of agricultural biotechnology – much larger than many have thought to identify, in economic sectors few would normally suspect. This discussion involves the most influential opponents, but by no means all of them.

Opponents of agricultural biotechnology

Aside from various ill-informed consumers and fringe elements in the pseudo-scientific community, it is difficult to find persons or organizations who oppose agricultural biotechnology *per se* [1,2]. However, there are substantial political or financial advantages which can be protected or gained by opposing this technology.

Chemical companies

Among the companies hardest hit by the biotech products currently on the market are chemical companies. Crops designed to resist attacks by hungry insects have dramatically reduced sales, and income, for producers of chemical insecticides. Crops designed to tolerate herbicides, such as glyphosate or glufosinate, have had a similar impact on producers of competing herbicides. In India, for instance, the introduction of insect-resistant cotton has been catastrophic for makers of chemical sprays, reducing sales by up to 70% in some regions [3]. India's chemical companies support opposition to GM cotton, and chemical companies there and elsewhere lobby government to restrict biotech crops [4–6].

Such a situation is far more likely to emerge in developing nations. In the USA, and in other developed nations where numerous biotech crops are legal, the producers of biotech seeds are also producers of chemical crop protection products. This allows the corporations to offset a decrease in chemical sales with an increase in seed sales. In developing nations, there is no such offset. Their chemical companies have no biotech seed technology, and therefore face financial ruin with the adoption of biotech crops.

Food companies

Food companies have substantial financial interests in opposing agricultural biotechnology, and support its opposition both in cash, and in kind. In 2006, the world's seven largest food advertisers spent nearly US$8 billion on advertising [7]. This represents a tremendous outreach effort, by the wealthiest food retailers, to the wealthiest consumers. In some countries, this outreach regularly includes advertising claims that certain food items are 'GM-free'.

Supermarkets

Such advertising behavior is exemplified by the major supermarkets in Britain, which shortly after the introduction of GM crops sought commercial advantage by advertising that their store-branded products contained no GM ingredients. The resulting competition led to a situation where all major British supermarket chains were advertising in 1999 their premium brands as GM-free [8]. In 2008, the eight largest British supermarket chains spent a total of 349 million pounds on advertising [9]. Advertising claims of 'GM-free' food necessarily communicate or reinforce anti-biotechnology sentiment.

Organic food industry

Producers and retailers of organic food advertise to the public that their foods are not genetically modified. However, they spend almost no money on advertising [10]. That is because most of their advertising is done by others. Direct advertising by producers and retailers of organic food has consistently been found false or misleading by advertising authorities, so non-governmental organizations (NGOs) make false and misleading claims on their behalf [11,12,35–38].

In 2007, the world market for organic food was estimated at US$40 billion, with over 90% of that market concentrated in the European Union (EU) and the USA [13]. Demand for organic food in these economies has outpaced supply, leading to shortages so acute that much or most organic food in wealthy markets is now produced for them in developing nations [14,15].

Paradoxically, this means that the poor in developing nations are themselves often too poor to be able to buy the organic crops they produce for Europeans and Americans [16]. Because organic standards prohibit the use of most modern agricultural technologies, including engineered seed, this is nothing more than paying farmers in the developing countries to not develop. Indeed, many of them are organic 'by default', that is, they practice organic farming methods because they cannot afford anything else [17].

This paradox has a wider impact. The organic food industry has by far the greatest financial interest in opposing agricultural biotechnology (Table 1). This makes the organic food industry, which has captured elements in nearly all financial and political interests opposed to modern biotechnology, the world's most profitable oppressor of agricultural development in developing nations.

Supply-chain services

Companies which provide services to those in commodities and food distribution benefit substantially from opposition to agricultural biotechnology.

GM testing

The more stringent and widespread the regulations of GM content in food and feed become, the more revenue is diverted to companies which offer tests to detect the presence of GM content. A wide variety of tests is available, with costs ranging from US$6 to US$600 per test [18,19]. Though expensive, these tests are fairly cheap in comparison to the global industry that emerged simply from the ability to test. In the US, which is comparatively friendly to GM crops and foods, the value of the GMO testing market was estimated at US$106 million in 2007 and forecast to reach US$193 million by 2012 [20]. In India, a developing country where the controversy over GM crops has reached epic proportions, the value of the GM testing market is estimated to be twice as large [21].

Segregation/traceability

The ability to test for GM content enables segregation and traceability of commodities, facilitating middlemen in the commodities pipeline who charge a premium for non-GM commodity grains and oilseeds.

The EU is the world's largest importer of soybean meal, and the second largest importer of soybeans. In 2008, premiums for non-GM soy were in the range of 60–80 € per metric ton [22]. With estimated EU demand for non-GM soy of 33 million metric tons in

2008, this yields an annual outlay of roughly 2.3 billion € in premiums for non-GM soy ([23], Table 1).

Equally salient are recent major purchases by Japanese trading firms of North American storage and shipping facilities, and contracts with North American farmers, for the production and distribution of non-GM maize and soybeans [24,25]. Such investments are not justified without the prospect of extraordinary profits, and represent the commitment of vested interests in maintaining public fears and regulatory restrictions directed at modified crops.

Politicians

Politicians have a great deal to gain from opposing agricultural biotechnology. Trade protectionism draws the support of domestic financial interests, while appeasement of NGOs gives politicians access to skilled media professionals. This works out differently in developed and developing countries.

Developed countries

In developed countries, notably those of Western Europe, bans and restrictions on the import and use of modified grains and oilseeds act as a trade protectionist price support for growers of grains and oilseeds, even after taking into consideration the productivity which would be gained if farmers were allowed to grow them [26,27]. It need not be explained how conferring commercial advantages on domestic interests translate into political support.

Restrictions on biotechnology also appeal to NGOs and to voters who find NGOs credible or persuasive. Politicians seeking restrictions on GM crops can look forward to political support from many quarters, which can even include NGO advertising on behalf of political candidates, or monetary contributions by NGOs to campaign finances [28–30].

Developing countries

The most prominent features of a developing country are a chronic shortage of food, and widespread poverty. Those in developing countries with food and money naturally wield political power, and in spite of food shortages, political leaders remain concerned with protecting export markets. These export markets supply the power elite with money in stable foreign currencies, an arrangement which they believe would be imperiled by the domestic adoption of genetically modified crops [31,32]. To protect their wealth and positions of power, these leaders have every incentive to oppose these crops – even to the point of calling them 'poisonous' [33,38].

Taking part in this dynamic requires that leaders in developing countries appease NGOs funded by developed nations. These organizations continually seek opportunities to disrupt export markets wherever genetically modified content can be detected, which could easily be considered to be a form of extortion [34]. NGOs also work to support decisions by corrupt leaders to deny farmers the use of modern biotechnology, by spreading lies among citizens. The lies include claims that modified crops cause homosexuality, impotence, illnesses like HIV/AIDS, baldness, allergies, liver and kidney toxicity, immune disorders, retarded growth, infertility and other things [35–38].

NGOs and the protest industry

The organizations which appear to be most bitterly opposed to agricultural biotechnology are known, sometimes ironically, as NGOs. These tax-exempt, but nonetheless profitable organizations are quite adept at portraying themselves as representing 'civil society', and the claim, to some extent, is true. In the case of agricultural biotechnology, these organizations derive much of their political influence by claiming to represent the concerns of consumers, farmers and others. However, these concerns are largely creations of the NGOs themselves [35–38]. At the same time, NGO efforts directly support commercial and political interests that rely on anti-biotech sentiment, often quite overtly. As a result of overlapping interests with politics and commerce, and the professional talent their lavish funding is able to attract, the operations of these organizations are coming closely to resemble private enterprise [39].

The sums of money diverted to these organizations are substantial and in Europe consist heavily of public funds. Perhaps the greatest beneficiary in this category is the Friends of the Earth (FOE). In 2006 alone, the FOE, directly and through member/affiliate/partner groups, was earmarked to receive roughly 790 million € from European governments. These governments appear to provide nearly all of its annual income [40]. Members of the European Parliament have called this diversion of public funds 'grotesque' and 'anti-democratic', and said that it amounts to government 'paying to have itself lobbied to take actions which, in the main, it would wish to take anyway' [41,42]. Even so, the sums diverted to the FOE are commensurate with the magnitude of the financial and political interests which benefit from its advocacy, and the influence of the FOE is not restricted to Europe. The organization now claims to be 'the world's largest grassroots environmental network, uniting 77 national member groups and some 5,000 local activist groups on every continent' [43]. The vast majority of the FOE's affiliate groups are found outside the EU, which means that Member States of the EU are paying the FOE to advertise the anti-biotech message around the world.

While the European Commission provides a good deal of money to the FOE, its main source of funding appears to be the Dutch government. The Netherlands is home to many of the world's largest agricultural kombinates, making this tiny country one of the world's three largest exporters of agricultural products [44]. This ensures that kombinates based in the Netherlands have some of the world's most significant interests in the regulation, testing, segregation and labeling of commodities and foods. At the same time, this helps to ensure political and economic support for Dutch agriculture, which is not well-equipped to compete with streamlined, low-cost, high-volume producers of agricultural products [45]. Such producers are invariably producers of modified crops.

European governments appear largely unaware of the extent to which they subsidize the FOE, and it is probably that there are similar problems with similar organizations. For instance, the European Commission says it paid nearly 520,000 € to the international headquarters of the FOE in 2006, an amount which the EC believed to be about 40% of the FOE's income. However, the FOE claims income of nearly five times that amount during the same period [46,47]. By way of comparison, European public funds earmarked for the FOE and its affiliates in 2006 are, at current rates of exchange, roughly equivalent to the regulatory compliance costs of 72 new biotech crops [40,55].

The vast sums paid to the FOE by European governments represent only a part of what is often called the 'international protest industry'. NGOs around the world are funded by governments,

foundations, corporations and individual donations. Since opposition to agricultural biotechnology can be rooted in nearly any political or economic motive, it is impossible to precisely determine the allocation of protest funds. In the US, sums paid annually to US NGOs with an anti-biotechnology campaign element are in the range of US$600 million [48–50]. The assets which generate these sums are substantial. For instance, the US-based Council on Foundations boasts an international membership of more than 2100 grantmaking foundations and corporations, whose assets total more than US$282 billion [51]. If the amounts they dedicate to environmentalism alone bear any resemblance to the spending habits of Greenpeace International, assets directed at opposing biotechnology in agriculture will account for roughly 16% of the total, or US$17 billion [52].

Multinational biotechnology corporations

With such a vast array of well-funded, influential groups, organizations, political interests and business enterprises engaged in restricting or preventing the use of biotechnology in food production, the position of the developers of biotechnology would appear hopeless. However, after a dozen years of commercialization, biotech crops now account for 125 million ha, or 309 million acres, worldwide. They are grown by 13.3 million farmers in 25 countries [53]. In 2007, the global market value of biotech seed was estimated at roughly 20% of the US$34 billion global commercial seed market [54].

The cost of gaining regulatory permission to commercialize a GM crop is in the range of US$6 million and US$15 million, although there exist higher estimates [55,56]. The costs of regulatory compliance are so high that, with few exceptions, they can be borne by only a select few multinational corporations – perhaps as few as five: BASF, Dow AgroSciences, Monsanto, Pioneer Hi-Bred (DuPont) and Syngenta [57]. It is widely claimed that the consolidation of the seed industry via the control of biotechnology by a select few corporations is because of 'patents on life'. However, patents are granted for GM and non-GM seeds alike, and all patents expire after a set number of years [58,59]. Rather, it is the regulatory costs imposed on biotechnology which limits the use of that technology. Since the costs of compliance will remain for as long as the regulations persist, this amounts to a perpetual patent in favor of the largest multinational corporations, not on individual inventions or discoveries, but upon an entire branch of crop development [60]. The net result is oligopolistic control of the technology and of the market for GM seed.

TABLE 1

Comparison of financial interests in restricting agricultural biotechnology

Organic industry sales, international	40,000
Sales of GM seeds, international	6800
Premiums paid for non-GM soy, EU	3409
Payments to Friends of the Earth (FOE) and affiliates, EU	1171
Payments to US groups opposed to GM	600
Supermarket advertising (eight largest supermarkets in UK)	575
Testing for GM content, US and India (excludes EU market)	318

Figures are annual, US$ millions.

Costs of opposing biotechnology in agriculture

The costs of opposing biotechnology are in the form of foregone benefits. For instance, if biotech traits currently on the market were incorporated into rice varieties and cultivated in India, Bangladesh, Indonesia and the Philippines, this would generate economic benefits of US$4.3 billion [61]. Annually, hundreds of thousands go blind or die as a result of vitamin A deficiency (VAD). As of November 2009, those who have died from VAD since the availability of Golden Rice total over 17 million, and those who have gone blind from VAD total nearly 4 million [62]. Where rice is the staple food, much of this enormous toll is directly attributable to regulatory restrictions on Golden Rice, which are imposed solely because the rice was developed using modern biotechnology.

Even so, the costs of opposing biotechnology in agriculture are not 'actual' costs, but merely, foregone benefits. Foregone benefits, also known as 'opportunity costs', do not reduce existing wealth. Such costs are merely profits which might have been [63]. Even the blind and dead do not count as actual costs, *per se*, as their destinies are merely part of the *status quo* of poverty and malnutrition.

Conclusion

The key players encompassed by the definition of 'opponent' of engineered crops reap billions annually from restricting agricultural biotechnology or the food that results. Indeed, more money can be made from restricting agricultural biotechnology than by delivering it. This dynamic ensures that access to the most recent advances in the technology of crop and food production is restricted to farmers in progressive nations with strong political and financial interests in agriculture. Those who most need access to this technology are those who have the least political and financial power, that is, subsistence farmers in the developing world.

In fact, it appears that the greatest money to be made by restricting access to agricultural biotechnology is made by intentionally keeping it out of the hands of those who need it the most – that is, by the organic industry. By linking political and financial interests in environmentalism, GMO testing, segregation and traceability, international trade and threatened disruptions, premiums for functionally identical goods, retailing, advertising, popular media and government subsidies for NGOs, the organic industry is able to monetize restrictions on agricultural biotechnology at nearly every point in the political/financial chain of interests.

The multinational seed developers capitalize on these interests as well, because restrictions on biotechnology prevent competition from smaller entities. In the context of development, however, this is not a meaningful barrier. If regulatory compliance costs were zero, subsistence farmers would still not represent a lucrative seed market. Indeed, the food production methods dictated by the poverty of farmers in developing nations make them an ideal source of organic food for European and North American retailers. Accordingly, the organic industry can monetize these farmers' poverty in a way that seed developers cannot.

There are no significant financial or political incentives to change this situation to the advantage of subsistence farmers in developing nations. If there were, this situation would not exist. It remains merely to consider the moral and ethical dimensions of this situation, which, upon serious examination, might prompt spontaneous changes based on more fundamental humanitarian concerns.

The case of Bt brinjals

On February 9, 2010, India's environment minister declared a moratorium on the cultivation of GM brinjals (eggplant, aubergine) [65]. The brinjals were engineered to withstand attack by the fruit and shoot borer, a destructive insect which inflicts 'opportunity costs' in the form of brinjal crop losses as high as 70%, even with chemical sprays. Without such sprays, the opportunity cost nears 100% [63,66]. Brinjals are grown on nearly 600,000 ha in India.
The cost of crop protection per hectare of brinjals is about US$400 [66]. This means that Bt brinjals directly threaten roughly US$240 million in revenues for India's crop protection industry. India's crop protection market differs from most. Globally, because of consolidation in the industry, five multinational corporations control almost 78% of the market. In India, the industry is very fragmented, with about 30–40 large manufacturers and about 400 formulators [67].
Currently, India's crop protection industry is experiencing a financial crisis. The causes given for this are rising costs of inputs, governmental duties and taxes and the cost of capital [68]. A good part of that crisis is probably the approval in India of Bt cotton. India's crop protection industry lobbied to prevent the approval of Bt cotton [4–6]. Were it not for the widespread illegal cultivation of Bt cotton that presented the government with a *fait accompli*, it would probably not have been legalized [69]. In the aftermath of its introduction, India's crop protection industry was devastated, with revenue losses of up to 70% in some regions [3].
Such an object lesson would necessarily lend urgency to the motives of chemical companies and formulators facing the loss of yet another lucrative market. With US$240 million at stake over the issue, the average company in that sector would see annual revenues decline by roughly US$540,000. With far greater combined political and financial resources than vegetable farmers, and the backing of NGOs (many of which are backed by Europe), and of producers of conventional seed, exporters and organic food interests, these companies and organizations were nearly destined to achieve the success with Bt brinjals that eluded them with Bt cotton [70].

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Challenges and responsibilities for public sector scientists

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Current agriculture faces the challenge of doubling food production to meet the food needs of a population expected to reach 9 billion by mid-century whilst maintaining soil and water quality and conserving biodiversity. These challenges are more overwhelming for the rural poor, who are the custodians of environmental resources and at the same time particularly vulnerable to environmental degradation. Solutions have to come from concerted actions by different segments of society in which public sector science plays a fundamental role. Public sector scientists are at the root of all the present generation of GM crop traits under cultivation and more will come with the new knowledge that is being generated by systems biology. To speed up innovation, molecular biologists must interact with scientists from the different fields as well as with stakeholders outside the academic world in order to create an environment capable of capturing value from public sector knowledge. I highlight here the measures that have to be taken urgently to guarantee that science and technology can tackle the problems of subsistence farmers.

Contents

The challenges

Public research institutions have always been engaged in innovations and developments aimed at ameliorating human living conditions. In the field of agriculture, thanks to the dedicated plant breeding scientists, the Green Revolution could make use of improved crop varieties that allowed food production to keep pace with worldwide population growth. The success of Norman Borlaug and the CIMMYT team in producing wheat and, later, rice high yield varieties, together with innovative cultivation methods, increased the grain yield at levels that led to the notion that the world hunger could be solved. This was true in the short run, however the on-going population growth and the eagerly anticipated industrialisation of developing countries have to be taken into account in the long run. These factors besides being energy and water demanding also compete for land and will ultimately exert pressure on global food production.

The media have always considered it *bon ton* to make anecdotal criticism of Malthus. We often read in the news about the arrogant intellectuals who keep quoting Malthus whilst the man has been wrong for more than 200 years. Indeed, while the world population tripled during the 50 years after the second World War, agricultural production increased by a factor of 3.5. But the scenario has now changed. The yield increase through classical breeding programs has reached a plateau and food production has

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to take into account the global pollution, a concept not considered in Malthus's time. We now realize that, unfortunately, Malthus's prediction of risks finally materialises. Current agriculture faces the challenge of doubling food production to meet the food needs of a population expected to reach 9 billion by mid-century whilst maintaining soil and water quality and conserving biodiversity. The task becomes particularly tough when it has to be accomplished with limited land. It is estimated that by the time the world's population passes the threshold of 8 billion people, there will only be 1.4 ha of arable land per capita [1].

These challenges are more overwhelming for the rural poor, who make up an estimated 80% of the world's 1.4 billon hungry people [2]. No segment of humanity depends more directly on environmental resources and services than the rural poor. They use soil and water for farming and fishing, forests for food, fuel and fodder, and the biodiversity of a wide range of plants and animals, both domesticated and wild. Their lives are interwoven with the surrounding environment in ways that make them both particularly valuable as custodians of environmental resources and particularly vulnerable to environmental degradation. When population pressure grows and food is scarce, hunger can drive them to plough under or overgraze fragile rangelands and forest margins, threatening the very resources upon which they depend.

The solutions

Solutions have to come from concerted actions of different segments of society. It will require political will and strong commitments on the part of the nations as it will lead to a full revision of the way we perceive our society and our interaction with the environment. In this context, science and technology alone obviously does not have the power to overcome the challenges, but it is a very relevant and essential instrument of the orchestra. The range of science and technology opportunities now available can mitigate the greater constraints imposed on poor farmers. As international organisations have stated repeatedly, there is a *moral imperative* that technologies that are pro-poor, pro-environment and pro-economy find their way to those who need them the most.

Plant biotechnology has produced numerous breakthroughs that can contribute significantly to alleviating many of the entrenched problems of poor nations, including hunger, malnutrition, diseases and environmental degradation (for review see Farre *et al.*) [3]. Public sector scientists are at the root of most innovations and practical achievements. Indeed all of the present generation of GM crop traits under cultivation can be traced back to discoveries in the public sector. The recent developments in systems biology are generating an explosion of information that public sector scientists are translating into new knowledge (see Figure 1). The next step, the generation of new products out of the knowledge gained, is beyond the scope of public research institutions. In general, the private sector takes charge of the knowledge application. Here stands the gap. Notwithstanding the scientific breakthroughs, the rate of development and commercialisation of new biotech crops is frustrating the expectation.

The responsibilities

Several factors have contributed to the knowledge application gap. One is the fact that the discoveries have not reached the group with expertise to generate innovation. There is a need for better

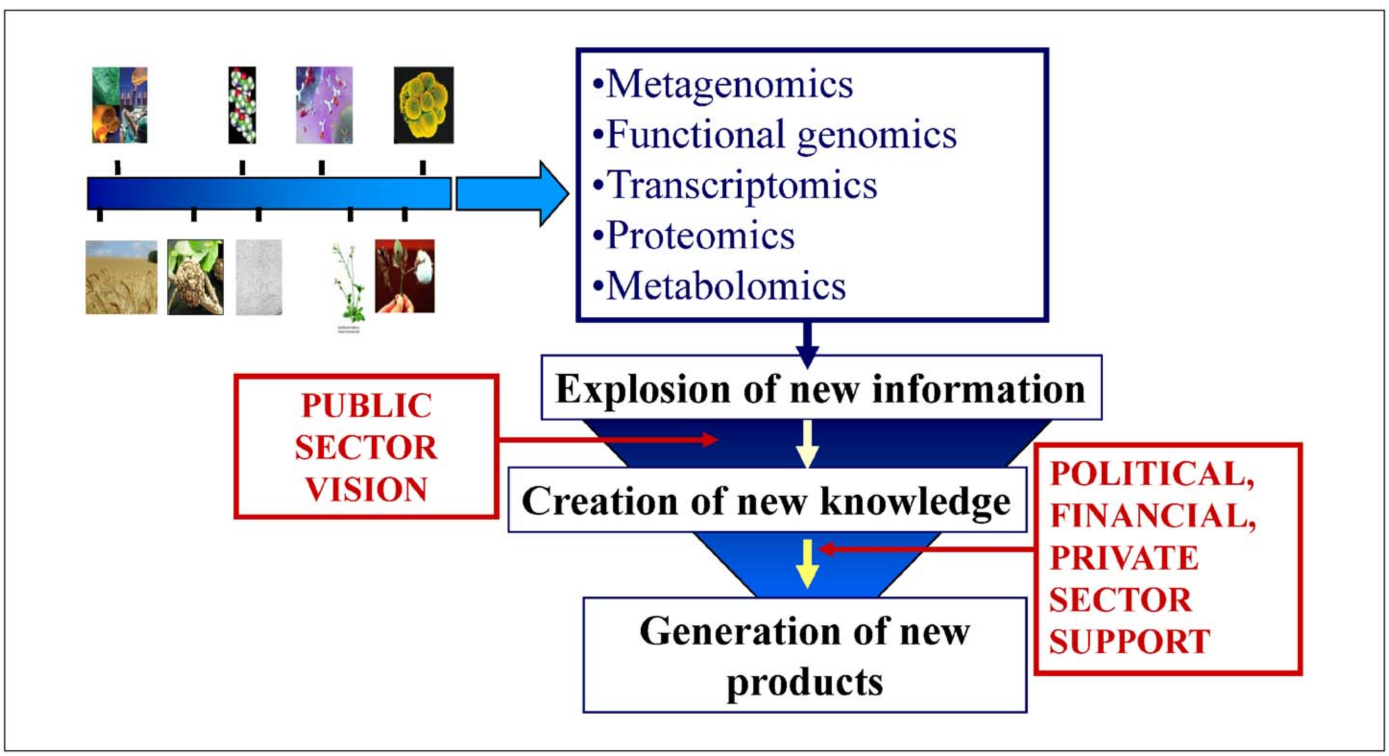

FIGURE 1

The innovation gap. Systems biology is generating an explosion of basic information from which scientists must derive tangible knowledge for the development of new products and services. A critical set of factors – political, financial and private sector support – will determine the rate at which this new knowledge will tackle the problems of subsistence farmers. Dialogue between the different players must be initiated now.

communication of the knowledge generated by the fundamental research. The communication channels of molecular biologists cannot be restricted any longer to specialised journals often enigmatic to those who do not belong to the clan. A better sharing of the knowledge and the generation of demand-driven technologies will require changes in the organisational structure of universities and public research institutions. To speed up innovation, molecular biologists must interact with scientists from the different departments that are tackling the same goal, for example departments of agronomy, forestry, tropical agriculture, agricultural economy, ecology, and nutrition. They also have to reach stakeholders outside the academic world, such as curators of seed banks, seed companies and small to medium size enterprises (SMEs). The latter are fundamental players, since they traditionally fill the application gap. Public research institutions have to be immersed into an environment fertile to generate spin-offs. This has been the strategy of the US and Europe and the results are clear. The investments in R&D accounted for 50% of the US economy growth in the last 40 years [4]. Similarly, in Europe, the experience of Flandres shows that when federal investments in universities' R&D increase, there is a corresponding increase in private sector investments, with the flourishing of SMEs in biotechnology.

Agricultural R&D in developing countries also requires the implementation of new organisational structures to promote the public–private partnership and the emergence of SMEs. Such environment is essential for capturing value from public sector knowledge and should be encouraged through policy measures that stimulate investments. Unfortunately the recent surveys [5] show that the trend is going in the opposite direction. The investments in agricultural research have stagnated over time despite the numerous studies showing that improvements in productivity are linked to increased investment in agricultural R&D. The consequences are clear and are already there. A recent review of the world's commercial pipeline of GM crops reveals that the contribution of Latin America and Africa to current and future GM events by 2015 is insignificant. The big actor in emerging countries is China, which will contribute with about 40% of the GM events that will be commercially available by 2015 [6]. Unsurprisingly, the Chinese government is stimulating public–private partnership and the emergence of a SME and start-up culture.

Another important issue must be highlighted. Society must understand that business is as usual everywhere. Commercial interests drive investments of the private sector in R&D both in developed and developing countries. Neglected pro-poor traits and orphan crops will remain as such if the returns of investments are not attractive. It is clear that, in this scenario, large private multinationals opt out. Private companies do not have it as their mission to accomplish the Millennium goals. But I do believe that SMEs in developing countries would invest in pro-poor GM crops because the returns can reach their expectations, provided that they can start with a rather finished product, ready to scale up. In view of the dimension of our challenge to overcome poverty, one may well say that what the private sector cannot do has to be the task of the public sector. Unfortunately this is not going to be so for now. The public sector has underinvested in R&D for smallholder crops and in biotechnology specifically. Public spending on R&D on transgenics is only a fraction of the US$ 1.5 billion spent each year by the four largest private companies [7]. The arguments are that it is not worthwhile to do research on pro-poor plant biotechnology, because the costly and unnecessary overregulation will anyway block the access to those who need it most. Society is then trapped into the loop reasoning that the technology is not worthwhile because the rich countries do not need it and it is not yet proven that it can have any humanitarian impact.

The importance of research developments to tackle the problems of subsistence farmers is acknowledged by governments and international organisations. It is now urgent to take measures to guarantee the accomplishment of this fundamental humanitarian task. I see the need for the following actions. (i) To increase funding for public sector programmes targeted to solve major constraints of poor farmers in trying to provide a sustainable, sufficient and safe supply of foods. They are many: higher productivity, enhanced nutrition, disease and insect resistance, drought tolerance, increased fertilizer use efficiency, and so on (ii) To promote and fund international cooperation to allow the knowledge transfer to developing countries scientists to develop of locally relevant crop improvement programmes. (iii) To support breeding programmes and quality seeds production in developing countries where a strong seed industry is inexistent and where the public sector is the major player. (iv) To develop mechanisms to empower developing country scientists so that they can participate in – and contribute to – the emerging global knowledge-based bio-economy. And last but not least, (v) to promote regulatory frameworks that are science-based, avoiding a costly overregulation that will halt pro-poor GM crops.

Indeed, the cumbersome and costly regulatory infrastructures constitute a major obstacle that adds to the chronic underinvestment in science and technology. Many public sector scientists cannot afford the regulatory compliance costs, which ranges from tens of thousands to millions of dollars [8]. The public sector scientists must be more actively involved in on-going biosafety regulation negotiations if we are to breach the present impasse that prevents many of the most promising pro-poor technologies reaching the farmers. Until recently, the public research sector has not provided scientific input in these negotiations, with the result that there is a misperception that biotechnology is only the domain of a handful of multinationals.

Critics of plant biotechnology have mounted a campaign of misinformation that warns that GM crops are the monopoly of the multinationals and will enslave the third world even more. The detractors go on saying that GM crops will lead to a loss of biodiversity and they have not been sufficiently tested. This is not the case. Despite the claims, no adverse effects of GM crops have been reported for consumer health or the environment; on the contrary, a number of health and environmental benefits have been reported. Sadly, the result of the present 'anti-GM' environment is that, currently, GM crops are one of the most over-regulated technology sectors in existence. Only the multinationals can afford to pay the costs associated with regulatory filings and bring new biotech products to market. No SME or third world country can develop and market such technology. Whilst decision making continues to ignore a science-based rationale, threats to food security and health problems will remain in the developing world, and the brain drain will continue in parts of the industrialised world. The public sector needs an improved understanding of the impact of the emerging regulatory framework on the

delivery of the public goods R&D agenda, it needs a better understanding of the consequences of the regulations on the total costs of research projects and needs to rethink research project definitions and funding criteria accordingly. Until then, regulatory policy that is poorly structured and implemented will continue to have a disastrous impact in Europe and all countries seeking to trade with Europe.

The public sector has taken steps to fight for the establishment of a regulatory framework less counterproductive in different countries. National regulations are strongly influenced by international agreements, such as the Cartagena Protocol on Biosafety (CPB). During the development of these international agreements, the public research sector, which numbers tens of thousands of researchers in several thousand research institutes in developing and developed countries, has until 2004 not been represented in an organised way. Aiming at filling this gap, public sector scientists involved in biotechnology research for the public good initiated, in 2004, a worldwide initiative – the Public Research and Regulation Initiative (PRRI) [9]. The objective of the PRRI is to offer public researchers involved in modern biotechnology a forum through which they participate in and/or are informed about relevant international discussions such as the Meetings of the Parties of the CPB (MOPs). The goal of participation in such meetings is to inform negotiators about the objectives and progress of public research in modern biotechnology, to bring science to the negotiations, and to inform the negotiators about concerns public researchers may have.

Another mechanism public sector scientists must use to reduce the unnecessary regulatory burden that halts the innovation chain is to engage in the dialogue with society. Regulatory policy is a political issue and as such sensitive to public opinion. Public sector scientists have to create channels to share with the different stakeholders the facts and information, as well as to discuss the concerns, potential and opportunities related to this new technology. We must convey this important message to society: agriculture, be it classical or organic, is very detrimental to the environment and biodiversity. GM agriculture is our biggest opportunity of having a less environmentally damaging agriculture and still meet the food needs of an ever-growing population. Actually biotechnology brings us as close as possible to the ideal agriculture system: a high yielding organic agriculture. Only through cooperation and mutual understanding will it be possible to capture and develop the true potential of this exciting technology to create a more livable and environmentally stable society.

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PAS Study Week, Vatican City, 15-19 May 2009

Transgenic Plants for Food Security in the Context of Development

A Study Week on the subject of 'Transgenic Plants for Food Security in the Context of Development' was held under the sponsorship of the Pontifical Academy of Sciences at its headquarters in the Casina Pio IV in the Vatican from 15 to 19 May 2009. During the course of the meeting, we surveyed recent advances in the scientific understanding of novel varieties of genetically engineered (GE) plants, as well as the social conditions under which GE technology could be made available for the improvement of agriculture in general and for the benefit of the poor and vulnerable in particular. The spirit of the participants was inspired by the same approach to technology that Benedict XVI expressed in his new Encyclical, in particular that 'Technology is the objective side of human action (1) whose origin and *raison d'être* is found in the subjective element: the worker himself. For this reason, technology is never merely technology. It reveals man and his aspirations towards development, it expresses the inner tension that impels him gradually to overcome material limitations. *Technology, in this sense, is a response to God's command to till and to keep the land* (cf. Gen 2:15) that he has entrusted to humanity, and it must serve to reinforce the covenant between human beings and the environment, a covenant that should mirror God's creative love'. (2)

Main Scientific Conclusions

We reaffirm the principal conclusions of the Study-Document on the Use of '"Genetically Modified Food Plants" to Combat Hunger in the World', issued at the end of the Jubilee Plenary Session on 'Science and the Future of Mankind', 10-13 November 2000. Summarised and updated, these include:

1. More than 1 billion of the world population of 6.8 billion people are currently undernourished, a condition that urgently requires the development of new agricultural systems and technologies.
2. The expected addition of 2-2.5 billion people to reach a total of approximately 9 billion people by 2050 adds urgency to this problem.

3. The predicted consequences of climate change and associated decreases in the availability of water for agriculture will also affect our ability to feed the increased world population.

4. Agriculture as currently practised is unsustainable, evidenced by the massive loss of topsoil and unacceptably high applications of pesticides throughout most of the world.

5. The appropriate application of GE and other modern molecular techniques in agriculture is contributing toward addressing some of these challenges.

6. There is nothing intrinsic about the use of GE technologies for crop improvement that would cause the plants themselves or the resulting food products to be unsafe.

7. The scientific community should be responsible for research and development (R&D) leading to advances in agricultural productivity, and should also endeavour to see that the benefits associated with such advances accrue to the benefit of the poor as well as to those in developed countries who currently enjoy relatively high standards of living.

8. Special efforts should be made to provide poor farmers in the developing world with access to improved GE crop varieties adapted to their local conditions.

9. Research to develop such improved crops should pay particular attention to local needs and crop varieties and to the capacity of each country to adapt its traditions, social heritage and administrative practices to achieve the successful introduction of GE crops.

Further Evidence

Since the preparation of that earlier study document, evidence that has been subjected to high standards of peer-reviewed scientific scrutiny, as well as a vast amount of real-world experience, has accumulated about the development, application and effects of GE technology. During our study-week we reviewed this evidence and arrived at the following conclusions:

1. GE technology, used appropriately and responsibly, can in many circumstances make essential contributions to agricultural productivity by crop improvement, including enhancing crop yields and nutritional quality, and increasing resistance to pests, as well as improving tolerance to drought and other forms of environmental stress. These improvements are needed around the world to help improve the sustainability and productivity of agriculture.

2. The genetic improvement of crop and ornamental plants represents a long and seamless continuum of progressively more precise and predictable techniques. As the U.S. National Research Council concluded in a 1989 report: ‘As the molecular methods are more specific, users of these methods will be more certain about the traits they introduce into the plants and hence less liable to produce untoward effects than other methods of plant breeding’.

There are many different terms used to describe the processes involved in plant breeding. All living organisms are made up of cells in which are contained their genes, which give them their distinctive characteristics. The complete set of genes (the genotype) is encoded in DNA and is referred to as the genome; it is the hereditary information that is passed from parent to offspring. All plant breeding, and indeed all evolution, involves genetic change or modification followed by selection for beneficial characteristics from among the offspring. Most alterations to a plant's phenotype or observable traits (such as its physical structure, development, biochemical and nutritional properties) result from changes to its genotype. Plant breeding traditionally used the random reshuffling of genes among closely-related and sexually compatible species, often with unpredictable consequences and always with the details of the genetic changes unexplored. In the mid-twentieth century this was supplemented by mutagenesis breeding, the equally random treatment of seeds or whole plants with mutagenic chemicals or high-energy radiation in the hope of generating phenotypic improvements; this, too, gave rise to unpredictable and unexplored genetic consequences from which the plant breeder selected the beneficial traits. Most recently, techniques have been developed allowing the transfer of specific, identified and well characterised genes, or small blocks of genes that confer particular traits, accompanied by a precise analysis of the genetic and phenotypic outcomes: this last category is called 'transgenesis' (because genes are transferred from a donor to a recipient) or 'genetic engineering' (abbreviated to GE in this report) but, in truth, this term applies to all breeding procedures.

3. The benefits have already been of major significance in countries such as the U.S., Argentina, India, China and Brazil, where GE crops are widely grown.

4. They also can be of major significance for resource-poor farmers and vulnerable members of poor farming communities, especially women and children. Insect-resistant GE cotton and maize, in particular, have greatly reduced insecticide use (and hence enhanced farm safety) and contributed to substantially higher yields, higher household income and lower poverty rates (and also fewer poisonings with chemical pesticides) in specific small-farm sectors of several developing countries, including India, China, South Africa and the Philippines.

5. The introduction of resistance to environmentally benign, inexpensive herbicides in maize, soybean, canola, and other crops is the most widely used GE trait. It has increased yields per hectare, replaced back-breaking manual weeding and has facilitated lower input resulting in minimum tillage (no till) techniques that have lowered the rate of soil erosion. This technology could be especially useful to farmers in the developing world who, for reasons of age or disease, cannot engage in traditional manual weed control.

6. GE technology can combat nutritional deficiencies through modification that provides essential micro-nutrients. For example, studies of provitamin A-biofortified 'Golden Rice' have shown that standard daily diets containing this biofortified rice would be sufficient to prevent vitamin A deficiency.

7. The application of GE technology to insect resistance has led to a reduction in the use of chemical insecticides, lowering the cost of some agricultural inputs and improving the health of agricultural workers. This relationship is particularly important in areas such as many European nations, where applications of insecticides are much higher than in most other regions, which may damage ecosystems generally as well as human health.

8. GE technology can reduce harmful, energy consuming, mechanical tilling practices, enhancing biodiversity and protecting the environment, in part by reducing the release of CO_2, the most important anthropogenic greenhouse gas, into the environment.

9. The predicted impact of climate change reinforces the need to use GE coupled with other breeding techniques appropriately and purposively, so that traits such as drought resistance and flooding tolerance are incorporated into the major food crops of all regions as quickly as possible.

10. GE technology has already raised crop yields of poor farmers and there is evidence of its generating increased income and employment that would not otherwise have taken place.

11. Costly regulatory oversight of GE technology needs to become scientifically defensible and risk-based. This means that regulation should be based upon the particular traits of a new plant variety rather than the technological means used to produce it.

12. Risk assessments must consider not only the potential risks of the use of a new plant variety, but also the risks of alternatives if that particular variety is not made available.

13. Significant public-sector efforts are currently underway to produce genetically improved varieties or lines of cassava, sweet potatoes, rice, maize, bananas, sorghum, and other major tropical crops that will be of direct benefit to the poor. These efforts should be strongly encouraged.

14. The magnitude of the challenges facing the world's poor and undernourished must be addressed as a matter of urgency. Every year nutritional deficiencies cause preventable illness and death. The recent rise in food prices throughout the world has revealed the vulnerability of the poor to competition for resources. In this context, forgone benefits are lost forever.

15. Given these scientific findings, there is a moral imperative to make the benefits of GE technology available on a larger scale to poor and vulnerable populations who want them and on terms that will enable them to raise their standards of living, improve their health and protect their environments.

In general, the application of GE technology has demonstrated its importance for improving agricultural productivity throughout the world, but it is still only one part of what must be a multifaceted strategy. As the Holy Father Benedict XVI has observed: 'it could be useful to consider the new possibilities that are opening up through proper use of traditional as well as innovative farming techniques, always assuming that these have been judged, after sufficient testing, to be appropriate, respectful of the environment and attentive to the needs of the most deprived peoples'. (3) Nevertheless, we recognise that not all developments of GE technology will realise their original promise, as happens with any technology. We must continue to evaluate the potential contribution of all appropriate technologies, which together with conventional plant breeding and additional strategies must be used to improve food security and alleviate poverty for future generations. (4) Many of them can be used synergistically with GE technologies. Strategies include the retention of topsoil through no-till and other conservation practices, the appropriate application of fertilizers, the development of new kinds of fertilizers and environmentally friendly

agrochemicals, water conservation, integrated pest management, conservation of genetic diversity, the adoption of new kinds of crops where appropriate and improving existing crops (particularly 'orphan crops' (5)) for wider use through public-private investment and partnerships. Other factors of vital importance to increasing food security or particular importance to resource-poor countries include improvements in infrastructure (transport, electricity supply and storage facilities), capacity building by way of the provision of knowledgeable and impartial advice to farmers about seed choice through local extension services, the development of fair systems of finance and insurance, and the licensing of proprietary technology. However, awareness that there is no single solution to the problem of poverty and discrimination against the poor in many regions should not prevent our use of GE varieties of crops where they can make appropriate contributions to an overall solution.

The Broader Public Debate

GE technology has aroused general public interest and debate around the world about the contribution of science in addressing many of the health and food related challenges that face society in the twenty-first century. This debate on the power and potential role and range of uses to which it can be applied is welcomed, but the discussion must rely on peer-reviewed or otherwise verifiable information if the science and technology are to be appropriately evaluated, regulated, and deployed for the benefit of mankind. Doing nothing is not an option, nor can science and technology be switched on and off like a tap to provide appropriate solutions to problems as they arise: if anything, the task of science is to foresee possible damage in order to avoid it and secure the greatest possible good. In this context, there are six domains of action that need attention: the public understanding of science; the place of intellectual property rights; the role of the public sector; the role of civil society; cooperation between governments, international organisations and civil society; and appropriate and cost-effective justifiable regulatory oversight.

The Public Understanding of Science

Participants at our meeting called attention repeatedly to the widespread misapprehensions about GE technology that pervade both public discussion and administrative regulation. For example, often ignored in the public debate is that all forms of plant breeding involve genetic modification and that some examples of what is called 'conventional' breeding – for example mutagenesis induced by radiation – have outcomes that are intrinsically much less predictable than the application of GE technologies.

All participants in the Study Week are committed to playing their part in contributing to public dialogue and debate in such a way that it is informed and enlightened. It is an obligation for scientists to make themselves heard, explain their science, and demystify technology, and make their conclusions widely available. We urge those who oppose or are sceptical about the use of GE crop varieties and the application of modern genetics generally to evaluate carefully the science

involved and the demonstrable harm caused by withholding this proven technology from those who need it the most. The common good can be served only if public debate rests upon the highest standards of scientific evidence and the civil exchange of opinion.

The Place of Intellectual Property Rights

Proprietary rights play an important role in developing any technology, including medical and agricultural biotechnology, as they do in all aspects of modern society. We are aware that the best practices of the commercial sector have made a significant contribution to the goals of eliminating poverty and food insecurity. However, in line with the social teaching of the Church, which indicates as a primary right the universal destination of the goods of the earth for all mankind, (6) we urge both private and public actors to recognise that the legitimate claims of their property rights should, as much as possible, be subordinated, often beyond the existing norms of civil society, to this universal destination and not allow unjust enrichment or the exploitation of the poor and vulnerable.

Public-private partnerships have become increasingly important in encouraging the development and distribution of improved varieties of crops regularly consumed by poor people in developing countries. The humanitarian 'Golden Rice' project provides an excellent example of such collaboration, where the patents held by the private companies were readily licensed, at no cost, to the public enterprises developing the varieties now ready to be deployed in farmers' fields for the benefit of the societies of which they are part. A number of similar examples are under development; such progress accords well with the belief that all human beings have a claim upon the fruits of the earth. When the private sector shows willingness to make proprietary technologies available for the benefit of the poor it deserves our congratulations, and we encourage it to continue to follow the highest ethical standards in this field.

For that matter, when we consider the relationship between business and ethics, every private company, and in particular a multinational, in the agricultural sphere as well, should not confine itself solely to economic gain. Above all else it should transmit human, cultural and educational values. For this reason, *Caritas in veritate* welcomes recent developments towards a 'civil economy' and an 'economy of communion', a composite reality which does not exclude profit but sees it as a means for attaining human and social ends. Indeed this encyclical affirms that the 'very plurality of institutional forms of business gives rise to a market which is not only more civilized but also more competitive'. (7) These reflections are particularly valid as regards the quality and quantity of food available to a population.

The Role of the Public Sector

The development of new crop varieties that made possible the Green Revolution of the twentieth century was largely achieved by public sector research laboratories in a number of countries. Although the public sector no longer has a near monopoly on such developments, its role is vital and still highly significant. In particular, it can use such funds as it has from national revenues and donor agencies to promote research relevant to those crop needs of the poorest and most vulnerable groups of people. The public sector has an important role to play in making widely available the results of research, and it can innovate in ways that are very difficult for the private sector, where the development of crop varieties for commercialisation is the central goal. If cooperation between private and public sectors has proved beneficial in the development of many applications of science and technology for human benefit particularly in areas of health, agriculture should not be an exception. Unfortunately, we must recognise that, in the case of crop improvement by modern biotechnological approaches, an unscientific and excessive regulation inflates the costs of R&D without any concomitant increase in safety, and makes its application and use by public sector institutions difficult and often impossible for financial reasons.

The Role of Civil Society

Governments, learned societies, NGOs, charities, civil society organisations and religions can all play a part in promoting an informed dialogue and a broad public understanding of the benefits that science can provide, as well as working to improve all aspects of the lives of the less fortunate. They must help to protect the poor from exploitation of all kinds for any purpose, but they also bear the responsibility for ensuring that these communities are not denied access to the benefits of modern science, to prevent them from being condemned to poverty, ill health, and food insecurity.

Cooperation between Governments, International Organisations and Civil Society

As has already been observed, GE technology has already made a significant contribution to crop improvement and increased food security. Appropriate application of the technology in combination with other molecular approaches to plant breeding offers the potential to make further major contributions to improve both major commodity crops and so-called orphan crops in the developing world. The use of these proven scientific advances can thus be considered a Global Public Good.

Because of the high cost of R&D of these new approaches to crop improvement, coupled with the inflated regulatory costs of bringing new traits to market, these technologies have primarily only

been applied by multinational companies to the major high volume commodity crops grown in the developed world. Public-good plant breeding using GE approaches has been limited for two major reasons:

1. The high cost involved and lack of investment by national governments. This has resulted in failure to apply this approach to the improvement and adaptation of locally grown crops, including important (so-called 'orphan') crops such as sorghum, cassava, plantains, etc., which are not internationally traded and have not justified commercial investment by multinational companies;

2. The excessive and unnecessary regulation of this technology compared with all others in agriculture has made it too expensive to apply it to 'minor' crops and those that cannot offer developers returns commensurate with the investment and risk undertaken. This, of course, does not apply solely to the private sector: all investment, private or public, has to be viewed in the light of likely returns. Therefore, the public sector as well as the private sector may refrain from developing products for limited use compared with major commodity crops as a result of the investment needed, problematic regulation and uncertainty of delivery.

Thus there is a need for cooperation between governments, international organisations and aid agencies and charities in this area. The potential benefits of such cooperation have already been demonstrated when multinational corporations have shown a willingness to negotiate with private-public partnerships that has led to the free donation of relevant patentable technologies for use in crop improvement. In the case of 'Golden Rice', this had led to technology transfers to many countries in Asia. Other examples include drought-resistant maize in Africa, insect-resistant vegetables and legumes in India and Africa, and many dozens of additional projects in Africa, Asia and Latin America.

Defining an Appropriate Approach to Regulatory Oversight

The realization of the benefits of any new technology requires an appropriate approach to regulation. Overly stringent regulation developed by wealthy countries and focused almost exclusively on the hypothetical risks of GE crops discriminates against developing and poor countries, as well as against smaller and poorer producers and retailers. This has placed the poor people of the world at an unacceptable disadvantage. The harm deriving from not being able to use more precise and predictable production technologies is irreversible, in the sense that the opportunity costs of lost investment, R&D and products (and their benefits) cannot be recovered.

The evaluation of new and improved crop varieties should be based on the traits of plant varieties and not on the technologies used to produce them: they should be judged in the light of their actual characteristics. This would facilitate the exploitation of the potential of the technology for our common benefit by delivering novel varieties of both major and local crops with improved traits.

This is emphatically not a matter of using the poor for experimentation, but of ensuring that the poor have access to technologies that have been proven to be safe, widely accepted and beneficial, in most of the developed and developing world. We cannot become more risk averse about science and technology – and the consequent risks of food and farming – than what we see as acceptable in the rest of our daily lives.

The hypothetical hazards associated with the genetic engineering of crop plants do not differ from those associated with other instances of the application of such genetic technology to other organisms (e.g., those used in medical biotechnology or biotechnology-enhanced enzymes used in cheese or beer processing). Short-term risks arising from the presence of toxic or allergenic products can be studied and excluded from new crop varieties, a procedure that is more precautionary than is usually the case in the cultivation of crop varieties produced by conventional breeding. As to longer-term evolutionary consequences, the present understanding of molecular evolution as it occurs at low rates in nature by spontaneously arising genetic variation, clearly shows that genetic modifications engineered into a genome can only follow the well-studied natural strategies of biological evolution. Viable modifications are only possible in small steps. This becomes understandable if one bears in mind that land plant genomes are like large encyclopaedias of several hundred books, while genetic modifications using modern genetic techniques affect only one or a few genes out of c. 26,000 genes in the average plant genome. Therefore, the possible evolutionary risks of genetic engineering events cannot be greater than the risks of the natural process of biological evolution or of the application of chemical mutagenesis, both responsible for generating extensive and poorly characterised degrees of genetic change. Statistical records show that the undesirable effects of such genetic change are extremely rare and, in the case of conventional breeding, selected against.

Given the developments in scientific understanding since the adoption of the Cartagena Protocol on Biosafety in 2000, it is now time to reassess that protocol in the light of a science-based understanding of regulatory needs and benefits.

Faith, Scientific Reason and Ethics

For a believer, the point of departure for the Christian vision is the upholding of the divine origin of man, above all because of his soul, which explains the commission that God gives to human beings to govern the whole world of living creatures on the earth through the work to which they dedicate the strength of their bodies guided by the light of the spirit. In this way human beings become the stewards of God by developing and modifying natural beings from which they can draw nourishment through the application of the methods of improvement. (8) Thus, however limited the action of humans may be in the infinite cosmos, they nevertheless participate in the power of God and are able to build their world, that is to say an environment suited to their dual corporeal and spiritual life, their subsistence and their wellbeing. Thus new human forms of intervention in the natural world should not be seen as contrary to the natural law that God has given to the Creation. Indeed, as Paul VI told the Pontifical Academy of Sciences in 1975, (9) on the one hand, the scientist must honestly consider the question of the earthly future of mankind and, as a responsible person,

help to prepare it, to preserve it for subsistence and wellbeing, and eliminate risks. Therefore, we must express solidarity with the present and future generations as a form of love and Christian charity. On the other hand, the scientist also must be animated by the confidence that nature has in store secret possibilities that are for human intelligence to discover and make use of, in order to achieve that level of development which is in the plan of the Creator. Thus, scientific intervention should be seen as a development of physical or vegetal/animal nature for the benefit of human life, in the same way that 'many things for the benefit of human life have been added over and above the natural law, both by divine law and by human laws'. (10)

Recommendations

1. Enhance the provision of reliable information to regulators, farmers and producers around the world so that they will be enabled to make sound decisions based on up-to-date information and knowledge about all aspects of farm management for productivity and sustainability.

2. Standardise – and rationalise – the principles involved in the evaluation and approval of new crop varieties (whether produced by so-called conventional, marker assisted breeding, or GE technologies) universally so that they are scientific, risk-based, predictable and transparent. It is critical that the scope of what is subject to case-by-case review is as important as the actual review itself; it must also be scientific and risk-based.

3. Re-evaluate the application of the precautionary principle to agriculture, reframing it scientifically and practically and making the regulatory requirements and procedures proportional to the risk, and considering the risks associated with lack of action. It must be borne in mind that prudence (*phronesis* or *prudentia*) is the practical wisdom that should guide action. (11) Although this practical wisdom or prudence needs precaution in order to have such a grasp of good as to avoid evil, the main component of prudence is not precaution but prediction. This means that the primary feature of prudence is not refraining from acting to avoid harm but using scientific prediction as a basis for action. (12) Thus, Pope Benedict XVI, in his address to the Pontifical Academy of Sciences on the occasion of the 2006 Plenary Session on 'Predictability in Science', emphasised that the possibility of making predictions is one of the main reasons for the prestige that science enjoys in contemporary society and that the creation of the scientific method has given science the capability of predicting phenomena, studying their development and thus keeping the habitat of human beings under control. 'Indeed we could say', affirms Pope Benedict, 'that the work of predicting, controlling and governing nature, which science today renders more practical than in the past, is itself a part of the Creator's plan'. (13)

4. Evaluate the Cartagena Protocol, an international agreement that regulates international trade in GE crop varieties, developed at a time when less was known about the science of GE crops, to ensure that it is in line with current scientific understanding.

5. Free GE techniques, the most modern, precise and predictable ones for genetic improvement, from excessive, unscientific regulation, allowing their application to enhance the nutritional quality and productivity of crops (and eventually also the production of vaccines and other pharmaceuticals) everywhere.

6. Promote the potential of technology to assist small farmers through adequate research funding, capacity building and training linked through to appropriate public policy.

7. Encourage the wide adoption of sustainable sound and productive agricultural practices and extension services, which are especially critical for improving the lives of poor and needy people throughout the world.

8. In order to ensure that appropriate GE and molecular marker-assisted breeding is used to improve relevant crops grown in food-insecure, poor nations, where they can be expected to have an important impact on improving food security, we urge that governments, international aid agencies and charities increase funding in this area. Given the urgency, international organisations such as the FAO, CGIAR, UNDP or UNESCO have the moral responsibility to guarantee food security for the current and future world population. They must use all their endeavours to mediate the establishment of private-public cooperative relationships to ensure the cost-free exploitation of these technologies for the common good in the developing world where they will have the greatest impact. (14)

Background

The PAS Study Week from 15-19 May 2009 was organised, on behalf of the Pontifical Academy of Sciences, by academy member Professor Ingo Potrykus, with support from academy members Professor Werner Arber, and Professor Peter Raven. The organisers knew that since 2000, when an earlier Study-Document was published by the same Academy on '"Genetically Modified Food Plants" to Combat Hunger in the World', a great deal of evidence and experience had accumulated about genetically engineered crops.

The aim of the Study Week was, therefore, to evaluate benefits and risks of genetic engineering and of other agricultural practices on the basis of present scientific knowledge and of its potential for applications to improve food security and human welfare worldwide in the context of a sustainable development. The participants were also aware of the social teaching of the Church on biotechnology and accepted the moral imperative to focus on the responsible application of GE according to the principles of social justice.

Participation was by invitation only and participants were selected for their scientific merits in their respective fields of expertise and their engagement for scientific rigour and social justice. The organisers had to make a selection of participants, and based their choice on the need to advance the principal purpose of the meeting, which was to review experience to date. Although there were differences of opinions, points of view and emphasis among the participants, all agreed on the broad principles contained in this statement.

The participants of the Study Week and their scientific competence are given below in alphabetic order

Members of the Pontifical Academy of Sciences:

Prof. em. Werner Arber • Switzerland, University of Basel: Microbiology, Evolution.

Prof. Nicola Cabibbo † • Italy, Rome, President Pontifical Academy of Sciences: Physics.

H.Em. Georges Cardinal Cottier, Vatican City: Theology.

Prof. em. Ingo Potrykus • Switzerland, Zurich, Swiss Federal Institute of Technology: Plant Biology, Agricultural Biotechnology.

Prof. em. Peter H. Raven • USA, St. Louis, President Missouri Botanical Garden: Botany, Ecology.

H.Em. Msgr. Marcelo Sánchez Sorondo • Vatican City: Chancellor Pontifical Academy of Sciences: Philosophy.

Prof. Rafael Vicuña • Chile, Santiago, Pontifical Catholic University of Chile: Microbiology, Molecular Genetics.

Outside Experts:

Prof. em. Klaus Ammann • Switzerland, University of Berne, Botany, Vegetation Ecology.

Prof. Kym Anderson • Australia, The University of Adelaide, CEPR and World Bank: Agricultural Development Economics, International Economics.

Dr. iur. Andrew Apel • USA, Raymond, Editor in Chief of GMObelus: Law.

Prof. Roger Beachy • USA, St. Louis, Donald Danforth Plant Science Center, now NIVA, National Institute of Food and Agriculture, Washington DC.,: Plant Pathology, Agricultural Biotechnology.

Prof. Peter Beyer • Germany, Freiburg, Albert-Ludwig University, Biochemistry, Metabolic Pathways.

Prof. Joachim von Braun • USA, Washington, Director General, International Food Policy Research Institute, now University of Bonn, Center for Development Research (ZEF): Agricultural and Development Economics.

Prof. Moisés Burachik • Argentina, Buenos Aires, General Coordinator of the Biotechnology Department: Agricultural Biotechnology, Biosafety.

Prof. Bruce Chassy • USA, University of Illinois at Urbana-Champaign: Biochemistry, Food Safety.

Prof. Nina Fedoroff • USA, The Pennsylvania State University: Molecular Biology, Biotechnology.

Prof. Dick Flavell • *USA*, CERES, Inc., Thousand Oaks: Agricultural Biotechnology, Genetics.

Prof. em. Jonathan Gressel • *Israel*, Rehovot, Weizmann Institute of Science: Plant Protection, Biosafety.

Prof. Ronald J. Herring • *USA*, Ithaca, Cornell University: Political Economy.

Prof. Drew Kershen • USA, University of Oklahoma: Agricultural Law, Biotechnological Law.

Prof. Anatole Krattiger • USA, Ithaca, Cornell University and Arizona State University, now: Director, Global Challenges Division, WIPO, Geneva, Switzerland: Intellectual Property Management.

Prof. em. Christopher Leaver • UK, University of Oxford: Plant Sciences, Plant Molecular Biology.

Prof. Stephen P. Long • USA, Urbana, Energy Science Institute: Plant Biology, Crop Science, Ecology.

Prof. Cathie Martin • UK, Norwich, John Innes Centre: Plant Sciences, Cellular Regulation.

Prof. Marshall Martin • USA, West Lafayette: Purdue University: Agricultural Economics, Technology Assessment.

Prof. *Henry Miller* • USA, Hoover Institution, Stanford University: Biosafety, Regulation.

Prof.em. Marc Baron Van Montagu • Belgium, Gent: President European Federation of Biotechnology: Microbiology, Agricultural Biotechnology.

Prof. Piero Morandini • Italy, University of Milan: Molecular Biology, Agricultural Biotechnology.

Prof. Martina Newell-McGloughlin • USA, Davis, University of California: Agricultural Biotechnology.

H.Em. *Msgr. George Nkuo* • Cameroon, Bishop of Kumbo: Theology.

Prof. Rob Paarlberg • USA, Wellesley College: Political Science.

Prof. Wayne Parrott • USA, Athens, University of Georgia: Agronomy, Agricultural Biotechnology.

Prof. Channapatna S. Prakash • USA, Tuskegee University: Genetics, Agricultural Biotechnology.

Prof. Matin Qaim • Germany, Georg-August University of Göttingen: Agricultural Economics, Development Economics.

Dr. Raghavendra S. Rao • India, New Delhi, Department of Biotechnology, Adviser to the Ministry of Science and Technology: Agriculture, Plant Pathology.

Prof. Konstantin Skryabin • Russia, Moscow, 'Bioengineering' Centre Russian Academy of Sciences: Molecular Biology, Agricultural Biotechnology.

Prof. Monkumbu Sambasivan Swaminathan • India, Chennai, Chairman, M.S. Swaminathan Research Foundation: Agriculture, Sustainable Development.

Prof. Chiara Tonelli • Italy, University of Milan: Genetics, Cellular Regulation.

Prof. Albert Weale • UK, Nuffield Council on Bioethics and University of Essex, now University College of London, Dept. of Political Sciences: Social & Political Sciences.

Prof. Robert Zeigler • Philippines, Metro Manila, Director General International Rice Research: Agricultural Biotechnology, Rice research and Development Policy.

Notes

1) Cf. John Paul II, Encyclical Letter *Laborem exercens*, 5: *loc. cit*., 586-589.

2) Caritas in veritate, § 69.

3) Caritas in veritate, § 27.

4) 'This is a principle to be remembered in agricultural production itself, whenever there is a question of its advance through the application of biotechnologies, which cannot be evaluated solely on the basis of immediate economic interests. They must be submitted beforehand to rigorous scientific and ethical examination, to prevent them from becoming disastrous for human health and the future of the earth' (John Paul II, *Address to the Jubilee of the Agricultural World*, 11 November 2000).

5) Orphan crops, also referred as neglected or lost crops, are crops of high economic value in developing countries. These crops include cereal crops (such as millet and tef), legumes (cow pea, grass pea and bambara groundnut), and root crops (cassava and sweet potato). Although orphan crops are vital for the livelihood of millions of resource-poor farmers, research in these crops is lagging behind that of major crops. To boost crop productivity and attain food self-sufficiency in the developing world, research on orphan crops should get more attention.

6) Centesimus annus, § 6.

7) Caritas in veritate, § 46.

8) 'God has sovereign dominion over all things: and He, according to His providence, directed certain things to the sustenance of man's body. For this reason man has a natural dominion over things, as regards the power to make use of them' (Thomas Aquinas, *Summa Theologica*, II-II, q. 66, a. 1 ad 1).

9) Cf. Paul VI, Address to the Plenary Session of the Pontifical Academy of Sciences of 19 April 1975, *Papal Addresses*, Vatican City 2003, p. 209.

10) St. Thomas Aquinas, *Summa Theologica*, I-II, 94, a.5. Cf. *loc. cit.* ad 3.

11) 'Prudence (*phronesis*) is a truth-attaining rational quality, concerned with action in relation to the things that are good for human beings' (Aristotle, *Eth. Nic*., VI, 5, 1140 b 20, Eng. tr. J. Bywater). Cf. also the rest of the chapter.

12) 'Prediction is the principle of prudence…Hence it is that the very name of prudence is taken from prediction [providential] as from its principal part' (St. Thomas Aquinas, *Summa Theologica*, II-II, q. 49, a. 6 ad 1).

13) Address of the Holy Father Benedict XVI to the Plenary Session of the Pontifical Academy of Sciences. Available online at http://www.vatican.va/holy-father/benedict _xvi/speeches/2006/november/documents/hf_ben-xvi_spec_20061106_academy-sciences_en.html

14) Cf. P. Dasgupta, 'Science as an Institution: Setting Priorities in a New Socio-Economic Context' in *World Conference on Science: Science for the Twenty-First Century, A New Commitment* (UNESCO, Paris, 2000).

The English Version represents the official Conference Statement of the Pontifical Academy of Science. It has been drafted and endorsed by all participants of the Study Week, and it was synthesized mainly by Ingo Potrykus, Peter Raven, Albert Weale and Chris Leaver.

أسبوع البحث العلمي للأكاديمية البابوية للعلوم (PAS)، مدينة الفاتيكان، في الفترة من 15 إلى 19 مايو 2009

النباتات المعدَّلة جينيًّا لأغراض سلامة الغذاء في سياق التنمية

تم تخصيص أسبوع كامل لدراسة موضوع "النباتات المعدلة جينيًّا لأغراض سلامة الغذاء في سياق التنمية"، تحت رعاية الأكاديمية البابوية للعلوم في مقرها في كاسينا بايو (Casino Pio IV)، في الفاتيكان في الفترة من 15 إلى 19 مايو 2009. وأثناء هذا الجمع، قمنا بعمل مسح لآخر التطورات في الفهم العلمي للتنوعات الجديدة في النباتات المعدَّلة وراثيًّا، وكذا الأوضاع الاجتماعية التي يمكن من خلالها إتاحة تقنية التعديل الوراثي (GE)، من أجل تحسين مستوى الزراعة في العموم ولإفادة الفقراء والضعفاء على وجه الخصوص. وقد كانت الروح الحماسية التي سادت المشاركين نابعةً من نفس المقاربة التي عبَّر عنها بنيديكت السادس عشر في بيانه البابوي، خاصةً أن "التكنولوجيا هي الجانب الموضوعي للعمل الإنساني[1]، الذي تأصَّل من خلال العنصر الذاتي، أي الفاعل نفسه. ولهذا السبب، لم تكن التكنولوجيا من أجل التكنولوجيا. إنها توجه الإنسان وطموحاته نحو التنمية؛ فهي تعبِّر عن القلق الداخلي الذي يدفع الإنسان بالتدريج للتغلب على القيود المادية. فالتكنولوجيا، بهذا المعنى، هي استجابة لوصية الله أن يعمِّر الإنسان الأرض ويحافظ عليها (انظر سفر التكوين 2:15) والتي أودعها أمانةً له، ويتوجب عليه أن يسعى لتعزيز العهد بين البشر والبيئة، وهو عهد يجب أن يعكس الحب الإبداعي الإلهي."[2]

النتائج العلمية الأساسية:

نعيد التأكيدَ على النتائج الأساسية للدراسة حول استخدام النباتات المعدَّلة وراثيًّا لأغراض الغذاء لمكافحة الجوع في العالم، والتي صدرت في اليوبيل الذهبي للجلسة كاملة الأعضاء حول "العلم ومستقبل الجنس البشري"، في الفترة من 10 إلى 13 نوفمبر 2000. وملخص هذه النتائج كالآتي:

1. أكثر من مليار شخص في العالم من مجموع 6,8 مليار يعانون من سوء التغذية، وهي حالة تتطلب ابتكار نظم زراعية وتقنيات جديدة على وجه السرعة.
2. الزيادة المتوقعة لـــ 2 أو 2,5 مليار شخص – ليصل عدد سكان العالم إلى 9 مليارات عام 2050 – تزيد من خطورة المشكلة.
3. سوف تؤثر كذلك العواقب المتوقعة للتغير المناخي والنقص المرتبط بها في إتاحة المياه للزراعة في قدرتنا على تغذية العدد المتزايد لسكان العالم.
4. إن الزراعة كما هي ممارسة الآن غير مستدامة، والدليل على ذلك الفقدان الرهيب في سطح التربة والاستخدامات المتزايدة على نحو غير مقبول لمبيدات الآفات في معظم أنحاء العالم.

5. يسهم الاستخدام الملائم للهندسة الوراثية وغيرها من تقنيات الجزيئات الحديثة في الزراعة نحو التصدي لبعض هذه التحديات.
6. ليس هناك ما هو جوهري في استخدام تقنيات التعديل الوراثي لتحسين المحاصيل مما سيسبِّب خطورة في النباتات ذاتها أو المنتجات الغذائية المصنعة منها.
7. يتوجب على المجتمع العلمي أن يتحمل مسئولية البحث والتطوير؛ مما يقود إلى تقدم في الإنتاجية الزراعية، ويتوجب عليه أيضًا محاولة البحث عن الفوائد المرتبطة بهذا التقدم والتي تتنامى لمصلحة الفقراء وكذلك لمصلحة الدول المتقدمة التي تتمتع الآن بمستويات معيشية عالية نسبيًّا.
8. يجب بذل جهود خاصة لإتاحة تنوعات في المحاصيل المعدَّلة وراثيًّا والملائمة للظروف المحلية الخاصة بالمزارعين الفقراء.
9. يجب أن توجه عناية خاصة من جانب أبحاث التطوير في المحاصيل المحسنة إلى الحاجات المحلية والتنوعات في المحاصيل، وكذلك إلى قدرة كل دولة على أن تكيف تقاليدها وموروثها الاجتماعي والممارسات الإدارية؛ من أجل تحقيق النجاح في إدخال المحاصيل المعدَّلة وراثيًّا.

أدلة أخرى:

منذ الإعداد لهذه الدراسة الأولية، تراكمت العديد من الأدلة التي خضعت للمقاييس العالمية للتحكيم العلمي الدقيق، وكذلك لعدد هائل من الخبرات الواقعية، حول تطوير تقنية الهندسة الوراثية وتطبيقاتها وآثارها. وخلال الأسبوع المخصص للدراسة، قمنا باستعراض هذه الأدلة والتوصل إلى النتائج التالية:

1. يمكن أن تسهم تكنولوجيا الهندسة الوراثية – المستخدمة على نحو ملائم وبشكل مسئول – بشكل أساسي في الإنتاجية الزراعية من خلال تحسين المحاصيل، بما في ذلك دعم الناتج المحصولي والجودة الغذائية وزيادة مقاومة الآفات، وكذلك تحسين درجة تحمل الجفاف وغيرها من أشكال الضغط البيئي. وهناك حاجة إلى هذه التحسينات حول العالم للمساعدة في تحسين استدامة الزراعة وإنتاجيتها.
2. يمثل التحسين الجيني للمحاصيل ونباتات الزينة سلسلةً طويلةً وغير سهلة للتقنيات الأكثر وضوحًا وتوقعًا. وكما استنتج تقرير مجلس البحث العلمي القومي في الولايات المتحدة عام 1989: "كما أن الأساليب الجزيئية أكثر تحديدًا، سوف يكون مستخدمو هذه الأساليب أكثر ثقةً حول الصفات التي تستخدم في النباتات ومن ثمَّ أقل عرضةً لإنتاج آثار غير مرغوبة من غيرها من الأساليب المستخدمة في زراعة النباتات".
3. كانت الفوائد ذات أهمية كبيرة في دول مثل الولايات المتحدة الأمريكية والأرجنتين والهند والصين والبرازيل، حيث يتم زراعة المحاصيل المعدلة وراثيًّا على نحو موسَّع.
4. يمكن أن تكون هذه الفوائد أيضًا ذات أهمية كبرى للمزارعين الفقراء والضعفاء من أبناء المجتمع الريفي، خاصةً النساء والأطفال. ولقد قللت محاصيل القطن والذرة الشامية المعدَّلة وراثيًّا، على وجه الخصوص، والمقاومة للآفات من استخدام مبيدات الآفات (ومن ثم دعم الأمن الزراعي) والإسهام في زيادة الناتج

الزراعي على نحو كبير، وفي زيادة الدخل الأسري، ومعدلات الفقر المتدنية (وكذلك تقليل حالات التسمم من جراء الآفات الكيميائية) في قطاعات محددة صغيرة في المزارع في العديد من الدول النامية، بما في ذلك الهند والصين وجنوب إفريقيا والفلبين.

5. إن إدخال مقاومة المبيدات النباتية الصديقة للبيئة وغير المكلفة في زراعة الذرة الشامية وفول الصويا والكانولا وغيرها من المحاصيل هو أوسع صفات التعديل الوراثي استخدامًا. لقد زادت من ناتج الهكتار واستبدلت إزالة الحشائش يدويًّا ويسَّرت من المدخلات الأقل؛ مما أدى إلى تقليل أساليب الحرث التي قللت بدورها من معدل تحاتّ التربة. وقد تكون هذه الحقيقة التقنية مفيدةً على نحو خاص للمزارعين في العالم النامي والذين لا يمكِّنهم السن أو المرض من الانخراط في مكافحة الحشائش يدويًّا بشكل تقليدي.
6. يمكن أن تحارب تكنولوجيا الهندسة الوراثية سوء التغذية من خلال التعديل الذي يقدم المكونات الغذائية الصغرى الضرورية. فعلى سبيل المثال، أوضحت دراسات حول البروفيتامينات (أ) المقوَّاة بيولوجيًّا والمستخدمة في "الأرز الذهبي" أن النظم الغذائية اليومية التي تحتوي على هذا الأرز المقوَّى قد تكون كافيةً لمنع نقص فيتامين (أ).
7. أدى استخدام تكنولوجيا الهندسة الوراثية في مقاومة الآفات إلى تقليص استخدام المبيدات الكيميائية؛ مما قلل من تكلفة المدخلات الزراعية وتحسين الحالة الصحية للعاملين الزراعيين. وهذه العلاقة مهمة على وجه الخصوص في مناطق مثل الدول الأوروبية؛ حيث يتم استخدام المبيدات بصورة أكبر من مناطق أخرى؛ مما قد يدمر النظام البيئي عامةً والصحة البشرية كذلك.
8. قد تقلص تكنولوجيا الهندسة الوراثية من الاستهلاك المضر للطاقة وممارسات الحرث الميكانيكية ودعم التنوع الحيوي وحماية البيئة من خلال تقليص انبعاثات ثاني أكسيد الكربون؛ أكثر الغازات المضرة بالغطاء الأخضر، إلى البيئة.
9. إن التأثير المتوقع للتغير المناخي يعزِّز الحاجة إلى استخدام الهندسة الوراثية بالإضافة إلى غيرها من تقنيات الزراعة على نحو ملائم وقوي، ومن ثم يتم إدراج صفات مثل مقاومة الجفاف وتحمل الفيضانات في المحاصيل الغذائية الأساسية لكل المناطق بأسرع وقت ممكن.
10. لقد زادت الهندسة الوراثية من النواتج الزراعية للمزارعين الفقراء، حيث توجد أدلة على زيادة الدخل وفرص العمل بصورة لم تكن ممكنة بأي طريق آخر.
11. يجب أن يكون الإشراف التنظيمي المكلف لتكنولوجيا الهندسة الوراثية في منعة علمية وأن يكون قائمًا على المخاطرة. وهذا يعني أن هذا التنظيم يجب أن يكون قائمًا على صفات خاصة للتنوع النباتي بدلاً من الوسائل التكنولوجية المستخدمة لإنتاج ذلك.
12. لابد وأن تضع تقديرات المخاطرة – ليس فقط المخاطر الممكنة لاستخدام تنوع نباتي جديدة – ولكن أيضًا مخاطر البدائل إذا لم تتم إتاحة التنوع الخاص.
13. هناك حاليًّا جهود مهمة للقطاع العام لتقليل التنوعات المحسنة وراثيًّا أو خطوط نبات المنيهوت والبطاطا والأرز والذرة الشامية والموز والذرة البيضاء وغيرها من المحاصيل الاستوائية الرئيسية التي سيكون لها فائدة مباشرة للفقراء، ويجب تشجيع هذه الجهود بقوة.

14. لابد من التصدي لفداحة التحديات التي تواجه فقراء العالم وسيئي التغذية كمسألة ملحة. فكل عام يتسبب سوء التغذية في أمراض يمكن الوقاية منها وكذلك في الموت الذي يمكن تفاديه. إن الزيادة الحالية في أسعار الغذاء في جميع أنحاء العالم قد أوضحت ضعف الفقراء وتعرضهم للكفاح من أجل الحصول على الموارد الغذائية. وفي هذا السياق، يتم فقدان الفوائد السابقة للأبد.

15. في ضوء هذه النتائج العلمية، هناك حتمية أخلاقية لجعل الفوائد الخاصة بتنمية التعديل الوراثي متاحةً على مدى أوسع للفقراء والضعفاء الذين هم في حاجة إليها، في أشكال تمكِّنهم من رفع مستوياقم المعيشية وتحسين صحتهم وحماية بيئاقم.

وفي عموم القول، أفصح تطبيق تكنولوجيا الهندسة الوراثية عن أهميته في تحسين الإنتاجية الزراعية في جميع أنحاء العالم، ولكنها لا تزال جزءاً واحدًا لما لا بد وأن تكون عليه استراتيجية متعددة الأوجه. وكما أشار البابا بنيديكت السادس عشر: "قد يكون من المفيد أن نفكر في إمكانيات جديدة تبرز من خلال الاستخدام الملائم للتقنيات التقليدية والمبتكرة للزراعة، مفترضين دائمًا أن هذه التقنيات لا بد وأن تخضع للدراسة، بعد تجريبها بشكلٍ كافٍ، والتأكد من أنها تحترم البيئة وتهتم بحاجات الشعوب الأكثر حرمانًا"[3]. إلا أننا نعترف بأنه ليست كل تطورات الهندسة الوراثية سوف تفي بوعدها الأصلي، كما هو الحال في أية تكنولوجيا. علينا الاستمرار في تقييم الإسهام الممكن لكل التقنيات الملائمة، والتي لابد وأن تستخدم مع الاستراتيجيات الإضافية التقليدية للزراعة من أجل تحسين سلامة الغذاء والتخوف من معدلات الفقر بالنسبة للأجيال القادمة[4]. ويمكن استخدام العديد منها بالتعاون مع تقنيات الهندسة الوراثية. وتتضمن استراتيجيات استعادة سطح التربة من خلال الممارسات غير القائمة على الحرث وغيرها من العوامل الوقائية، والاستخدام الملائم للمخصبات، واستحداث أنواع جديدة من المخصبات والكيماويات الزراعية صديقة البيئة وحفظ المياه والإدارة المتكاملة للآفات وحفظ التنوع الجيني وتبني أنواع جديدة من المحاصيل كلما أمكن ذلك وتحسين المحاصيل الحالية (خاصةً المحاصيل "اليتيمة") [5] لتستخدم على نطاق أوسع من خلال الاستثمار العام والخاص والشراكات. وتتضمن العوامل الأخرى ذات الأهمية الحيوية في زيادة سلامة الغذاء أو الأهمية الخاصة للدول فقيرة الموارد – تحسينات في البنية التحتية (المواصلات والكهرباء ومرافق التخزين) وبناء الطاقات من خلال توفير المشورة الواعية وغير المنحازة للفلاحين حول اختيار الحبوب عبر الخدمات المحلية الإضافية وابتكار نظام نزيه للتمويل والتأمين وترخيص تكنولوجيا الملكية. ولكن يجب ألا يمنع الوعي بعدم وجود حل واحد لمشكلة الفقر والتفرقة ضد الفقراء في العديد من المناطق من استخدامنا لمحاصيل منوَّعة معدَّلة وراثيًّا أينما كانت قادرةً على تقديم إسهامات ملائمة نحو حل متكامل.

الجدل الأوسع نطاقًا:

لقد أثارت تقنية الهندسة الوراثية الاهتمام والجدل حول العالم فيما يخص إسهام العلم في التصدي للعديد من تحديات الصحة والغذاء التي تواجه المجتمع في القرن الواحد والعشرين. وهذا الجدل أمر مقبول، ولكن النقاش لابد وأن يعتمد على معلومات محكمة أو مثبتة إذا توجب تقييم العلم والتكنولوجيا على نحو ملائم وتنظيمهما ونشرهما لخدمة الجنس البشري. إن الوقوف مكتوفي الأيدي ليس خيارًا ممكنًا، ولن يستطيع العلم والتكنولوجيا أن يفتحا ويغلقا كالصنبور لتقديم الحلول الملائمة عندما تظهر المشكلات، وعلى أية حال، إن مهمة العلم هي

استشراف الدمار الممكن من أجل تجنبه، وضمان أكبر قدر من المصلحة الممكنة. وفي هذا السياق، هناك ستة مجالات للعمل تحتاج إلى التركيز عليها، وهي: تفهم العامة للعلم، ومكانة حقوق الملكية الفكرية، ودور القطاع العام، ودور المجتمع المدني، والتعاون بين الحكومات والمنظمات الدولية والمجتمع المدني، والمسئولية المنظمة المبررة التي تقلل التكلفة وتتسم بالملاءمة.

تفهم العامة للعلم:

لفت المشاركون في لقائنا الانتباه مرارًا إلى المغالطات المنتشرة حول تقنية الهندسة الوراثية التي تتسرب إلى المناقشات العامة والتنظيمات الإدارية. فعلى سبيل المثال، كثيرًا ما يتجاهل الجدل العام أن كل أشكال الزراعة النباتية تتضمن تعديلاً وراثيًّا، وأن بعض أمثلة ما يُطلق عليها الزراعة "التقليدية" (مثل التعديل الجيني من خلال الإشعاع) لها نتائج جوهرية أقل توقعًا من استخدام تقنيات الهندسة الوراثية.

ويتعهد كل المشاركين في هذه الأسبوع بالقيام بدورهم في الإسهام في الحوار والجدل العام بشكل مطلع ومستنير. إنه إلزام على العلماء أن يدلوا بآرائهم وينشروا علمهم، ويزيلوا الغموض الذي يكتنف التكنولوجيا، ويتيحوا نتائج أبحاثهم على نطاق واسع. إننا نحضُّ الذين يعارضون أو يشككون في استخدام المحاصيل المعدلة وراثيًّا ويطبقون علم الجينات الحديث أن يقيِّموا بدقة العلم المتضمن فيه والضرر المحدق الذي ينتج عنه منع هذه التكنولوجيا عمن يحتاجون إليها. ويمكن تحقيق المصلحة العامة إذا قام الجدل العام على أعلى معايير الأدلة العلمية والتبادل المدني للآراء.

مكانة حقوق الملكية الفكرية:

تلعب حقوق الملكية الفكرية دورًا هامًّا في تطوير أية تكنولوجيا، بما في ذلك التكنولوجيا الحيوية الطبية والزراعية، كما هو الحال في كل جوانب المجتمع الحديث. إننا على دراية بأن أفضل ممارسات القطاع التجاري قد أسهمت بأهمية في تحقيق أهداف القضاء على الفقر والمخاطر الغذائية. إلا أنه فيما يتعلق بالتعاليم الاجتماعية للكنيسة، والتي تشير إلى الانتشار العالمي لكل خيرات الأرض لكل أفراد الجنس البشري، كحق أولي[6]، فنحن نحضُّ كلاًّ من القطاعَين العام والخاص على الاعتراف بأن الادعاءات الشرعية لحقوق الملكية الفكرية لابد وأن تخضع قدر الإمكان، وفي الأغلب فيما وراء المعايير الحالية للمجتمع المدني، لهذا الهدف العالمي ولا تسمح بالثراء الفاحش أو استغلال الفقراء والضعفاء.

لقد أصبحت الشراكات العامة والخاصة ذات أهمية متزايدة في تشجيع تطوير ونشر التنوعات المحسنة للمحاصيل التي يستهلكها الفقراء بانتظام في الدول النامية، ويقدم المشروع الإنساني "الأرز الذهبي" مثالاً ممتازًا على هذا التعاون، حيث تم ترخيص براءات الاختراع التي تحملها الشركات الخاصة دون تكلفة وتحويلها إلى مشروعات عامة تطور التنوعات الجاهزة التي هي جزء فيها. وثمة عدد لأمثلة أخرى مشابهة في طريقها إلى الظهور، وهذا التقدم يتواكب جيدًا مع الاعتقاد بأن كل البشر لهم حق استخدام خيرات الأرض. وعندما يبدي القطاع الخاص استعدادًا

لإتاحة تكنولوجيا الملكية لصالح الفقراء، فإن ذلك يستحق تهانينا ويشجعنا على الاستمرار في اتباع أعلى المعايير الأخلاقية في هذا المجال.

ولذلك، عندما نفكر في العلاقة بين الأعمال التجارية والأخلاق، فإنه يتعين على كل شركة خاصة، ولاسيما الشركات متعددة الجنسيات، والعاملة في المجال الزراعي، ألا تتحدد بالربح الاقتصادي فحسب؛ فعلاوة على ذلك، يجب أن تنقل القيم الإنسانية والثقافية والتعليمية. ولهذا السبب، ترحب جمعية "كاريتاس" بالتطورات الحديثة نحو "الاقتصاد المدني" و"اقتصاد الجماعة"، وهو أمر مركَّب لا يهدف إلى الربح ولكن ينظر إليه كوسيلة لتحقيق غايات إنسانية واجتماعية. والحق أن البيان البابوي يؤكد بأن "التعددية في الأشكال المؤسسية للأعمال تعطي مجالاً لسوق ليس متقدمًا فحسب بل أيضًا منافسًا." [7] وهذه الأفكار صالحة فيما يتعلق بكم وكيف الغذاء المتاح للأفراد.

دور القطاع العام:

لقد توصلت معامل الأبحاث العلمية بالقطاع العام في عددٍ من الدول إلى تطوير أنواع جديدة من المحاصيل التي مكنت من تحقيق الثروة الخضراء في القرن العشرين. وبالرغم من أن القطاع العام لم تعد له أية احتكارات على هذه التطورات، فإن دوره لا يزال حيويًّا ومهمًّا للغاية. فهو قادر، على وجه الخصوص، على استخدام التمويل المتاح له من خلال العوائد القومية ووكالات التبرعات لدعم البحث ذي الصلة بهذه المحاصيل التي تحتاجها الشرائح الأكثر فقرًا وضعفًا. إن للقطاع العام دورًا هامًّا في إتاحة نتائج البحث العلمي على نطاق واسع، ويمكن أن يبتكر أساليب يصعب على القطاع الخاص التوصل إليها؛ حيث يكون ابتكار تنوعات للمحاصيل تستخدم لأغراض تجارية هدفًا رئيسيًّا. وإذا ثبت أن التعاون بين القطاعين العام والخاص مفيدٌ في ابتكار العديد من استخدامات العلم والتكنولوجيا للصالح الإنساني خاصةً في مجالات الصحة، فلا يجب أن تظل الزراعة استثناءً. وللأسف، علينا أن نعترف بأنه في حالة تحسين المحاصيل باستخدام أساليب بيوتكنولوجية حديثة، فإن تنظيمًا غير علمي وصارم يضخم من تكاليف البحث والتطوير دون أية زيادة مكافئة في السلامة، وهذا يجعل استخدامها وتطبيقها في مؤسسات القطاع العام صعبًا وكثيرًا ما يكون مستحيلاً لأسباب مالية.

دور المجتمع المدني:

تستطيع الحكومات والجمعيات العلمية والجمعيات الأهلية والمؤسسات الخيرية ومنظمات المجتمع المدني والدين أن تؤدي دورًا في نشر الحوار الواعي والفهم العام الواسع لفوائد العلم وكذلك العمل على تحسين كل جوانب حياة البائسين. على تلك الجهات أن تساعد في حماية الفقراء من الاستغلال بكل أشكاله وكل أغراضه، ولكن تقع على عاتقهم أيضًا مسئولية ضمان عدم حرمان هذه الجماعات من الحصول على فوائد العلم الحديث، حتى تتم حمايتهم من وطأة الفقر والمرض وغياب السلامة الغذائية.

التعاون بين الحكومات والمنظمات الدولية والمجتمع المدني:

كما لاحظنا آنفًا، قدمت تكنولوجيا التعديل الوراثي إسهامًا مهمًّا في تحسين المحاصيل ورفع مستوى سلامة الغذاء. ويقدم التطبيق الملائم للتكنولوجيا مع الاتجاهات الجزيئية الأخرى لزراعة النباتات إمكانية توفير إسهامات أخرى رئيسية لتحسين المحاصيل التجارية الأخرى والمحاصيل "اليتيمة" في العالم النامي. واستخدام هذا التطور العلمي الدامغ قد يعتبر خيرًا للعالم بأسره.

وبسبب التكلفة العالية للبحث والتطوير في هذه الاتجاهات الجديدة لتحسين المحاصيل، وفي ضوء التكاليف التنظيمية المتضخمة الخاصة بإيجاد خصائص جديدة في الأسواق، فلقد طبقت الشركات متعددة الجنسيات هذه التكنولوجيات على المحاصيل التجارية الرائجة والرئيسية التي يزرعها العالم المتقدم. ولقد تم تحديد زراعة النباتات للمصلحة العامة باستخدام الهندسة الوراثية لسببين رئيسيين:

1. التكلفة العالية وقلة الاستثمار من جانب الحكومات الوطنية. ولقد أدى هذا إلى الفشل في تطبيق هذا الاتجاه في تحسين وتهيئة المحاصيل المزروعة محليًّا، بما في ذلك المحاصيل الهامة (أو اليتيمة) مثل الذرة السكرية والمنيهوت وأذن الجدي وغيرها، التي لا يتم الاتجار فيها عالميًّا، وليس هناك مسوغ للاستثمار فيها من قبل الشركات متعددة الجنسيات.
2. لقد أدى التنظيم المبالغ فيه وغير الضروري لهذه التكنولوجيا مقارنةً بالتقنيات الأخرى في الزراعة إلى جعلها مكلفة للغاية بحيث لا يمكن تطبيقها على المحاصيل "الثانوية" والتي لا يمكن أن تقدم للمطورين عوائد تتماشى مع الاستثمار والمخاطرة. ولا ينطبق ذلك بالطبع على القطاع الخاص فحسب؛ فكل الاستثمارات العامة والخاصة لابد وأن ينظر إليها في ضوء العوائد الممكنة. ولذلك، قد يأنف القطاعان العام والخاص من تطوير منتجات لاستخدام محدود مقارنةً بالمحاصيل التجارية الرئيسية كنتيجة للاستثمار المطلوب والتنظيم المعقد وعدم ضمان الحصول عليها.

وبذلك، فإن هناك حاجة للتعاون بين الحكومات والمنظمات الدولية ووكالات الإغاثة والمؤسسات الخيرية في هذا المجال. ولقد تم إيضاح الفوائد الممكنة عندما أبدت الشركات متعددة الجنسيات استعدادًا للتفاوض مع الشراكات العامة والخاصة مما أدى إلى التبرع بالتقنيات ذات الصلة وذات براءات الاختراع لتستخدم في تحسين المحاصيل. وفي حالة "الأرز الذهبي"، أدى ذلك إلى نقل التكنولوجيا للعديد من الدول في آسيا. وتتضمن الأمثلة الأخرى الذرة الشامية المقاومة للجفاف في إفريقيا والخضروات المقاومة للحشرات والبقوليات في الهند وإفريقيا وعشرات المشروعات الأخرى الإضافية في إفريقيا وآسيا وأمريكا اللاتينية.

تحديد المقاربة الملائمة للمسئولية المنظمة:

يتطلب تحقيق فوائد أية تكنولوجيا جديدة مقاربة ملائمة لمسألة التنظيم. إن القوانين الصارمة التي وضعتها الدول الغنية والمتركزة حصريًّا في المخاطر الافتراضية للهندسة الوراثية تميز ضد الدول النامية والفقيرة وكذا ضد الأصغر والأفقر وتجار التجزئة. ولقد وضع الأمر فقراء العالم في موقف حرج، ويعتبر الضرر الناجم عن عدم القدرة على استخدام تقنيات أكثر دقةً وتنبؤًا ضررًا فادحًا، بمعنى أنه لا يمكن التعافي من فرص تكاليف الاستثمارات والبحث والتطوير.

يجب أن يؤسس تقييم تنويعات المحاصيل الجديدة والمحسنة على الصفات الخاصة بالنباتات، وليس على تقنيات مستخدمة لإنتاجها؛ فيجب أن تقيم في ضوء خصائصها الحقيقية. وقد يؤدي ذلك إلى استغلال قدرة التكنولوجيا للصالح العام من خلال توفير تنويعات جديدة لكلٍّ من المحاصيل الرئيسية والمحلية ذات الصفات المحسنة. وهذا بالتأكيد ليس مسألة استخدام الفقراء كفئران تجارب، ولكن لضمان أن الفقراء قادرون على الحصول على التكنولوجيا التي ثبت أنها آمنة ومقبولة ومفيدة على نحو واسع في معظم أنحاء العالمين النامي والمتقدم. ونحن لا يمكن أن نكون متخوفين من المخاطر حيال العلم والتكنولوجيا (والمخاطر النابعة من الغذاء والزراعة) أكثر مما نراه مقبولاً في حياتنا اليومية.

ولا تختلف المخاطر الافتراضية المرتبطة بالهندسة الوراثية للمحاصيل عن هذه المرتبطة بالأمثلة الأخرى لاستخدام تلك التكنولوجيا الجينية في الكائنات الأخرى (مثل المستخدمة في التكنولوجيا الحيوية الطبية أو الإنزيمات المدعمة بهذه التكنولوجيا المستخدمة في تصنيع الجبن أو الخمر). ويمكن دراسة واستبعاد المخاطر قصيرة الأجل التي تنجم عن وجود منتجات سامة أو مسببة للحساسية من تنوعات المحاصيل الجديدة، وهو إجراء أكثر احترازًا مما هو معمول به في حالة المحاصيل التي تنتجها الزراعة التقليدية. وبالنسبة للعواقب طويلة الأجل، يوضح الفهم الحالي للتطور الجزيئي كما هو في المعدلات المتدنية في الطبيعة من خلال زيادة التنوع الجيني تلقائيًّا أن التعديلات الجينية التي أصبحت جينومًا قد تسير وفق الاستراتيجيات الطبيعية المدروسة جيدًا للنشوء البيولوجي. ويصبح ذلك واضحًا إذا وضعنا في الاعتبار أن جينوم النباتات الأرضية مثلها مثل الموسوعات الكبيرة بها مئات الأجزاء، بينما تؤثر التعديلات الجينية التي تستخدم التقنيات الحديثة في جين أو اثنين فقط من بين حوالي 26,000 جين في الجينوم النباتي العادي. ولذلك، لا يمكن أن تكون المخاطر النشوئية المحتملة لعمليات الهندسة الوراثية أكبر من مخاطر العملية الطبيعية للنشوء البيولوجي أو استخدام التعديل الجيني الكيميائي، وكلاهما مسئول عن إيجاد درجات موسعة وضعيفة من التغير الجيني. وتوضح السجلات الإحصائية أن الآثار غير المرغوبة لهذا التغير الجيني نادرةً للغاية وفي حالة الاستزراع التقليدي غير موجودة.

وفي ضوء التطورات في الفهم العلمي منذ تبني بروتوكول قرطاجنة حول الأمن الحيوي في عام 2000، حان الآن وقت إعادة تقييم البروتوكول في ضوء الفهم العلمي للحاجات التنظيمية والفوائد.

الإيمان والمنطق العلمي والأخلاق:

في سياق ديني وأخلاقي، لمفهوم "المصير العالمي لخير الأرض"[1] المُطبق في مجال التكنولوجيا الحيوية تبعات للجميع. فأصناف المحاصيل المعالجة بالهندسة الوراثية لا تختلف من أي جانب ملموس عن تلك التي تم إنتاجها بطرق أخرى؛ فهي لا تمثل خطرًا مثبتًا أو محتملاً على الصحة أو البيئة. ومن ثم، فلا يوجد منطق وراء رؤية تطبيق تقنيات النقل الجيني في تحسين المحاصيل على إنه مخالف لقوانين الطبيعة التي وضعها الخالق سبحانه.

بالنسبة للمؤمن، فإن نقطة الانطلاق في الرؤية المسيحية هي التمسك بالأصل الإلهي للإنسان، وذلك قبل كل شيء بسبب روحه التي تشرح الحق الذي أعطاه الله للإنسان كي يحكم عالم المخلوقات الحية بأسره على وجه الأرض من خلال العمل الذي يكرِّسون له قوة أجسامهم مهتدين بنور الروح. وبهذه الطريقة، يصبح البشر خدامًا لله من خلال تعديل الكائنات الطبيعية التي يمكن من خلالها أن يحصلوا على الغذاء عبر تطبيق أساليب التحسين[8]. وبذلك، بالرغم من الأعمال المحدودة للبشر في الكون اللانهائي، فإنهم يشاركون في قدرة الله وهم قادرون على بناء هذا العالم، أي في البيئة المناسبة لحياتهم الجسدية والروحية المزدوجة ومعيشتهم ونمائهم. ومن ثم لا يجب النظر إلى الأشكال البشرية الجديدة للتدخل في العالم الطبيعي كمناقضة للقانون الطبيعي الذي منحه الله للخلق. والحق أنه، كما قال بولس السادس للأكاديمية البابوية للعلوم في عام 1975[9]: "إن العالم لا بد وأن يفكر بصدق في مسألة مستقبل الجنس البشري على الأرض، وبوصفه شخصًا مسئولاً، أن يساعد في إعداده والحفاظ عليه والتخلص من المخاطر. ولذلك، علينا أن نعبر عن تضامننا مع الأجيال الحالية والمستقبلية كشكل من أشكال الحب والخير المسيحي. ومن ناحية أخرى، على العالم أيضًا أن يصدر عن الثقة بأن الطبيعة لديها أسرار في جعبتها وعلى الذكاء البشري أن يكتشفها ويستغلها حتى يحقق مستوى من التنمية قدره الخالق من قبل. ومن ثم، يجب النظر إلى التدخل العلمي كنمو للطبيعة الملموسة أو النباتية/ الحيوانية من أجل صالح الحياة البشرية بنفس الأسلوب الذي "قد تمت به إضافة العديد من الأمور لصالح الحياة البشرية إلى القانون الطبيعي من خلال القانون الإلهي والقوانين البشرية. [10]

التوصيات:

1. توفير المعلومات الموثقة للمنظمين والمزارعين والمنتجين حول العالم حتى يتسنى لهم اتخاذ قرارات منطقية بناءً على معلومات حديثة ومعرفة بكل جوانب إدارة المزارع لتحقيق الاستدامة والإنتاجية.
2. معايرة ومنطَقَة المبادئ المتضمنة في تقييم التنوعات المحصولية الجديدة وإجازتها (سواءً أكان منتجها هي الكاشفات التقليدية أم تقنيات التعديل الوراثي) على نحو عالمي حتى تصبح قائمةً على أساس علمي وعلى أساس المخاطرة ويمكن التنبؤ بها وتتسم بالشفافية. إنه من الضروري أن يكون مجال ما هو خاضع للدراسة حالة بحالة ذي أهمية تضاهي عملية الدراسة ذاتها.
3. إعادة تقييم استخدام المبدأ الاحترازي في الزراعة وإعادة تأطيره علميًّا وعمليًّا وجعل المتطلبات التنظيمية وإجراءاتها متناسبة مع المخاطرة، وإعادة النظر في المخاطر المرتبطة بغياب الفعل[11]. لابد من الأخذ في الحسبان أن الحرص هو الحكمة العملية التي يهتدي بها العمل. وعلى الرغم من أن هذه الحكمة العملية أو الحرص تحتاج إلى الاحتراز من أجل السيطرة على الخير وتجنب الشر، فإن المكون الرئيسي للحرص ليس

الاحتراز بل التنبؤ. ويعني ذلك أن الملمح الأولي للحرص ليس البعد عن العمل من أجل تجنب الضرر، بل استخدام التنبؤ العلمي كأساس للعمل.[12] وبذلك، في خطابه في الأكاديمية البابوية للعلوم بمناسبة الجلسة مكتملة الأعضاء حول "القدرة على التنبؤ في العلم" عام 2006، أكد البابا بنيديكت السادس عشر أن إمكانية التنبؤ هي أحد الأسباب الرئيسية في الهيبة التي يتمتع بها العلم في المجتمع المعاصر وأن ابتكار الأسلوب العلمي قد أعطى العلم القدرة على التنبؤ بالظواهر ودراستها ومن ثم السيطرة على البيئة التي يعيش فيها البشر. ويؤكد البابا بنيديكت: "إننا نستطيع أن نقول إن التنبؤ، والتحكم والسيطرة على الطبيعة، والذي حوله العلم إلى أمر عملي أكثر من الماضي، هو نفسه جزء من خطة الخالق." [13]

4. تقييم بروتوكول قرطاجنة، وهو اتفاقية دولية تنظم توزيع أنواع المحاصيل المعدلة وراثيًّا في المناطق المختلفة. وقد تمت صياغته في ضوء النقص في المعلومات التي كانت متاحة حول علم المحاصيل المعدلة وراثيًّا أقل، وذلك لضمان تماشي التوزيع مع الفهم العلمي الحالي.
5. التوصل إلى تقنيات مجانية للتعديل الوراثي، وهي التقنيات الحديثة والدقيقة والمتوقعة للتحسين الجيني، من خلال التنظيم غير العلمي الصارم، مما يسمح لها بالتطبيق لدعم الجودة الغذائية وإنتاجية المحاصيل (وفي النهاية إنتاج الأمصال وغيرها من المواد الصيدلانية) في كل مكان.
6. تعزيز إمكانيات العلم لمساعدة صغار المزارعين من خلال التمويل الكافي للبحوث وبناء الطاقات والتدريب المرتبط بالسياسة العامة الملائمة.
7. تشجيع التبني الواسع للممارسات الزراعية المستدامة والإنتاجية المناسبة والمرافق التابعة لها، والتي هي ضرورية للغاية لتحسين حياة الفقراء والمعوزين في جميع أنحاء العالم.
8. لضمان أن يكون التعديل الوراثي مناسبًا، وأن الزراعة بالكاشفات مستخدمة لتحسين مستوى المحاصيل المزروعة في الدول غير الآمنة غذائيًّا والفقيرة، حيث يمكن التنبؤ بأن لها تأثيرًا مهمًّا في تحسين السلامة الغذائية، فإننا نحث الحكومات ووكالات الإغاثة الدولية والمؤسسات الخيرية على زيادة التمويل في هذا المجال. وفي ضوء هذا الإلحاح، فإنه يقع على عاتق المنظمات الدولية مثل الفاو والمجموعة الاستشارية للبحوث الزراعية الدولية (CGIAR) وبرنامج الأمم المتحدة الإنمائي واليونسكو مسئولية أخلاقية لضمان سلامة الغذاء لسكان الأرض حاليًّا ومستقبلاً. عليهم أن يستخدموا كل طاقاتهم للتوسط في إقامة علاقات تعاونية بين القطاعين العام والخاص لضمان الاستغلال المجاني لهذه التقنيات لما فيه خير الجميع للنهوض بالعالم.[14]

معلومات أساسية:

تم تنظيم أسبوع البحث العلمي للأكاديمية البابوية للعلوم من 15 إلى 19 مايو 2009 بالنيابة عن الأكاديمية البابوية للعلوم، من جانب البروفيسور عضو الأكاديمية إنجو بوتروكس، بدعمٍ من عضوَي الأكاديمية البروفيسور ورنر أربر والبروفيسور بيتر رافن. وقد كان المنظمون يعلمون أنه منذ عام 2000، عندما نشرت

الأكاديمية دراسة مسبقة عن "النباتات المعدلة وراثيًا لأغراض الغذاء لمكافحة الجوع في العالم"، تراكمت العديد من الأدلة والخبرات حول المحاصيل المعدلة وراثيًا.

ولذلك، كان هدف هذا الأسبوع هو تقييم فوائد ومخاطر الهندسة الوراثية وغيرها من الممارسات الزراعية على أساس المعرفة العلمية الحالية وتطبيقاتها الممكنة لتحسين سلامة الغذاء وتحقيق الرخاء الإنساني حول العالم في سياق التنمية المستدامة. ولقد كان المشاركون أيضًا على وعي بأن التعاليم الاجتماعية للكنيسة حول البيوتكنولوجيا والالتزام الأخلاقي المقبول حول التركيز على التطبيق المسئول للهندسة الوراثية وفق مبادئ العدالة الاجتماعية.

وكانت المشاركة من خلال دعوة رسمية فقط، وتم اختيار المشاركين بناءً على تميزهم العلمي في مجالاتهم وانخراطهم في البحث العلمي والعدالة الاجتماعية. وكان على المنظمين أن يختاروا المشاركين، ولقد بنوا اختيارهم على الحاجة إلى دعم الغرض الرئيسي للقاء، الذي كان متركزًا في استعراض آخر الخبرات لدى المشاركين، فقد اتفق الجميع على المبادئ العامة المتضمنة في هذا التقرير.

وفيما يلي قائمة بالمشاركين ودرجاتهم العلمية مرتبة ترتيبًا أبجديًّا:

أعضاء الأكاديمية البابوية للعلوم:

- البروفيسور ورنر آربر – سويسرا، جامعة بازل: الميكروبيولوجيا والنشوء والارتقاء.
- البروفيسور نيكولا كابيبو — إيطاليا، روما، رئيس الأكاديمية البابوية للعلوم: الفيزياء.
- الكاردينال جورج كوتييه، مدينة الفاتيكان: اللاهوت.
- البروفيسور إنجو بوتريكوس– سويسرا، زيوريخ، أستاذ متفرغ بالمعهد السويسري الفيدرالي للتكنولوجيا: بيولوجيا النباتات والبيوتكنولوجيا الزراعية.
- البروفيسور بيتر رافن – الولايات المتحدة، سانت لويس، رئيس المشتل العلمي بولاية ميسوري: علم النبات وعلم البيئة.
- المونسينيور مارسيللو سانشيز سوروندو — مدينة الفاتيكان، مستشار الأكاديمية البابوية للعلوم: الفلسفة.
- البروفيسور رافاييل فيكونا – تشيلي، الجامعة الكاثوليكية بتشيلي: الميكروبيولوجيا، مبحث الجينات الجزيئية.

خبراء خارجيون:

- البروفيسور كلاوس أمان – سويسرا، جامعة برن: علم النبات، بيئة النباتات
- البروفيسور كيم آندرسون– أستراليا، جامعة أديليد، مركز أبحاث السياسات والاقتصاد (CEPR) والبنك الدولي: اقتصاديات التنمية الزراعية، والاقتصاد الدولي.
- الدكتور آندرو آبل – الولايات المتحدة، رئيس تحرير "GMObelus": القانون
- البروفيسور ورنر آربر – سويسرا، جامعة باسيل.

- البروفيسور روجر بيتشي – الولايات المتحدة، سانت لويس، مركز دونالد دانفورث العلمي للنباتات، وحاليًا بالمعهد القومي للأغذية والزراعة (NIFA)، واشنطن العاصمة.
- البروفيسور بيتر باير – ألمانيا، فريبورج، جامعة آلبرت لودفيج، فرايبرج: الكيمياء الحيوية، المسارات الاستقلابية.
- البروفيسور خواكيم فون براون – الولايات المتحدة، واشنطن العاصمة، مدير عام المعهد الدولي لبحوث سياسات الغذاء، وحاليًا بجامعة بون، مركز الأبحاث التنموية (ZEF): اقتصاديات الزراعة والتنمية.
-– الدكتور مويزيس بوراتشيك – الأرجنتين، بوينس أيريس، المنسق العام لقسم البيوتكنولوجيا: البيوتكنولوجيا الزراعية، والأمن الحيوي.
- البروفيسور بروس تشاسي – الولايات المتحدة، جامعة إلينوي في إيربانا شامبين: الكيمياء الحيوية والأمن الغذائي
- البروفيسور نينا فيدرروف – الولايات المتحدة، جامعة ولاية بنسلفانيا، البيولوجيا الحيوية والتكنولوجيا الحيوية
- البروفيسور ديك فلافيل – الولايات المتحدة، شركة ديك فلافيل – الولايات المتحدة، شركة "CERES".
- البروفيسور جوناثان جريسل – إسرائيل، معهد وايزمان للعلوم.
- البروفيسور رونالد جي هيرنج – الولايات المتحدة، جامعة كورنيل.
- البروفيسور درو كراشين – الولايات المتحدة، جامعة أوكلاهوما.
- البروفيسور أناتولي كراتيجر – الولايات المتحدة، جامعة كورنيل.
- البروفيسور كريستوفر ليفر – المملكة المتحدة، جامعة أوكسفورد.
- البروفيسور ستيفن بي لونج – الولايات المتحدة، معهد علوم الطاقة.
- البروفيسور كاثي مارتن – المملكة المتحدة، مركز جون أنز، نوريتش.
- البروفيسور مارشال مارتن – الولايات المتحدة، جامعة بردو.
- البروفيسور هنري ميللر – الولايات المتحدة، مؤسسة هوفر، جامعة سانفورد.
- البروفيسور مارك بارون فان مونتاجيو – بلجيكا، رئيس الاتحاد الأوروبي للبيوتكنولوجيا.
- الدكتور بيرو مورانديني – إيطاليا، جامعة ميلان.
- البروفيسور مارتينا نويل– ماكجوغلن – الولايات المتحدة، جامعة كاليفورنيا، ديفيز.
- معالي جورج نكيو – الكاميرون، أسقف كومبو.
- البروفيسور روب بارلبرج – الولايات المتحدة، كلية ويليزلي.
- البروفيسور وايني باروت – الولايات المتحدة، جامعة جورجيا.
- البروفيسور إنجو بوتروكس–سويسرا، أستاذ متفرغ بالمعهد السويسري الفيدرالي للتكنولوجيا.
- البروفيسور سي إس براكش – الولايات المتحدة، جامعة تسكيجي.
- البروفيسور مارتن كايم–ألمانيا، جامعة جورج أوجست في جوتنجن.

- الدكتورة راجافندرا راو – الهند، نيودلهي، قسم البيوتكنولوجيا، مستشار وزارة العلوم والتكنولوجيا: الزراعة وأمراض النبات.
- البروفيسور كونستنتين سكرايبين – روسيا، موسكو، الأكاديمية الروسية للعلوم، مركز "الهندسة الحيوية": البيوتكنولوجيا الجزيئية والبيوتكنولوجيا الزراعية.
- البروفيسور مونكومبو سامباسيفان سواميناثان – الهند، تشيناي، رئيس مجلس مؤسسة إم إي سواميناثان للبحث العلمي: الزراعة والتنمية المستدامة.
- البروفيسور كيارا تونيللي – إيطاليا، جامعة ميلانو: مبحث الجينات والتنظيم الخلوي.
- البروفيسور آلبرت ويل – المملكة المتحدة، مجلس نافيلد للأخلاقيات الحيوية وجامعة إسكس، حاليًا جامعة لندن، قسم العلوم السياسية: العلوم الاجتماعية والسياسية.
- البروفيسور روبرت زايجلر – الفلبين، مترو مانيلا، مدير المعهد الدولي لأبحاث الأرز: البيوتكنولوجيا الزراعية، وأبحاث الأرز والسياسات التنموية.

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(1) انظر رسالة البابا يوحنا بولس الثاني بشأن "مزاولة العمل"، 5، المرجع السابق ذكره، من ص 586 إلى ص 589.

(2) "الخير في الحقيقة"، 69.

(3) "الخير في الحقيقة"، 27.

(4) "هذا مبدأ يجب تركزه في الإنتاج الزراعي ذاته، أينما كانت هناك مسألة التقدم من خلال تطبيق تقنيات البيوتكنولوجيا، وهو ما لا يمكن تقييمه فقط على أساس الفوائد الاقتصادية القريبة. لابد من إخضاعها أولاً للفحص العلمي والأخلاقي المدقق لمنعها من أن تصبح كارثيةً للصحة البشرية ومستقبل الأرض" (يوحنا بولس الثاني، "خطاب يوبيل العالم الزراعي" نوفمبر 2000).

(5) المحاصيل اليتيمة، أو المشار إليها كمهملة أو خاسرة، هي محاصيل ذات قيمة اقتصادية عالية في الدول النامية. وهذه المحاصيل تتضمن الحبوب (مثل التحف والدخن والبقول (مثل اللوبيا واللوبيا الجذرية وحبوب بامبارا، والمحاصيل الجذرية (المنيهوت والبطاطا). وبالرغم من حيوية المحاصيل اليتيمة بالنسبة لحياة الملايين من المزارعين الفقراء، فإن البحث العلمي في هذه المحاصيل متخلف. ولدعم الإنتاجية المحصولية والحصول على الكفاية الغذائية في العالم النامي، يجب توجيه مزيد من الانتباه لهذه المحاصيل.

(6) "العام المائة"، 6.

(7) "الخير في الحقيقة"، 46.

(8) "لله ملك كل شيء، ووفقًا لعنايته، وجه أشياء معينةً لغذاء جسم الإنسان. ولهذا السبب، للإنسان سيطرة طبيعية على الأشياء فيما يخص القدرة على استغلالها" (توماس الأكويني، "اللاهوت الأسمى"ii-ii، ق 66، أ-1، أ وأ).

(9) انظر بولس السادس، خطاب في الجلسة الكاملة لأعضاء الأكاديمية البابوية للعلوم، في 19 إبريل عام 1975، الخطابات البابوية، مدينة الفاتيكان، 2003، ص 209.

(10) القديس توماس الأكويني، "اللاهوت الأسمى"، I-II ، 94، أ-5، انظر 3.

(11) "الحرص هو صفة عقلانية تصل إلى الحقيقة وترتبط بالعمل في علاقته بالأشياء التي فيها خير البشر" (أرسطو، الأخلاق، 1140،5،6،ب 20، الترجمة الإنجليزية لجي بايووتر)، انظر كذلك بقية الفصل.

(12) "التنبؤ هو مبدأ الحرص... ومن ثم هو نفس الاسم الذي اشتق منه الحرص كجزء رئيسي فيه" (القديس توماس الأكويني، "اللاهوت الأسمى"، I-II ، 49، أ-5).

(13) خطاب البابا بنيديكت السادس عشر للجلسة المكتملة الأعضاء للأكاديمية البابوية للعلوم. متاح على الإنترنت:
www.vatican.va/.../benedict_xvi/.../2006/.../hf_ben-xvi_spe_20061106_academy-sciences_en.html -

(14) انظر بي داسجوبتا "العلم كمؤسسة: تحديد الأولويات في السياق الاجتماعي والاقتصادي"، المؤتمر الدولي للعلوم: العلم للقرن الحادي والعشرين، التزام جديد (اليونسكو، باريس،2000).

Head Secretary of the Library of Alexandria ,Hanan Mounir :Translation

罗马教皇科学院研讨会　2009. 5. 15-19 梵蒂冈城

发展背景下转基因作物与粮食安全

2009 年 5 月 15 日至 19 日，罗马教皇科学院在其总部庇护四世别墅举办了主题为“发展浪潮下转基因作物的粮食安全问题”的研讨会，回顾了转基因（GE）植物新品种的最新科学进展，分析了利用转基因技术实现农业改良的社会条件，并且详细阐明了此技术为贫困人口带来的福利。教皇本笃十六世的通谕给予参会人员极大鼓舞，他说：“技术是人类行为的客观方面，而其起源却由于人类本身而具有了主观因素。从这个意义上讲，技术不仅仅只是技术，它揭示了人类发展的强烈愿望和逐渐克服物质局限的内在动力。因此，技术是遵照上帝的旨意去耕耘和保有土地（圣经创世纪，第 2 章第 15 节）(1)，它要依托于人道，服务于人类与环境的和谐共存，反映上帝的造物之爱”。(2)

主要的科学研究结论

2000 年 11 月 10 日至 13 日“科学与人类未来”周年全体会议结束后，发行了一份题为《转基因粮食作物征战饥荒》的研究报告，本次会议上重申了报告中的主要结论，并根据最新情况概述如下：

1. 世界 68 亿人口中超过 10 亿的人口正处于营养不良的困境，因此急需新型的农业系统和技术来解决这一问题；
2. 到 2050 年世界人口将会增加 2～2.5 亿，总人口达到约 9 亿，人口剧增使得第一条中的问题更加严重；
3. 气候变化和农业用水的减少将会影响我们解决粮食问题的能力；
4. 目前的耕种模式是非可持续发展的，例如大量的表层土壤流失、世界范围内大量使用杀虫剂等；
5. 在农业上合理使用转基因和其他现代分子技术可以为解决上述问题提供新思路；
6. 没有任何实质性证据表明利用转基因技术改良作物会造成作物本身或者其产物的“不安全”；
7. 科学界应承担起研究与发展的重任，提高农业生产能力，致力用农业上的增产来使贫困人口获得福利，事实上，目前相对享有较高生活水平的发达国家也可以从中获益；
8. 努力使第三世界的贫困农民获得适合当地条件的转基因作物；
9. 改良作物的研究应着眼于当地需要、作物品种、不同国家的接受能力、社会传统和政府政策，从而能更好地引进转基因作物。

进一步证据

早先的研究文件已得到高质量的同行评议，加之大量的实际经验表明转基因作物已在发展应用之中，并且产生了不小的影响。研讨会中我们回顾相关的内容并得出以下结论：

1. 合理、有目的地使用转基因技术改良作物可为提高农业生产能力做出贡献，包括提高作物产量和营养水平，提高作物抗虫、抗旱或其他逆境的能力。这将促进全球农业生产力的发展并提高其可持续性。
2. 作物和观赏植物的遗传改良中提出了一种逐渐更为精确、可预测的技术，这种技术将形成一个长期的准确无误的连续体系。美国国家研究中心在 1989 年的报告中提到：“随着分子技术的特定化，使用者对转入植物的性状更为确定，并更倾向于使用转基因技术而不是其他无法确定效果的育种手段”。
3. 在广泛种植转基因作物的国家如美国、阿根廷、印度、中国和巴西，其收效十分显著。
4. 转基因作物对资源匮乏农民和农村弱势群体特别是妇女和儿童有重要的意义。种植转基因抗虫棉

花和玉米大量减少了杀虫剂的使用，化学杀虫剂中毒事件因此减少，这不仅提高农业劳动保护，增加作物产量，而且使农民收入增加，同时降低某些发展中国家（如印度、中国、南非和菲律宾）小农地区的贫困比例。

5. 在转基因玉米、大豆、油菜和其他作物中转入最多的是环境友好、低成本除草的基因。这些作物亩产量高，人们不必为繁琐的除草工作担忧，耕作成本减少，同时减少土壤流失。尤其在发展国家，这种转基因技术可以替代传统的人力除草，前景良好。
6. 转基因技术可以通过改良作物使其含有基本微量元素，摄取这种作物可以改善营养不良的状况。生物改造后含有维他命原 A 的“黄金水稻”可以从膳食中向人类提供足量的维他命 A，减少营养不良。
7. 转基因抗虫作物的应用减少了化学杀虫剂的使用，降低某些农业生产成本，改善农民健康状况。这对于大量使用杀虫剂的欧洲国家来说至关重要，因为杀虫剂的使用不仅破坏生态系统也不利于人类健康。
8. 转基因技术可以减少有害的高耗能机械耕种模式，增加生物多样性，保护环境，减少温室气体二氧化碳的排放。
9. 气候变化迫使我们要更加合理有目的地使用转基因和其他育种技术，让全球范围内的主要作物尽快具有抗旱抗涝的功能。
10. 转基因技术的应用使得贫困地区的粮食产量增加，改善了当地耕作者的收入和就业情况。
11. 监督转基因技术的法规政策应当科学、基于风险考虑，也就是说这些法规政策要注重新作物品种的优良性状而不是转入性状的技术手段。
12. 转基因作物的风险评估不仅要考虑新型作物品种种植的潜在风险，也要考虑不种植这种作物品种的风险。
13. 目前许多政府部门加大力度引进转基因改良的木薯、红薯、水稻、玉米、香蕉、高粱和其他热带作物，给贫困人民带来直接福利。对于这种做法我们应该大力支持。
14. 世界人口贫困和营养不良的巨大挑战迫在眉睫，每年由于营养缺乏而引起不少疾病和死亡。最近世界范围内的粮价上涨也反映了穷困人民在资源竞争方面处于劣势，事实上，他们现在若得不到这些资源，将来获取的可能性更是微乎其微。
15. 以上证据表明，大规模使用转基因技术是从人道上帮助贫困人民，让他们的生活水平有所提高，健康状况有所改善，生活环境得到保护。

大体而言，转基因技术的使用彰显其提高世界农业生产力的重要性，然而这只是多方面策略中的一部分。正如本笃十六世所说：“在未来，合理使用新型农业技术可以和传统农业技术相辅相成，而新型技术的使用必须经过严格的审查以保证它们满足贫困人们的需要并且不对环境产生危害”。(3) 尽管如此，不是所有的转基因技术发展都能像它预期的结果一样，这和其他技术的发展没有差别。因此我们必须继续评估所有合理技术的潜在优势，把它们和传统的育种技术结合起来提高粮食安全性、免除子孙后代的贫困。(4) 很多技术可以和转基因技术同时使用，例如非耕作和其他保护措施以保持表层土壤，合理使用肥料，发展新型肥料和环境友好型农业化学产品，害虫防治，节约用水，保护遗传多样性，合理引进作物新品种，通过公私投资与合作改善现有作物特别是广泛应用的“孤儿作物 (5)”。加强第三世界的粮食安全具有十分重要的意义，其他方面的工作包括加强基础设施建设（交通、电力和仓库储备），提供明智且不带偏见的种子挑选意见和推广服务，发展良好的金融和保险系统以及技术产权认证许可系统。世界上许多地区的贫困人口处于贫困和受歧视的境地，这个问题不可能由一个单独的方法来解决，我们利用转基因作物，并让它联合其他的方法来共同解决上述问题。

广泛的公众议论

转基因技术已引起全球公众的广泛关注和讨论，科学技术是否可以解决二十一世纪社会面临的许多健康和粮食相关问题？一方面人们不反对转基因技术的使用，但另一方面它必须经过同行评议或者其他的认证以保证得到合理评估、约束和使用，最终有利于人类。面对问题什么都不做不是一个好的选择，但科学技术也不是像水龙头那样可开可关，可以轻易地解决任何问题。科学的任务是预见可能的危害并尽可能避免，保证最大程度的利益。因此以下六方面需要特别注意：公众对科学的理解，知识产权的归属，政府责任，民间组织的力量，政府、国际机构和民间组织的合作，以及合理、低成本、公正的法规监督。

公众对科学的理解

本次研讨会的成员多次指出在公众讨论和行政法规中人们对转基因技术的误解，比如公众讨论中很容易忽视一点：所有涉及遗传修饰的作物育种，如“传统育种”中利用辐射诱变的手段，跟转基因技术相比其实质上结果预知的程度大为降低。

所有与会人员承诺他们会在公众对话中给民众提供大量的信息让他们正确了解转基因技术。科学研究者们需要广纳意见，阐明他们的研究和技术，使他们的研究结论能够广泛应用于实际。一些人反对或怀疑转基因作物及使用现代遗传手段，我们强烈要求他们认真评估这些技术中的科学因素，进而阻止那些急需转基因技术的群体因得不到此种技术而造成的危害。公众讨论只有建立在高水平的科学证据和民事法规观念改变的基础上，公共利益才能发挥到极致。

知识产权归属

在发展任何一种技术的过程中，包括医药、农业技术以及现代社会的各个层面，知识产权起到了重要作用。金融部门为减少贫困和粮食风险做出了不可估量的贡献。然而，正如教会社会思想中以追求全人类的福利作为人类共同目标 (6)，我们希望政府和私人机构对于他们知识产权的要求能够尽可能地从属于上面提到的共同目标，而不应该造成剥削他人和弱势群体以及非法致富的情况。

发展中国家发展和推广转基因作物品种主要依靠公私合作，“黄金水稻”工程就是一个很好的例子，私人机构把知识产权无偿转移给政府部门以引进黄金水稻，给当地民众带来福利。还有一些相似的计划也在进行之中，这正反映了人民要求享有人类成果的合理愿望。我们应该鼓励私人机构把享有知识产权的技术成果无偿推广，并对他们这种高尚的道德加以赞扬。

由此，每一个私有公司特别是跨国公司在涉及商业和道德的关系时，不应该仅仅考虑经济利益，而要把人民、文化和教育价值放在首位。所以，《真理之仁爱》通谕赞同最近出现的“公民经济”和“共享经济”的说法，即不排除谋取利益，但只把它作为一种满足人类和社会需求的手段，通谕也强调“这种混合型商业模式促发了更加文明、竞争的市场 (7)”。

公共部门的责任

二十世纪绿色革命中新型作物品种的研发主要依靠公共部门及其研究机构的力量，虽然现今公共部门已不再是推动发展的主导力量，但它们的作用还是不可估量的。特别是公共部门可以从国家税收和募捐机构筹集资金，研发相关的作物品种，帮助极度贫困的人口和弱势群体。它们可以推广研究成果商业化，而这对于私有机构来说绝非易事。既然公私合作已经在许多科学技术的应用方面特别是公众医疗中取得成功，那么在农业方面的应用也不应该是例外。但是我们要意识到，在利用现代生物技术改良作物的过程中，一些非科学且过度的规章制度提高了生物技术研发的成本，不但没有解决安全性问题，而且增加了公共部门推广其应用的难度。

民间组织的力量

政府部门、学术团体、非政府组织、慈善机构、民间组织和宗教团体有责任让民众了解科学技术能够造福人类，同时要致力于改善不幸人群生活的各个方面，确保他们接受现代科学的福利，保

护他们免受任何目的的剥削，远离贫穷、疾病和粮食风险。

政府部门、国际组织和民间组织的合作

事实证明，转基因技术已在作物改良和粮食安全方面取得了显著成效，在作物育种过程中，联合使用转基因技术和其他分子技术为将来第三世界主要经济作物和“孤儿作物”的发展提供了可能性。应用这种科学上的发展进步将会带来全球公众利益。

应用转基因技术研发改良作物的成本较高，而且受到法律法规的限制其投放入市场也需要大量资金，因此主要是一些跨国公司承担转基因技术的研发应用，研究对象也只是发达国家中的主要作物，那些具有公共利益的作物育种主要受到以下两方面的制约：

1. 大量的资金需求和国家政府投资缺乏，导致无法应用转基因技术改良当地作物，例如高粱、木薯和大蕉等等，这些作物由于不在世界范围内贸易而不被跨国公司投资研发。
2. 过度非必要的法规政策使转基因技术应用于这些非主要作物的费用过于昂贵，这就使得投资和风险承担的差距过大。

因此，这就需要政府部门、国际机构、援助机构和慈善机构的通力合作。当跨国机构愿意与政府部门协商合作，把具有知识产权的技术无偿用于作物改良，那么这将会带来潜在效益，例如在应用于亚洲的“黄金水稻”，非洲的抗旱玉米，印度和非洲的抗虫蔬菜和豆类，以及非洲、亚洲、南美洲的许多项目。

制定有效的法规政策

实现任何一项新技术的价值都需要一种合适有效的方法来加以控制。发达国家发展起来的管理政策过于苛刻，几乎只关注转基因粮食作物将会带来的风险，这一管理方式无形中遏制了发展中国家以及小规模生产者、零售商的发展，使得世界上穷苦的人们被迫处于不利地位。如果不去利用这种更精确、结果可预知的生产技术，那么带来的危害将是不可逆转的；也就是说资金投入、研发和产品（和它们带来的利益）的机会成本是不能被补偿的。

我们应该评估新作物品种的性状而不是生产这些新品种的技术：即评价它们的实际特点性状。通过投放性状改良的主要作物和地方作物的新品种，转基因技术的开发潜力将大为提升，最终实现全民利益。而在使用转基因技术的过程中，贫穷国家绝不是实验对象，只是让他们有机会利用这些已经在大多数发达国家和发展中国家证明是安全的、广泛接受的和有效益的技术。不相信科学技术的力量其实会给食品和农业带来更大的风险，这比我们日常生活中看似安全的事情更具风险。

在粮食作物和其他生物体中应用转基因技术所带来的的风险没有什么区别（比如，生物技术医药或者在奶酪和啤酒生产中添加生物技术改造过的酶）。新的作物品种中有毒性或过敏性的副产物所带来的短期风险可以通过研究去除，这比传统育种选育的作物品种更具有预测性。按照目前对分子进化的理解：遗传突变是长期进化中自发性的低频率事件，而我们对基因组的改造技术必须遵照生物进化的自然法则，一步一个脚印的工作才能实现真正意义上的基因改造。打个比方来说：陆地植物的基因组就像好几百本大百科全书，而运用现代基因工程技术的基因改造只影响到了植物基因组 26,000 基因中的一个或很少几个基因。因此，基因工程带来的可能进化风险并不会比自然突变或化学诱变带来风险更大，后两者都会导致基因产生大量不良的突变。统计数据显示这种遗传变化的不良后果是非常稀少的，在传统育种中也不会被选择。

自从 2000 年签署《卡塔赫纳生物安全议定书》后，随着科学认识的不断发展，我们现在应该科学理解管理需求和利益，重新评估该协议。

信念，科学理性和道德规范

对于一个信仰者而言，追寻基督教教义的要点就是支持人的神圣起源即灵魂，灵魂通过支配人类的躯体去辛勤劳作，以完成上帝赋予人类的使命——统治地球上整个生物界。这样说来，人类是

上帝的管理者，通过改进方法的应用，发展和改造自然万物从中获得食物 (8)。因此，虽然人类的活动限制在无限的宇宙之中，但他们拥有上帝的力量，能够建造物质和精神的双重世界，以适于他们的生存和福利。因此，人类对自然界的介入不应该对立于上帝赋予生物的自然法则，正如保罗六世 1975 年对罗马教皇科学院所说的 (9)，一方面，科学家必须认真思考地球人类的未来问题，作为一个负责的人，科学家们应该为将来做好准备，保护生存环境为人类谋福利，并且消除可能的风险，这就需要我们心怀仁爱和子孙后代共同努力；另一方面，科学家亦必须充满信心，用智慧去发现和利用自然界的奥秘，以便达到造物主计划的发展水平。自然或是动植物原本就具有为人类生活服务的本性，因此，科学的介入只是建立在这一基础之上，同时“为人类生活带来利益的许多事物都已经被加入自然法则（神律和法律 (10)）。”

建议

1. 给全世界管理者、农民和生产者提供可靠信息，让他们了解农业生产发展管理的全方位最新信息，以便他们能够做出合理的决策。
2. 在评估和批准新的作物品种时采用标准化、理性化的普遍性原则（无论是传统育种、分子标记辅助育种或者基因工程技术），保证评估是建立在科学、风险有据以及结果可预知的基础上。逐个案例考察与实际自身考察是同等重要的，它必须也是科学的且有风险根据的。
3. 重新评价农业预防原则的应用，科学且实际的重新制定这一评价系统并且使管理需求和程序与风险成比例，还要考虑与执行不利相关的风险。切记谨慎是实践的智慧，谨慎应该指导行动 (11)。尽管这个实践的智慧或者说是谨慎需要预防措施，以便抓住有利的一面避免有害的一面，但谨慎的主要组成部分不是预防措施而是预测。这意味着谨慎的主要特点不是要限制行为来避免伤害而是利用科学的预测作为行动的基础 (12)。 因此，本笃十六世在 2006 年罗马教皇科学研究院全体会议上发表的《科学的预测性》中强调，预测性是科学在当今社会上享有声誉的主要原因，科学方法能够预测现象，通过研究这些现象的发展，维护人类的生活环境在我们的控制能力之内。本笃十六世说：“事实上我们可以认为，预测、控制以及管理自然的工作比过去更为实际，它们本身就是造物者旨意的一部分（13）。”
4. 评估《卡塔赫纳生物安全议定书》，确保它和现今的科学理解一致（《卡塔赫纳生物安全议定书》是一份约束转基因作物全球贸易的国际约定，制定之时人们对转基因还没有太多的了解）。
5. 最为现代化、精准、结果可预知的转基因技术若可以无偿使用，则可以提高作物产量，增加作物营养水平（也可用于生产疫苗和药物）。
6. 通过获得足够的研究资金、加强能力建设和采取合适的政府政策提升转基因技术的潜力，帮助世界各地的小农。
7. 鼓励那些可持续、健全、有效的农业行为和推广服务，这对于改善全球贫困人口的生活至关重要。
8. 为了保证合适的转基因技术和分子标记辅助育种技术能够在粮食缺乏的贫困国家应用，以改良相关作物解决粮食安全问题，我们强烈要求政府部门、国际救援机构和慈善机构在这方面增加投入。类似于联合国粮农组织、国际农业研究磋商小组、联合国开发计划署和联合国教科文组织的机构在道义上应该保证当代和未来世界人口的粮食安全，竭尽全力促进公私合作，确保转基因技术的无偿使用，给予第三世界最大的公共利益（14）。

背景

2009 年 5 月 15 日至 19 日的研讨会由罗马教皇科学院主办，科学院成员英格 • 包崔克斯教授组织，并得到了沃纳 • 亚伯教授和彼得 • 雷文教授的支持。组织者知道自从 2000 年以来，即科学院《转基因粮食作物征战饥荒》的报告发表后，转基因作物已经积累了大量的证据和事实经验。

因此，本次研讨会的目的一方面是以科学知识为基础，评估转基因技术和其他农业手段的效益与风险，另一方面是在可持续发展背景下，分析利用转基因技术确保粮食安全并提高全人类福利的

潜力。与会人员同样意识到教会对生物技术的社会教化作用，并且接受在社会公正前提下推广转基因技术的道德使命。

承办方根据各个专家在其各自科研领域的贡献、科学作风和社会公信力来挑选与会人员，挑选之后邀请条件符合的专家参加研讨会，目的在于了解、交流最新的科学进展。虽然大家各抒己见，但都同意这份文件中的主要观点。

补充：

植物育种过程中涉及很多的专业术语。一切活体生物由细胞组成，细胞中含有它们的基因，而基因决定了生物个体的特殊性状。整套基因（基因型）由 DNA 编码，也称为基因组，亲代通过基因把遗传信息传递到子代。所有的植物育种包括进化，涉及遗传变异或者修饰，之后在子代中筛选优良特性。大多数植物表型或可见性状的改变，例如形态结构、发育过程、化学物质或营养物质组成等，都是因为基因的改变。传统植物育种采用近缘生殖非隔离的品种进行随机杂交，这种方式只会获得不确定的结果和未知的遗传改变。二十世纪中叶出现诱变育种，即使用化学诱变剂或者高能辐射随机处理种子或整株植物，以获得表型改良，而这种方法同样也只能获得无法预知的遗传改变。最近发展出可以转入特定良好性状基因（或具有特定性状的一组基因）的技术，同时可以详细分析其基因和表型改变，这种新型的技术被称为“转基因”（因为基因是从一个供体转移到另一个受体）或“基因工程”，实际上，这个术语适用于所用的育种进程。

参会人员名单（后附其研究领域，按姓氏的字母顺序排列）

罗马皇家科学院成员：

Werner Arber 教授，瑞士，University of Basel：微生物学，进化学。

Nicola Cabibbo 教授，罗马，President Pontifical Academy of Sciences：物理学。

Georges Cottier 枢机主教，梵蒂冈：神学。

Ingo Potrykus 教授，瑞士，Swiss Federal Institute of Technology：植物生物学，农业生物技术。（退休）

Peter H. Raven 教授，美国，President Missouri Botanical Garden：植物学，生态学。

Marcelo Sánchez Sorondo 教士，梵蒂冈，Chancellor Pontifical Academy of Sciences：哲学。

Rafael Vicuña 教授，智利，Pontifical Catholic University of Chile：微生物学，分子遗传学。

其他专家：

Klaus Ammann 教授，瑞士，University of Bern，土耳其，伊斯坦布尔：植物学，生态学。

Kym Anderson 教授，澳大利亚，The University of Adelaide, CEPR and World Bank：农业发展经济学，国际经济学。

Andrew Apel 博士，美国，Editor in Chief of GMObelus：哲学，法学。

Roger Beachy 教授，美国，Donald Danforth Plant Science Center, now NIVA, National Institute of Food and Agriculture, Washington DC.,：植物病理学，农业生物技术。

Peter Beyer 教授，德国，Albert-Ludwig University, Freiburg，弗莱堡：生物化学，生理代谢途径。

Joachim von Braun 教授，美国，Director General, International Food Policy Research Institute now University of Bonn, Center for Development Research (ZEF), Agricultural and Development Economics.：农业与发展经济学。

Moisés Burachik 博士，阿根廷，General Coordinator of the Biotechnology Department：农业生物技术，生物安全。

Bruce Chassy 教授，美国，University of Illinois at Urbana-Champaign：生物化学，食品安全。

Nina Fedoroff 教授，美国，The Pennsylvania State University：分子生物学，生物技术。

Dick Flavell 教授，美国，CERES, Inc.：农业生物技术，遗传学。

Jonathan Gressel 教授，以色列 Weizmann Institute of Science：植物保护，生物安全。

Ronald J. Herring 教授，美国，Cornell University：政治经济学。

Drew Kershen 教授，美国，University of Oklahoma：农业法，农业生物技术。

Anatole Krattiger 教授，美国，Cornell University and Arizona State University：知识产权管理。

Christopher Leaver 教授，英国，University of Oxford：植物科学，植物分子生物学。

Stephen P. Long 教授，美国，Energy Science Institute：植物生物学，作物科学，生态学。

Cathie Martin 教授，英国，John Innes Centre，诺里奇：植物科学，细胞调控。

Marshall Martin 教授，美国 Purdue University：农业经济学，技术评估。

Henry Miller 教授，美国，Hoover Institution, Stanford University：生物技术，政策研究。

Marc Baron Van Montagu 教授，比利时，President European Federation of Biotechnology：微生物学，农业生物技术。

Piero Morandini 博士，意大利，University of Milan：分子生物学，农业生物技术。

Martina Newell-McGloughlin 教授，美国，University of California, Davis：农业生物技术。
George Nkuo 教士，喀麦隆，Bishop of Kumbo：神学。
Rob Paarlberg 教授，美国，Wellesley College：政治学。
Wayne Parrott 教授，美国，University of Georgia：农学，农业生物技术。
Channapatna S. Prakash 教授，美国，Tuskegee University：遗传学，农业生物技术。
Matin Qaim 教授，德国，Georg-August University of Göttingen：农业经济学，发展经济学。
Raghavendra Rao 博士，印度，Department of Biotechnology, Ministry of Science and Technology：农学，植物病理学。
Konstantin Skryabin 教授，俄罗斯，'Bioengineering' Centre Russian Academy of Sciences：分子生物学，农业生物技术。
Monkumbu Sambasivan Swaminathan 教授，印度，Chairman, M.S. Swaminathan Research Foundation：农学，可持续发展学。
Chiara Tonelli 教授，意大利，University of Milan：遗传学，细胞调控。
Albert Weale 教授，英国，Nuffield Council on Bioethics and University of Essex, now University College of London, Dept. of Political Sciences：社会政治科学。
Robert Zeigler 教授，菲律宾，Director General International Rice Research Institute：农学，植物病理学。

1) 罗马教皇约翰保罗二世，通谕《论人的工作》，5: *loc. cit.*, 586-589
2) 《真理之仁爱》，§ 69
3) 《真理之仁爱》，§ 27
4) 这是农业生产本身的原则，每当我们考虑生物技术的使用时，不能光从其快速的经济效益来评估，而应该以严格的科学和道德标准来检验
而应该以严格的科学和道德标准来检验，以免使其成为人类健康和未来世界的灾难。（约翰保罗二世，《致农业世界周年会议的一封信》，2000 年 11 月）
5) 孤儿作物，又称为被忽视或遗失作物，即在发展中国家有极高经济效益的作物品。包括谷类的黍米、画眉草，豆类的豇豆、草豆和班巴拉花生，根类的木薯和红薯。孤儿作物是资源贫困人口的日常粮食来源，但对于这些作物的研究却远远落后于其他的主要作物，为了加强第三世界的作物生产率，提高粮食自给自足的能力，应在孤儿作物的研究中投入更多力量。
6) 《百年献辞》§ 6
7) 《真理之仁爱》§ 46

8)　“上帝是一切事物至高无上的统治者，他指定某些东西作为人类摄入的食物。因此，人类天生具有支配万物的权利，通过这种权利来利用万物。”（托马斯•阿奎奈，《神学总纲》II-II, q. 66, a. 1 ad 1）
9)　保罗六世，《致罗马教皇科学院 1975 年全体会议》，1975 年 4 月 19 日，梵蒂冈 2003，p.209。
10) St•托马斯•阿奎奈，《神学总纲》I-II, 94, a.5. Cf. *loc. cit.* ad 3
11)　“谨慎（phronesis）是获得真理的理性行为，与对人类有利的行为相关”（亚里士多德，《尼各马可伦理学》VI, 5, 1140 b 20, Eng. tr. J. Bywater）
12)　“预测是谨慎的原则，因此谨慎就是从预测的重要部分中提取出来的名字”（St..托马斯•阿奎奈，《神学总纲》II-II, q. 49, a. 6 ad 1）
13）　本笃十六世在罗马教皇科学院全体大会上的讲话：http://www.vatican.va/holy-father/benedict_xvi/speeches/2006/november/documents/hf_ben-xvi_spec_20061106_academy-sciences_en.html

14）P. 达斯古普拉，“科学制度：在新的社会经济学背景下建立优先权“*世界科学大会：二十一世纪的科学，新义务*（联合国教科文组织，巴黎，2000）

Translations facilitated through Clive James, and Mariechel Navarro,
the International Service for the Acquisition of Agri-biotech Applications (ISAAA)

<u>संवर्धन के संदर्भ में खाद्य सुरक्षा के लिए पारजीनी पादप</u>

''संवर्धन के संदर्भ में खाद्य सुरक्षा के लिए पारजीनी पादप'' इस विषय पर ''पॉन्टिफिकल अकादमी ऑफ साइंसस'' के प्रायोजन के अंतर्गत अकादमी में 15 से 19 मई 2009 को एक अध्ययन सप्ताह का आयोजन किया गया था । इस बैठक के दौरान हमने आनुवंशिकतः अभियंत्रित (GE) पादपों की नई विधाओं को वैज्ञानिक दृष्टि से समझने में जो अधुनातन वृद्धि हुई है, उसका सर्वेक्षण किया और सामाजिक स्थितियों की भी चर्चा की जिसमें GE प्रौद्योगिकी को सामान्यतः कृषि के विकास के लिए और विशेषतः गरीब तथा दुर्बल वर्ग के हित के लिए प्राप्त कराया जा सके ।

<u>प्रमुख वैज्ञानिक निष्कर्ष</u>

10-13 नवंबर 2000 को ''विज्ञान और मानव जाति का भविष्य'' पर संपन्न संपूर्ण सत्र के अंत में दिये गये ''विश्व में भूख मिटाने के लिए आनुवंशिकतः रूपांतरित खाद्य पादपों की उपयोगिता ''संबंधी अध्ययन-दस्तावेज़ के मुख्य निष्कर्षों को हम पुनर्स्वीकार करते हैं ।

इसमें अद्यतन विवरण सम्मिलित है -

1. 6.8 अरब विश्व की जनसंख्या में से एक अरब से अधिक लोग फिलहाल अपोषित हैं । ऐसी स्थिति में नयी कृषि व्यवस्था तथा तकनीकी की अभिवृद्धि अत्यावश्यक है ।

2. अपेक्षित 2-2.5 अरब लोगों की वृद्धि होकर 2050 तक लगभग कुल 9 अरब होने की संभावना है जो इस समस्या को और गंभीर बनाती है ।

3. जलवायु-परिवर्तन के अनुमानित परिणामों के साथ-साथ कृषि के लिए जल प्राप्ति में कमी के कारण विश्व की बढ़ती जनसंख्या को खिलाने की हमारी सामर्थ्य को धक्का पहुँचेगा ।

4. विश्व-भर में आजकल की कृषि पद्धति अप्रतिपालित है, जो शीर्षमृदा के बृहत् घटाव और अमान्य उच्च प्रमाण में कीटनाशक व सस्यनाशी के अनुप्रयोग के द्वारा प्रमाणित हो चुका है ।

5. इनमें से कुछ चुनौतियों का सामना करने में कृषि क्षेत्र में GE और अन्य आधुनिक आण्विक तकनीकों का सही अनुप्रयोग, अपना योगदान दे रहा है ।

6. यह वास्तविकता नहीं है कि फसल की अभिवृद्धि में GE तकनीकों के प्रयोग से स्वयम् पादप या खाद्य उत्पाद हानिकारक होते हैं ।

7. वैज्ञानिक समुदाय का दायित्व होना चाहिए कि वह अनुसंधान तथा विकास के क्षेत्र में कार्य करे जिससे कृषि उत्पादकता में वृद्धि हो और प्रयास करे कि ऐसी वृद्धि गरीबों के साथ-ही-साथ विकसित देशों के लोगों के लिए लाभदायक हो, जो अब उन्नत स्तर के जीवन के आदी हो गये हैं ।

8. विकासशील देशों के गरीब किसानों को अपनी स्थानीय स्थितियों के अनुकूल उपयोग करने के लिए सुधारित विभिन्न प्रकार की GE फसल उपलब्ध कराने की दिशा में विशेष प्रयत्न करने चाहिए ।

9. ऐसी उन्नत फसल की वृद्धि में अनुसंधान को स्थानीय आवश्यकता और विभिन्न प्रकार की फसल तथा कृषि पंरपराओं के उपयोग करने में प्रत्येक देश की सामर्थ्य, सामाजिक रूढ़ियाँ, प्रशासनिक व्यवस्था तथा आनुवंशिकतः रूपांतरित फसल के सफल प्रचार की ओर विशेष ध्यान देना चाहिए ।

[पादप प्रजनन संबंधी प्रक्रियाओं का वर्णन करने के लिए बहुत सारे शब्द प्रचलित हैं । सभी जीवंत जीव कोशिकाओं से बनते हैं, जिनमें उनके जीन उनको विशेष लक्षण प्रदान करते हैं । संपूण जीन समुदाय (जीनी संरचना) DNA के द्वारा सूचित किया जाता है और उसे जीनोम (संजीन) कहते हैं ; आनुवंशिकता संबंधी लक्षण जन्मदाता से संतान धारण करते हैं । सभी पादप प्रजनन, वास्तव में सभी विकास, आनुवंशिक परिवर्तन या रूपांतरण और संतान के लाभदायक लक्षणों के चयन से जुड़ा रहता है । पादप के लक्षणप्ररूप में अत्यधिक बदलाव अथवा योग्य लक्षण (शारीरिक संरचना, विकास, जैवरासायनिक तथा पोषणज गुणधर्म आदि) उसकी जीनी संरचना के परिवर्तन का परिणाम होता है । पादप प्रजनन में निकट संबंधी और लैंगिकता की दृष्टि से सुसंगत जाति के जीनों का परंपरागत अनियमित समवकुलन का ज्यादातर अनिरीक्षित परिणामों और हमेशा आनुवंशिक परिवर्तन के विवरणों की जाँच किये बिना ही प्रयोग किया गया । बीसवीं सदी के मध्य में इसको उत्परिवर्तजनी प्रजनन द्वारा संपूरित किया गया, समलक्षणी अभिवृद्धि की उम्मीद में उत्परिवर्तजनी रासायनिकों से बीजों का अथवा संपूर्ण पादपों का अनियोजित उपचार अथवा तेज-ऊर्जा विकिरण ; इससे भी अनपेक्षित तथा अनिरीक्षित आनुवंशिक परिणाम निकले जिनसे पादप प्रजनक ने लाभदायक लक्षणों को चुना । हाल ही में, विशिष्ट तथा अच्छे लक्षणों के जीन या जीनों के छोटे समूह जिनमें खास लक्षण प्रतिपादित थे, उनकी तबदीली की सुविधा द्वारा और उसके साथ ही जीनी व

लक्षणप्ररूपी के परिणामों के संक्षिप्त विश्लेषण द्वारा नई तकनीकों का निर्माण हुआ । इस अंतिम वर्ग को ''पारोत्पत्ति'' कहा जाता है (क्योंकि जीनों को एक दाता से प्राप्तकर्त्ता में तबदील किया जाता है) या ''आनुवंशिकतः अभियंत्रित'' (इस रिपोर्ट में संक्षेप में GE), लेकिन सच्चाई यह है कि यह शब्द सभी प्रजनन प्रक्रियाओं के लिए लागू होता है ।]

उस पहले के अध्ययन दस्तावेज़ को तैयार करने के समय से अब तक GE तकनीक के विकास, अनुप्रयोग और प्रभाव के संबंध में साक्ष्य एकात्रित हुए हैं, जिनका बड़े अनुभवी लोगों के अवलोकन के अधीन अत्युन्नत स्तरीय वैज्ञानिक परीक्षण किया गया है । हमारे अध्ययन सप्ताह के दौरान इन साक्ष्यों का पर्यवेक्षण कर निम्नांकित निष्कर्ष पर पहुँचे हैं :

1. GE तकनीक का सही और जिम्मेदारी से उपयोग किया जाए तो फसल की सुधारक उन्नति, कृषि उत्पाद की संवृद्धि, पोषणज गुण, कीट और रोगों के विरुद्ध प्रतिरोधक शक्ति में बढ़ोत्तरी, अकाल और अन्य प्रकार के वातावरणीय तनाव को सहने की शक्ति में वृद्धि आदि के द्वारा कई परिस्थितियों में कृषि उत्पादकता में अत्यावश्यक योगदान प्राप्त हो सकता है ।

2. फसल की आनुवंशिक अभिवृद्धि और सजावटी पादप, लंबे और अंतहीन व निरंतर प्रगतिशील, विशिष्ट तथा अपेक्षित तकनीकों का प्रतिनिधित्व करते हैं । 1989 में अमेरिका राष्ट्रीय अनुसंधान परिषद (US National Research council) ने अपनी एक रिपोर्ट में कहा था, 'आण्विक विधान अधिक विशिष्ट होने के कारण जो इनका इस्तेमाल करते हैं, वे पादपों में जिन लक्षणों को धरते हैं उनके बारे में अधिक विश्वस्त होते हैं । इसीलिए अन्य पादप प्रजनन के विधानों से कम अवांछनीय परिणाम उत्पन्न करते हैं ।''

3. अमेरिका, अर्जेंटीना, ब्रेज़ील आदि देशों में जहाँ ज्यादातर GE फसल को उत्पन्न किया जाता है, इनके लाभ महत्वपूर्ण बन चुके हैं ।

4. संसाधन-हीन कृषक और कृषि समुदाय के दुर्बल सदस्य, विशेषकर महिलाओं और बच्चों के लिए ये अत्यंत महत्वपूर्ण हो सकते हैं । इस तरह से कीट-प्रतिरोधक GE कपास और मक्के ने कीटनाशक का उपयोग बहुत हद तक कम किया है (अतः खेतों की सुरक्षा को बढ़ाया है) और अधिक घरेलू आमदनी तथा गरीबी के प्रमाण में कमी द्वारा (रासायनिक कीटनाशकों से विष प्रयोग में भी कमी) विकासशील देशों जैसे भारत, चीन, दक्षिण अफ्रीका और फिलिपीन्स के छोटे खेती के क्षेत्रों में अधिक उत्पादन में काफी योगदान दिया है ।

5. उत्कीर्णाकृति के मक्का, सोयाबीन, कैनोला और अन्य फसलों में सौम्य, सस्ते प्रतिरोधक

सस्यनाशी का ज्यादातर प्रयोग करना GE लक्षण है । प्रति हेक्टेर में इसने फसल की वृद्धि की है, हाथ से करनेवाली निराई जो अत्यंत कठिन होती है उसको बदला है और कम निवेश के द्वारा न्यूनतम जुताई तकनीकों की सुविधा प्रदान की है जिससे मिट्टी के क्षरण के अनुपात में कमी हुई है । यह तकनीक विशेष रूप से विकासशील देशों के क्षेत्रों में उपयोगी है जहाँ पर कृषक समुदाय में ज्यादातर लोग रोगग्रस्त या बूढ़े हैं और परंपरागत शारीरिक विधियों द्वारा घासपात का नियंत्रण नहीं कर सकते ।

6. GE प्रौद्योगिकी आवश्यक सूक्ष्म-पोषक तत्वों को प्रदान करते हुए रूपांतरण द्वारा पोषणज अभावों को दूर कर सकती है । उदाहरण के लिए, प्रोविटामिन "A" से सुदृढ़ ''स्वर्णिम चावल'' (गोल्डन राइस) का अध्ययन यह प्रमाणित करता है कि

विटामिन - A की कमी को दूर करने के लिए इस प्रकार के चावल के नियमित दैनंदिन भोजन काफी है । अतः अनुचित परिमाण में चावल खाने की आवश्यकता नहीं है, जैसा कि विरोधी दावा करते हैं ।

7. कीट-अवरोध के लिए GE प्रौद्योगिकी के अनुप्रयोग ने रासायनिक कीटनाशकों के प्रयोग में कमी की है । परिणामतः कृष्टि निवेश के खर्च में कमी और कृषि कर्मियों के स्वास्थ्य में सुधार आया है । अधिकतम क्षेत्रों के मुकाबले अनेक यूरोपीय देशों में, जहाँ कीटनाशकों का अनुप्रयोग बहुत ज्यादा होता है, जो पारिस्थितिकतंत्र तथा मानवीय स्वास्थ्य के लिए हानिकारक है, वहाँ यह संबंध विशेष महत्वपूर्ण है ।

8. ऊर्जा ग्रहण करनेवाली यांत्रिक जुताई की विधियों की हानि को GE प्रौद्योगिकी कम कर सकती है और अत्यंत महत्वपूर्ण मानवोद्भवी पौधा घर के गैस, कार्बन डाईऑक्साइड के निस्तार में कमी करते हुए जीव विभिन्नता तथा पर्यावरण की रक्षा में वृद्धि करती है ।

9. जलवायु परिवर्तन का अनिवार्य प्रभाव GE के साथ-साथ अन्य प्रजनन तकनीकों के सही और तीव्र प्रयोग की आवश्यकता को अधिक प्रबल कर देता है, ताकि अतिशीघ्र अनावृष्टि और बाढ़ को सहने की क्षमता तथा अवरोधक शक्ति आदि लक्षणों को सभी क्षेत्रों के प्रमुख खाद्य फसल में सम्मिलित कर सकें ।

10. GE प्रौद्योगिकी ने एक दर्जन से अधिक विकासशील देशों जैसे चीन, भारत, दक्षिण अफ्रीका और फिलिपीन्स के गरीब किसानों के फसल-उत्पादन को बढ़ा दिया है और अधिक आमदनी तथा रोजगार को उत्पन्न किया है जो अन्यथा संभव नहीं था । भारी मात्रा में

कीटनाशकों के अनुप्रयोग की आवश्यकता को भी कम किया है, मानवीय तथा पारिस्थितिकतंत्र के स्वास्थ्य को सुधारा है और शीर्षमृदा के संरक्षण में भी सहायता की है ।

11. GE प्रौद्योगिकी की नियमित दृष्टि (अत्यधिक खर्च के साथ), अद्यतन नहीं किंतु वैज्ञानिक-रक्षा तथा आपत्ति-आधारित होनी चाहिए । अर्थात् वह नियमन किसी नये प्रकार के पादप के विशिष्ट लक्षणों पर आधारित होने चाहिए, उनके उत्पादन में जिन तकनीकी विधानों का प्रयोग किया गया है, उन पर नहीं ।

12. अगर विशेष प्रकार के पादप को उपलब्ध नहीं कराया जाता है तो नये प्रकार के पादप के उपयोग करने में सभाव्य विपत्ति मात्र पर ध्यान नहीं देना चाहिए, बल्कि अन्य विकल्पों की विपत्तियों पर भी ध्यान देना होगा ।

13. आनुवंशिकतः सुधारित कैसावा, शकरकंद, चावल, मक्का, केले और अन्य प्रमुख उष्णकटिबंधीय फसल के उत्पादन के लिए अब सरकारी संस्थाओं द्वारा सार्थक प्रयास किये जा रहे हैं, जो प्रत्यक्ष रूप से गरीबों के लिए लाभदायक होंगे । इन प्रयासों को संपूर्ण प्रोत्साहन मिलना चाहिए ।

14. विश्व के गरीब तथा अपोषितों के सम्मुख जो बृहत्तर चुनौतियाँ हैं, वह अत्यंत महत्वपूर्ण विषय है जिसे तुरंत निपटाना आवश्यक है । प्रतिवर्ष पोषणज कमी की समस्याएँ निवारण योग्य बीमारी और मृत्यु के प्रमुख कारण बन जाती हैं । विश्व भर में खाद्य के दामों में बढ़ोत्तरी ने संसाधन के लिए प्रतिस्पर्धा करने में गरीबों की दुर्बलता को दर्शाया है । इस संदर्भ में कहना होगा कि जो लाभ छूट जाते हैं, वे हमेशा के लिए खो जाते हैं ।

15. इन वैज्ञानिक निष्कर्षों के अनुसार एक नैतिक कर्तव्य बनता है कि इस प्रौद्योगिकी का लाभ प्राप्त करें, जो कि स्पष्टतः अमेरिका तथा अन्य देशों में गरीब और दुर्बल जनता के लिए इस शर्त पर उपलब्ध कराया गया है जिससे कि उनके जीवन-स्तर में और स्वास्थ्य में सुधार हो सके और पर्यावरण की रक्षा करने में भी सहायक हो सके ।

विश्वभर में कृषि उत्पादन की वृद्धि करने में GE प्रौद्योगिकी के अनुप्रयोग ने अपने महत्व को निरूपित किया है, लेकिन आज भी यह बहुमुखी युक्तियों का एक भाग मात्र है । हमें सभी सम्यक् प्रौद्योगिकियों के संभाव्य योगदान का सतत मूल्यांकन करना चाहिए, जिसका खाद्य सुरक्षा तथा आगामी पीढ़ियों की गरीबी को हटाने के लिए रूढ़िगत पादप प्रजनन और अतिरिक्त युक्तियों के साथ उपयोग किया जाय । GE प्रौद्योगिकी के साथ उनमें से बहुतों का

प्रभावपूर्ण प्रयोग किया जा सकता है । इन युक्तियों में –– बिन जुताई के शीर्षमृदा की धारणा और अन्य सुरक्षा-आचरण, सही खादों का अनुप्रयोग, नये-नये प्रकार के खाद और पर्यावरण स्नेही कृषि रासायनिकों की अभिवृद्धि, जल संरक्षण, एकत्रित कीट प्रबंधन, आनुवंशिक भिन्नता की सुरक्षा, उचित क्षेत्र में नये प्रकार की फसल उत्पन्न करना - आदि शामिल हैं । सार्वजनिक-निजी निवेश और साझेदारी के द्वारा विस्तृत उपयोग के लिए प्रस्तुत फसल के सुधार द्वारा अंशतः ऐसी फसल प्राप्त हो सकती है ('अनाथ फसल') । खाद्य सुरक्षा की वृद्धि में अन्य अत्यंत महत्वपूर्ण तत्व अथवा संसाधनहीन देशों के लिए विशेष महत्वपूर्ण तत्व हैं ––– संरचनात्मक विकास (परिवहन, बिजली की आपूर्ति और संग्रहण सुविधाएँ), स्थानीय विस्तरण सेवाओं द्वारा किसानों को बीज चयन संबंधी ज्ञानयुक्त और पक्षपातरहित सुझाव देकर योग्यता-निर्माण, वित्तीय और बीमा की प्रचुर व्यवस्था का विकास और अधिकाराधीन प्रौद्योगिकी की अनुज्ञा प्राप्ति आदि । खैर, यह जानकारी कि गरीबी की समस्या के लिए कोई एक समाधान नहीं है और कई क्षेत्रों में गरीबों के प्रति भेदभाव, GE प्रकार की फसल के उपयोग को रोक नहीं सकता क्योंकि वह फसल अपने सही योगदान द्वारा समग्र समाधान दे सकती है ।

<u>विस्तृत सार्वजनिक वितर्क</u> :

21वीं सदी में अनेक स्वास्थ्य तथा खाद्य संबंधी चुनौतियों का सामना करने में विज्ञान के योगदान पर GE प्रौद्योगिकी ने साधारण जनता में कौतूहल और समस्त विश्व में वितर्क उत्पन्न कर दिया है । क्षमता और संभाव्य भूमिका तथा उसकी उपयोगिता और अनुप्रयोग के परिमाण के संबंध में वितर्क का स्वागत हुआ है, लेकिन अगर विज्ञान एवं प्रौद्योगिकी का सही मूल्यांकन, नियमन तथा मानव जाति के लाभ के लिए विस्तरण करना हो तो यह चर्चा अनुभवी-अवलोकन अथवा प्रामाणित सूचनाओं पर निर्भर होनी चाहिए । जैसे-जैसे समस्याएँ उत्पन्न होती हैं उनके समाधान के लिए 'कुछ नहीं करना' एक विकल्प नहीं हो सकता अथवा विज्ञान और प्रौद्योगिकी को एक नल के जैसे खोला या बंद नहीं किया जा सकता । इस संदर्भ में पाँच कार्य प्रक्षेत्र हैं जिनकी ओर ध्यान देने की आवश्यकता है : विज्ञान की सार्वजनिक समझ ; बौद्धिक संपत्ति के अधिकारों का स्थान ; सरकारी संस्थाओं की भूमिका ; नागरिक समाज की भूमिका ; सही और प्रभावित मूल्य तथा औचित्यपूर्ण व्यवस्थित दृष्टि की परिभाषा ।

<u>विज्ञान की सार्वजनिक समझ</u> :

GE प्रौद्योगिकी के संबंध में विस्तृत रूप से सार्वजनिक परिचर्चा तथा प्रशासनिक

व्यवस्था में जो गलत समझ फैल गयी है, उस ओर हमारी बैठक के प्रतिभागियों ने बार-बार ध्यान आकर्षित किया । उदाहरण के लिए, सार्वजनिक वितर्क में पर्याप्त जोर दिया जाता है कि सभी प्रकार के पादप प्रजनन में आनुवंशिक रूपांतरण अवश्य होता है और उसके कुछ उदाहरणों को ''रूढ़'' प्रजनन कहा जाता है, जैसे विकिरण द्वारा प्रेरित उत्परिवर्तजन के ऐसे परिणाम निकले हैं जो स्वाभाविक रूप से GE प्रौद्योगिकी के अनुप्रयोग के मुकाबले कम निरीक्षित हैं । इन समस्याओं के बावजूद इन सभी तकनीकों ने संस्थापित, संपूर्ण रूप से स्वीकृत और विस्तृत रूप से उपभुक्त खाद्य उत्पादों के उत्पादन को अग्रसित किया है ।

सभी प्रतिभागी अध्ययन सप्ताह में अपनी भूमिका निभाने के लिए और सार्वजनिक संवाद एवं वितर्क में अपने ज्ञान युक्त और शिक्षा प्रद योगदान के लिए समर्पित हैं । वैज्ञानिकों का कर्तव्य है कि वे अपने विचारों को सुनायें, अपने विज्ञान की जानकारी दें, प्रौद्योगिकी की अस्पष्टता को दूर करें और अपने निष्कर्षों को विस्तृत रूप से उपलब्ध करायें । GE प्रकार की फसल और आधुनिक आनुवंशीकी के अनुप्रयोग के संबंध में जो विरोध करते हैं और जो संदेहशील हैं, उनसे हम अनुरोध करते हैं कि वे इसमें अनुप्रयुक्त विज्ञान का और उन जरूरतमंदों तक पहुँचने से इस प्रौद्योगिकी को रोक रखने से संभाव्य हानियों का सावधानी से मूल्यांकन करें । सामान्य भलाई तभी संभव है जब सार्वजनिक वितर्क, अत्युत्तम स्तर के वैज्ञानिक प्रमाणों तथा विचार-विनिमय पर आधारित होता है । जवाहरलाल नेहरू जी का कथन है कि ''भविष्य, विज्ञान का तथा उनका होगा जो विज्ञान से मैत्री करते हैं ।''

बौद्धिक संपत्ति के अधिकारों का स्थान :

जैसे आधुनिक औद्योगिक समाज के सभी पहलुओं में अधिकृत अधिकारों की महत्वपूर्ण भूमिका होती है, वैसे ही चिकित्सा तथा कृषि जैवप्रौद्योगिकी में भी या फिर किसी भी प्रौद्योगिकी के विकास में इन अधिकारों की प्रमुख भूमिका होती है । हम जानते हैं कि खाद्य असुरक्षा तथा गरीबी के उन्मूलन के लक्ष्यों में वाणिज्य क्षेत्र का महत्वपूर्ण योगदान है । चर्च के सामाजिक शिक्षण में सूचित किया गया है कि पृथ्वी की संपत्ति के वैश्विक गंतव्य पर सभी मानव जाति का प्रमुख अधिकार है । उसी के अनुरूप हम निजी तथा सार्वजनिक क्षेत्र दोनों से अनुरोध करते हैं कि इस वैश्विक गंतव्य के लिए नागरिक समाज में विद्यमान नियमों के अनुसार वे यथासंभव अपनी संपत्ति के अधिकारों की जायज़ मांगों को अवश्य पहचानें और अपने अधीनस्थ कर लें और अनुचित समृद्धि अथवा गरीब तथा दुर्बल वर्ग का शोषण होने न

दें । विकासशील देशों में गरीब लोगों द्वारा नियमित रूप से उपभुक्त विभिन्न प्रकार की फसल की अभिवृद्धि तथा वितरण व विकास के प्रोत्साहन में सरकारी-निजी साझेदारी अत्यंत महत्वपूर्ण बन गयी है । ऐसे सहयोग का मानवोपकारी स्वर्णिम चावल (गोल्डन राइस) परियोजना एक अत्युत्तम निदर्शन हो सकता है, बिना कोई खर्च के ही निजी कंपनियों के पेटेंट का अनुज्ञा-पत्र सरकारी उद्योगों को प्राप्त होता है, जो विभिन्न प्रकारों को विकसित कर रहे हैं और उस समाज के हित के लिए जिसके किसान प्रमुख अंग हैं, उन किसानों के खेतों में वितरित करने के लिए अब तैयार है । ऐसे मिलते-जुलते अनेक उदाहरण विकासाधीन हैं ; ऐसी प्रगति इस विश्वास के साथ संबंधित है कि धरती के लाभों पर सभी मनुष्यों का अधिकार है । अधिकृत प्रौद्योगिकियों को उपलब्ध कराने के लिए इच्छुक उन निजी उद्योगों को हम बधाई देते हैं, जो गरीबों की भलाई के लिए इन प्रौद्योगिकियों का प्रयोग कर रहे हैं और ऐसे मामलों में उच्च स्तर का अनुसरण करने के लिए उन्हें प्रोत्साहित करते हैं ।

<u>सरकारी संस्थाओं की भूमिका</u> :

कई देशों की सरकारी अनुसंधान प्रयोगशालाओं में खोज द्वारा विभिन्न प्रकार की नई फसल के विकास से बीसवीं सदी की हरित क्रांति संभव हो पाई । यद्यपि सरकारी संस्थाओं का अब ऐसी खोज पर एकाधिकार नहीं है, फिर भी इसमें इनकी भूमिका अत्यंत महत्वपूर्ण है । विशेष रूप से अनुसंधान को बढ़ावा देने के लिए राष्ट्रीय आय तथा दाता एजेन्सियों से प्राप्त पूँजी का उपयोग किया जा सकता है जो कि अत्यंत दुर्बल एवं गरीब लोगों की फसल आवश्यकताओं के लिए प्रासंगिक है । अनुसंधान के परिणामों को विस्तृत रूप से उपलब्ध कराने में सरकारी संस्थाओं की भूमिका महत्वपूर्ण है और ये नये बदलाव ला सकती हैं जो कि निजी संस्थाओं के लिए अत्यंत कठिन है, जहाँ पर वाणिज्यीकरण के लिए विभिन्न प्रकार की फसल का विकास करना उनका केन्द्रीय लक्ष्य होता है । मानव के हित के लिए विशेषकर स्वास्थ्य के क्षेत्र में विज्ञान और प्रौद्योगिकी के अनेक अनुप्रयोगों की वृद्धि में निजी तथा सरकारी संस्थाओं के बीच का सहकार लाभकारी सिद्ध हुआ है और कृषि क्षेत्र इसका अपवाद नहीं है । आधुनिक जैवप्रौद्योगिकीय पद्धतियों द्वारा फसल अभिवृद्धि की दिशा में हम जानते हैं कि अवैज्ञानिक, विभेदकारी और अतिशय नियमन ने अनुसंधान एवं विकास संबंधी खर्च को बढ़ा दिया है, GE प्रौद्योगिकी का उपयोग तथा अनुप्रयोग सार्वजनिक क्षेत्र की संस्थाओं के लिए कठिन और कभी-कभी आर्थिक कारणों से असंभव हो गया है ।

नागरिक समाज की भूमिका

सरकार, विद्वत समाज, NGOs (गैर-सरकारी संस्थाएँ), दानी संस्थाएँ, नगरीय सामाजिक संगठन और धर्म -- ये सब सुव्यवस्थित संवाद और जनता में विज्ञान द्वारा उपलब्ध फायदों की विस्तृत समझ को प्रोत्साहित करने में मुख्य भूमिका निभा सकते हैं । साथ ही, नागरिक जो गरीब एवं ग्रामीण समुदायों के सदस्य हैं, उनके जीवन के सभी पक्षों में सुधार लाने के लिए कार्य कर सकते हैं । किसी भी उद्देश्य के लिए सभी प्रकार के शोषण से गरीबों की रक्षा करने में सहायता कर सकते हैं, लेकिन यह ध्यान रखने का उत्तरदायित्व भी उनका है कि आधुनिक विज्ञान के लाभों से यह समुदाय वंचित नहीं रहे, जो उन्हें और अधिक गरीबी, अस्वस्थता और खाद्य असुरक्षा से बचा सकता है ।

सही और औचित्यपूर्ण व्यवस्थित दृष्टि को परिभाषित करना

किसी भी नयी प्रौद्योगिकी के लाभों को समझने के लिए औचित्यपूर्ण व्यवस्थित अप्रोच की आवश्यकता होती है । अब अनुचित लगता है कि दो दशकों के अत्यंत शुद्ध और निरीक्षित आनुवंशिक अभियंत्रिकी फसल प्रौद्योगिकी पर नई केंद्रित अतिशय आपत्ति-प्रतिकूल नियमन के कारण कई क्षेत्रों में अनेक नई प्रौद्योगिकियों तथा उत्पादों को प्रारंभ करने से रोका गया, जिसने संसार के गरीब लोगों को हानिकारक व अनुचित परिस्थितियों में रखा । ऐसे नियमन के प्रारंभ एवं प्रवर्तन को -- यह अवैज्ञानिक और अनुचित है -- इस बात पर वैज्ञानिकों का एकमत होने पर भी पॉलिसी-निर्माण प्रक्रिया में कार्यरत सम्यक् ज्ञान-हीन सदस्यों द्वारा उकसाया गया और प्रोत्साहित किया गया । अन्य उत्पादन प्रौद्योगिकियों से संभाव्य लाभ अगर छूट गये तो उसे बदला नहीं जा सकता, अर्थात् प्रदत्त अवसर, पूँजी निवेश के खर्च में हानि, अनुसंधान एवं विकास तथा उत्पाद (और उनके लाभ) को पुनः प्राप्त करना असंभव है ।

नये और सुधारित फसल प्रकारों का मूल्यांकन पादप प्रकारों के लक्षणों पर आधारित होना चाहिए, न कि उनको उत्पन्न करने में प्रयुक्त प्रौद्योगिकी पर । उनके प्रत्यक्ष स्वभाव पर उनको आँकना चाहिए, जो हमारे सामान्य लाभ के लिए प्रौद्योगिकी की पूरी क्षमता का फायदा उठाकर सुधारित लक्षण युक्त प्रधान और स्थानीय फसल के नये प्रकारों को प्रदान करने में सहायक होगा । यह प्रयोग के लिए गरीबों को इस्तेमाल करने का विषय नहीं है, बल्कि उनको अधिक विकसित देशों में विस्तार से स्वीकृत और सुरक्षित प्रौद्योगिकी को प्रदान करना है । खाद्य और खेतीबारी के संबंध में हम जरूरत से ज्यादा प्रौद्योगिकी और आपत्ति-प्रतिकूल नहीं

हो सकते, जो हमारे दैनंदिन जीवन के लिए स्वीकारने योग्य होता है ।

बिंदु पादपों की आनुवंशिक अभियंत्रिकी से जुड़े जुए अनुमानित खतरे, अन्य जीवों के लिए (उदाहरण : चिकित्सा जैवप्रौद्योगिकी) प्रयुक्त ऐसी आनुवंशिक प्रौद्योगिकी से संबंधित खतरों से भिन्न नहीं हैं । विषैले अथवा प्रत्यूर्जक वस्तुओं के कारण उत्पन्न अल्पकालीन संकटों का अध्ययन हो सकता है और नये फसल प्रकारों से आसानी से अलग किया जा सकता है ; रूढ़ प्रजनन द्वारा उत्पन्न फसल प्रकारों की खेती के लिए इस प्रक्रिया का प्रयोग नहीं किया जाता । विकसन के दीर्घकालीन परिणामों के संबंध में आनुवंशिक विभेद से प्रकृति में स्वतः कम परिणाम में घटित होने वाले आण्विक विकास का अद्यतन ज्ञान, स्पष्टतः दर्शाता है कि जीनोम में अभियंत्रित आनुवंशिक रूपांतरण केवल जैविक विकास के स्वाभाविक युक्तियों के सम्यक् अध्ययन का अनुसरण कर सकता है । योग्य रूपांतरण छोटे पैमाने पर ही संभव है । यह तभी समझने योग्य बनता है यदि कोई याद रखता है कि भूमि पादप जीनोम बृहत् विश्वज्ञानकोश के सैकड़ों किताबों के अनुरूप होते हैं ; जबकि साधारण पादप जीनोम में आधुनिक आनुवंशिक तकनीक के प्रयोग से आनुवांशिक रूपांतरण सेन्टिआर 26,000 जीनों में से केवल एक या कुछ जीनों को प्रभावित करता है । अतः आनुवंशिक अभियंत्रिकी घटनाओं से संभाव्य विकसन संबंधी खतरे, जैविक विकास की स्वाभाविक प्रक्रिया के खतरों से बड़े नहीं हो सकते अथवा रासायनिक उत्परिवर्तजनी के अनुप्रयोग के या दोनों जो विस्तृत और दुर्बल स्वभावगत आनुवंशिक परिवर्तन के लिए जिम्मेदार हैं, आँकड़ों के अभिलेखों से प्रमाणित होता है कि उनके अवांछित प्रभाव अत्यंत विरल हैं और इसके विरुद्ध चयनित रूढ़ प्रजनन के विषय भी ।

सन् 2000 में ''कार्टजीना प्रोटोकॉल ऑन बयोसेफ्टी'' के संस्थापन से वैज्ञानिक समझ में वृद्धि के उपरांत नियमन आवश्यकताओं तथा लाभों के विज्ञान-आधारित समझ के परिप्रेक्ष्य में उस प्रोटोकॉल के पुनर्मूल्यांकन का अब समय आ चुका है ।

विश्वास, वैज्ञानिक तर्क तथा नैतिकता

एक धार्मिक और नैतिक संदर्भ में ''पृथ्वी की संपत्ति का वैश्विक गंतव्य'' (1) की परिकल्पना का अनुप्रयोग कृषि जैवप्रौद्योगिकी के लिए हो, तो सबके लिए इसका संकेत मिलता है । GE प्रकार की फसल अन्य पद्धतियों से उत्पन्न फसल से कोई खास भिन्न नहीं होतीं, वे स्वास्थ्य अथवा पर्यावरण के लिए कोई विशेष प्रमाणित या शंकित संकट के कारण भी नहीं बनतीं । फसल की वृद्धि के लिए पारजीनी तकनीकों के अनुप्रयोग को विधाता के द्वारा स्थापित

प्रकृति के नियमों के विपरित मानने में कोई तर्क नहीं है । एक भरोसेमंद के लिए मानव के पवित्र उद्‌गम को प्रतिष्ठित करना ही ईसाई दृष्टि का प्रस्थान बिंदु होता है, विशेषकर उसकी आत्मा के कारण, जो अधिकार को समझाता है कि भगवान मनुष्यों को पृथ्वी के जीवित प्राणियों के संपूर्ण संसार पर कार्य द्वारा शासन करने का अधिकार प्रदान करता है, जिसके प्रति वह आत्मा के पथ प्रदर्शन में अपनी शारीरिक शक्ति को समर्पित करता है । इस तरह मनुष्य भगवान के कारिंदे होते हैं और प्राकृतिक उपादनों की अभिवृद्धि और रूपांतरण करते हैं, जिनसे वे विकास की पद्धतियों के अनुप्रयोग द्वारा पोषण प्राप्त कर सकते हैं । यद्यपि इस असीम ब्रह्माण्ड में मनुष्यों का कार्य सीमित होता है, फिर भी वे भगवान की हुकूमत में भाग लेते हैं और उसके संसार को सुदृढ़ बनाते हैं, जिससे स्पष्ट होता है कि उनके शारीरिक तथा आध्यात्मिक जीवन, उनके जीवनोपाय और उनके कल्याण के लिए उपयुक्त परिवेश बनता है । प्राकृतिक संसार में नये मानवीय हस्तक्षेप को भगवान के निर्माण में प्राकृतिक नियमों के विरुद्ध नहीं मानना चाहिए । दरअसल, 'पॉन्टिफिकल अकादमी ऑफ साइंसस' में 1975 (3) में पॉल IV ने कहा था कि एक ओर, वैज्ञानिक को ईमानदारी से मानव जाति की पृथ्वी संबंधी विषय में सोचना है और एक जिम्मेदार व्यक्ति होने के नाते पृथ्वी को तैयार करने में सहायता करनी है, जीविका और भलाई के लिए उसका संरक्षण करना है और संकट का उन्मूलन करना है । अतः उपकार के रूप में वर्तमान तथा भविष्य की पीढ़ियों का समर्थन करना है और दूसरी ओर, वैज्ञानिकों को इस विश्वास से संचालित होना चाहिए कि स्तरीय अभिवृद्धि को हासिल करने के लिए प्रकृति में जो पर्याप्त गुप्त संभावनाएँ हैं, उन्हें मानव ज्ञान को खोज निकालना है और उनका उपयोग करना है, जो कि उस जगन्निर्माता की योजना के अंतर्गत है । इसलिए वैज्ञानिक हस्तक्षेप को मानव जीवन के हित के लिए भौतिक या जैविक प्रकृति का विकास मानना चाहिए जैसे सकारात्मक नियमों द्वारा प्राकृतिक नियम के साथ मानव जीवन के लिए उपयोगी कई प्रबंध जोड़े गये हैं ।

इसलिए GE प्रौद्योगिकी के न्यायसंगत और सामाजिक रूप से निष्पक्ष उपयोग को टालने के लिए कोई वैज्ञानिक, नैतिक या धार्मिक आधार नहीं हैं । वस्तुतः भगवान ने मनुष्य को जो ज्ञान एवं जाँचने की योग्यता का उपहार दिया है, उसकी तुलना में इस प्रौद्योगिकी की प्रगति, इसके मूल्यांकन और विस्तरण को अस्वीकार करना असंगत होगा । विभिन्न क्षेत्रों में चर्च (Church) के लिए जिम्मेदार व्यक्तियों से हम अनुरोध करते हैं कि वे अपने लोगों को, विशेषकर

गरीबों को सुधारने के सभी साधनों के संबंध में सावधानीपूर्वक विचार करें और राजनैतिक प्रवृत्ति के आधारहीन तर्कों से विचलित न हो जायें ।

सुझाव :

1. संपूर्ण विश्व के कृषकों व उत्पादकों के लिए विश्वसनीय सूचनाओं को प्रदान करने में बढ़ावा देना है, जिससे कि वे जीविकोपार्जन तथा उत्पादन के लिए अद्यतन सूचनाओं तथा कृषि प्रबंधन के सभी पहलुओं के ज्ञान के आधार पर उचित निर्णय लेने के योग्य होंगे ।

2. पूरे संसार में नये प्रकार की फसलों (रूढ़ आण्विक सहायता से उत्पन्न या GE प्रौद्योगिकी से) के मूल्यांकन एवं अनुमोदन में संलग्न तत्वों का तर्कसंगत मानकीकरण होना चाहिए ताकि वे वैज्ञानिक, आपत्ति-मूलक, संभावित और पारदर्शी हों । यह विचारणीय है कि एक-एक विषय का जो पुनर्निरीक्षण हुआ है, उसका प्रयोजन वास्तविक पुनरावलोकन जितना ही महत्वपूर्ण है ; यह भी अवश्य वैज्ञानिक एवं आपत्ति-मूलक होना चाहिए ।

3. आपत्ति के अनुपात में वैज्ञानिक एवं व्यावहारिक रूप से पुनर्गठित करते हुए, नियमित आवश्यकताओं और पद्धतियों को निर्मित करते हुए, कृषि के पूर्वोपाय तत्वों के अनुप्रयोग का पुनर्मूल्यांकन करना चाहिए । उसी तरह यद्यपि बुराई को त्यागकर अच्छाई को थामने के लिए समझदारी में सावधानी की आवश्यकता होती है, पर भविष्य का अंदाजा लगाते हुए सावधानी बरतना उस समझदारी का प्रमुख अंग नहीं है ।

अर्थात्, समझदारी का प्रमुख लक्षण सावधानी के कारण कार्य करने से रोकना नहीं, बल्कि वैज्ञानिक भविष्यवाणी को कार्य करने के लिए आधार के रूप में स्वीकारना है (1) । पोप बेनेडिक्ट XVI ने 'पॉन्टिफिकल अकादमी ऑफ साइंसस' में 2006 संपूर्ण सत्र के अवसर पर 'विज्ञान में भविष्य कहने की योग्यता' विषय पर अपने वक्तव्य में इस बात पर ज़ोर दिया था कि समकालीन समाज में विज्ञान के सम्मान का एक प्रमुख कारण है उसमें भविष्यवाणी करने की संभावना और वैज्ञानिक पद्धति के निर्माण ने विज्ञान को प्राकृतिक घटनाओं के संबंध में भविष्य को व्यक्त करने की तथा उनकी वृद्धि के अध्ययन करने की योग्यता दी है जिससे वह मनुष्य के वासस्थान को नियंत्रित करती है । 'वस्तुतः हम कह सकते हैं कि -- यह पोप बेनेडिक्ट का दृढ़तापूर्ण कथन है -- भविष्यवाणी करने का कार्य, नियंत्रण और प्रकृति पर शासन, जो आज विज्ञान का पहले से ज्यादा वर्तमान में व्यावहारिक बताना ही स्वयं उस विधाता की योजना का एक भाग है ।' (2)

4. कार्टजीना प्रोटोकॉल, जो विभिन्न क्षेत्रों में GE फसल के प्रकारों के वितरण को अवरुद्ध करता है, उसका संशोधन करना चाहिए और उसे आज की वैज्ञानिक समझ के अनुरूप लागू करना है । अपने मूल रूप में प्रोटोकॉल वैज्ञानिक दृष्टि से अतीव दोषयुक्त है ।

5. आनुवंशिक सुधार के लिए GE तकनीक जो अत्यंत आधुनिक, विशुद्ध और संभावित हैं, उन्हें अतिशय नियमन से मुक्त करना चाहिए और पौष्ठिक गुणों की वृद्धि और फसलों के उत्पादन (कालांतर में वैक्सीनों तथा अन्य औषधियों के उत्पादन) के लिए सर्वत्र उन तकनीकों का अनुप्रयोग कराना है ।

6. अनुसंधान के लिए पर्याप्त धनराशि, योग्यता निर्माण और सम्यक् सार्वजनिक नीति से जुड़े प्रशिक्षण के द्वारा दुर्बल कृषकों की सहायता करने के लिए इस प्रौद्योगिकी की संभाव्यता को बढ़ावा देना चाहिए ।

7. सुदृढ़ तथा उत्पादक कृषि प्रयोगों का अनुपालन और विस्तरण सेवाओं को प्रोत्साहित करना चाहिए जो विशेषतः गरीब एवं जरूरतमंद लोगों के जीवन को सुधारने के लिए अत्यावश्यक हैं ।

पहले से ही खाद्य सुरक्षा की वृद्धि और फसल सुधार में GE प्रौद्योगिकी का महत्वपूर्ण योगदान रहा है । बड़े पैमाने पर पण्य फसलों के व्यापार में वृद्धि और अनाथ फसल जिन्हें कहा जाता है, उन दोनों की दृष्टि से विकासशील देशों में पादप प्रजनन के लिए अन्य आण्विक अप्रोचों के साथ इन तकनीकों के सही अनुप्रयोग में महत्तर योगदान की क्षमता है । इन प्रमाणित वैज्ञानिक विकासों के प्रयोग को भूमण्डलीय सार्वजनिक भलाई के रूप में स्वीकारा जा सकता है । फसलों की वृद्धि करने में और नये प्रकारों को बाजार में लाने के लिए इन अप्रोचों के नियामक लागत के साथ-साथ अनुसंधान और विकास में अधिक खर्च होने के कारण इन प्रौद्योगिकियों का केवल प्रमुख उच्च प्रमाण की पण्य फसलों के लिए अनुप्रयोग होता है, जिन्हें विकसित संसार में बहुराष्ट्रीय कंपनियों द्वारा उत्पन्न किया जाता है ।

GE अप्रोचों के प्रयोग द्वारा सार्वजनिक रूप से अच्छे पादप प्रजनन को सीमित करने के दो प्रमुख कारण हैं : (1) इसमें लगनेवाले अत्यधिक लागत और राष्ट्रीय सरकारों द्वारा निवेश की कमी । परिणामतः स्थानीय महत्वपूर्ण ('अनाथ' कही जानेवाली) फसल जैसे सोरघम, कसावा, केले आदि जिनका अंतर्राष्ट्रीय व्यापार नहीं होता और बहुराष्ट्रीय कंपनियों द्वारा व्यावसायिक निवेश का समर्थन नहीं होता, उनको सुधारने और उनके अनुकूलन करने में इस

अप्रोच का अनुप्रयोग असफल हुआ है ; (2) कृषि क्षेत्र में दूसरों की तुलना में इस प्रौद्योगिकी के अतिशय तथा अनावश्यक नियमन ने इसके अनुप्रयोग को ज्यादा खर्चीला बना दिया है । इसलिए 'लघु' और अन्य फसलों के लिए इसका प्रयोग नहीं हो सकता और यह आपत्ति मोलने के साथ-साथ निवेश के बराबर लाभ भी नहीं दे सकता । यह सिर्फ निजी क्षेत्र के लिए लागू नहीं होता ; निजी या सार्वजनिक, सभी निवेशों को संभाव्य लाभ के परिप्रेक्ष्य में ही आँकना चाहिए । इस तरह प्रमुख पण्य फसलों की तुलना में निवेश की आवश्यकता, समस्यापूर्ण नियमन तथा परिणाम की अनिश्चितता के कारण सीमित उपयोग के लिए सार्वजनिक क्षेत्र के साथ-साथ निजी क्षेत्र भी उत्पादों के विकास को रोक सकता है ।

अगर खाद्य असुरक्षित निर्धन देशों में उत्पन्न प्रासंगिक फसलों को सुधारने में सम्यक् GE तथा आण्विक चिह्न युक्त सहायक प्रजनन को स्थिर किया जाय तो खाद्य सुरक्षा की वृद्धि पर उनका महत्वपूर्ण प्रभाव हो सकता है । अतः सरकारों, अंतर्राष्ट्रीय सहायता एजेन्सियों और दानी संस्थाओं से हम अनुरोध करते हैं कि इस क्षेत्र में अवश्य लागत बढ़ायें । हम यह भी संस्तुति करते हैं कि विकासशील संसार में, जहाँ पर इनका अधिक विस्तृत प्रभाव होगा, सामान्य भलाई के लिए इन तकनीकों के लागत मुक्त संपूर्ण प्रयोग को स्थिर करने में CGIAR, UN या UNESCO जैसे अंतर्राष्ट्रीय संगठन, निजी-सार्वजनिक सहकारी संबंधों के संस्थापन में मध्यस्थता निभायें । पहले से ही ऐसे सहकार के संभाव्य लाभों को प्रमाणित किया गया है । फिलीपीन्स में स्वर्णिम चावल (गोल्डन राइस), अफ्रीका में अकाल प्रतिरोधक मक्का और भारत तथा अफ्रीका में कीट अवरोधक फली आदि के विषय में प्रांसगिक पेटेंट योग्य तकनीकों का मुक्त दान कर फसल संवर्धन में उनके प्रयोग करने में बहुराष्ट्रीय निगमों ने भी निजी-सार्वजनिक साझेदारी के संबंध में सौदा करने के लिए सम्मति दर्शायी है ।

निष्कर्षतः संगोष्ठी के प्रतिभागियों ने निर्णय लिया कि इस यथार्थ की अब और ज्यादा उपेक्षा नहीं करनी चाहिए, इसमें विस्तृत वैज्ञानिक एकमत है, प्रौद्योगिकी-अंतर्निहित असामान्य आपत्ति नहीं है और इसके लिए वैज्ञानिक प्रमाण एवं व्यावहारिक अनुभव की ऐसी संपत्ति है कि अनुमानित आपत्तियों के संबंध में चर्चा जारी रखना न्यायसंगत नहीं है । इसके बदले निर्धनों की गरीबी तथा भूख संबंधी ज्ञात आपत्तियों को ध्यान में रखते हुए GE प्रौद्योगिकी के दायित्वपूर्ण अनुप्रयोग करने का अनिवार्य नैतिक कर्तव्य है, किंतु सामाजिक न्याय के रूप में ।

पृष्ठभूमि एवं प्रतिभागी

प्रोफेसर वर्नर अर्बर तथा प्रोफेसर पीटर रावेन के सहयोग से अकादमी के सदस्य, प्रोफेसर इंगो पॉट्रिकस द्वारा 'पॉन्टिफिकल अकादमी आफ साइंसस' की ओर से 15-19, मई 2009 के PAS अध्ययन सप्ताह का आयोजन किया गया था । केवल निमंत्रण पर ही इसमें भाग लिया गया था और उनकी अपनी निपुणता के क्षेत्रों में वैज्ञानिक योग्यता, सामाजिक न्याय तथा वैज्ञानिक दृढ़ता के अनुपालन के आधार पर प्रतिभागियों का चयन हुआ था । प्रमाणित विकास के संदर्भ में विश्वभर में मानव कल्याण के लिए आनुवंशिक अभियंत्रिकी तथा प्रस्तुत वैज्ञानिक ज्ञान के आधार पर अन्य कृषि प्रयोगों के लाभ एवं आपत्तियों का मूल्यांकन करना और खाद्य सुरक्षा संवर्धन में उसके अनुप्रयोग की क्षमता को जाँचना, अध्ययन सप्ताह का लक्ष्य था । इस कठिण कार्य के लिए प्रतिभागियों की सूची अत्यंत ''संतुलित'' है । अध्ययन सप्ताह के प्रतिभागियों के नाम वर्णमाला के क्रम में निम्नांकित है :

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प्रो.रोनाल्ड जे.हेरिंग - यू एस ए
कार्नेल यूनिवर्सिटी
प्रो.ड्रयू कर्शेन - यू एस ए
यूनिवर्सिटी ऑफ ओक्लाहोमा
प्रो.अनाटोले क्रटि्टगर - यू एस ए
कार्नेल यूनिवर्सिटी
प्रो.क्रिस्टोफर लीवर - यू के
यूनिवर्सिटी ऑफ आक्सफर्ड
प्रो.स्टीफन पी लांग - यू एस ए
एनर्जी साइंस इंस्टिटयूट
प्रो.केती मार्टिन - यू के
जॉन इन्स सेंटर, नार्विच
प्रो.मार्शल मार्टिन - यू एस ए
पर्ड्यू यूनिवर्सिटी
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हूवर इंस्टिटयूशन, स्टानफर्ड यूनिवर्सिटी
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प्रेसिडेंट यूरोपियन फेडेरेशन ऑफ बयोटेक्नॉलजी
प्रो.पीरो मोरांदिनी - इटली
यूनिवर्सिटा डेगली स्टडी डी मिलानो
प्रो.मार्टीना नेवेल - मेकग्लौलिन - यू एस ए
यूनिवर्सिटी ऑफ कालिफोर्निया, डेवीस
मॉनसिनोर जार्ज एनकूओ - कैमेरून
बिशप ऑफ कुंबो
प्रो.राब पार्लबर्ग - यू एस ए
वेल्लेस्ली कॉलेज
प्रो.वेन पारट - यू एस ए
दि यूनिवर्सिटी ऑफ जार्जिया
प्रो.इंगो पॉट्रिकस - स्विज़रलैंड
एमिरिटस, स्विस फेडेरल इंस्टिटयूट ऑफ टेक्नॉलजी
प्रो.सी.एस.प्रकाश - यू एस ए
टस्केजी यूनिवर्सिटी

प्रो.माटिन खैम - जर्मनी

जार्ज-अगस्त यूनिवर्सिटी ऑफ गोटि्ंटजेन

डॉ.राघवेन्द्र राव - इंडिया

डिपार्टमेंट ऑफ बयोटेक्नॉलजी, मिनिस्ट्री ऑफ साइंस एण्ड टेक्नॉलजी

प्रो.पीटर एच.रावेन - यू एस ए

प्रेसिडेंट, मिस्सौरी बोटानिकल गार्डन

मॉनसिनोर मार्सेलो सांचेस सारोंडो - वाटिकन

चान्सेलर पॉन्टिफिकल अकादमी ऑफ साइंसस

प्रो.कोंस्टांटिन स्क्रैयाबिन - रसिया

सेंटर 'बयोइंजीनियरिंग' रसियन अकादमी ऑफ साइंसस

प्रो.एम.एस.स्वामिनाथन - इंडिया

चेयरमन, एम.एस.स्वामिनाथन रिसर्च फाऊंडेशन

प्रो.चियारा तोनेल्ली - इटली

यूनिवर्सिटी ऑफ मिलान

प्रो.राफेल विकुना - चिली

पॉन्टिफिका यूनिवर्सिडाड कटोलिका डी चिली

प्रो.अल्बर्ट वीले - यू के

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प्रो.रोबर्ट ज़िग्लर - फिलिपीन्स

डायरेक्टर जनरल, इंटरनाशनल राइस रिसर्च इंस्टिट्यूट

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Juma La mafunzo ya Taaluma Ya Sayansi Ya Papa, Jijini Vatikani Mei 15 – 19, 2009

Mimea ya Ubadilishaji Jeni Kwa Usalama wa Chakula Katika Muktadha wa Maendeleo

Juma la mafunzo kuhusu Mimea ya Ubadilijeni kwa usalama wa chakula Katika Muktadha wa Maendeleo uliofanywa chini ya ufadhili wa Taaluma ya Sayansi ya Papa katika makao yake makuu kwenye CasinaPio IV huko Vatikani kutoka Mei 15 hadi 19, 2009. Wakati wa kukutana hapo, tulichunguza maendeleo ya hivi karibuni katika kuelewa aina mbalimbali za mimea ambayo imebadilishwa Jeni, na wakati huo huo kuchunguza hali ya kijamii ambayo teknolojia ya Ubadilishaji Jeni ingeweza kuenezwa ili kuboresha kilimo kwa ujumla na kwa faida ya maskini na hasa wasiobahatika.

Ari ya washiriki ilivutiwa na mkabala huo wa teknolojia ambao Benedict XVI aliuelezea katika Waraka wa Baba Mtakatifu kuwa, 'Teknolojia ni lengo ambalo (1) chimbuko lake na sababu ya kuwepo kwake kunapatikana kwenye hali ya kujitawala: mfanyikazi mwenyewe. Kwa sababu hiyo, teknolojia haiwi teknolojia tupu tu. Inamwangazia binadamu na ari yake kwenye maendeleo, inaonyesha mgongano wa ndani unaomshurutisha kuvishinda vikwazo taratibu. *Teknolojia kwa hali hiyo, ni matokeo ya amri ya Mungu ya kulima na kutunza ardhi*. (Mwanzo 2:15) kwamba amemkabidhi mwanadamu, na inapaswa kuendeleza agano kati ya wanadamu na mazingira, agano ambalo lapaswa kuonyesha kioo cha upendo wa Mungu kwenye uumbaji' (2).

Masuluhisho makuu kisayansi

Tunasisitiza mahitimisho makuu ya Makala ya Mafunzo Katika Matumizi ya "Mimea ya Chakula ya Ubadilishaji Jeni" ili Kupambana na Njaa katika Ulimwengu iliyotolewa mwishoni mwa Kikao cha Jubilii chenye uwezo juu ya 'Sayansi na Maisha ya Baadaye ya Binadamu', Novemba 10 – 13, 2009. Muhitasari wa makala haya yanajumuisha:

1 Zaidi ya watu bilioni moja ya idadi ya ulimwengu ya watu bilioni 6.8 kwa sasa ni maskini, hali ambayo inahitaji kwa haraka sana kuendelezwa kwa kanuni mpya za kilimo na teknolojia.

2 Idadi inayotazamiwa ya watu bilioni 2 – 2.5 ili kufikia takribani watu bilioni tisa (9) ifikapo 2050 inaongeza umuhimu wa tatizo hili

3 Matokeo yanayotarajiwa ya mabadiliko ya hali ya hewa ikiandamana pamoja na upungufu wa upatikanaji wa maji kwa ajili ya kilimo pia utaathiri uwezo wetu wa kulisha idadi ya watu duniani iliyoongezeka.

4 Kilimo kama kinavyotekelezwa kwa sasa hakiwezi kutosheleza, kikithibitishwa na hasara kubwa ya upoteaji wa udongo wenye rutuba na utumizi wa kiwango cha juu cha dawa za kunyunyuzia wadudu kwenye maeneo mengi ya duniani.

5 Utumizi sahihi wa uzalishaji wa Jeni na mbinu zingine za kisasa za kimolekule kwenye kilimo unachangia katika kushughulikia changamoto hizi.

6 Hakuna chochote ambacho ni cha asili halisi kwenye utumizi wa teknolojia ya uzalishaji wa Jeni ili kuboresha upanzi ambacho kitafanya mimea yenyewe au bidhaa za chakula zisiwe salama.

7 Jamii ya kisayansi inapaswa kuwajibika katika kufanya Utafiti na Maendeleo (tafiti na Maendeleo U + M) utakaoleta maendeleo kwenye kilimo na uzalishaji mavuno, na ni lazima pia kutia juhudi ili kuona kuwa faida inayohusiana na maendeleo hayo itaongeza faida ya maskini na vilevile kwenye nchi zilizoendelea ambazo kwa sasa zinafurahia kuishi kiwango cha juu.

8 Juhudi maalum zinapaswa kufanywa ili kuwafanya wakulima maskini katika nchi zinazoendelea wapate aina za mazao yaliyoboreshwa ya Ubadilishaji Jeni wayalime katika sehemu zao.

9 Utafiti wa kuendeleza mazao bora unapaswa kuangalia kwa makini mahitaji ya wenyeji na aina za mazao na uwezo wa kila nchi wa kuzingatia mapokeo yake, urithi wa kijamii na utawala ili kupata ufanisi wa kutumia mazao ya Ubadilishaji Jeni.

Ushahidi zaidi

Tangu maandalizi ya makala ya mafunzo ya awali; ushahidi kwamba kumekuwa na kiwango cha juu cha uchunguzi na uhakiki wa kisayansi pamoja na kiasi kingi cha tajiriba, kimekusanywa kuhusu maendeleo,

matumizi na athari za teknolojia ya Ubadilishaji Jeni. Wakati wa juma-la mafunzo tulirejelea huu ushahidi na kufikia masuhuhisho yafuatayo:

1. Teknolojia ya Ubadilishaji Jeni inapotumiwa kwa usahihi na inavyowajibika, kwa wakati mwingi italeta mchango wa maana kwenye uzalishaji wa kilimo kwa kuboresha mazao, ikiwa ni pamoja na kuimarisha mavuno ya mazao na ubora wa lishe, na kuongeza ukinzani wa wadudu, vile vile ustahimilivu wa ukame na adha zingine za kimazingira. Uboreshaji huu unahitajika kote duniani ili kusaidia kuboresha uendelezaji kilimo na uzalishaji wake.

2. Uboreshaji wa mazao na kuremba mimea kwa kutumia jeni inawakilisha mwendelezo wa mfululizo usio na mipaka wa mbinu za uhakika na zinazotabirika kama Baraza la Utafiti la Marekani lilivyohitimisha katika taarifa mwaka 1989: kwa kuwa njia za kimolekule ni mahsusi zaidi, watumiaji wa njia hizi watakuwa na uhakika zaidi kuhusu sifa watakazozianzisha kwenye mimea na hivyo inastahili kuwa na athari chache zaidi kuliko njia zingine za kuzalisha mimea.

Kuna njia nyingi zilizotumiwa kuelezea hatua zinazohusika katika uzalishaji wa mimea. Viumbe vyote vyenye uhai vimeundwa kwa seli ambazo zimo ndani ya jeni zao, ambazo huzipa tabia zilizo tofauti (viumbe vingine). Seti moja ya jeni (Jenotaipu) imefichwa katika DNA na inaitwa jenomu, ni taarifa inayohusu urithi wa uzao unaopitishwa kutoka kwa mzazi hadi mtoto. Uzalishaji wote wa mimea na kwa kweli mabadiliko yote, yanahusisha mabadiliko ya jeni au mageuzi yakifuatiwa na uteuzi wa tabia zenye manufaa kutoka miongoni mwa watoto, mageuzi mengi ya fenotaipu au sifa zinazochunguzika (kama ilivyo kwenye maumbile halisi, maendeleo, bayokemikali na sifa za lishe hutokana na mabadiliko ya jenotaipu zake. Uzalishaji wa mimea ambao kijadi ulitumia uhamishaji usio na mpango kamili wa jeni kati ya zile zenye uhusiano wa karibu na zinatangamana vyema na jinsia tofautu, aghalabu huna na madhara yasiyotabirika na daima kuwa na mabadiliko ya kijeni ambazo hazijavumbuliwa.

Katikati ya karne ya ishirini hii iliongezwa kuzalisha kwa mutajenisis, njia ya kutibu mbegu au mimea mizima kwa kemikali za mutajeni au mionzi yenye nguvu nyingi kwa tegemeo la kuanzisha fenotaipu iliyoboreka, hii pia ilizusha jeni zisizotabirika na madhara ambayo hayajagundulika ambayo kizalishi cha mmea kilivyochagua sifa bainishi zenye manufaa. Hivi karibuni, mbinu zimeendelezwa zinazoruhusu uhamishaji wa jeni maalum, na zaidi tabia njema, au vibonge vidogo vya jeni ambazo zinatuza sifa bainishi fulani

3. Faida tayari zimekuwa za umuhimu zaidi kwenye nchi kama Marekani, Ajentina, India, Uchina na Brazili ambapo mazao ya Ubadilishaji Jeni yanalimwa kwa mapana.

4. Pia zinaweza kuwa na umuhimu mkubwa kwa wakulima maskini wasio na mtaji na wanaoishi katika mazingira magumu ya jamii za kilimo duni, hasa zinaweza kuwa muhimu kwa wanawake na watoto. Mazao ya Ubadilishaji Jeni yanavyokinzana na wadudu, hasa pamba na mahindi, yanaweza kupunguza utumiaji wa dawa za wadudu (na kwa hivyo kuimarisha usalama wa kilimo) na kuchangia kwa uthabiti mavuno ya juu, mapato ya juu ya kaya na kushusha kiwango cha umaskini (na pia kupunguza sumu kwa njia ya kemikali za wadudu) katika sekta ndogo za shamba kwenye nchi kadhaa za nchi zinazoendelea ikiwemo India, Uchina, Afrika Kusini na Ufilipino.

5. Uanzilishaji wa ukinzani mwepesi wa kimazingira, sumu ya mimea rahisi katika mahindi, maharage ya soya, kanola na mazao mengine ndizo sifa bainishi za Ubadilishaji Jeni zinazotumika zaidi. Zimeongeza mavuno kwa kila hekta, na zimerejesha uondoaji wa magugu yanayoota na huendeleza upunguzaji wa pembejeo ambazo zimepunguza zaidi uchimbuaji wa udongo mbinu ambayo itapunguza kiwango cha mmomonyoko wa udongo. Teknolojia hii inaweza kuwa na manufaa hasa kwa wakulima wa nchi zinazoendelea ambao, kutokana na sababu za umri na magonjwa, hawawezi kujihusisha na njia za jadi za kudhibiti magugu.

6. Teknolojia ya Ubadilishaji Jeni inaweza kupambana na uhaba wa lishe kwa kupitia ugeuzaji ambao hutoa virutubishi vidogo muhimu. Kwa mfano mafunzo ya kukubali vitamini katika uimarishaji wa 'Mchele wa Thamani' yameonyesha kuwa kiwango cha maakuli ya kila siku ya mchele huo kitatosha kuzuia upungufu wa vitamin A.

7. Matumizi ya teknolojia ya Ubadilishaji Jeni imesababisha kupunguza utumiaji wa dawa za kunyunyuzia wadudu, na kupunguza gharama za baadhi ya pembejeo za kilimo hivyo kuboresha afya ya wafanyikazi wa kilimo. Uhusiano huu ni muhimu hasa katika maeneo mengi kama Mataifa ya Ulaya, ambapo utumizi wa dawa ya wadudu ni wa kiwango cha juu zaidi ya sehemu zingine zote, jambo ambalo linaweza kupunguza uwiano kwa ujumla na vilevile afya ya binadamu.

8. Teknolojia ya Ubadilishaji Jeni inaweza kupunguza utumiaji wa nishati wenye madhara, uchimbaji wa kutumia mitambo, utaimarisha uhai anuai na kulinda mazingira kwa kiasi Fulani, kwa kupunguza utoaji wa hewa ya karboni, ambayo ni gesi muhimu ya kianthropojenia kwenye nyumba ya kuhifadhia mimea.

9. Athari zinazotarajiwa za mabadiliko ya hali ya hewa hulazimisha kuwepo na utumiaji wa Ubadilishaji Jeni pamoja na mbinu nyingine za uzalishaji kwa usahihi ili sifa bainifu kama uzuiaji ukame, ustahimilivu wa mafuriko vijumuishwe kwenye mazao makuu ya chakula ya maeneo yote kwa haraka inavyowezekana.

10 Teknolojia ya Ubadilishaji Jeni tayari imeinua mazao ya wakulima maskini na kuna uthibitisho wa ongezeko la mapato katika uzalishaji na ajira vitu ambavyo havingeweza kutokea.

11 Usimamizi wa urekebishaji wa gharama za Ubadilishaji Jeni zinafaa ziegemezwe kwenye sababu na madhara yaliyopo.Hii ina maana kwamba usawazishaji uegemezwe kwenye sifa bainishi maalum za aina ya mmea mpya kuliko kuegemezwa kwenye njia za teknolojia za uzalishaji wake.

12 Uchunguzi wa hatari au madhara ni lazima uzingatie, sio tu hatari za uwezo wa kutumia mmea mpya bali pia hatari za mmea mbadala kama aina yenyewe haiwezi kupatikana.

13 Juhudi dhahiri za sekta ya umma kwa sasa zinaandaliwa ili kukuza aina zilizoboreshwa kwa kutumia jeni, kama mihogo, viazi vitamu, mchele, mahindi, ndizi, mtama na mazao makuu ya kitropiki ambayo yatakuwa ya faida moja kwa moja kwa maskini. Juhudi hizi zinahitaji kusisitizwa mno.

14 Ukubwa wa changamoto unaokabili watu maskini na wenye afya duni ni lazima lishughulikiwe kama jambo la dharura. Kila mwaka ukosefu wa lishe bora husababisha magonjwa na kifo ambavyo vingeweza kuzuilika. Kupanda kwa gharama za chakula ulimwenguni mwote kumeonyesha udhaifu wa maskini katika ushindani wa raslimali. Kutokana na hayo faida zinaachiliwa zipotee milele.

15 Ukizingatia matokeo haya ya kisayansi, kuna maadili muhimu ya teknolojia hii ambayo hupaswa yafikie idadi kubwa ya maskini na wale wasiobahatika ambao wanazihitaji ili faida hizo ziwawezeshe kuinua kiwango cha maisha yao, waboreshe afya zao na kulinda mazingira yao.

Kwa ujumla, utumizi wa teknolojia ya Ubadilishaji Jeni imeonyesha umuhimu wake kwa kuboresha bidhaa za kilimo ulimwenguni mwote, lakini ni sehemu moja tu ya mikakati ambayo ni ya ncha nyingi. Kama vile Baba Mtakatifu Benedict XVI alivyoona: 'Inaweza kuwa na manufaa kufikiria uwezekano mpya ambao unafunguka kwa kupitia mbinu sahihi za kienyeji pamoja na ugunduzi wa mbinu za ukulima, wakati wote tuamini kuwa mbinu hizi zimekubalika, baada ya majaribio ya kutosha, yanayofaa na yanayothamini mazingira na yanayothamini mahitaji ya watu walio wengi ambao wamekandamizwa'. (3) Hata hivyo, tunatambua kwamba siyo maendeleo yote ya teknolojia ya Ubadilishaji Jeni yatakayoweza kufikia ahadi zake za hapo awali, kama inavyokuwa kwenye teknolojia yoyote ile. Ni lazima tuendelee kutathmini uthabiti wa mchango wa teknolojia zote zinazofaa, ambazo pamoja na njia za desturi za kuzalisha mimea na mikakati ya ziada zinapaswa kutumiwa ili kuboresha uhifadhi wa chakula na kupunguza umaskini kwa vizazi vijavyo. (4) Mikakati mingi kati ya hiyo inaweza kutumika ili kwa kuongezea nguvu zaidi pamoja na teknolojia za Ubadilishaji Jeni. Mikakati hiyo ni pamoja na kuhifadhi udongo wa juu kwa kutouchimbua na njia zingine za kutunza udongo, njia inayofaa ya utumizi wa mbolea, maendeleo ya aina mpya za mbolea na kutumia pembejeo za kilimo zisizodhuru mazingira, kuhifadhi maji, udhibiti wa vijidudu kwa kuunganisha njia nyingi, uhifadhi jeni tofauti, upanzi wa aina tofauti za mazao inapowezekana na kuboresha mazao yaliyopo (hasa 'mazao yatima' (5)) kwa matumizi mapana kwa kupitia njia za uwekezaji za umma na kibinafsi na ubia. Mambo mengine yaliyo muhimu mkuu kwenye kuongeza uhifadhi wa chakula au umuhimu mahsusi kwa nchi zisizo na raslimali ni pamoja na uboreshaji wa miundo msingi (usafiri, utoaji umeme na ghala za kutunzia) ukuzaji wa uwezo kwa njia ya kutoa ushauri wa ujuzi na wa haki kwa wakulima kuhusu uteuzi wa mbegu kwa kupitia huduma za mashamba ya majaribio ya mahali pahusikapo, uendelezaji wa mipango ya haki ya fedha na bima, na ukataji leseni ya umilikaji wa teknolojia. Hata hivyo, utambuzi kwamba hakuna suluhisho moja pekee kwa tatizo la umaskini na ubaguaji dhidi ya watu maskini katika sehemu nyingi haupaswi kuzuia utumiaji wetu wa Ubadilishaji Jeni kwenye mazao mbalimbali wakati ambapo yataweza kutoa mchango ufaao kwa suluhisho la ujumla.

Mjadala Mpana wa Umma

Teknolojia ya Ubadilishaji Jeni imeibua mvuto wa jumla kwa umma na mjadala duniani kuhusu mchango wa sayansi katika kuelezea changamoto nyingi zinazohusika na afya na chakula ambazo zinaikumba jamii katika karne ya ishirini na moja. Mjadala huu kuhusu nguvu na dhima ya uwezo na masafa ya utumizi yatakapoweza kutumiwa unakaribishwa lakini majadiliano ni lazima yategemee marekebisho yaliyo sawa au vinginevyo kuwe na taarifa zilizothibitishwa ikiwa sayansi na teknolojia zinahitaji kutathminiwa, kusawazishwa, na kutumiwa kwa faida ya binadamu.

Kukaa tu bila kufanya kitu, siyo uchaguzi mzuri, wala sayansi na teknolojia haziwezi kufunguliwa na kufungwa kama bomba ya maji ili kutoa masuluhisho mwafaka kwa matatizo yanapozuka:

Kwa vyovyote vile, kazi ya sayansi ni kuangalia mbele na kuona uwezekano wa hasara za baadae kabla, ili kuzikwepa na kupata uwezekano mzuri zaidi ufaao. Katika muktadha huu, kuna nyanja za kielimu sita zinazohitaji kuangaliwa: uelewaji wa umma kuhusu sayansi; pahali pa haki za umilisi wa kiakili; wajibu wa sekta ya umma; wajibu wa wafanyikazi wa serikali ushirikiano kati ya serikali; mashirika ya kimataifa na waajiriwa wa serikali; na usimamizi unaofaa na gharama zinazostahili za haki na urekebishaji.

Kuelewa Sayansi kwa Umma

Washiriki katika mkutano walikazia marambili kuhusu kutofahamu teknolojia ya Ubadilishaji Jeni ambako kumesambaa kwenye majadiliano ya umma na kwenye sheria za kiutawala. Kwa mfano, kitu ambacho hakitiliwi mkazo katika majadiliano ya umma ni kwamba aina zote za uzalishaji wa mimea unahusisha ubadilishaji wa vinasaba (genetic) na kwamba baadhi ya mifano ya kile kinachoitwa 'uzalishaji wa kidesturi' – kwa mfano ubadilishaji dutu kwa njia ya mionzi mategemeo yake ni madogo zaidi kuliko utumizi wa teknolojia za Ubadilishaji Jeni. Washiriki wote wa juma la mafunzo wamejitolea kutekeleza wajibu wao katika kuchangia hoja kwenye dayolojia za umma na mijadala ili waweze kupata taarifa na mwangaza. Ni wajibu wa wanasayansi wenyewe watafute mbinu ili wasikike, waelezee sayansi yao na waiweke wazi na kufanya masuluhisho yao yaweze kupatikana kwa mapana.

Tunawahimiza wale ambao wanapinga au wenye shaka kuhusu utumiaji wa kilimo cha aina tofautitofauti cha Ubadilishaji Jeni na utumizi wa Jeni za kisasa kwa ujumla watathmini kwa uangalifu sayansi iliyotumika na kuonyesha madhara ya kuzuilia teknolojia thabiti kwa wale wanaoihitaji zaidi. Uzuri kamili unaweza kutolewa tu kama majadiliano ya umma yameegemezwa kwenye ithibati ya viwango vya juu kabisa vya kisayansi na kubadilishana maoni kwa raia.

Mahali pa Kumiliki haki za Kiakili

Umilikaji wa haki una wajibu mkubwa katika kuendeleza teknolojia yoyote, ikiwa ni pamoja na bayoteknolojia ya kitabibu na kilimo, kama inavyofanyika katika vipengele vyote vya jamii ya kisasa. Tunatambua kuwa sekta ya kibiashara imetekeleza mengi kwenye kuchangia katika malengo ya kuondoa umaskini na uhaba wa chakula. Hata hivyo, kufuatana na mafundisho ya kijamii ya Kanisa, ambayo inaonyesha kuwa ni haki za kimsingi za watu wote za kufikia mali zilizomo duniani, (6) tunasisitiza kwa wahusika wote wa kibinafsi na umma kutambua madai yao halali ya kumiliki haki zao wanapaswa kama inavyowezekana, kuwa wasaidizi wa kisheria za raia kuufikisha ujuzi huu kwa wote na wasiruhusu kujitajirisha kusiko kwa haki au unyonyaji wa maskini na wasiobahatika. Ubia wa umma na watu binafsi umeendelea kuwa muhimu mno katika kuendeleza maendeleo na usambazaji wa mazao mbalimbali yaliyoboreshwa ambayo kwa kawaida hutumiwa na watu maskini katika nchi zinazoendelea.

Mradi wa kiubinadamu wa 'Mchele wa Thamani' umekuwa ni mfano bora sana wa ushirikiano kama huo, ambapo vibali vya kampuni za kibinafsi vilitolewa bila malipo, kwa umma kuwapa ujasiri wa kuendeleza aina ambazo sasa ziko tayari kutumiwa kwa mashamba ya wakulima kwa faida ya wanajamii ambao pia wao wamo. Mifano kadhaa kama hiyo inatayarishwa, maendeleo kama hayo huenda vyema na imani kuwa binadamu wote wana haki kumiliki matunda ya dunia.

Wakati sekta za watu binafsi zinaonyesha nia ya kutoa umilikaji wa teknolojia kwa faida za watu maskini wanastahili pongezi zetu, na tunawahimiza waendelee kufuatia kiwango cha juu sana cha maadili katika uwanja huu. Kwa sababu hiyo, tukizingatia uhusiano kati ya biashara na maadili, kila kampuni ya kibinafsi, na hususan za kimataifa, pia uwanja wa kilimo, haupaswi ujikite kipekee kwa faida za kiuchumi. Zaidi ya hayo yote inapaswa kuruhusu manufaa ya kibinadamu, kimila na ya kielimu. Kwa sababu hii, '*Karitas in Ventate'* hukaribisha maendeleo ya hivi karibuni kwenye maendeleo ya 'Uchumi wa raia' na 'Uchumi wa Ujima' mchanganyiko ambao hautengi faida bali huiona kuwa ni njia ya kufikia hatima ya kibinadamu na kijamii. Kwa hakika huu waraka wa baba mtakatifu unathibitisha kwamba 'Umilikaji kwa wingi wa aina za taasisi za kibiashara huleta kupanda kwa soko ambalo si kuwa limeendelea tu bali ni lenye ushindani zaidi.' (7) Fikara hizi ni za manufaa hasa kuhusiana na wingi na ubora wa chakula unapopatikana kwa wakazi.

Jukumu la Sekta ya Umma

Maendeleo ya mazao ya aina mpya ambayo ndiyo yaliyowezesha 'Mapinduzi ya Green' ya karne ya ishirini kupatikana kwenye maabara ya utafiti wa sekta ya umma kwa kiasi kikubwa kwenye nchi kadhaa. Ingawa sekta ya umma haina tena ukiritimba katika maendeleo hayo, jukumu lake muhimu bado ni la maana sana.

Kwa kweli hasa, inaweza kutumia fedha hizo kama inavyofanya kutoka mapato ya kando ya kitaifa na mashirika ya wafadhili ili kukuza utafiti wa mazao utakaofaa kwa walio maskini zaidi na makundi ya watu waliokandamizwa. Sekta ya umma ina jukumu muhimu katika kuleta upatikanaji wa matokeo ya utafiti, na unaweza kuvumbua kwa njia ambayo ni vigumu kwa sekta ya kibinafsi, ambapo maendeleo kilimo kwa ajili

ya kibiashara ndilo lengo kuu. Kama ushirikiano kati ya sekta za kibinafsi na umma zimeleta faida katika maendeleo ya utumizi mwingi wa sayansi na teknolojia kwa faida ya kibinadamu hasa katika maeneo ya kiafya, kilimo hakipaswi kuachwa kando. Kwa bahati mbaya, hatuna budi kutambua kuwa, katika shughuli za uboreshaji wa mazao na mbinu za kisasa zilizoboreshwa kwa mikabala ya kibayoteknolojia, usawazishaji uliokithiri na usio wa kisayansi unaongeza gharama za Utafiti na Maendeleo bila ongezeko lolote la kiambata cha usalama, na huifanya utumizi wake na asasi za umma kuwa mgumu na mara nyingi usiowezekana kwa sababu za kifedha.

Jukumu la raia

Serikali, jamii zilizoelimika, mashirika yasiyo ya kiserikali, mashirika ya kiraia na dini yote yanawajibu katika kuendeleza mazungumzo ya taarifa na kueleweka kwa mapana kwa umma kuhusu faida ambayo sayansi inaweza kuleta, na vilevile kuendelea kuboresha nyanja zote za maisha ya wale wasio na bahati. Ni lazima wasaidie kulinda maskini kutokana na unyonyaji wa aina zote kwa madhumuni yoyote yale, lakini pia kubeba jukumu la kuhakikisha kuwa jamii hizi hazizuiliwi kupata faida ya kisasa ya kisayansi, ili kuwazuia wasilaumiwe kwa hatia ya kuwa maskini, kukosa afya na uhaba wa chakula.

Ushirikiano kati ya serikali, Mashirika ya kimataifa na raia

Kama ilivyoonyeshwa tayari. Teknolojia ya Ubadilishaji Jeni tayari imetoa mchango muhimu wa uboreshaji wa mazao na kuongeza usalama wa chakula. Matumizi yanayofaa ya teknolojia hii ikichanganywa na mikabala mingine ya kimolekule kwenye uzalishaji mimea unaleta uwezekano wa nguvu wa kuendelea kuboresha bidhaa zote kuu na zile zinazojulikana kuwa ni Mazao Yatima katika nchi zinazoendelea. Matumizi ya maendeleo hayo yaliyothibitishwa kisayansi hivyo yanaweza kuzingatiwa kuwa Jambo Zuri kwa Umma Kiutandawazi. Kwa sababu ya gharama za Utafiti na Maendeleo ya hizi njia mpya kwenye uboreshaji mazao, ikichangiwa na udhibiti wa gharama za kuleta sifa mpya bainishi sokoni, teknolojia hizi za kimsingi zimekuwa zikitumika tu kwa makampuni ya kimataifa kwa leo bidhaa zenye kiwango cha juu cha ujazo mkubwa zinazolimwa katika nchi zilizoendelea.

Kuzalisha kwa kutumia Mmea Mzuri wa Umma kwa kutumia mkabala wa Ubadilishaji Jeni umekuwa na upungufu kwa sababu kuu mbili:

1 Gharama za juu zilizohusika na upungufu wa uwekezaji kwa serikali za kitaifa. Hii imesababisha kushindwa kutumia njia hii ili kuboresha na kurekebisha mazao yanayolimwa kienyeji, ikijumuisha yale mazao muhimu (yanayojulikana 'Yatima') kama mtama, mihogo, mkonotembo, n.k., ambayo haya si ya

kufanyiwa biashara na kimataifa na hayaruhusiwi kwenye uwekezaji wa kibiashara na makampuni ya kimataifa;

2 Urekebishaji uliokithiri na usio muhimu wa teknolojia hii ukilinganishwa na zingine zote, umesababisha ikawa ghali mno kwenye utumizi wake kwa mazao 'madogo' na yale ambayo hayawezi kutoa faida kwa wanamaendeleo kulingana na uwekezaji na hatari zilizoko. Hii bila shaka haihusiani tu na sekta ya kibinafsi: uwekezaji wote, wa kibinafsi au wa umma, unapaswa kuangaliwa katika mwanga wa faida zake zinazopatikana. Kwa hivyo, sekta ya umma vilevile ile ya kibinafsi zinaweza kujizuia kwenye kuendeleza bidhaa kwa matumizi machache ikilinganishwa na bidhaa za mazao makubwa kulingana na uwekezaji unaohitajika, tatizo la udhibiti na utoaji usio na hakika.

Hivyo kuna haja ya ushirikiano kati ya serikali, Mashirika ya kimataifa na wakala wa ufadhili na misaada ya eneo hili. Uwezekano wa faida wa ushirikiano wa aina hii tayari umeonyeshwa wakati mashirika ya kimataifa yanapoonyesha ari ya kujadiliana ubia na sekta za kibinafsi na umma ambao umeleta utoaji bure wa teknolojia kwa matumizi ya uboreshaji wa mazao. Kuhusu suala la 'Mchele wa thamani', hii ilikuwa imefanya uhamishaji wa teknolojia hadi kwenye nchi nyingi za Asia.

Mifano mingine ni pamoja na mahindi yanayostahimili ukame huko Afrika, mboga zinazostahimili wadudu na maharage huko India na Afrika, na dazeni nyingi za miradi ya ziada huko Afrika, Asia na Amerika Kusini.

Kuelezea wazi Mtazamo Unaofaa na Uangalizi wa Udhibiti

Utambuzi wa faida za teknolojia yoyote mpya unahitaji mtazamo unaofaa na urekebishaji. Urekebishaji uliozidi mno kiasi ulioundwa na nchi tajiri na kuwa na mwelekeo ambao karibu wote umejikita kwenye hatari za kubuni za mazao ya Ubadilishaji Jeni hubagua dhidi ya nchi zinazoendelea na nchi maskini, vile vile dhidi ya wazalishaji wadogo na maskini na wauzaji reja reja. Hii imewaweka watu maskini duniani katika hasara isiyokubalika. Madhara yanayotokana na hali ya kutoweza kutumia teknolojia halisi yenye matokeo bora haiwezi kugeuzika, ikiwa na maana kuwa gharama ya kupoteza fursa ya uwekezaji Utafiti na Maendeleo na bidhaa (na faida zake) haviwezi kurudishwa.

Tathimini ya aina mpya za mazao na zilizoboreshwa zinapaswa kuegemezwa kwenye sifa za aina za mmea na siyo kwenye teknolojia iliyotumika kuzikuza: zinapaswa kutolewa uamuzi kufuatana na sifa zao halisi. Hii ingeweza kurahisisha utumiaji wa uwezo wa teknolojia kwa faida yetu wote kwa kutoa aina ngeni ya mazao yote makuu na ya kienyeji yakiwa na sifa zilizoboreshwa. Hii kwa namna fulani siyo suala la kuwatumia maskini kwa majaribio, lakini ni kuhakikisha kuwa maskini wanaweza kuzipata teknolojia ambazo zimethibitishwa kuwa ni salama, zilizokubalika kwa mapana na zenye faida, katika sehemu kubwa za nchi zilizoendelea na zinazoendelea. Hatuwezi kuwa na chuki zaidi kwa ajili ya hatari za Sayansi na teknolojia na wakati huo huo kuwa na hatari za chakula na ukulima zaidi ya yale tunayoona yanayokubalika katika maisha yetu yaliyobakia.

Hatari zisizo za hakika zinazohusishwa na uzalishaji mazao kwa kubadili Jeni zao hazitofautiani na zile zinazohusishwa na zile zingine kama za matumizi ya teknolojia ya kijeni kwa viumbe hai (k.v., zile zinazotumiwa katika bayoteknolojia ya tiba au vimeng'enywa vilivyoongezewa uwezo kwa bayoteknolojia vinavyotumika katika jibini au utengenezaji wa bia). Hatari za muda mfupi zinazotokana na kuwepo kwa sumu au bidhaa za mzio zinaweza kuchunguzwa na kutengwa kwenye aina mpya za zao, hatua ambazo ni za hadhari zaidi kuliko ilivyo kawaida katika kulima aina za mazao zinazozalishwa kwa kubadilisha uzao. Kufuatana na athari za mabadiliko ya muda mrefu, kuelewa kwa sasa kwa mabadiliko ya kimolekule kwa kuwa hutokea kwa kiwango cha chini kiasili kwa kujianzishia zenyewe na kuleta mabadiliko ya kijeni, huonyesha dhahiri kuwa Ubadilishaji Jeni unatumiwa kwenye jumla za Jeni (jenomu) zinaweza tu kufuatisha mikakati asilia iliyochunguzwa ya mabadiliko ya kibayolojia.

Mabadiliko yenye kujitegemea yanawezekana tu kwenye hatua ndogo. Hii inaeleweka kama mtu anazingatia akilini kuwa jenomu za mimea ardhini ni kama vitabu vikubwa vya encycolopedia vyenye mamia ya vitabu kadhaa, wakati mabadiliko ya kiJeni kwa kutumia mbinu za awali zinaathiri Jeni moja au Jeni chache kati ya Jeni 26,000 kwa wastani kwenye jenomu za mmea.

Kwa hivyo, madhara yanayowezekana kutokana na mabadiliko ya kijeni hayawezi kuwa makubwa zaidi ya madhara ya hatua za kiasili za kibayolojia au za utumizi wa kemikali za mutajenisis, zote zinawajibika kwa uanzishaji mkubwa na dhaifu wa sifa za Jeni za mabadiliko kwa kiwango fulani.

Rekodi za kitakwimu zinaonyesha kuwa athari zisizokubalika kama hizo za ubadilishi Jeni ni za nadra sana na, katika hali ya ubadilishaji wa kiuzao hazitengwi.

Kutokana na maendeleo na kuelewa kisayansi tangu kupitishwa kwa itifaki ya Kartagena ya usalama uhai katika 2000, huu ndio wakati wa kuchunguza tena itifaki hiyo katika mwanga wenye msingi wa kisayansi wa kuelewa mahitaji ya urekebishaji na faida.

Imani, Sababu za Kisayansi na maadili

Kwa muumini, hoja ya mkristo ya maono yake ni kushikilia chanzo cha kiungu cha mwanadamu, hii ni kwa sababu ya nafsi ya binadamu, inayoeleza kwamba Mungu amewapa amri binadamu kutawala dunia nzima ya viumbe hai duniani ambavyo amevitumia kupitia mwangaza wa kiroho kufanya kazi yake. Katika njia hiyo wanadamu huwa wadhamini wa Mungu kwa kuendeleza na kubadilisha vitu asilia na kupata lishe bora kwa kutumia njia za mabadiliko. (8) Hivyo, ingawaje binadamu wana upungufu wamo kwenye ulimwengu, hata hivyo wataweza kushiriki katika nguvu ya Mungu na kuwa na uwezo wa kujenga ulimwengu wao, hivyo ni kusema kuwa mazingira yafaayo kwa maisha mawili ya kimwili na maisha ya kiroho, chakula chao na kuishi kwao vyema, kwa hivyo kuna njia mpya za binadamu za kuingilia dunia ya kiasili na isionekane kama ni kinyume kwa sheria za asili ambazo Mungu amezitoa katika uumbaji.

Kwa hakika, kama Paulo VI alivyosema katika Taaluma ya Papa ya Sayansi katika 1975, (9) upande mmoja, mwanasayansi pia lazima asisimuliwe na kuamini kuwa maumbile yana siri ambazo zinataka akili ya binadamu ivumbue na kuitumia, ili aweze kufikia kiwango cha maendeleo ambacho kiko katika mpango wa Muumbaji. Kwa hivyo, mwingilio wa kisayansi unapaswa uonekane kwamba ni maendeleo ya kimwili au vegetal/maumbile ya mnyama kwa faida ya maisha ya binadamu, katika njia hiyo 'vitu vingi kwa ajili ya manufaa ya maisha ya binadamu vimeongezewa zaidi kwenye sheria zote za kimaumbile, za kiungu na sheria za binadamu.' (10)

Mapendekezo

1 Kuimarisha upatikanaji wa taarifa zenye uhakika kwa warekebishaji, wakulima na watengenezaji bidhaa ulimwenguni ili waweze kutoa maamuzi yafaayo kutegemea taarifa za kisasa na ujuzi wa vipengele vyote vya uendeshaji kilimo kwa ajili ya, uzalishaji bidhaa na kuzihimili/ kuziendeleza.

2 Sanifisha – na razinisha - kanuni zinazohusika katika kutathmini na kuwa na makubaliano ya aina mpya za mazao (Iwe ni teknolojia iliyotokana na zile wanazoziita za kutayarishwa, kusaidiwa kuzaliana kwa kuziweka alama na kuteua au teknolojia ya Ubadilishaji Jeni) Zinaundwa ili ziwe za kisayansi, ziepuke madhara, ziwe za kuaminika na dhahiri. Ni jambo la umakinifu kwamba uwanja wa mada husika unapofanyiwa uhakiki; ni ni lazima uhakiki wenyewe uwe wa kisayansi na uzingatie madhara yaliyopo.

3 Tathmini tena matumizi ya kanuni za kutoa tahadhari katika kilimo, ziundwe tena kisayansi na kiutendaji na kufanya marekebisho ya mahitaji na hatua zinazolingana na madhara, na kufikiria madhara yanayohusishwa na ukosefu wa utendaji. Ni lazima iwekwe akilini kwamba busara ni hekima inayopaswa kuongoza kitendo. Ingawaje hiki ni kitendo cha hekima au busara kinahitaji kutolewa tahadhari tena ili kuweza kuwa na mshiko wa ubora ili kuzuia uovu, sehemu kubwa ya busara siyo tahadhari bali ni utabiri huo. Hii ina maana kwamba msingi wa hulka ya busara sio kuzuia utekelezaji ili uzuie madhara bali ni kutumia utabiri wa kisayansi kama msingi wa utekelezaji. (11) Hivyo Papa Benedict XVI, katika hotuba yake kwenye chuo cha Kipapa cha Taaluma ya Sayansi kwenye ufunguzi wa 2006 kipindi cha Uwezo kamili wa 'Ubashiri kwenye Sayansi', alikazia kwamba uwezekano wa kutoa ubashiri ni sababu mojawapo ya fahari ambayo sayansi hufurahia katika jamii za kisasa na kwamba ni uundaji wa njia za kisayansi ndizo zimeipa sayansi uwezo wa kutabiri jambo la shani, kuchunguza maendeleo yake, na hivyo kudhibiti mazingira ya wanadamu. (12) 'Kwa hakika tungeweza kusema', alithibitisha Papa Benedict, 'kwamba kazi ya utabiri, kudhibiti na kutawala maumbile ambayo leo sayansi inaimudu kimatendo kuliko zamani, yenyewe ni sehemu ya mpango wa Muumba. (13)

4 Tathmini Itifaki ya Kartagena, makubaliano ya kimataifa yanayorekebisha biashara za kimataifa kwenye aina za Ubadilishaji Jeni, ziliendelezwa wakati ambapo hapakuwa na habari zilizojulikana za sayansi ya Ubadilishaji Jeni, ili kuhakikisha kuwa zinakuwa mstari mmoja na uelewano wa sasa wa kisayansi

5 Mbinu huru za Ubadilishaji Jeni, ambazo ndizo za kisasa zaidi, za hakika na kutabirika kwa ajili ya uboreshaji wa kijeni, kutoka ile iliyokithiri urekebishaji usio wa kisayansi unaoruhusu matumizi yake ili kuimarisha ubora wa lishe na uzalishaji wa mazao (na hatimaye pia utengenezaji wa chanjo na dawa zingine)

6 Kukuza uwezo wa teknolojia kusaidia wakulima wadogo kwa kupitia matokeo ya utafiti wa kutosha, uwezo wa kujiendeleza na mafunzo yaliyoambatanishwa na sera zifaazo za umma

7 Kuhamasisha ukubalifu mpana wa utekelezaji wa kilimo chenye nguvu na chenye kuleta mazao na huduma za majaribio, ambavyo hasa ni makinifu kwa uboreshaji wa maisha ya watu maskini na wahitaji duniani kote.

8 Ili kuhakikisha kwamba Ubadilishaji Jeni unaofaa na uzalishaji wa kusaidiwa wa uteuzi wa kimolekule unatumiwa kuboresha mazao yanayohusika kupandwa kwenye mataifa yenye upungufu wa chakula na yaliyo maskini, ambapo hutegemewa kuwa na athari muhimu kwenye kuboresha usalama wa chakula, tunakazia kwamba Serikali, mashirika ya ufadhili ya kimataifa na ya misaada iongeze ufadhili wa fedha kwenye eneo hilo.

Ukizingatia umuhimu huo, mashirika ya kimataifa kama FAO, CGIAR, UNDP au UNESCO yana jukumu la kimaadili la kuhakikisha usalama wa chakula kwa idadi ya watu duniani sasa na siku zijazo. Ni lazima watumie juhudi zao zote kuleta ustawishaji wa uhusiano wa mashirika ya binafsi – umma ili kuhakikisha utumiaji usio na gharama wa teknolojia hizi kwa manufaa ya wote katika nchi zinazoendelea mahali ambako watakuwa na athari kubwa zaidi. (14)

Usuli

Juma la mafunzo la Taaluma ya Sayansi ya Papa, kuanzia May 15 – 19, 2009 ilitayarishwa, kwa niaba ya Taaluma ya Sayansi ya Papa, na mwanachama wa taaluma hiyo Profesa Ingo Potrykus, kwa msaada kutoka wanachama wa taaluma Profesa Werne Arber, na Profesa Peter Raven. Watayarishaji walijua kuwa kuanzia 2000, wakati ambapo makala ya mafunzo ya awali yalipochapishwa na Taaluma hiyo juu ya “Mimea ya chakula iliyobadilishwa kwa kutumia Jeni” ili ‘kuondoa Njaa Duniani’, uthibitisho mwingi mkubwa na tajriba zimekusanywa kuhusu mazao yaliyoundwa kijenetik.

Madhumuni ya juma la mafunzo kwa hivyo lilikuwa, kutathmini faida na madhara ya uundaji wa kijeni na wa utekelezaji mwingine wa kilimo kwenye misingi ya sasa ya ujuzi wa kisayansi na uwezo wake kwa matumizi ili kuboresha usalama wa chakula na ustawi wa binadamu kote ulimwenguni kwa muktadha wa kuendeleza wa maendeleo. Washiriki pia walifahamu mafundisho ya kijamii ya kanisa kuhusu bayoteknolojia na walikubali kanuni za maadili na kusisitiza matumizi yaafayo ya Ubadilishaji Jeni kufuatana na kanuni za haki kijamii.

Ushiriki ulifanywa kwa mwaliko tu na washiriki walichaguliwa kutegemea sifa zao za kisayansi kwenye nyanja zao tukufu za kiujuzi, shughuli na msimamo wao mkali kwenye haki za kijamii.

Watayarishaji walilazimika kuchagua washiriki, na walifanya uchaguzi kutegemea mahitaji ya kuendeleza malengo makuu ya mkutano, ambao ulihakiki tajriba ya awali hadi wakati huu. Ingawaje kulikuwa tofauti ya kimaoni, mitazamo ya hoja na mkazo miongoni mwa washiriki, wote walikubaliana kwenye kanuni nyingi zilizoko kwenye taarifa hii.

Washiriki wa Juma la Mafunzo ya kisayansi na umahiri waowanaonyeshwa hapa chini

katika mpangilio wa herufi za alfabeti.

Wajumbe wa Kipapa Taaluma ya Sayansi:

Prof em. Werner Arber • Uswisi, Chuo Kikuu cha Basel: Microbiology, Evolution.
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H.Em. Georges Kardinali Cottier, Vatikano City: Theolojia.
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Prof em. Peter H. Raven • Marekani, Rais Missouri botaniska Peponi: Ukuaji, Ikolojia.
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Prof Rafael Vicuña • Chile, Santiago, Chuo Kikuu cha Kipapa Katoliki Chile: Microbiology, Vinasaba Masi.

Wataalam nje:

Prof em. Klaus Ammann • Uswisi, Berne University: Ukuaji, Ikolojia.
Prof Kym Anderson • Australia, Chuo Kikuu cha Adelaide, CEPR na Benki ya Dunia: Maendeleo ya Kilimo Uchumi, Uchumi Kimataifa.
Dr iur Andrew Apel • Marekani, Raymond, Mhariri Mkuu GMObelus: Philosophy, Sheria.
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Prof Peter Beyer • Ujerumani, Albert-Ludwig Chuo kikuu cha, Freiburg: Biokemia, Metabolic Pathways.
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Prof Nina Fedoroff • USA, The Pennsylvania Chuo cha Kitaifa: Masi ya Biolojia, Biotechnology.
Prof Dick Flavell • Marekani, ceres, Inc: Bayoteknolojia ya Kilimo, Genetics.
Prof em. Jonathan Gressel • Israeli, Rehovot, Weizmann Taasisi ya Sayansi: Kuhami Mimea,, biosäkerhet.
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Prof Drew Kershen • Marekani, Chuo Kikuu cha Oklahoma: Sheria ya Kilimo, Bayoteknolojia ya Kilimo

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Prof Monkumbu Sambasivan. Swaminathan • Uhindi, Mwenyekiti, M.S. Swaminathan Msingi wa Utafiti: Kilimo, Kuhimili Maendeleo.
Prof Chiara Tonelli • Italia, Chuo Kikuu cha Milano: Genetics, Cellular lagstiftning.
Prof Albert Weale • Uingereza, Nuffield Baraza Bioethics na Chuo Kikuu cha Essex, University College of London, Dept. of Political Sciences: Social & Political Sciences.
Prof Robert Zeigler • Filipino, Manila, Mkurugenzi Mkuu wa Taasisi ya Utafiti wa Kimataifa Rice: Agronomy, Plant Pathology.

Notes

1. Waraka wa Baba Mtakatifu
2. Mungu kwenye uumbaji'
3. Caritas in veritate
4. Hii ni kanuni ya kukumbukwa katika uzalishaji wa kilimo chenyewe, wakati kunapokuwa na swali linalohusu utumizi wa bayoteknolojia, ambalo haliwezi kutathiminika kipekee kwa misingi ya faida za kiuchumi. Ni lazima kwanza zichunguzwe kwenye majaribio ya kisayansi na ya kimaadili, ili kuzuia maangamizi ya afya ya binadamu na kuharibu dunia baadaye' (John Paul II, Hotuba ya Jubilii ya Kilimo ya Dunia, Novemba 11, 2000).
5. Mazao yatima' ambayo pia huitwa mazao yaliyokataliwa au mazao yaliyopotea, haya ni mazao ya thamani ya juu kiuchumi katika nchi zinazoendelea. Haya mazao ni pamoja na mazao ya nafaka (kama vile mtama na tef) aina ya maharage (mbaazi, majani ya njegere na karanga za bambara), na mazao ya mizizi (mihogo na viazi vitamu). Ingawa mazao yatima ni muhimu kwa uhai wa maisha kwa mamilioni ya wakulima maskini wasio na mtaji, utafiti wa mazao haya umezorota nyuma ya yale mazao makuu. Kukuza mavuno ya kilimo na kufikia hali ya kujitosheleza kwa chakula kwenye nchi zinazoendelea, utafiti wa mazao yatima unapaswa utiliwe mkazo zaidi.
6. Centesimus Annus & 6
7. Caritas in Veratate
8. Mungu ana mamlaka yote juu ya vitu vyote; na yeye, kutokana na utoaji wake aliagizia vitu fulani vitumike kwenye kuhimili mwili wa binadamu kwa sababu hiyo mwadamau ana mamlaka juu ya kiasili ambayo juu ya vitu vyote kuvitumia na kuvituma. (Thomas Aquinas, *Summa Theologica,* II-II, q.66, a. 1 ad 1)
9. Cf. Paul VI Hotuba ya Kipindi cha kwanza cha Papa kwa Taalimu ya Sayansi ya 19 Aprili 1995 Hotoba za Papa, Vatican City 2003, p.209
10. St. Thomas Acquinas, *Summa Theologica,* I-II, 94 a.5. cf loc. Cit. ad 3.
11. Busara ni njia razini ya kufikia kiwango cha juu cha ukweli, unaohusika na vitendo vya vitu ambavyo ni vizuri kwa maisha ya wanadamu. (Aristotle, *Eth, Nic.,* VI 4, 1140 b 20, Eng,tr. J, Bywater). Cf pia mwisho wa sura hiyo.

12. Utabiri ni kanuni ya busara… Hivyo kwamba neno hilo la busara limechukuliwa kutokana na Utabiri (kupata kile cha manufaa) kutokana na sehemu yake kuu' (St. Thomas Acquinas, *Summa Theologica*, I-II q. 49, a. 6 ad 1)

13. Papa Mtakatifu Benedict XVI, katika hotuba yake kwenye chuo cha Kipapa cha Taaluma ya Sayansi. Inapatikana kwenye mtandao http://www.vatican.va/holy-father/benedict_xvi/speeches/2006/november/documents/hf_ben-xvi_spec_20061106_academy-sciences_en .html

14. Cf. P. Dasgupta, 'Sayansi kama Asasi: Kuweka mikakati katika Uchumi Mpya wa Kijamii' katika Kongamano la Dunia la Sayansi *: Sayansi kwa Karne ya Ishirini na Moja, Kujitolea Upya (*UNESCO, Paris, 2000).

Translations facilitated by Clive James, and Margareth Karembu,
International Service for the Acquisition of Agri-biotech Applications (ISAAA)

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http://www.ask-force.org/web/Vatican-PAS-Statement-FPT-PDF/PAS-Statement-Bahasa-FPT.pdf

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