Pharmaceutical crops
Monitoring and Advisory report

CGM/041214-01/02

Summary

Netherlands Commission on Genetic Modification (COGEM)

COGEM's task is to advise the government at their request or independently about the risks of using genetically modified organisms (GMOs) and to inform the government about ethical and societal issues associated with genetic modification. COGEM's task is described in the Environmental Management Act.

Summary

Biopharming

In recent years a lot of research has been carried out into the production of pharmaceutical proteins in genetically modified plants (biopharming). Examples of such products are antibodies, vaccines, or proteins for medicinal purposes. Cultivating crops to produce medicines is nothing new. Since time immemorial, countless medicines have been isolated from plants, such as digitoxin from foxgloves. In biopharming, however, one or more foreign genes are incorporated into the plant by means of genetic modification, so that a plant produces a pharmaceutical protein that it would not otherwise produce.

Risks for humans and the environment and risk management

The purpose of pharmaceuticals is to induce certain effects in humans, and some pharmaceuticals will be toxic or allergenic. Due to mixing, pharmaceuticals produced in genetically modified plants may unintentionally end up in the food chain of humans and animals. Furthermore, as a result of outcrossing, the inserted genes may spread to wild relatives or other crops cultivated for food production.

General statements about the potential risks of biopharming are impossible due to the large number of different proteins that may be produced and the considerable range of plants or crops that may be used for production purposes. Some products will not be toxic or allergenic and will not cause any environmental effects. These will, therefore, effectively be the same as other proteins or characteristics that can be incorporated into genetically modified plants. Other products might, however, cause effects but will be produced in non-food crops or in crops from which outcrossing is not possible. COGEM therefore advises a case-by-case approach.

A number of recommendations can nevertheless be made to prevent potential problems from arising. Firstly COGEM argues that food or fodder crops should not be chosen but instead other crops such as bulbous plants or hemp. Not only will this reduce the risk of food chain contamination, but it will also circumnavigate potential problems with European and Dutch legislation. Under the current legislation it is unlikely that a licence would be granted for the commercial cultivation, under field conditions, of a genetically modified food or fodder crop into which a toxic pharmaceutical protein has been inserted. In order to avoid contamination of the human and animal food chain with pharmaceuticals COGEM also calls for a strictly regulated supply chain separation by means of certification. Supply chain regulation applies to all stages of the production process, from seed to pharmaceutical, and also to transport and waste processing. The certification should preferably be supervised by an independent supervisory authority recognised by the government. Further COGEM recommends the incorporation of external characteristics, such as a different colour, into the genetically modified plant. Giving pharmaceutical crops a different external appearance may help to prevent their unintended

consumption. Finally, COGEM wishes to emphasise the importance of further exploratory research into, for example, the possibilities for separating supply chains and the consequences of such systems being breached, as well as the possibilities for remedial action should such chains become contaminated.

Legislation

COGEM notes that the present legislation on genetically modified crops with respect to the safety of food, fodder and the environment, is sufficient to guarantee the safety of both humans and the environment and that new legislation is, therefore, not necessary. Pharmaceutical crops form a category within the cultivation of genetically modified crops. The cultivation of pharmaceutical crops under field conditions can be assessed and regulated using the present legislation, which is based on EU Directive 2001/18. If food crops are used for production purposes then an assessment within the framework of food safety will also take place on the basis of EU Regulation 1820/2003/EC, even if these plants are not intended for consumption. Requests to cultivate genetically modified plants under strictly contained conditions such as growth chambers and greenhouses are assessed according to the Genetically Modified Organisms Decree (Environmentally Hazardous Substances Act). Agreements and regulatory measures that have been declared applicable to the coexistence of GM, conventional and organic cultivation will equally and fully apply to pharmaceutical crops.

Public debate

Biopharming is a rapidly developing area. In the US, large-scale field experiments are being carried out and several pharmaceutical crops are in the last phases of commercial development. Although Europe is lagging behind with respect to these developments, many research groups in Europe are working on the development of pharmaceutical crops. Meanwhile in the US the first case of contamination has occurred. A consignment of soya was found to be contaminated with maize that produced a pharmaceutical protein. US policy has been tightened in response to this and the government policy now includes a strict supply chain separation, with the associated monitoring.

This incident has also led to an intensification of the public debate, and to a highlighting of the possible risks of pharmaceutical crops in particular. Interestingly, the pharmaceutical crops currently under development have mainly made use of food crops. To a certain extent this was inevitable because of the choice to produce a vaccine in an edible crop. The underlying intention is to distribute appropriate quantities of the edible parts of the plant which will induce protection against pathogens upon oral intake. Yet in the majority of cases, food crops have been chosen due to the considerable prior experience in cultivating and processing the harvested products. Furthermore, seeds such as maize kernels have the advantage that they can be harvested in large quantities and the proteins they contain are not broken down during subsequent storage.

The objections against pharmaceutical crops focus on the alleged risks of contaminating the food chain. Contaminations with pharmaceuticals do not automatically imply a safety risk, as many products are not toxic or allergenic. Despite this, consumers are strongly dismissive about the contamination of food by a pharmaceutical, even in the absence of a safety risk. The food industry therefore fears a loss of reputation, should its products contain traces of pharmaceuticals. As a result of this, not only consumer organisations but also the food industry are pushing for tough requirements and strict regulation. COGEM points out that any future contamination of the food chain with pharmaceuticals, even if the safety and health of humans and animals is not threatened, is likely to damage public support for biopharming.

Contaminations and the safety of humans, animals and the environment are not the only fears. Other objections to biopharming are raised, such as the principal rejection of genetic modification in general.

COGEM points out that the supposed advantages and disadvantages need to be carefully considered when formulating policy. Biopharming would seem to provide considerable advantages for both the producer and society. With the help of genetically modified plants, proteins can be produced quickly, relatively easily and cheaply on a large scale. This could result in a lower price, greater availability and shorter development time for drugs and vaccines, as well as a more flexible production level. Furthermore the investments required would be relatively small, as knowledge about the cultivation of corresponding 'normal' crops can be further built upon. Moreover, it should not be forgotten that biopharming also offers opportunities for Dutch agriculture, due to the considerable experience with cultivation in greenhouses. This is an attractive option, as the contained greenhouse environment can counteract spreading and unintended mixing.

Biopharming is also expected to provide considerable advantages for consumers, i.e. patients, such as a lower price and a quicker and wider availability. A further consideration is that at present, animal cells are often used for the production of pharmaceutical proteins. Not only are these systems more expensive and more difficult to manage than plant-based systems, but there is also the risk that viruses be present in the animal which could contaminate the final product, thereby forming a public health threat. Animal systems are strictly controlled with respect to such risks, whereas plant systems are free of such problems. Furthermore, biopharming could also satisfy the considerable demand in developing countries for effective, safe, acceptable and cheap vaccines against life-threatening diseases such as cholera, dysentery or hepatitis B.

However, there are widespread doubts about all of the advantages stated and so they must first of all be proven. In addition to this, opponents of biopharming also cite all of its previously stated disadvantages, such as contamination of the food chain with toxic pharmaceuticals and outcrossing to food crops.

Conclusions

COGEM believes that despite the advantages it may provide, biopharming also may pose risks for both humans and the environment, the severity of which depends on the nature of the product and the crop. Moreover, mixing might lead to a loss of consumer confidence. The introduction of biopharming to the Netherlands will therefore require a case-by-case approach to assess the risks and to guarantee a strict supply chain separation.