3.4.4
Field releases and Commercialisation of GMOs in CEE Countries

Until 2003, only experimental field trial releases have been authorised by the competent authorities of the CEE countries. Examples on field trial releases authorised in the CEE countries are:

Hungary	Herbicide and insect-tolerant corn, herbicide-resistant oilseed rape, virus-resistant potato and tobacco, improved protein in wheat
Poland	Herbicide-resistant sugar beet, virus-resistant potato, herbicide-resistant oilseed rape, virus-resistant plum,
Czech	RepublicVirus-resistant plum, potato with reduced sweetening, improved flax

3.4.5
Information Sources

Biosafety regulations in CEE countries. All important latest documents on Biosafety and Regulation and texts of National Laws are available at http://www.biosafety-CEE.org

European Federation of Biotechnology (1999) Biotechnology legislation in Central and Eastern Europe, Briefpaper 9

3.5
Genetically Modified Plants and Risk Analysis

Anne-Katrin Bock

Risk analysis includes risk assessment, risk management and risk communication. Risk assessment is the first and crucial part of the risk analysis process of GMOs. The principal approach on a case-by-case basis and proceeding step-by-step is generally accepted, but harmonisation of the different methods used on an international basis is needed. Risk assessment needs to comply with high scientific standards. Scientific uncertainty in assessing potential risks needs to be acknowledged and dealt with in an open and transparent way that also includes the public. More research is necessary to fill some of the knowledge gaps.

3.5.1
Introduction

Risk assessment has a long tradition in regulating human activities with the aim to minimise or avoid risk to human health and the environment. Examples can be found in the production of medical products, chemistry or nuclear power. According to European regulations, the safety of GMOs has to be assessed prior to releases into the environment and placing on the market. The approach is described in more detail in Directive 2001/18/EC on the deliberate release into the environment of GMOs, which was adopted in April 2001 and repealed Directive 90/220/EEC in October 2002. In the Annex II of this Directive the principles

for the so-called environmental risk assessment, which also includes human health effects, are laid down. Concerning food, Regulation (EC) 258/97 on Novel Food and Novel Food Ingredients stipulates risk assessment for foods that have not been used for human consumption to a significant degree in the European Union before. Foods and feed containing or consisting of or derived from GMOs are covered by Regulation (EC) 1829/2003, requiring one single risk assessment, carried out by the newly founded European Food Safety Authority. The overall aim is to release only those GMOs that do not pose any risk to human health or the environment. Possible positive effects of GMOs are not subject to risk assessment. Please also refer to König et al. (2004) for a thorough review of food safety assessment and regulation.

3.5.2 What is Risk Assessment?

Risk assessment, the first part of risk analysis, is followed by risk management and risk communication (see also Sects. 2.5, 3.6, 4.2 and 4.5). Environmental risk assessment is defined by Directive 2001/18/EC as the evaluation of risks to human health and the environment, whether direct or indirect, immediate or delayed, which experimental deliberate release or deliberate release by placing GMOs on the market may pose.

Direct effects refer to primary effects, which are due to the GMO itself, e.g. allergenicity of the derived novel GM food. In contrast, indirect effects occur through a causal chain of events, e.g. interaction with other organisms or effects due to a change of agricultural management due to the use of GM crops. Immediate effects could be observed during the period of release of the GMO, e.g. the establishment of weedy GM plants outside the agriculturally used fields. They can be direct or indirect. Delayed effects would be observable at a later stage as a direct or indirect effect as such as long-term effects from changed consumption patterns due to GM food. Additionally, cumulative long-term effects on the environment and human health have to be assessed.

The objective of environmental risk assessment, according to European legislation, is to identify and evaluate potential adverse effects of a GMO and to elucidate if there is a need for risk management and suitable measures to be taken.

In the context of this section, the terms hazard and risk are defined as follows: A hazard is a potential harmful characteristic (here of a GMO), which is an intrinsic property of the organism investigated. Hazards can give rise to negative consequences. These consequences can have different orders of magnitude and different likelihood of actually coming true. Risk can be quantified by combining the likelihood of consequences of a specific hazard with their magnitude.

The principal approach to assess the safety of GMOs is largely accepted. First of all risk assessment should be science-based and carried out ensuring a very high scientific standard. For every GMO the risk assessment is done on a case-by-case basis and in a stepwise manner. This means that for example each GM plant is tested first in the laboratory then on a small scale in a field trial, followed by a large-scale field trial before authorisation for placing on the market can be requested. The following step can only be carried out if the preceding step

has shown that the GMO does not pose any risk to human health or the environment.

In contrast, the interpretation and use of the results of the risk assessment differ within the European Union Member States and internationally, depending for example on the models used for comparisons. For example, Germany and the UK compare the use and the effects of GM crops to conventional agriculture, while Austria or Sweden take an organic-oriented input reduced agriculture as the scale.

3.5.3 How is Risk Assessment Carried Out?

The steps in environmental risk assessment are outlined in Table 3.2. Potential adverse effects on the environment and human health depend strictly on the specific characteristics of the GMO and thus to a certain extent on the inserted transgene(s) and the respective traits. Potential hazards associated with GM crops are listed in a general way in Table 3.3 and will partly be explained in the following sections, distinguishing between environmental hazards and hazards for human health.

3.5.3.1 *Spreading of the GMO in the Environment*

What is the degree of invasiveness of conventional crops, and can transgenic traits increase the potential of survival in non-cultivated surrounding areas or as volunteers on the same plot? Many GM crops developed today carry herbicide tolerance as a new trait, which is not expected to increase the fitness of the plants in the absence of the selecting factor, i.e. the respective herbicide. The situation might be different when new traits such as increased tolerance to dryness, salt or a reduced need for nutrients are developed (see also Sect. 2.5.3).

3.5.3.2 *Vertical and Horizontal Gene Transfer*

The transfer of transgenes from GM crops to other related crops or weeds (vertical gene transfer, out-crossing) is a very intensively studied and discussed issue.

Table 3.2. Steps in environmental risk assessment

1	Identification of characteristics that may cause adverse effects
2	Evaluation of the potential consequences of each adverse effect if it occurs
3	Evaluation of the likelihood of the occurrence of each identified potential adverse effect
4	Estimation of risk posed by each identified characteristic of the GMO
5	Application of management strategies for risks from the deliberate release or marketing of the GMO
6	Determination of the overall risk of the GMO

Table 3.3. Potential hazards associated with GM crops

Expression of toxic or allergenic compounds	Potential for production of substances that are toxic or allergenic to human beings or other species
Effects on biogeochemistry	Potential to negatively influence decomposition processes in the soil and thus causing changes in nitrogen and carbon recycling
Increased persistence on the environment and invasiveness	Potential to confer an ecological fitness advantage to the GM crop causing persistence and invasiveness (superweeds)
Transfer of genetic material	Potential to transfer the newly introduced genetic material to other crops or weeds via cross-pollination or to other organisms via horizontal gene transfer. Depending on the transferred trait such gene transfer might not present a hazard
Instability of genetic modification	Potential of reversing down-regulation of a naturally occurring hazardous trait
Unintended effects	Potential that genetic modification leads to unintended effects, e.g. influencing other genes of the organisms, which might lead to unexpected hazards.

The risk of gene transfer to related weed species depends very much on the GM plant itself. Maize and potato do not have any compatible indigenous related weeds in Europe that could receive transgenes via pollen flow. In contrast, oilseed rape is a cross-pollinating species for which several related species exist, so out-crossing cannot be ruled out. The extent of out-crossing depends on climatic conditions, agricultural practices, viability of pollen, and availability of out-crossing partners. The establishment of a trait in the wild population depends on the selective advantage the new trait might confer. The possibility of gene transfer within the same crop species depends on the specific crop. It can present a potential problem for agriculture, as in the case of organic agriculture where only very low levels of GM plants might be tolerated in the harvest.

The term horizontal gene transfer describes non-sexual gene transfer e.g. from plant to micro-organisms. Micro-organisms, especially bacteria have the ability to take up DNA from other organisms or their environment and to integrate the DNA into their genome. Horizontal gene transfer has been discussed as a risk of gene escape into the environment without any control. During evolution, horizontal gene transfer has taken place, but it is considered to be a very rare event. Still, it cannot be ruled out and in the context of antibiotic-resistance marker genes this possibility has attracted a lot of attention. According to Directive 2001/18/EC antibiotic-resistance marker genes should be phased out for GMOs to be placed on the market until the end of 2004. Of course, alternative marker genes such as those conferring the possibility of metabolising new substrates, have to undergo new risk assessments.

3.5.4 Potential Trait-Specific Environmental Effects

The potential consequences of the general effects discussed above depend mainly on the transgenic trait of the GMO. Up to now, the main traits for GM crops are herbicide tolerance and pest resistance.

Herbicide tolerance genes confer tolerance to broad spectrum herbicides like glyphosate (Round-Up) or glufosinate (Basta). This trait represented 75% of all GM crops planted commercially in the year 2002. Possible trait-specific environmental effects, apart from the ones discussed in the previous section, are mainly due to the application of the respective herbicide and changes in crop management. Glyphosate and glufosinate are said to be more environmentally friendly than other herbicides in use. Easier and less applications might lead to less pollution of soil and ground water. The possibility of a later application during cultivation could lead to a better soil coverage with plants (weeds) and less erosion. On the other hand a permanent use could reduce biodiversity of weeds and related animals considerably.

In 2002, 17% of commercially planted GM crops world-wide were insect-resistant through the expression of a toxin from the soil bacterium *Bacillus thuringiensis* (Bt) (see also Sect. 2.2). The Bt toxin has been used for many years as a spray in organic agriculture. Out-crossing of Bt-crops resulting in certain advantage for Bt-producing weeds is a potential negative effect. Of greater concern are the unintended effects of Bt plants. This issue has been widely discussed in the context of assumed damage to larvae of the Monarch butterfly in the USA after being fed pollen of Bt-maize in a laboratory setting. Adverse effects could not be confirmed by field trials. Soil organisms might come into contact with the Bt toxin, as it is exuded via the plant roots. The effect on the soil ecosystem is still unclear.

Another important issue is the development of resistance mechanisms against the toxin by the targeted pests. This is a normal process, taking place for conventional synthetic pesticides after approximately 10 years. Development of insect resistance is therefore assumed, which would also render the Bt toxin useless for organic agriculture. The application of certain risk management strategies, with refuge areas where non-Bt-plants are grown to delay the development of resistance, is requested in the USA.

3.5.5 Potential Effects on Human Health

Food consisting of, or derived from, GMOs is tested for potential negative effects on human health according to Regulation (EC) 1829/2003. The assessment includes tests for toxic effects, allergenicity and unfavourable changes in nutrient composition. Not only genetic modification but also plant breeding in general could potentially lead to unexpected or unintended changes in concentration of toxic substances, anti-nutrients or nutrient composition. However, conventional food is not subject to similar examinations.

A starting point for the safety evaluation of GM foods is the application of the concept of substantial equivalence (see also Sect. 4.2.5). This concept was first

formulated by OECD in 1993 as a guiding tool and has been developed further since then. Meanwhile it has been internationally accepted, although criticised as being too general and poorly defined. In the EU, with the introduction of Regulation (EC) 1829/2003, the concept has been abandoned. Substantial equivalence is based on the comparison of the GM crop with the appropriate conventional counterpart (considered to be safe on the basis of long experience of use) with respect to phenotype, agronomic characteristics and food composition (key nutrients, antinutrients, toxicants typical of the plant). Three scenarios are distinguished:

1. The GM food or plant is substantially equivalent to its conventional counterpart and is thus considered to be as safe as this conventional counterpart. This is the case when the end product does not contain the newly introduced protein, e.g. sugar from GM sugar beets, or the newly introduced protein has been part of human diet before. No further safety testing would be necessary.
2. The GM food or plant is substantially equivalent except for the inserted trait e.g. the Bt-protein from GM maize. The safety tests would apply only to the newly introduced protein.
3. The GM food or plant is not equivalent to its conventional counterpart. This would be the case for oil from oilseed rape with changed oil composition. In this case the whole plant or food would be subject to safety assessment.

An analysis of key components is carried out to compare GM plants or food with conventional counterparts. The OECD has compiled so called Consensus Documents, the minimal key components of specific crops that should be checked for comparing GM and non-GM crops. Consensus Documents are available for potato, sugar beet, soybean and low erucic acid oilseed rape. International harmonisation is considered necessary to prevent trade barriers. In July 2003 the Codex Alimentarius Commission adopted the "Principles for the risk analysis of foods derived from biotechnology".

Toxicology assessments are not considered to pose any problems with highly purified substances but are more difficult with whole foods. Many conventional crops produce low levels of known toxic substances (e.g. lectins in beans, solanine in potatoes, erucic acid in rapeseed) or antinutrients (e.g. trypsin proteases inhibitors interfering with protein digestion, phytic acid binding minerals). These substances are present at levels significant to human health but are inactivated by food processing, e.g. cooking.

It is difficult to assess the potential for allergenicity. Until today there have been no methods that allow the identification of new proteins as allergenic. Indirect methods are used, based on general characteristics of known allergens as such as typically large protein size, exceptional stability, amino acid sequence homology to known allergens and the quantity of the respective protein in the crop (generally above 1%). Of the huge number of proteins in food, only very few are allergens. Known allergens are found in milk, eggs, peanuts, tree nuts, soybean, fish, crustaceans and wheat. Currently, only in one case has a transgenic protein been shown to be allergenic. A protein from Brazil nut, which was transferred to soybean to enhance the nutritive value for feed purposes, turned out to be a major allergen. This GM soybean has never been marketed. Starlink maize is another GM crop for which potential allergenicity of the newly introduced

protein has been discussed. This GM maize contains the Bt protein Cry9C, which could be a potential allergen because it shows some of the general features of allergenic proteins, e.g. molecular weight and relative resistance to gastric proteolytic degradation as well as to heat and acid treatment. For this reason Starlink maize was only authorised to be used for feed in the U.S. However, Starlink maize has been detected in small amounts in maize food products, which put in question the segregation systems in place. Some consumers reported allergic reactions after consumption of maize products, but a connection to Starlink and thus to the Cry9C protein has not been found by U.S. Centers for Disease Control and Prevention (CDC). However, due to some shortcomings in carrying out the investigation, the question of whether or not Cry9C is an allergen still cannot be answered with absolute certainty.

3.5.6 Scientific Uncertainty

In many cases of potential environmental or health risks, the scientific knowledge base is not good enough to assess potential risks in a quantitative way and with sufficient certainty. Profound understanding of complex ecological systems is lacking as well as knowledge to predict the long-term effects of novel food in the diet on the health status. However, it is important to be aware of the fact that this is not only true for GM crops and GM food but also for new varieties of conventional crops and novel exotic foods that have not been consumed in Europe before. It should also be noted that GM crops and food are examined to a much higher extent than any other conventional crop or food.

As quantitative risk assessment is not possible in many cases, a qualitative evaluation system has been developed. The magnitude of potential consequences can be described as negligible, low, moderate and severe. Also the likelihood that these consequences will come into effect can be assigned as negligible, low, moderate or high. The risk must then be assessed by combining the likelihood with the magnitude of consequences. For example, a high magnitude of consequences of an adverse effect combined with a low likelihood of the adverse effect being realised could result in a moderate risk. The final evaluation depends on the specific GMO and needs to be considered on a case-by-case basis.

3.5.7 Risk Management

If the risk assessment identified a risk, a risk management strategy may be developed to minimise or mitigate it (see also Sect. 4.5). A 100% safety or 0% risk is not achievable as a result of risk assessment, therefore uncertainty is an unavoidable part of risk assessment and risk management. Risk management measures could include:

- Confinement strategies, e.g. certain GM crops are only allowed to be grown in greenhouses.
- Restricted use, e.g. the growth of GM crops could be restricted to certain geographical areas.

- Monitoring following experimental release of GM crops or commercialisation of GM crops or GM food. Monitoring can be used to identify predicted or unforeseen effects.
- Guidelines and technical support, e.g. introduction of refuge areas to minimise resistance development of pests or advice for good agricultural practices as such as crop rotation and weed control to avoid weediness of GM crops and GM volunteer plants.
- Record keeping (the use of documentation), e.g. as foreseen in Regulation (EC) 1830/2003 on traceability of GM crops and food as an important part of risk management.

In addition, the design of GM crops could be changed towards male sterile varieties or to the production of sterile seeds (e.g. terminator technology). The latter is especially controversial as the production of sterile seeds will prevent farmers from saving seeds, forcing them to buy new seeds every year.

3.5.8 The Precautionary Principle as Part of Risk Management

Very often scientific data is not available or is insufficient to assess a possible risk in relation to a GM crop in a significant manner (see also Sect. 4.2). Several questions are not addressed due to lack of data on fundamental biological phenomena as such as out-crossing behaviour in oilseed rape or the effects of GM crops on the soil ecosystem. Scientific uncertainty in risk assessment leads to the question of how to deal with risks that cannot be sufficiently quantified. The precautionary principle was introduced at the 1992 Rio Conference on the Environment and Development in Article 15 of the Rio Declaration:

> In order to protect the environment the precautionary approach shall be widely applied by States according to their capability. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be pursued as a reason for postponing cost-effective measures to prevent environmental degradation.

The precautionary principle is also included amongst the other international treatise and declarations, and referred to in Directive 2001/18/EC. However, the application of the precautionary principle is not clearly defined and harmonised and gives rise to different interpretations. Generally, the precautionary principle encompasses a forward-looking approach, which includes the prevention of damage, and has a cost-benefit analysis of action or lack of action and the ratio of this response refers to the cost-effectiveness of the action. The application of the precautionary principle should be non-discriminatory and consistent, i.e. comparable situations should not be treated differently and measures should be consistent with measures adopted under similar circumstances. Measures taken have to be reviewed as new scientific developments evolve.

3.5.9 Risk Communication

Risk communication to stakeholders is a key area of risk analysis. The expression of each risk assessment should be unambiguous, transparent and relevant. Key rules, identified by the Scientific Steering Committee (SSC) of the European Commission include:

- Completeness of information
- Public access to documentation
- Transparency of discussions and motivations
- Frank acknowledgement of the various positions and contrasting view, including speculations
- Clarity in wording and accuracy in use of specific expressions
- Recognition of different interests and stakeholders
- Recognition of social, cultural and ethical issues

Awareness of risk perception is another important factor in communicating risk. Risk perception of experts and the general public might differ considerably, because personal opinions are formed by information from different sources and integrated with personal experiences. Among the factors influencing public perception of risk are, for example, the extent to which the risk is voluntary, controllability of the risk and the novelty of the risk form. The SSC suggests expressing conclusions of risk assessment in a more user-acceptable manner by putting them into some form of context, e.g. through risk ranking by comparing risk assessments of different, but related, sources of risk, the risk of possible replacements and by using risk benefit analysis.

3.5.10 Information Sources

Codex Alimentarius (2003) Principles for the risk analysis of foods derived from modern biotechnology. ftp://ftp.fao.org/codex/standard/en/CodexTextsBiotechFoods.pdf

Custers R (ed) (2001) Safety of genetically engineered crops. The report gives a state-of-the-art review on different biological risks of genetically engineered crops. Obtainable from VIB, www.vib.be

EC Scientific Steering Committee (2000) First report on the harmonisation of risk assessment procedures. http://europa.eu.int/comm/food/fs/sc/ssc/out83_en.pdf

European Parliament and Council (1990) Council Directive 90/220/EEC of 23 April 1990 on the deliberate release into the environment of genetically modified organisms. Off J Europ Commun L117:15

European Parliament and Council (1997) Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients. Off J Europ Commun L43:1

European Parliament and Council (2001) Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms. Off J Europ Commun L106:1 http://europa.eu.int/eur-lex/en/search_lif_simple.html

European Parliament and Council (2003) Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed. Off J Europ Commun L268:1

European Parliament and Council (2003) Regulation (EC) 1830/2003 Concerning the traceability and labelling of genetically modified organisms and the traceability of food and feed products produced from genetically modified organisms and amending Directive 2001/18/EC. Off J Europ Commun L268:24

König et al (2004) Genetically modified crops in the EU: food safety assessment, regulation, and public concern. Office for Official Publications of the European Communities

Kuiper et al (2001) Assessment of the food safety issues related to genetically modified foods. Plant J 27(6):503–528

OECD (2000) Report of the task force for the safety of novel foods and feeds. Provides an overview on scientific issues and current approaches to food safety assessment. http://www.olis.oecd.org/olis/2000doc.nsf/LinkTo/C(2000)86-ADD1

OECD (2000a) Report of the working group on harmonisation of regulatory oversight in biotechnology. This report is complementary to the report of the task force for the safety of novel foods and feeds (see above). It focuses on the environmental safety implications of the use of products of modern biotechnology. http://www.olis.oecd.org/olis/2000doc.nsf/LinkTo/C(2000)86-ADD2

OECD Consensus documents for the work on the safety of novel foods and feeds. These documents provide information on compositional considerations for new (GM) varieties of several food and feed crops. http://www.oecd.org/EN/document/0,EN-document-0-nodirectorate-no-27–24778–0,00.html

3.6 Monitoring of GMOs

Paul Pechan, Ervin Balazs

Plant biotechnology holds the promise of becoming an increasingly valuable tool in the efforts to improve our heath and achieve sustainable solutions for agriculture and the environment. Improved vaccines, increased food production and more effective waste treatment of polluted lands are but some of the results we may expect (see Sects. 5.1–5.3). However, plant biotechnology may create undesirable side effects. In order to reduce these risks and at the same time fully exploit the potential of this technology, a number of actions need to be taken. The first is the creation and implementation of rules and regulations to govern the application and trade of plant biotechnology products and second, enforcement of these rules through risk assessment, risk monitoring and transparent management. For regulatory related issues please see Sects. 3.3, 3.4 and for risk assessment and management see Sect. 3.5. This section concentrates on the issue of monitoring of GM crops, especially as it relates to their detection.

3.6.1 Why the Need for Monitoring of GM Products

The rapid increase in the commercial scale of transgenic plant in the world from 1.6 million ha in 1996 up to more than 80 million ha today indicates the increasing importance of GM crops worldwide. Public attitude towards GM products varies from total rejection to full acceptance. The many and complex reasons for such varied attitudes are dealt with in Sects. 4.3–4.5. In order to address the societal and environmental concerns, EU legislators have agreed on the general

http://www.springer.com/978-3-540-20178-6

Genes on the Menu
Facts for Knowledge-Based Decisions
Pechan, P.; de Vries, G.
2005, XII, 217 p. 6 illus. in color. With CD-ROM.,
Hardcover
ISBN: 978-3-540-20178-6