

# Values in risk assessment and risk management of GMO

Knut G. Berdal  
National Veterinary Institute  
P.O. Box 750 Sentrum  
0106 OSLO  
NORWAY

Arne Holst-Jensen  
National Veterinary Institute  
P.O. Box 750 Sentrum  
0106 OSLO  
NORWAY

## 1. Introduction

Plant breeding has had, and still has, an immense importance to human beings. The present human population could not have been fed without the many fold increases in crop yields that plant breeding has provided. However, the use of new varieties, can also involve risks at several different levels - the agricultural system, ecosystem, environment, human and animal health, economy, society, trade and international relations. This is true for the so called genetically modified organisms (GMOs) as well as for non-GMOs. Notably, both GMOs and other breeding products are genetically altered, so the term genetically modified (GM) which refers to products of a particular technology may be confusing. The safety of foods from plants genetically altered through plant breeding was not questioned until transgenic crop plants came into commercial production in the 1990-ies. GM varieties, which are derived through recombinant DNA technology, are by legislation required to be subject to extensive and costly safety research, public safety assessment and regulatory authorisation before they are accepted for cultivation or use as food or feed.

From a food safety perspective it is fair to ask the questions: Do plant varieties developed through other techniques than recombinant DNA technology also pose similar risks that should be assessed in a similar manner? Is the current safety evaluation standard for GM plants justifiable, especially relative to the safety evaluation of varieties developed through other techniques? Here we will provide some analysis and discussion on these complex questions. When lack of coherence between the regulatory regimes for GMOs and traditional plant breeding is observed, this will be evaluated from an ethical point of view.

## 2. Plant breeding and GMO

GMO crops were introduced commercially in 1996. Since then the global area planted with GMO crops has increased rapidly (see figure 1).

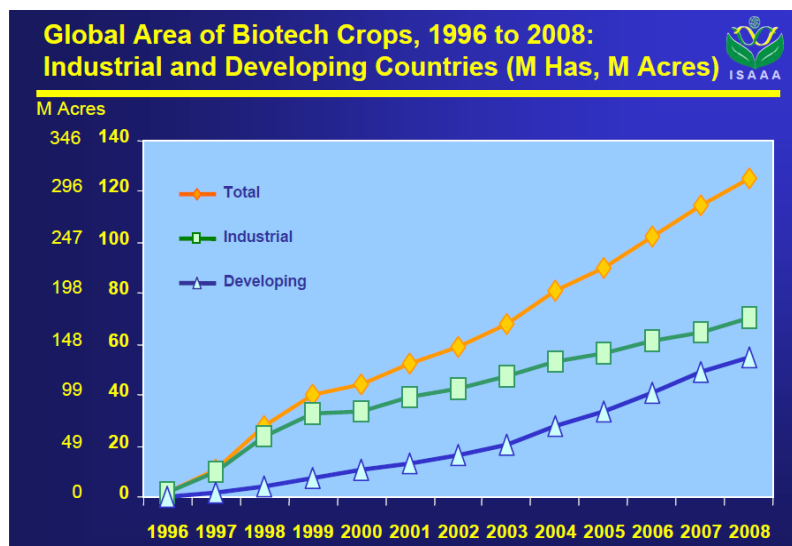


Figure 1. Global area of GMO crops. Reprinted with permission from Global Status of Commercialized Biotech/GM Crops. International Service for the Acquisition of Agri-biotech Applications (James, 2008).

Here we focus on risks to human health from new plant crop varieties, such as GMOs. In the USA, there have been issued 13 000 permits for field trials, and in the order of 100 GMOs have been deregulated for

commercialisation (GAO, 2008). However, in Europe many GMOs are only authorised for importation as GMO foods. Unless the imported material may be viable and can grow in the receiving country, the main risks derived from the GMO will therefore have to come from consumption. There are at present approx. 20 GMOs authorised for food use in the European Union (EU), while only one GMO is authorised for growing. Even though Norway has a similar regulatory regime as in the EU, there is not yet a single GMO authorised for use in food in Norway.

All breeding material is evaluated throughout the breeding process, and individuals with obvious unfavourable traits are usually discarded. This screening is generally limited to easily observable traits, that is, morphological (visible) or agronomic traits. Contents of toxic compounds, allergens and nutrients are sometimes measured in plants where they are known or expected to be of relevance to human or animal health (e.g. solanine in potato which is known to be toxic to humans). However, in general very little safety related research is conducted on non-GMO varieties, primarily because of the lack of legal requirements for safety research on new non-GMO varieties (except in Canada regarding non-GMO varieties with novel properties).

While GM varieties in many jurisdictions around the globe are legally required to be subjected to extensive and costly safety research, public safety assessment and regulatory authorisation before being accepted for cultivation or food purposes, similar requirements are normally not in place for non-GMO varieties. However, it may well be that non-GMOs can pose similar to, or other risks than, GMOs. This can only be clarified on a scientific basis if the different breeding techniques are compared with regards to potential for unintended and adverse effects. The potential benefits of breeding techniques may also deserve to be considered as part of a comprehensive risk benefit analysis.

At the beginning of the 20<sup>th</sup> century, plant breeders started to use hybridisation (through crossing) of different plant materials as a tool to increase the genetic variability within a crop on which selection could be imposed. Crossing can be done within a species or between relatively closely related species. Some species hybridise in nature, while others can be subject to induced crossing through chemical and/or physical treatments (stress). Embryo rescue was used to obtain an interspecific cross as early as in the 1920-ies. The protoplast fusion technique was developed from the 1970-ies. Crossing of a crop species with a related, non-domesticated species is commonly done in order to introduce genes not present in the gene pool of the crop species. However, there might be toxic or other undesirable side-effects genetically linked with the desired traits.

By exposing plant material to chemical mutagens or ionising radiation, the mutation rate can be increased dramatically above the natural background mutation rate. Proof of mendelian inheritance of changes induced by X-rays was presented in the late 1920-ies, but induced mutagenesis did not come into practical plant breeding until the 1950-ies. Induced mutations include both mutations in genes and chromosomal rearrangements. In the IAEA Mutant Variety Database (<http://www-mvd.iaea.org> accessed March 8<sup>th</sup> 2009) there are listed 2570 released varieties developed through mutagenesis. Around 90 % of the varieties have been mutated using radiation. Recent analyses of induced mutant populations indicate a mutation rate of 5000-50000 per cell (Waugh et al., 2006).

Selection for one trait may lead to correlated effects on other traits. This may occur when one gene affects several traits or it may occur due to effects of closely linked genes. Disease and pest resistance is often based on the production of certain enzymes or chemical compounds (secondary metabolites) that are toxic to plant pathogens or insects. These substances are sometimes toxic to human beings or other non-target organisms as well, in which case selection for resistance may have adverse effects.

Independent of the breeding technique involved the novel trait found in any new variety will have its basis in genetic alterations and will co-exist with additional unintended alterations. Some unintended alterations may be discovered while others remain unknown. These alterations may be unwanted as they may impose adverse effects on the plant, the environment or human health.

There are not yet any well documented examples of adverse health effects associated with commercialized GMOs. Regarding non-GMOs there are a limited number of well documented incidents with adverse health effects associated with the breeding (Cellini et al., 2004). One example of this is selection for pest resistance leading to increased levels of furanocoumarins in celery. Furanocoumarins can cause severe skin irritations in humans and are carcinogenic. A variety bred for enhanced insect resistance in celery has caused skin problems among workers that handle these plants. Selection for disease resistance can lead to increased levels of the toxin solanine in potato. There is also an example of adverse effects from eating a certain squash variety.

A number of genes closely linked to the genes encoding the desired trait are likely to be co-introduced into any new variety descending from such a cross (linkage drag). In most cases the identity and function of these genes will be completely unknown. Introduction by transformation (GMO), on the other hand, does not involve the linkage drag described above and thus it is unlikely that irrelevant genes linked to the gene of interest will be introduced.

The safety of foods from plants genetically altered through plant breeding was not questioned until transgenic crop plants came into commercial production in the 1990-ies. A large number of food crop varieties cultivated during the last century were developed using induced mutagenesis or introgression (crossing in) of genes from related species. There are relatively few examples of food crops with documented adverse effect on human health where this effect is believed to be caused by the breeding process and not by characteristics intrinsically present in (one of) the species involved in the breeding process. This may indicate that there is not a strong need for safety assessment of foods derived from crop varieties developed with these techniques. However, subtle, long-term differences in the effect of genetically altered plants and their non-altered counterparts are difficult to detect.

To our knowledge there is presently only one study published which reports on the comparative safety of various breeding techniques. This is the National Academy of Sciences report from 2004 on approaches to assess unintended health effects in genetically engineered foods (NAS, 2004). Various breeding techniques are scored along the scale likelihood of unintended effects (figure 2). The main finding in this assessment is that there are risks associated with all breeding techniques and that there is no particular high risks associated with GMOs relative to some of the older or more conventional breeding techniques. Thus, the belief that risks associated with foods derived from GMOs are qualitatively different from risks associated with foods from other crop breeding techniques are not supported by scientific inquiry so far. Indeed, most if not all of the biological mechanisms active when a GMO is generated, are also found to be active to a smaller or greater extent when the other breeding techniques are applied.

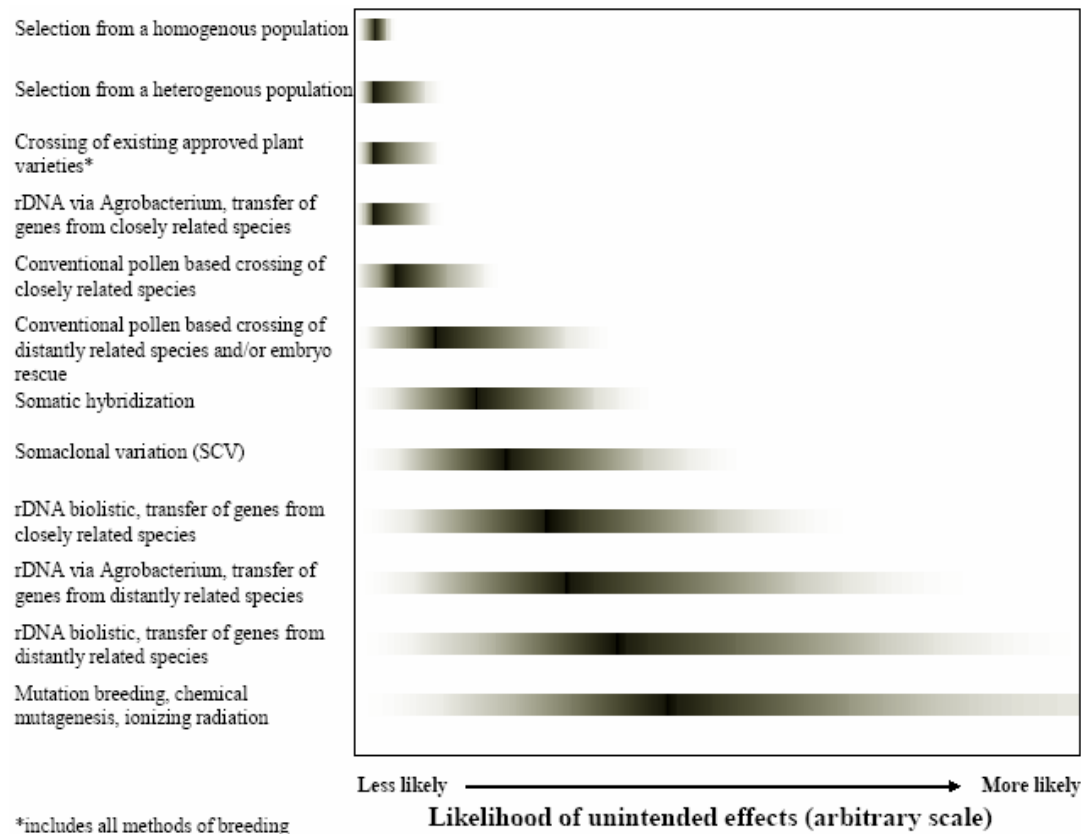


Figure 2. Likelihood of unintended effects from different breeding techniques. The GMOs are made from different rDNA techniques associated with different levels of risk. Reprinted with permission from Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects, 2004 © by the National Academy of Sciences, Washington, D.C.

### **3. The values accentuated by the introduction of GMOs**

The questions related to use of GMO in the food chain have generated extensive debates over the last two decades. While medical use of e.g. pharmaceuticals from GMOs is widely accepted, the use of GMOs to produce food is in many countries rejected by a majority of those who have taken a stand, especially in Europe (Eurobarometer, 2006). It is important to take into account that attitudes to GMO may have “value-expressive” functions to consumers rather than being a strict risk benefit calculation assumed by models of technical rationality (Frewer et al., 2004). Let’s take a look at the values that are frequently reiterated in relation to the use of GMO in agriculture and food.

#### **3.1 Protection of health and the environment**

In the early days, after the introduction of gene technology, the possibility of rewriting the genetic code of living beings raised several deeply philosophical and religious questions. However, as research provided more information and the technology lost some of its power to generate normative shocks, the arguments became more and more profane. What were the risks to health and environment? Such questions, however, normalise the debate on GMOs because the question of health and environmental risk is the same that is asked for any human activity, even those that are not associated with any particular ethical or religious concern.

Even though the value of human health and the integrity of the environment are more and more often used as normative critique against agricultural GMOs there may be other values that are arguably threatened or promoted by GMOs. Some of these are discussed below:

#### **3.2 The sacredness of nature and living systems**

Even though the idea of evolution by natural selection is not new, the sacredness of living beings is a central value in several cultures, including Christianity and Buddhism. When breeding was used to modify plants and animals since pre-historic time, it was predominantly the natural variation between individuals and closely related species that was exploited. Gene technology, however, has enabled humans to read and rewrite in much greater detail the genome of living beings. This is seen by many as a violation of the integrity or sacredness of living beings. The potential use of “terminator” technology, which would render GMO plants sterile, is one such example.

#### **3.3 Economic and social equality**

Most of the commercialised GMOs are owned by USA-based multinational biotechnology companies. Farmers are often keen on using new seeds when these are expected to increase the income. GMO seed prices have included a large premium and the farmers have been obliged not to harvest seeds for their own future sowings, but rather to buy new seeds every year if they want to grow that particular variety. This scheme has not been popular in many circles, despite being a common agricultural practice on IPR protected goods. The agrobiotechnology and in particular the GMO business has been a vector of capitalism and industrialisation of agriculture and it is easy to argue that the power of the biotech companies has risen while the autonomy of small farmers has been reduced. Like any new technology that increase productivity, as seen with GMOs, a choice is imposed on the actors in the market- use the technology or become less competitive relative to your competitors.

#### **3.4 The right of consumer choice**

In the 1990-ies many European countries established a legal framework that opened up for GMOs that were documented to be safe as part of an elaborate authorisation procedure. However, since the issue of GMOs was extensively debated, and the general population was sceptical, it was decided that food containing GMOs should be labelled. This was intended mainly to ensure consumer choice.

#### **3.5. The basic value of sufficient, safe, and nutritious food**

The major cause of famine today is not a general shortage of food in the world but the lack of optimal distribution. Historically, however, food production has been a major limiting factor. Recent, dramatic increase in food prices has put focus on the effects of an anticipated increase in world population. Economic growth in countries with large populations is also expected to redirect foods to consumption as feed for meat production. Thus, increased food production is necessitated. GMOs may contribute to food security. Maybe more important, the content of nutrients in the major staple crops may be optimized. An additional point is that food safety may be improved. Many food crops contain hazardous levels of toxins due to microorganisms like fungi. GMOs may be developed that are resistant to toxic microorganisms or less susceptible to secondary infections through wounds caused by insects. Thus, GMOs may contribute to the basic value of sufficient, nutritious and safe food.

### **3.6. The value of the autonomy of science and personal freedom**

Modern liberal societies are based on freedom in many areas, including the acquisition of knowledge through scientific inquiry and the civil freedoms. This includes the opportunity to develop new businesses based on technological invention. This freedom is in principle only limited by duty not to impose harm on others.

### **3.7. Prudence and precaution**

The first decades after the Second World War were set in the light of unbound optimism in progress and technological inventions. The realisation that new technologies may introduce risks that were not foreseen (such as DDT, greenhouse gases, and mad cow disease) made the general population and the regulators of novel technologies more sceptical. Risks were becoming an increasingly important aspect of modern society. Indeed, in many cases the risks, both their nature and magnitude are not known. There is a higher level risk that must be taken into account, namely that we in some cases do not know what we do not know about risks. Thus, the prudent attitude “better safe than sorry” was translated into national and international policies becoming known as the precautionary principle. In cases where there are large risks and ignorance affiliated with a certain technology, and consequently sufficient risk assessment is precluded, the risk managers should seriously consider the option to reject or postpone the technology.

## **4. The clash of values in risk assessment and risk management of GMOs**

While technology and science has been the driving force in the development of GMOs, science has also played an important role as the competent expertise and arbiters in the discussion on the risk aspects of GMOs.

Since the values that have accentuated the GMO debate have been so strong and emotional, some of the fundamental values of science, such as truth and independence, have been set under pressure.

### **4.1 The problem of social values both within and after risk assessment**

Out of the 180 member states in the intergovernmental UN framework CODEX Alimentarius, which deals with international trade related guidelines and standards of food safety, only two states generally rejected GMO in food production at the 2008 summit. These two states are Sudan and Iran, and the arguments were that of food safety, even though other legitimate factors, such as ethics, may be invoked in CODEX. There are two main explanations for the rejection of GMO food by this minority of states. These two countries may have scientific evidence of risks that other states do not possess. Another explanation may be that there are other values or interests behind the rejection of GMO food, but that the use of the main normative “currency” of CODEX - that is food safety – is more likely to achieve international support of national policies..

The above example may be rather obvious, but in the field of GMO risk is only one of many important values that are considered and negotiated. However, health risks are a universally agreed value with a high degree of legitimacy. Thus, even when risks are forwarded as the arguments against GMOs there may be other values that lure behind. The majority of GMOs that have been risk assessed by scientific experts in governmentally established committees have been found to be equivalent to traditional food crops with regards to safety. Simultaneously, many interest groups and non-scientific actors have claimed that the same GMOs constitute unbearable risks. Like the case above, with Sudan and Iran, other values – or interests - may be the underlying objection to the technology. If this is the case, the risk assessments that are forwarded publicly are merely substitute arguments hiding the underlying motivation.

The biotech companies primarily develop and sell GMOs to earn money. The fear of many, however, is that the aim of making money may prevent the companies from disclosure of adverse effects. Indeed, there are cases where adverse effects of products already on the market have been withheld. On the other hand, there may not be many cases where products have been introduced to the market after identification of adverse effects in the pre-marketing process. The popular conception is that industrially funded research is biased and not trustworthy and that publicly funded research is necessary to ensure independence. This notion is not necessarily correct. While national research councils have in place review procedures focusing on scientific quality, direct funding from stakeholders may be channelled to small niche institutes with a proven track record of biased researchers (NENT, 2004).

The ideal of collective reasoning and democratic decisions is that it should be based on a certain level of open and unbiased knowledge of the world as it is. A rational and critical discourse is hampered if the factual inputs are biased. The scientific assessments should be a foundation upon which social deliberation takes place.

#### **4.2 The issue of normative consistency**

Risks derived from GMOs are not managed in a consistent way relative to risks derived from other breeding technologies. A fundamental ethical principle is that equal cases should be treated equally. This principle is the ideal in modern democracies as well. Thus, risks arising from GMOs should be treated along the same principles as identical or similar risks arising from other breeding techniques.

In Norway there is a specific law dealing with GMOs, i.e. the Gene Technology Act from 1993. According to this act, it is not only a requirement that GMOs shall not constitute a risk to health or the environment. There are three additional considerations that should be taken into account for each new GMO, that is 1) how it contributes to a sustainable development, 2) ethical considerations, and 3) social consequences. Indeed, the Norwegian Biotechnology Advisory Board has required documentation that each of these considerations is secured. The industry, on the other hand, is reluctant to provide such documentation because of the cost and scientific problems associated with such documentation of beneficence. The compliance costs for regulatory approval, to ensure health and environmental safety, are 6 to 14 million USD (Kalaitzandonakes, 2007). The costs associated with documentation of additional considerations have not been put to a test.

There are additional problems associated with documentation of the three additional requirements. The requirements are not consistent based on several different interpretations. Firstly, there are no requirements for documenting the safety of other breeding technologies, which may pose higher or lower risks. Contrarily, GMOs for which the safety must be documented also have to fulfil additional requirements. Moreover, the three additional requirements are not found in relation to food production or agricultural practices. The fundamental duty to be respected when introducing products to the market in the food sector, and in other sectors as well, is that the products do not cause harm to health or environment. A product without such adverse effects may be legally introduced to the market. In modern democracies, it is not the state that determines which products consumers should buy or which products that are the better. Therefore, the inconsistency is not only seen when comparing breeding techniques, but also when considering general principles regarding trade and the market. In addition, these extra requirements are only found in Norway. Thus, there are issues found at the level of international trade and standardisation as well. These issues indicate that the regulatory regime on GMO was established as a relatively rapid response to a new technology threatening important values and associated with risks and uncertainties. In such circumstances, the value of food and environmental safety trump the ideal of consistency.

#### **4.3 Publicly ensured food safety versus consumer choice**

GMO labelling was developed to ensure consumer choice. Additionally, a secondary argument was that this would provide a "safety net" which would allow for more easy withdrawal of products if adverse effects were identified after products were brought to the market. Unlike most other labelling requirements do labelling of GMOs (and organic products) not provide information on what the product consist of. Rather, the label provides information on some steps in the production process. GMO labelling allows consumer to respect all their GMO related values.

In addition to this, the question of labelling is as much a fight on the issue of stigmatizing. Some countries claim that GMO labelling constitutes unduly trade barriers since there are no documented food safety issues related to authorised GMOs. The effect of stigmatizing is also seen with irradiation of food to kill pathogenic bacteria and improve food safety. This technique has, despite its proven record in improving food safety, not been used to any large extent due to the labelling requirement and the stigmatization of a "radioactivity" label. In European countries where GMOs have been authorised the consumers do not have the opportunity to choose, possibly less expensive, GMO-labelled products because they are basically absent from the market. Companies do not dare to introduce the products possibly due to protests from different consumer groups, and the fear of losing reputation. Notably, the labelling requirement was followed by traceability requirements that may be costly and difficult to implement for small and medium enterprises in the food sector. Consequently, the availability of niche products may be reduced, partly as a consequence of a desire to ensure consumer choice.

#### **4.4. The problem of co-existence and low level presence of GMOs**

The relatively wealthy Europeans have no immediate problems with a restrictive policy on GMOs with regard to food security or availability of nutrients. Europeans may in stead be facing other problems as a consequence of their restrictive practice with respect to GMOs. The availability of food and feed material without GMOs is generally becoming more and more limited and the price of such products increases. Imported foods and feeds containing detectable but non-authorised GMO are presently rejected from the EU market even if the GMO has been evaluated with regard to safety and is authorised in other countries. The number of countries where GMOs have been authorised is increasing and the diversity of GMOs grown commercially or in field trials is also increasing, partly as a consequence of regional preferences and needs for local adaptations. Consequently, the

probability of introduction of non-authorised GMOs in the food supply chain is likely to increase too. The consequence of this is that it will become increasingly difficult to maintain or establish GMO free supply chains. Another, somehow connected issue is that of territorial co-existence of GMO and non-GMO crops. GMOs may be introduced at low levels into non-GMO fields by several different means. The consequence of low-level presence of GMO is that international trade, consumer choice and farmer's autonomy may be harmed. In these situations, there is no food safety concern. The GMOs are present at low levels, and they have been authorised after thorough safety assessments by the state or other states according to international guidelines. Thus, the problem is due to the fear that a stigmatized technology will violate consumers preferred choice to avoid eating any GMOs. The policy of totally segregated production chains and labelling may rapidly become nonviable from a practical perspective. Currently, there are extensive national and international initiatives to facilitate co-existence of GMO and non-GMO.

#### **4.5 The issue of the overall good**

There are risks to health and the environment associated with GMOs as there are with any effective breeding technique. However, after decades of intensive research and commercial production and consumption since 1996 there is yet no evidence of a single harm to human or animal health. Some environmental issues are unique to GMOs, but at the same time there are elaborate risk assessments, authorisation procedures and mitigations with the aim to ensure environmental safety. Thus, the risk aspects seem to be manageable. The question that naturally follows is; what are the overall effects of the risk aversion specifically directed against GMO of, particularly, the Europeans? This question will not be answered here but one issue will be mentioned.

There are very large potential gains promised by the proponents of the biotechnology revolution. Even though there is a certain level of hype associated with any ascending technology, there are also important dilemmas that must be faced such as the need for a doubling of the world food production over the next forty years (FAO, 2008). Moreover, there are very serious nutritional and environmental deficiencies associated with the current agriculture and food supply in certain parts of the world. Even though most people obtain sufficient energy from their food there are serious nutritional deficiencies in major crops such as rice and maize.

GMOs may undoubtedly contribute to increase food production as well as to ameliorate some of the nutritional and environmental deficiencies associated with food production today.

Annually, new millions of people die or become victims to chronic diseases due to food deficient of vitamins, amino acids and other micro- and macro nutrients. Vitamin A deficiency is a leading cause of preventable blindness and mortality among children and pregnant women, and is a public health problem in more than half of all countries. According to the WHO and CDC (Center for Disease Control, USA), 250 million preschool children are vitamin A deficient. Half a million are estimated to become blind every year, of which a majority (70%) dies within one year after becoming blind.

Rice varieties have been developed with sufficient levels of vitamin A to strongly reduce the problem of vitamin A deficiency (Yu et al., 2000). New varieties could have been on the market within a few years if the increased vitamin A content had been achieved with traditional breeding techniques such as mutagenesis or wide-hybridisation. However, since gene technology was a part of the breeding process the regulatory requirements and heavy documentation needs are still not passed. And more years are still to pass before golden rice will reach the millions that are affected by vitamin A deficiency.

## **5. Conclusion**

The management of GMO is argued to be risk based and founded on scientific risk assessment. We have tried to show that several values make the GMO policies a pragmatic mixture of value assessments and risk assessments. However, the normative shock that was generated by the introduction of GMOs in their first years is gradually disappearing. Over the last decade GMOs have become accepted by many countries, provided the GMOs are subjected to thorough safety assessment and safety management on a case by case basis.

This regime captures and manages a variety of confrontations between GMO related values. Despite the growing awareness that the risks associated with GMOs are comparable to risks associated with alternative technologies, the regulatory and normative framework is radically different. GMOs are understood as highly risky until their safety is proven, while food crops generated with other technologies are considered safe and no documentation or authorisation is needed.

The current regime is a pragmatic response to widespread popular scepticism towards GMO. The ideological and normative bitterness of the “GMO-pill” is in Europe sweetened by a regulatory framework that is focusing on guaranteed safety and consumer choice. The broader consequences on the global level are a threat to values such as liberal rights and business opportunities, coupled with lost opportunities to introduce better crops that may contribute to food security and human health.

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