GENETICALLY MODIFIED FOOD:
Objectives for EU funded research and development

Final Study

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Genetically modified food : objectives for EU funded research and development

RESTRICTED CALL FOR TENDERS No. EP/IV/A/STOA/99/0501/01

ABSTRACT

This study provides a concise review and analysis of key issues concerning the current state of research in genetically modified (GM) food in the EU and in the world. It takes into account, among other issues, the strategies of private companies and public research organisms, the developments of consumer and other actors' perceptions and the problems which trade in raw materials for the production of GM food may involve.

The shortcomings of European legislation affect the organisation of the monitoring and evaluation of the introduction of GMO in the food chain. Several options have been put forward concerning future research on GMOs in food, including the need for : the development of new methods for the evaluation of risks associated with GMO in food, the harmonisation of detection methods, the assessment of antibiotic marker genes and other techniques aimed at the control of gene expression, addressing the question of responsibility in the introduction of GMOs in food.

These options are backed by evidence of recent changes in the organization and role played by public research and advances in genetic modification applied to plants and animals. Scientific results concerning field trials, the risk-benefit assessment of GM food (the study includes three case studies on the subject) and a technical file on genetic engineering techniques, provide additional information in order to gain insight into the debate.

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OPTIONS BRIEF

Objectives of the study

This study provides a concise review and analysis of key issues concerning the current state of research in genetically modified (GM) food in the EU and in the world.

Considering the European policy-making context, the study identifies the most significant policy options in the field of EU funded research in genetically modified food to be adopted or recommended by the European Parliament.

Options

The shortcomings of European legislation affect the organisation of the monitoring and evaluation of the introduction of GMO in the food chain. Several options have been put forward, particularly in terms of the level of expertise and transparency needed in future research on GMOs in food and the relevant legislation :

- New methods for the evaluation of risks associated with GMO in food should be developed in the future and should be integrated in the official evaluation procedure. This is because, in terms of human health, there is still insufficient knowledge on the possible chronic toxicity due to the consumption of food containing GMO. As techniques are developed but their evaluation does not follow at the same pace, would there be a role for the public sector in promoting the development of evaluation methods? Furthermore, the introduction of GMOs in agriculture should not be to the detriment of other, more sustainable modes of production for which research funds are currently limited. Research on GMOs should include the environment in its own dimension, considering the multiple factors which make up the ecosystem.

- The analysis on which the definition of substantial equivalence between GM and GMO-free food is based should be reviewed. This is because the application of the principle is controversial : the USA are convinced that genetic modification does not bring about essential changes in food products, i.e. GMO and non-GMO foods are "substantially equivalent". The equivalence is based on the analysis of only a few food components, which is, according to certain scientists, insufficient. The concept of "substantial equivalence" is problematical since a GMO recognized as such under one circumstance would no longer be equivalent for a different crop, environment or other specific conditions which may have caused a deregulation of the gene. For a more reliable and complete risk assessment, the concept should be extended to cover knowledge of : the transgenes used, the products expressed and "non intentional" effects resulting from the action of genetic modification. It should be possible to declare, *a priori*, that GM food is not substantially equivalent to traditional food and that its innocuity should therefore be proven.

- A harmonisation of detection methods for GM food should be seeked. The identification of a particular genetic modification requires the knowledge of a specific DNA fragment linking part of the transgene and part of the chromosome on which the transgene itself is inserted. However, this information remains inaccessible to the general public and there is no centralized database for these fragments, which would be a useful reference for the traceability of GMOs throughout the food chain, from the field to the consumer. Companies depositing a demand for a marketing authorisation should provide national and European authorities with the information concerning border fragments. Beyond detection methods, research should also concentrate on the study of the interactions within the cells and the possible unpredicatble effects on the organism and its environment.

- The use of antibiotic marker genes and other techniques aimed at the control of gene expression should be evaluated further and closely monitored and assessed for their effects on human health and the environment. Today, at least half of GM plants which are cultivated, tested or awaiting authorisation in the world, contain antibiotic marker genes. The risks associated with these genes concern the spread of human and animal resistance to antibiotics.

- A moratorium on GMO in food would benefit research efforts. Research could continue to be carried out in a confined environment, benefitting from a reduction in pressure to produce economically viable results. Without a clear-cut legislative framwork, the current situation is destabilising the EU, faced with pressures from the USA on the one hand and the refusal of the development of GMOs in food from a large share of the European population.

- The creation of a European over-arching body responsible for GM products with a solid juridical base could be useful. At present, the contradictory results of research on the effects of GMO in food are not always available to European authorities, consumers and other actors due to the commercial interests involved. This is linked to the differences existing in the current approaches to evaluation in GM food , which are also favouring the build up of international commercial trade disputes.

- It is urgent to address the question of responsibility in the introduction of GMOs in food. The problem of responsibility in case of ex-post risks such as damage to the environment or health is not tackled by European legislation. Consumer claims concern risk and safety, which have an ethical dimension when they raise further questions about responsability. This implies that if ethical aspects are to be taken into account in the discussion concerning the introduction of GMO, the question of responsibility should be addressed.

- More research into the best ways to convey complex scientific information to the public should be carried out. The evaluation of GMOs in food should be multidisciplinary, away from the belief that a complex science should be confined to specialists who can understand it. Restoring public trust in food, following the recent protests on food quality in Europe should to be the main priority today. Assessments made by European research should not only be limited to purely technical, scientific questions, since public concern involves broader questions such as the implications of changing farming practices for the conservation of biodiversity or for eating habits.

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EXECUTIVE SUMMARY

Introduction

This study provides a concise review and analysis of key issues concerning the current state of research in genetically modified (GM) food in the EU and in the world.

Considering the European policy-making context, the study identifies the most significant policy options in the field of EU funded research in genetically modified food to be adopted or recommended by the European Parliament.

The review of the current state of research into GM food takes into account in Part A, among other issues, the strategies of private companies and public research organisms (Chapter 2), the developments of consumer and other actors' perceptions and the problems which trade in raw materials for the production of GM food may involve (Chapter 3), as well as the current developments in relevant EU legislation (Chapter 4).

This international and holistic perspective is intended to provide specialist and non-specialist readers with the necessary tools in order to gain insight into the debates on genetically modified organisms (GMO) and the derived food thereof.

Part A - OPTIONS

1. EU-funded research in GM food

Against the background of existing obstacles which research is facing (i.e. the absence of a scientific consensus and the lack of knowledge concerning the best ways to convey information

concerning nutrition), the "Quality of life and management of living resources" thematic programme of the 5th Framework Programme seeks to satisfy the needs of consumers and to reinforce the competitivity of the European food industry. To this end, it seeks to develop methods and strategies for a risk-free introduction, utilisation, monitoring and detection of GMO in food and the environment. Research efforts are thus directed at the improvement of the quality of food, whereby the study of the genome is of strategic importance.

2. Future needs for research at European level

The role played by public research has changed considerably, in both the USA and in Europe. The first developments in partnerships between public research institutes, universities and private companies have started in the USA, and have only recently appeared in Europe.

In terms of human health, there is still insufficient knowledge on the possible chronic toxicity due to the consumption of food containing GMO. As for the environment, it is questionable whether GM crops can have wide-ranging and unpredictable effects on the environement, upsetting the ecological balance.

The contradictory results of research on the effects of GMO in food are not always available to European authorities, consumers and other actors due to the commercial interests involved. The benefits and risks of GMO in food are therefore not easy to assess.

3. Issues of world competition

The area devoted to growing GM crops reached 27.8 million hectares in 1998 (against 1.7 million in 1997), 75% of which in the USA. Around 60 GM plant species are cultivated in the United States and 10 species in Europe represent 80-90% of field trails.

There has been an increase in the number of alliances and mergers between agro-chemical companies and seed producing companies over the last years. The profitability of investments, the rationalisation of activities and the competitivity of companies are major issues in research into GMOs in food today.

The implications of a review of the Trade Related Aspects of Intellectual Property Rights (TRIPS) Agreement at World Trade Organisation (WTO) level for the rights of nations over biodiversity and related knowledge should not be overseen.

4. Policy options

The shortcomings of European legislation affect the organisation of the monitoring and evaluation of the introduction of GMO in the food chain. Several options have been put forward, particularly in terms of the level of expertise and transparency needed in future research on GMOs in food and the relevant legislation :

- New methods for the evaluation of risks associated with GMO in food should be developed in the future and should be integrated in the official evaluation procedure.
- The application of the principle of substantial equivalence between GM and GMO-free food is controversial. The analysis on which its definition is based should be reviewed. Also, a harmonisation of detection methods for GM food (should companies working on GM food bear the costs of detection and in which way?) should be seeked.
- The use of antibiotic marker genes and other techniques aimed at the control of gene expression should be evaluated further and closely monitored and assessed for their effects on human health and the environment, although antibiotic marker genes are supposed to be eliminated in the near future.
- A moratorium on GMO in food would not imply a halt in research efforts, if these are carried out in a confined environment and would benefit from a reduction in pressure to produce economically viable results.
- The creation of a European over-arching body responsible for GM products with a solid juridical base could be useful.
- It is urgent to address the question of responsibility in the introduction of GMOs in food.
- More research into the best ways to convey complex scientific information to the public should be carried out.

Part B - ARGUMENTS AND EVIDENCE

1. Scientific definition of genetically modified food

The majority of demands for GMO market licences concern plants and most of them include a gene for herbicide resistance. The identification of a particular genetic modification requires the knowledge of a specific fragment linking part of the transgene and part of the chromosome on which the transgene itself is inserted, but this information remains inaccessible to the general public.

2. Field trials

Isolating fields where GM plants are grown by allowing for a sufficiently large area of land around them (refuge area) has been considered as a possibility for limiting the environmental impact of the introduction of GMOs, but appears as impossible in practice due to the large areas involved.

The genes coding for the toxins produced by Bacillus Thurengiensis (Bt) have been directly integrated in the plant through genetic modification techniques. This continuous production of toxins in the plant causes however a constant selection pressure, with the development of insect resistance.

The reliability of field trials for the assessment of risks for the environment such as gene flow, carried out on a small scale, remains questionable.

3.Risk-benefit assessment of GM food

Two food crops (tomato and maize) and animals on which experiments are currently carried out, have been chosen in order to see the implications for food security of the introduction of GMOs in food (Annex IV).

The risks for human health are twofold : toxic and allergic. One potential danger is the intake of new, unknown pathogens together with modified plants, which may have appeared due to the modification which has made plant species resistant to viral infections. The evaluation of allergenic risks is complicated by the uncertainties linked to the prediction and future of the behaviour of transferred genes.

It seems that there are potential hazards for biodiversity associated with the (uncontrolled) dissemination of GMO in the environment, sometimes compared to the introduction of a species in a new area in the past. The difficulty is that *a priori* estimates on the effects of these disseminations cannot be made.

Arguments in favour of biotechnology for farmers include the provision of means for the simplification of agricultural practices and lowering production costs. However, the introduction of GMOs in agriculture should not be to the detriment of other, more sustainable modes of production for which research funds are currently limited. At present, few research teams study the environment in its own dimension, considering the multiple factors which make up the ecosystem.

Due to the very nature of the subject studied (genes, their variation, transmission and organisation in the genome), research on GMOs raises philosophical and ethical questions.

4.Utilisation of antibiotics resistance factors

Today, at least half of GM plants which are cultivated, tested or awaiting authorisation in the world, contain antibiotic marker genes. The risks associated with these genes concern the spread of human and animal resistance to antibiotics.

5.Objectives of current research outside Europe

The International Agricultural Research Centres (IARCs) are today adapting to the rapid transformation of agricultural sciences through genetic engineering by developing links with private sector research. Research has shifted from original crop specific research to the integration with the concepts of sustainability and eco-regionality, which is yet to be achieved; and a change in scientific paradigm, from conventional plant breeding towards biotechnology.

Part C - TECHNICAL FILE

There is no universally accepted definition of biotechnology, even though many attempts have been made to find an exhaustive definition. It entails a number of techniques using micro-organisms, plant and animal cells or their constituents in order, in particular, to produce substances useful to man.

Genetic engineering, (also referred to as genetic modification, genetic manipulation and gene technology), can be thought of as a subset of biotechnology and is a set of techniques where individual genes can be copied and transferred to another living organism to alter its genetic make up and thus incorporate or delete specific characteristics into or from the organism.

Gene sequencing techniques have been developed in order to locate the genes for the expression of the agronomic traits of plants on the chromosomes and to study the interaction between genes and their environment. It is presupposed that successful manipulation of genes brings real insights into the underlying effects of the manipulation. However, many fundamental questions remain unresolved.

No scientific consenus exists at the moment on the risks involved in the use of GMO in food, but several experts have underlined possible hazards justifying the development of more reliable and precise evaluation methods.

The improvement of the evaluation methods for food risks, through the definition of "global" methods to determine the exact composition of GM varieties should be able to contribute to the assessment of the impact of GMO in food.

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FINAL STUDY

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PART C - TECHNICAL FILE

PART A - OPTIONS

1. Objectives for the options for EU funded research into GM food in Europe

According to article 130 F of the Maastricht Treaty, Framework Programmes have the following aim : "to reinforce the scientific and technological base of industry in the Community, to favour its international competitivity and to support the other Community policies". The accent was thus put on the competitivity of the European industry, the main objectives being economic in nature. Other concerns have since been added, as can be seen by the objectives of the 5th Framework Programme, as far as the thematic programme "Quality of life and management of living resources" is concerned.

1.1 Fifth Framework Programme (1998-2002)

Objectives

The improvement in the quality of life and health of European citizens is today part of the concerns of the 5th Framework Programme - which sets out the priorities for the European Union's research, technological development and demonstration (RTD) activities. These considerations were not the case in the early days of the European Community, when priorities were rather linked to market needs rather than societal needs.

Within this programme, research efforts are thus directed at the improvement of the quality of food1. In order to qualitatively improve human nutrition, the study of the genome becomes of strategic importance and the social sciences can contribute to a better understanding of the changing consumer demands for better quality food.

The obstacles which research has to face are the absence of a scientific consensus and the insufficient knowledge concerning the best ways to convey information concerning nutrition. Furthermore, the Commission has stated that the complex legal framework existing in Europe is not conducive to the development of new products which could have a positive impact on consumer's health and industrial competitivity2.

Key action 1 of the Quality of life programme (Food, nutrition and health) has thus the following objectives :

- to satisfy the needs of consumers and to reinforce the competitivity of the European food industry.
- to guarantee food security and integrity.
- to understand the role of nutrition for health and well-being (including the benefits of GM food).

Key action 3 (the "Cell factory") in particular seeks to favour a better integration of research and industry in order to gain new knowledge on the functioning of cells as "biological factories".

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1 See Work programme of the 5 th Framework Programme for the live sciences, March 1999.
2 Ibid., 1999.

Means

The objectives of key action 1 should be achieved through projects able to :

- develop new technologies for the production of high quality food which is safe for human consumption.
- develop tests for the detection of toxic substances in food.
- study the role of nutrition in health promotion and protection.

As far as GMO and the environment are concerned, projects in key action 3 should focus on the development of methods and strategies for a risk-free introduction, utilisation, monitoring and detection of GMO in food and the environment.

Through the creation of industrial platforms, the participation of small and medium enterprises to the Programme is favoured, i.e. the collaboration between research and industry; facilitating contacts between small companies and researchers; identifying industry's preferences and favouring the participation of industrial partners to the programmes.

1.2 Sixth Framework Programme (2002-2006)

Possible orientations and priorities for the 6th Framework Programme concerning the quality of life will be given on the basis of additional information gathering and assessment of the current situation of research in Europe, with the views expressed from professionals in this field. What seems to be already desirable, is to take a closer look at the development of research in food biotechnology. This is because research has all too often been dictated by short-term commercial interests, which did not take into account the importance of the long-term usefulness and profitability of research to society, several areas for the improvement of the quality of life through better food quality remaining under-researched. This is where the member States and the European Union could intervene, ensuring also a better coordination of European research in order to create added value.

2. Future needs for research at European level

2.1 Agri-food industry vs. "independent" public research

Research projects

Partnerships between public research institutes, universities and private companies have recently been started in Europe, years after the first developments in the USA, prompted by the creation of the Plant Genome Initiative Program, with a budget of 130 million US$ to study the genome of four plant species : *Arabidopsis thaliana*, rice, maize and soya.

The UK is probably the European country with the longest tradition in the field of biotechnology at an international level and cooperation between research and industry. Several national programmes managed by the Office of Science and Technology of the Department of Trade and Industry, assist small enterprises in biotechnology projects associating researchers and industries. Zeneca has recently signed an agreement with the John Innes Centre on the study of the wheat genome, with a budget of 82.5 million US$ over several years.

In France, the Génoplante programme was launched in February 1999, associating public research institutes (INRA, CNRS, IRD, CIRAD) (financing 40%), companies such as Rhône-Poulenc and seed companies Biogemma and Bioplante (financing 30%) and the Ministries of Agriculture and Research. At first, its mission is to study the plant genome of *Arabidospis* and rice and should extend to maize, wheat and oilseed-rape at a later stage. Managing patents on genetic material is also seen as important. According to P. Vialle, INRA's director-general, "the risk was that certain genes of great interest be patented by foreign competitors and that they could be introduced in varieties which would not be perfectly adapted to the European and French production conditions" (Vialle, 1999). As a result, many companies which had expressed an interest in joining Génoplante, but which were US-based, have been turned down.

The way in which research is conducted, in partnership with private companies, has been the subject of a recent study commissioned by the Technology Directorate of the Ministry of Research and Technology, due to be published shortly in France (Philipon, 1999).

Other research programmes on plant genomes have been initiated in Germany, where the negative opinion of the population on research in biotechnology has long restrained its development. The "Gabi" programme is the result of the coming together of agro-chemical companies, seed producers, variuos research institutes and the Ministries of Research and Agriculture. Its aim is to describe the key functions of plants, based on a study of the model plant Arabidopsis and to develop, based on the analysis of the barley genome, tools which can be used for cereals with a more complex genome, such as wheat. A more specific programme, "Zigia" (initiated by AgrEvo, KWS, DSV and the Max Plank Institute) will work more closely on the functional analysis of *Arabidospis*.

The creation of Aventis between Rhône Poulenc and Hoescht is likely to favour the creation of research networks between France and Germany.

In The Netherlands, the breeding centre at Wageningen University, CPRO-DLO, has recently launched a research programme of three years on plant genomes : *Arabidopsis*, potatoes and rice.

The *Arabidopsis* genome should be completely identified by next year. *Arabidopsis thaliana* has

more than 90% of its genes in common with other plant species. As a result, the identification of the maize genome should follow, as well as the rice, oilseed-rape, wheat and sugarbeet genomes.

Privatised public research

At a European level, the creation of links among the different actors of research in biotechnology has been favoured through, for instance, the European Commission's initiative called "Biotechnology and Finance Forum". In June 1998, it set up a European plant biotechnology network in order to promote the exchange of results from research in this field in Europe.

The role played by public research has changed considerably, as there has been a tendency for public research to comply to a supply driven economy rather than to public demand (Pisani, 1993). Today, due to the commercial interests involved, public research is often reticent to publicly give full details of the research conducted in partnership with the private sector and knew knowledge with potential commercial value seeks to be protected by a patent. This is the case for Génoplante : the identification of the likelyhood for the outcome of a research programme to be patented is essential and the patent is deposited before the publication of research results1.

The patenting of research techniques and plant production associated with transgenic plants will, in the long-term, limit the action of individual research teams. Furthermore, progress in research is likely to be confined to those teams which have patented the utilisation of a transgenic plant, and less performing teams will be rapidly distanced.

The concentration of the efforts of public research on short-term commercial interests will certainly have an impact on the role it has played in teaching and fundamental research (Goupillon, 1996). This is reflected in the increasing amount of funds allocated to research in molecular biology in universities, whereby less botanists and other specialists able to assess the ecological impacts of the introduction of GMO in the environment are formed.

Even though it is difficult to determine society's needs, efforts should be directed at the identification of benefits which research could bring to society from the application of one particular innovation and that the relevant research results be transparent and accessible, despite the commercial interests. What can be seen it that the development of intellectual property rights in the field of biotechnology is however not conducive to making such an effort easily operational and public-funded research becomes increasinlgy involved in the market economy.

New research areas

The questions which the introduction of GMO in the food sector and the environment raise are to be answered through, in particular, the determination of a reliable method for the identification of GMOs and on an in-depth knowledge of the environmental impact.

Those who see the introduction of GMOs as a potential threat, are convinced that Europe should

1 Company interviews; Haynes, 1999.

favour strategies directed at the improvement of the quality of food.1

What can be seen is that, in general, technology develops at a faster rate than legislation which is supposed to regulate its application. As a result, massive investments have been made in the research on the production of transgenic plants rather than on the evaluation of their impact. Multidisciplianry research on the usefulness of biotechnology, which would involve economic, sociological, juridical, ethical and ecological aspects, could be carried out by public research.

2.2 Which research in the field of GMO in food is needed in the future?

Human nutrition and the environment

Due to the fact that discoveries in the field of GMO are relatively recent, insufficient knowledge on the possible chronic toxicity due to the consumption of food containing GMO is available today. Tests of chronic toxicity would have to last over a period of 20-40 years2. More research is needed on the possible negative long-term impact on health of the consumption of GM food (see Part B).

There are tens of thousands of allergenic substances and only about 300 are known. Current research is yet to assess whether genetic changes may result in allergenic reactions. Toxicological studies on GM plants resistant to herbicides do not take into account the long-term impact of agro-chemicals which have been introduced into the plant. Furthermore, up-to date studies are not always considered in the evaluation of imported products such as glyphosate in France, the actual marketing authorisation having been given prior to the issue of the results of full toxicological tests3.

No official tests exist today which are able to prove whether the proteins coded by the modified DNA can be transmitted, in their entirety or partially, to GM plants and animals or animals fed with GMOs.

An evaluation of the risks involved with genetic modifications in food should be taken into account in future European research, as all the consequences of the introduction of GMOs have not yet been identified.

As far as the detection of GMO in food is concerned, a valid and universally recognized detection method is still to be developed (see Part B).

Economic

From the point of view of the European agricultural trade balance, protein-rich crops such as

1 Que choisir n° 356, January 1999.
2 M. Messean, CETIOM, France. personal comm.
3 Cultivar Le Enjeux n° 6, July-August 1999.

soyabeans for animal feed are mostly imported. The development of GM crops with a higher protein content is of major economic interest for the competitivity of the European agricultural industry.

Public research becomes increasingly internationalised, away from strictly national organisational models and through the build-up of research networks and initiatives, highlighting the fact that it can no longer exclusively work for national industries.

The development of a gene bank with models of genomes accessible by all Member States and constantly updated, was the aim of the conservation of genetic resources programme, managed by DG VI. The work carried out was to contribute to achieving synergy between actors involved in European research in this field. However, the current reorganization of the Commission's services have been partly responsible for the fact that this programme will not be reconducted, away from the initial aim (conservation of genetic resources supported by EU funds).

The question remains however of whom should (and can) benefit from the results achieved, given the development of intellectual property rights for living organisms.

3 Issues of world competition

3.1 Technical

According to the International Service for the Acquisition of Agri-biotechology Applications (ISAAA), the area devoted to growing GM crops reached 27.8 million hectares in 1998 (against 1.7 million in 1997). 85% of transgenic plants are cultivated in industrialised countries. The USA cover 75% of the area (i.e. 30 million ha), followed by Argentina (15%), Canada (10%) and only a few European countries (less than1%).

In 1999, 40% of the area planted to maize and 50% of the area planted to soya was GM in the US. In Argentina, 70% of soya was planted in Roundup Ready. In Europe, there were only about 200 ha in France, 500 ha in Germany and between 20.000 and 30.000 ha in Spain1.

Around 60 GM plant species are cultivated in the United States and 10 species in Europe represent 80-90% of field trails2. These include tobacco (the first transgenic plant created) and tomato (the first transgenic plant to be marketed) and other economically important crops such as maize and potato and, more specifically, soyabeans in the United States and sugarbeet in Europe. Major advances have been made in soyabeans and maize, which are also the main US export crops. Wheat (a major European export crop) only represents about 1% of field trials due to the difficulties encountered in the identification of its DNA (see Part B).

The development of GMO in agriculture has followed three directions :

1. The improvement of the agronomic characteristics of plants (input traits). This concerns herbicide resistance (to Roundup Ready for Monsanto, a technology used on soya, oilseed rape, cotton, maize and sugarbeet), insect resistance (for potatoes, cotton, maize), fight against diseases and viruses (potato).

2. The improvement in the qualitative characteristics of plants and the composition of the final product (output traits). The aim is to alter the plant's composition in order to improve its nutritional qualities. The plant produces elements which it did not produce before and is made more appetising to animals. Pioneer and DuPont in particular are already marketing maize with a high oil content (8-9% inseatd of the usual 2-3%) (Dupount-Fauville, 1999) and have created a subsidiary company (Optimum Quality Grain) to this end.

3. The production of substances destined to health (such as vitamine B) and the industry. Limagrain has, for instance, invested in an important programme ("Molecular pharming") to develop pharmaceutical molecules and the plants concerned have been tobacco (production of haemoglobin) and maize. DuPont has started to use maize starch in its chemical activities (Diemer, 1999).

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1 Agrapresse n° 2719, Monday July 5th, p. 5.
5% of Spain's maize production are genetically modified and the country imports US GM soyabeans. While other European countries like France have suspended nearly all cultivation (1500 ha GM crops in 1998, 200 ha in 1999). The debate over GM farming is virtually absent in Spain, while it is lively in countries such as the UK.
2 Database 1987-1998 for the USA and 1992-1998 for Europe (Ditner and Lemarié, INRA Grenoble, 1999).

3.2 Economic

Biotechnology and the life sciences

Biotechnology1 concerns both plant and animal species. Only the marketing of GM plants has however been largely developed, particularly since 1996, when field crops such as maize and soyabeans have first been marketed. Biotechnology has brought together the sectors of agriculture, food and health into a new sector called the "life sciences".

The main reasons for this development are :

- the end of the product life cycle for some agrochemical products (such as Monsanto's glyphosate) and the added value created by the adaptation of chemical products to GM seeds by seed companies.
- the synergy existing between the agro-chemical and pharmaceutical sectors, whereby considerable investments have been made in genetics, bio-informatics and toxicological studies.
- the increase in the number of alliances and mergers between agro-chemical companies and seed producing companies over the last years, as chemical pesticides are increasingly rejected by popular opinion.

As a result, six multinational companies, with important R&D budgets, hold most of the genes used worldwide for commercial purposes. The distribution networks they are building on the European and US market are important (Joly and Lemarié, 1998) (see Annex II). Monsanto has invested considerably in mergers and acquisitions (more than 8 billion US$) (Lerner and Merges, 1997). DuPont has invested 9.4 billion US$ for the acquisition of Pioneer. In total, since 1995, technology acquisitions and alliances have been made. Monsanto, Novartis, DuPont and Aventis (Mattei, 1999) are the "big four" of the Life Siences sector. Dow and Zeneca are much smaller since they integrated the sector at a later stage and are in a consolidation phase.

Competitivity

Technical progress has been felt by many as contributing to the competitivity of the sector. As a result, each element of the GM food chain (farmers, seed companies, agrochemical companies, transformers, traders, distributors,...) has an interest in evaluating the value added created by transgenic plants (Joly, 1998). This is not an easy endavour, as contrasting opinions on the risks and benefits of GMO plants subsist (see Part B). The profitability of investments and products, the rationalisation of activities and the competitivity of companies remain nevertheless major issues :

- Advances in traditional breeding, genetic engineering and cultural practices have brought about an increase in *crop yields*.
- Companies are working towards the improvement in seed production, the reduction of costs for farmers, by reducing inputs and making their use more simple (Tobelem and Briand, 1998). The adoption of GM seeds by interested farmers in the US is mainly due to promised increases in

1 For a definition of biotechnology and related terms, see Part C.

productivity (10-20% according to estimates by Monsanto).1

- Large agrochemical companies have bought biotechnology firms in order to acquire new techniques (*innovation*) and, in the case of seeds, avoid paying royalties (Joly and de Looze, 1996). This has occured while transgenic plants have started to enter the commercial phase.
- Companies must be able to reorient their strategy according to changes in market demand (*flexibility*).
- *Quality* enables product differentiation. It applies to second generation GMO, whereby the added value of genetic modification should be more visible to consumers (nutritional advantages). This poses the question of traceability and who should pay the additional costs involved. The industry believes that the consumer who would like to purchase GMO-free food will have to pay the additional costs of something he has not even asked for.
- The *organisation of the supply chain* seeks to optimise the added value of GMOs. The added value created and distributed to each element of the food chain is dependent upon the risk premium (price), the quantity produced and the quality offered (Kalaitsandonakes, 1998). Risks linked to the creation of a GM food sector can be reduced by : the integration of agrochemical companies, seed companies and start-ups2, alliance strategies between agrochemical companies and processors3, and contracts between farmers and agrochemical companies or processors.

The strongest research structure for modern biotechnology is found in the US (see Annex III), and some authors stress that "if this situation does not change, Europe will soon find itself excluded from what may be considered one of the great "business opportunities" of history, to the detriment not only of European industry but particularly economic development in terms of market demand" (Marabini, 1993).

The future

The biotechnology industry is shifting from the control of marketing channels to the control and ownership of genetic material through patents.

Farmers have warned against vertical integrations (agrochemical and seed companies) likely to lead to a monopoly. The seed sector in both the US and Europe is considered by some as remaining quite fragmented (the first 10 companies control 32% of the world market estimated at 23 billion $), compared to the 10 first agrochemical companies, which have a turnover of 85% of the world market for pesticides and herbicides, estimated at 31 billion$.

However, the number of acquisitions and mergers in this sector has increased considerably over the last decade4 and the future situation might be very diffferent from what we see today. Even if in Europe, for the moment, a large number of seed companies exists, market domination has largely been achieved by the development of high-yielding hybrid seeds, forcing farmers to buy seeds from their suppliers every year. As for cereals, the number of varieties available is rather small and, in France, 34% of the capital of the largest cereal seed company (Etablissements Benoît) is held by

1 This cannot be generalised, however, as climatic and soil variations between regions have pushed farmers to go back to non GM crops, despite premiums offered by agrochemical companies.

2 Dow has bought Mycogen, DuPont has bought Pioneer.

3 Monsanto-Cargill or Novartis-Béghin Say.

4 See Annex II for an overview of the development of industrial groups in the Life Sciences sector.

Novartis1.

As far as quality GMO are concerned, the valorisation strategies seem to depend on a more vertical form of company integration (Joly, 1998b), with a tendency towars monopoly. Too little investment in a number of important crops, such as wheat and peas in France, for instance, would have a negative impact on the competitivity of those sectors. Seed producers defining themselves as independent, do however show that they consider international alliances as a way to increase their negociation power2. The increasing integration of the agri-food sector today can be seen as a future increase in the dependency of consumers on a restricted choice of food products (Rouvillois and Le Fur, 1999).

Growing interest in the development of a GMO-free supply chain

The number of agri-food industries having chosen to import GM-free raw material has grown recently. This was the case in Mexico, South Corea, Japan and the United States.3

In Europe, France has also seen initiatives for the separation of GM-free maize and soyabeans from GM varieties. Starch factories have been under pressure from clients such as brewers and biscuit manufacturers in order to exclude GM maize (Young, 1999). Industries whose main output is soya products have developed labels guaranteeing that they are GM-free and retailers have set up traceability schemes up to the fields4.

Company interviews revealed that agro-chemical companies would create added value through concentrating efforts on output traits (quality GMOs) or through GM-free products. The European position has certainly favoured a shift of company strategies towards the development of a GMO-free supply chain. An evaluation is needed of the extent that this chain could reach.

3.3 Political aspects

International negotiations on the release and marketing of GMO

At the end of the Uruguay Round of the GATT, in 1994, it was decided that the Trade Related Aspects of Intellectual Property Rights (TRIPS agreement) should be reviewed under the auspices

1 Yves Manguy, personal comm.

2 See, for instance, the case of Limagrain Agro-Industries in France, with its biotechnology company Biogemma and four activity hubs in several European countries and the United States (Company interviews).

3 In the USA, the main miller, Archer Daniels Midland, has demanded collectors to separate GM and non-GM cereals (Wall Street Journal, September,1999).

4 Linéaires n° 142, 1998.

of the new WTO in 1999. TRIPS relates to seven areas of intellectual property, including plant varieties. The review of TRIPS in November this year shall re-examine Article 27.3b, i.e. the "biodiversity provision" which states that "…members shall provide for the protection of plant varieties either by patents or by an effective *sui generis* system [breeders' rights] or by any combination thereof". The implications that such as agreement will have for the rights of nations over biodiversity and related knowledge should not be overseen.

However, the picture is complicated by the existence of the Convention on Biodiversity1 (CBD), decided at the Rio Earth Summmit in 1992 and which stipulates that countries should regulate access to genetic resources. The world CBD conference on bio-security held in Cartagena (Colombia) between February 14th-24th 1999, was not able to achieve the signature of an international protocol on the trade of products derived from GMO. This failure was due to the refusal of the "Miami group" of GMO exporting countries to accept to provide information and a clear identification (labelling) of goods containing GMO.

One of the priorities of the European Union is to reconcile environmental and commercial concerns. At international level, the EU is in favour of the precautionary principle, asking for the labelling of GM food and considering that an international protocol on biosecurity should prevail over other international agreements such as the TRIPS. In view of the forthcoming WTO negotiations, options for environmental and sanitary measures concerning GMO in food, acceptable and recognized by all, should be defined.

Two further agreements with the framework of the WTO have en impact on national sanitary and food policies : the agreement on sanitary and phytosanitary measures (SPS) and the agreement on technical barriers to trade (TBT).

These two agreements authorise WTO members to fix the level of sanitary protection judged "appropriate". Each State has thus the freedom to determine the level of acceptable risk. However, in order to avoid sanitary measures having as hidden aim the restriction of imports, the level of acceptable risk must be defined in a coherent manner between various products. These measures should not discriminate between national and foreign production and should be proportional to the accepted level of risk.

The main problem is that the WTO does not give a clear answer in the case when risk evaluation is made difficult given the current state of scientific knowledge. Only Art. 5.7 of the SPS agreement stipulates that provisional measures can be taken while further scientific studies are carried out, but this has never ben used by the European Union. It is within this framework that the "precautionary principle" should find an application within the WTO.

However, the concept has been used by NGOs, the media and politicians, but its juridical weight is questionable, given that zero risk doesn't exist and that the total innocuity of a product cannot be demonstrated. To demand the demonstration that a product doesn't constitute an abnormal risk for the consumer becomes legitimate. The precautionary principle should enable the refusal of the marketing of a product if the risk and uncertainties concerning its innocuity go beyond a certain level deemed acceptable by the scientific community.

Progress should be made in four main areas :

1 The CBD has not been ratified by the USA.

- The definition of norms and environmental and sanitary practices universally accepted and recognized. This should be the prerogative to any real progress within the framwork of the WTO.

- The creation of several organisations (agencies, offices, laboratories) of a very high scientific level, independent from the government and private companies, transparent and aimed at the control of all new products having direct or indirect consequences on health and the environment. The European Union could have an Agency for Food and Sanitary Security which would be able to issue decisions which would be less dependent upon economic and political influences. A sound juridical base is necessary in order to decide on the marketing of new products and proceed to risk evaluation.

- A cooperation should be started between this Agency and related organisms would reduce the differences in the current approaches to evaluation, which are favouring the building up of commercial trade disputes.

- The relationships between multilateral rules and regulations and the precautionary principle should be clarified so that this principle be recognized within the WTO. However, the USA have been strongly opposing the fact that the term of "precuationary principle" be present in the final *communiqué1*.

4 Policy options to be considered by the European Parliament

4.1 Regulatory issues

Background - European level

A legislative framework has been set up in order to accompany the developments of techniques in genetic engineering. This was partly due to the concerns associated with possible hazards linked to

1 For the USA, decisions should be taken on the basis of the "available scientific evidence" which does not, at the moment, set doubts on the innocuity of GMOs.

the development of new genetic manipulation techniques and to avoid trade distortions (Wybe and Matthee, 1999). The introduction of GMO has been felt as introducing new risks1 for human health and the environment which had to be evaluated according to certain standards.

This prompted the issue of two EC directives : Directive 90/219/EEC2 on the Contained Use of GMO3s and Directive 90/220/EEC4 on the deliberate release into the environment of GMOs. These directives are process-oriented (horizontal), i.e. focusing on the genetic manipulation rather than the product being genetically manipulated.

More recent legislation includes :

- Council Regulation 258/97/EEC5 on Novel foods, which sets the principles for the labelling of GM food. However, it does not cover genetically modified food additives, flavourings and solvants. At the end of October 1999, the EU Scientific Committe on Food issued a favourable opinion on two Commission regulation proposals for GMO labelling, including the choice of the tolerance level of 1% for the (accidental) presence of GMO in food.

- Directive 98/95/EEC on genetically modified plant varieties and plant genetic resources. This legislation is vertical, i.e. product-oriented, dealing with specific aspects or products resulting from genetic modification.

Several criticisms have been made on the current EU regulatory system for GMOs, namely :

- The risk assessments6 mandated by the 1990 regulations are not standardised and vary considerably between Member States. They are qualitative in nature and rely on expert judgment.
- The 90/219 and 90/220 Directives are technology based rather than product based.
- They are considered by many as being excessively precautionary.
- They are seen as adversely affecting the competitiveness of European companies, which are therefore encouraged to make biotechnology investments in the US.
- The problem of responsibility in case of ex-post risks such as damage to the environment or health is not tackled by European legislation.

These criticisms have brought about a series of proposals and EU Member countries declarations for a review of the legislation concerning GMOs and Directive 90/220 in particular :

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1 Risk : the probability that a particular adverse event (a hazard) occurs during a stated period oftime, or results from a particular challenge (Rogers, 1995). The calculation of societal risk (risk to society as a whole) is particularly difficult and risk perception by the general public should not be overlooked.
2 Council Directive 90/219/EEC, O.J. 1990, L 117/1 (amended by Council Directive 98/81/EC, O.J. 1998, L 330/13).
3 A genetically modified organism (GMO) has been definded as "an organism in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural genetic recombination" (Art.2 of the 90/220/EEC Directive).
4 O.J. 1990, L 117/15.
5 O.J. 1997, L 043/1.
6Risk assessment : the process of obtaining quantitative or qualitative measures of risk levels, inlcuding estimates of possible health effects and other consequences as well as the degree of uncertainties in those estimates (Fiksel, J. and Covello, V.T., 1986)

Box I 4.1 - On the review of Directive 90/220 (follow-up work to the initial directive)

- 1994 - Commission Communication (COM(94)219)
- 1996 - Commission evaluation (COM (96)630)
- 1997 - Report of the EP Committee on the Environment, Public Health and Consumer Protection on the Report from the Commission on the Review of Directive 90/220/EEC, Rapporteur David Bowe, MEP (A4-0239/97)
- 1998 - Commission proposal (COM(98)85)
- 11.02.1999 - EP amendments on COM(98)85
- 26.03.1999 - Commission revised proposal (COM(99)139 final)
- 24/25.06.1999 - 2149th Ministerial Meeting of the Environmental Council of the EU

The Commission's revised proposal (COM(99)139final) has not included the banning of the use of antibiotic marker genes and has rejected the proposals of the European Parliament to include the precuationary principle explicitely in the Directive. It also ignored the proposal made by the Parliament to introduce a liability regime and does not provide for sanctions in case of damages caused by unintentional GMO releases. The idea of introducing a certification system for GMO products, which would aim to detect the GMO at all stages of the production process (going further than labelling, since it has not only the aim of informing the public, but also the traceability of the GMOs) has not been included in the revised proposal. The safeguard clause was modified taking into account the Parliament's proposal : "new" information has been modified by "additional" information.

The Parliamentary Assembly of the Council of Europe also issued declarations on GMOs in June and September 1999 (Recommendation 1425). It mentioned the fact that "...a balance between private and public interests...[...]... is nearly impossible to find" and yet the necessity for researchers in the field of biotechnology of conforming with the Convention on Biological Diversity (CBD) of 1992 (see previous chapter) and the WTO to comply with it.

As a result of the declarations issued by the EU Member countries at the - 2149th Ministerial Meeting of the Environmental Council of the EU on 24/25 June 1999, the granting of new GMO licences has been blocked until a new revised directive is adopted. During the meeting, a majority of Member States (11 out of 15) were in favour of at least a thoroughly precautionary approach, meaning not to grant applications unless it is demonstrated that there is no adverse effect on the environment and human health. Amongst the four countries which were not in favour (UK, Ireland, Spain and Portugal), Ireland has recently adopted a policy statement on GMOs and taking into account the precautionary principle and the UK has strong public resistance to GMOs (Matthee, personal com.). Future policy statements might however be influenced by the WTO conference in Seattle due to start on November 30th 1999.

The current situation in the EU has been assimilated to a *quasi* or *de facto* moratorium. NGOs such as Friends of the Earth demand a global moratorium on GMOs while a new directive is defined and the innocuity of GMOs for health and the environment is clearly established.

Recommendations

Risk assessment

New methods for the evaluation of risks associated with GMO in food should be developed in the future and should be integrated in the official evaluation procedure. Meanwhile, the precautionary principle1, whose introduction has been prompted by increased scientific uncertainties in the evaluation of risks for the environment ("irreversible damage")2 - and which states what should be done in a situation of uncertainty, without waiting for scientific proofs to take the necessary measures to reduce a potential risk - should be applied. This principle remains, however, largely ill-defined and its application is not universal nor compulsory.

Is the standardisation of risk assessment possible? In order to be used as a management and regulatory tool, risk assessment should result in precise measures.

Ethical and scientific questions

The reliability of expert judgement and the defininition of scientific knowledge are often questioned. This might be due to the fact that scientific and technical knowledge is today in the hands of the main industrial actors worldwide and, amongst the researchers of public research institutes, only a few do not work in partnership with industry. As a result, the credibility of control procedures, as some experts might find themselves in a situation of judge and party is questioned. Nevertheless, most warnings on GMOs today are mainly issued by experts which are fully independent from the interest groups involved in the debate.

At European level, the Commission has proposed to rely on the European Group on Ethics in Science and Technology, created in 1997, for ethical advice, which should become the "Ethical committee" (12 members in 1998).

Legislation3

European legislation should be able to ensure an independent evaluation of GMO, whereby deliberations are transparent towards consumers and independent from private commercial interests4

1 The Precautionary Principle is set out in Art 174 (2) of the EU Treaty. The European Commission has recently been working on guidelines for taking into account the precautionary principle (M. Matthee, personal comm.).
2 Rio Declaration on the environment and development (June 1992).
3 See Annex V for a short review of recent regulatory initiatives for GMOs.
4 The US Food and Drug Administration has been sued by the International Center for Technology Assessment (ICTA) in June 1998 for failing to require manufacturers to label genetically modified foods. One of the plaintiffs,

a) Revision of directives and regulations

The Directives 90/219 and 90/220 have been criticised as being technology based rather than product based. Would product-based legislation be more appropriate? What would this imply? A product-based regulatory system, such as the US system, enables the application of the principle of substantial equivalence, whereby the equivalence of the final product containing GMOs can be considered as equivalent to a non-GMO product. Furthermore, the equivalence is based on the analysis of only a few food components, which is, according to certain scientists (Philipon, 1999), insufficient. It should be possible to declare, *a priori*, that GM food is not substantially equivalent to traditional food and that its innocuity should therefore be proven.

b) Detection methods, herbicides and animal feed

How far has work towards a harmonisation of detection methods gone? The revision of Directive 90/220/EEC should involve the need for companies depositing a demand for a marketing authorisation to provide national and European authorities with the information concerning border fragments. This would avoid that the costs involved in the analyses carried out for the detection of GMOs are borne by public authorities.

The lack of knowledge on the metabolic products of the herbicides used in plants and which enter animal feed together with the concentration of herbicide residues in the food chain, show, on the one hand, a need for the traceability of food derived from animals "fed with GMO" (Seralini, 1998)1. On the other hand, herbicides used in GM plants should be subject to a new authorisation procedure, given their new application (gliphosate and glufosinate are corrently authorised as weed-killers, without a direct relationship with crops destined to food consumption).

c) Antibiotic marker genes

The ban on the marketing of GMOs containing antibiotic marker genes should be included in the revision of directive 90/220/EEC and the previously authorised GMOs containing such genes should also be concerned. The evaluation prior to issuing authorisations should also cover other techniques aiming at controlling gene expression (such as seed sterilisation, 'switch' mechanisms), with case by case studies.

d) The implications of a moratorium on GMOs

A moratorium would mean putting a halt to the marketing of GMO food products (whether they are produced in the EU or imported). Research on GMOs could however go on, if the necessary experiments are conducted in a confined environment. Research could benefit from an opportunity to develop without an economic pressure, being possibly better able to respond to the questions it generates (the evaluation of the impacts on health and the environment could be carried out relying on expertise from a variety of sectors and the setting up of pertinent evaluation models could be seeked).

P.Regal, professor of ecology at the University of Minnesota, claims that the FDA is too close to the industries it is supposed to regulate (Nature, 393,404 (1998)).

1 The future European legislation on novel feed for animals should include the obligation of using labelling for GM animal feed (van Dam and de Vriend, 1998).

A moratorium might provide more space for enlarging the debate on GMOs to include other production methods, thus not being limited to a cost/benefit analysis of GMOs. A "technology induced" approach would be replaced by a "problem induced" approach, involving the assessement of all solutions which might provide an answer to a given problem (Levidow, 1999).

Furthermore, there might be scope for a more complete analysis of risks at a global level. This would involve socio-economic, environmental and ethical issues and the situation of developing countries. Another aspect would be the development and set up of a suitable legislative framework. The current situation is destabilising the EU, faced with pressures from the USA on the one hand and the refusal of the development of GMOs from a large share of the European population.

On the whole, a moratorium can be useful if it is not assimilated to the sentencing of a technology but rather to the possibility of clarifying the issues at stake and fixing from the research stage onwards the conditions for the control of progress. The evaluation stages should be multidisciplinary, away from the belief that a complex science should be confined to specialists who can understand it. The views of non-specialists can be critical, whereby what seems evident to specialists is not admitted *a priori*. As a result, specialists may be able to question their own views, clarifying the situation.1

The question remains whether a moratorium could be sustained in the long-term and whether viable alternatives exist, considering the implications of such decisions at international level (WTO).

International level

In the United States and Canada, GM food is not considered substantially different from non GM food. No specific authorities have been set up to regulate their introduction.

The USA are particularly keen on eliminating the precautionary principle from the forthcoming WTO negotiations (Millenium Round), as they are convinced that genetic modification does not bring about essential changes in food products, i.e. GMO and non-GMO foods are "substantially equivalent" (see Part B). There is a risk of WTO trade sanctions if unilateral bans by EU countries on GM plants and products are announced and put into practice.

4.2 Interactions between research policy and regulatory issues

The shortcomings of European legislation affect the organisation of the monitoring and evaluation of the introduction of GMO in the food chain. Several options have been put forward, particularly in terms of the level of expertise and transparency needed :

A scientific body at European level, independent from the public and private sector, to test all new GM food products which could have direct or indirect consequences on health and the environment, has often been put forward as an option. This body would certainly need a solid juridical base in order to be able to take decisions, including the marketability of those products. According to EuropaBio (European Association for BioIndustries), the federating organization of the 942

1 Courrier de l'environnement, INRA, n° 16, April 1992.

biotechnology (pharmaceutical and agro-chemical) firms in Europe, there is a need for a European over-arching body responsible for GM products.

The lenght of tests necessary for the evaluation of risks for human nutrition in particular have been mentioned in section 2.2. Regulations should take into account the fact that the evaluation of the impact of GMO in food is a lenghty process which should not be ignored. Setting up a monitoring system for novel food is needed, as the determination of minimum daily intake may not take into account the important evolutions which are taking place in the consumption of these novel foods.1

The patentability of living organisms has implications for research policy. Directive 98/44//EEC, which entered into force on July 30th 1998 and has to be codified into national law of the member States by July 30th 2000 recognizes the "principle of farm exemption", protecting farmers by enabling them to freely reseed in their own fields the seeds obtained from the harvest of the produced varieties without having to request authorization from the original breeder2 to do so, so long as the seeds are effectively used for this purpose and not for commercial ends (Marabini, 1993). The principle of research exemption is however not recognized : a licence must be obtained by those research institutes or companies wanting to use a patented gene.

4.3 Added value of EU funded research

Recent public concern and protests about GM food has been fuelled by dramatic illustrations of unanticipated dangers such as the epidemic of bovine spongiform encephalopathy (BSE) in cattle. Given the existence of significant scientific uncertainties about the potential ecological and health impact of GM crops, restoring public trust should to be the main priority.

Consumer claims concern risk and safety, which have an ethical dimension when they raise further questions about responsability.3 This implies that if ethical aspects are to be taken into account in the discussion concerning the introduction of GMO, the question of responsibility should be addressed.

1 Pierre Besançon, Communication at AFSSA Scientific Seminar.
2 Original holder of protected variety.
3 Cambridge Biomedical Consultants (1999) Ethical Aspects of Agricultural Biotechnology.

Assessments made by European research should not only be limited to purely technical, scientific questions, since public concern involves broader questions such as the implications of changing farming practices for local wildlife or for eating habits.1 The challenge lies in facilitating public access to credible scientific information, stressing its significance and limitations. It should be understood that "the best research can do is to narrow the limits on uncertainties, not eradicate them".2

Consensus conferences, which involve a citizen panel and an expert panel on specific scientific subjects, started in Denmark in the 1980's, where the recommendations made by both panels were useful to the Parliament's work and were a means of drawing decision-making and public debate together3. However, research should address the difficult question of synthetising and translating results into viable options. The information which should be provided to consumers who can then make informed choices should take into account the fact that different groups have different concerns for ethical, religious and medical reasons.

Other issues include the creation of a GMO-free food chain : for some, this decision implies that GM food is substantially different from non-GM food and that it would be more logical for GM-food to be clearly labelled4.

B – ARGUMENTS AND EVIDENCE

1 Scientific definition of genetically modified food

1.1 Characterisation

Fifth Framework P demands for GMO market licences concern plants and most of them include a gene for herbicide resistance. In Europe, oilseed rape and maize are the main GM plants for which requests for market licences have been submitted and the only ones present on the market.

In the world, other GM plants have been developed and their market is expanding :

1 See Nature 394 , 605 (1998).
2 See Nature 398, 639 (1999).
3 Courrier de la Planète, July-August 1998
4 Yves Manguy, personal comm.

Table B 1.1 Transgenic plant varieties in the world

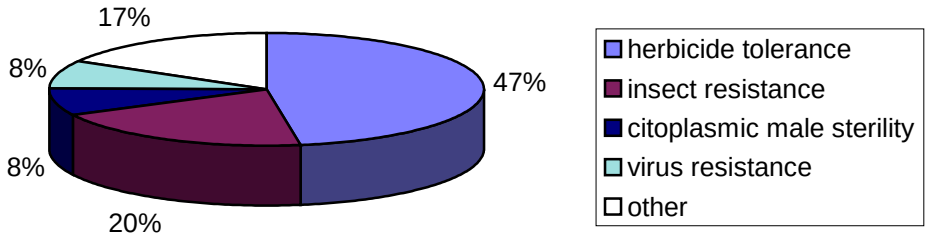
Crop	**Country**
Maize	On the market in USA, Canada, Japan, Argentina, Europe
Oilseed rape	On the market in USA, Canada, Japan, under moratorium in Europe
Soya	On the market in USA, Europe (import and human consumption), Japan, Argentina
Wheat	Research and development stage in Europe and the USA, a variety is examined for market licence in Canada
Rice	Development stage in Japan and the USA
Sugarbeet	Development stage : research in Europe and elsewhere
Tomato	On the market in the USA, Canada, Japan, stand-by in Europe and import under moratorium in the UK
Potatoes	On the market in the USA and Canada
Chicory	On the market in the USA, stand-by for seed production and cultivation licence in Europe
Papaya	On the market in the USA
Courgettes	On the market in the USA and Canada

Source : F. Hervieu, French Ministry of Agriculture, personal comm.

Other products derive from genetic modification but they do not contain DNA molecules. These include enzymes (e.g. alpha-amylase used in bread-making and brewing, chymosine used in cheese-making).

The main traits for which marketing applications were made in Europe between 1987 and 1997 concerned :

Fig. B1.1 : Distribution of traits introduced in GM plants subject to a marketing authorization 1987-1997



Source : CGB activity report, 1997.

It can be seen that the main trait is herbicide tolerance, where plants (maize, soya bean, oilseed rape and others) have been engineered to allow broad-spectrum herbicides to be used to greater effect1. Contrary to what is generally announced, the development of biotechnology does not principally concern quality traits. The latter are above all referring to crops with industrial applications such as potatoes, tomatoes and sugarbeet, directly linked to their market outlets (retailers and industry, which are taking into account new consumer demands).

1.2 Detection

Detection methods mainly concern proteins and DNA. Those concerning proteins cover products which are only slightly processed or not processed at all and are based on immunochemical reactions. Proteins derived from the expression of a gene of interest introduced in the plant are specifically recognized by antibodies ("Elisa" method, whose cost is relatively modest).

The detection of DNA is done through a method called polymerase chain reaction (PCR) (Campaniol, 1999). This method can be applied on processed products since DNA is degraded at a lower rate that proteins. It enables the multiplication of a large number of copies of the DNA fragment which is of interest and thus detects even very small quantities of DNA.

In general, a genetic modification can be detected because of the existence of common DNA fragments between GM plants. A weak point of this method is however the impossibility of asserting the absence of foreign DNA if it is not detected (Laurent, 1999).

The identification of a particular genetic modification requires the knowledge of a specific fragment linking part of the transgene and part of the chromosome on which the transgene itself is inserted. However, this information remains inaccessible to the general public and there is no centralized

1 This reflects the development of agricultural applications of GM by mainly US agrochemical companies which have turned to genetics to integrate the areas of seed production and pesticide use (production of a seed/herbicide package) (POST, 1998).

database for these fragments, which would be a useful reference for the traceability of GMOs throughout the food chain, from the field to the consumer.

2 Field trials

2.1 Environmental impact

Gene flow

In February 1999, the UK's Royal Society gave its view on the risks linked to gene transfer from a GM plant to a non-GM plant based on the following three cases (Royal Society, 1998):

a) Maize and potato : the risks of gene flow are nil. There are no wild varieties of the same species since these crops have been originally imported. They are also unable to outcross with wild plants from related species if these exist in the area, due to sexual incompatibility. The strong allogamy of maize may bring about the formation of hybrid seeds, but maize is still heavily dependent upon specific cultural techniques.

b) Rice and autogamous plants : these plants are self-reproducing and gene flow is therefore impossible. Soya has a low allogamy and seeds survive with difficulty in the soil, the propagation of hybrids being thus limited.

c) Other plants, like oilseed rape (*Brassica napus*), for which the risk of gene flow remains important if GM plants and non GM plants are situated in the same culture area, flower at the same time and are pollinised by the same insect (Scientific Committee on Plants, 14/7/98).

Research has shown that crossings of *Brassica napus* and *Brassica campestris* (a related species) have given vigorous hybrids (F1) (Jorgensen et al, 1994) which backcrossed with *Brassica campestris*, without being more vigorous nor invading (Mikkelsen et al.,1996).

The risk of environmental impact can be defined as : the probability of transfer x the consequences linked to the transfer (Ahl Goy and Duesing,1996). The probability of transfer will depend upon the crop's biological characteristics, the risks of interspecific crossing1 with wild relatives, the strong density of weeds, the presence of vectors (e.g. pollen), the persistance of grains in the soil. The consequences are linked to : hybrid vigour and the hybrids' fertility.

Other authors stress that even in autogamous species, environmental conditions may favour the exchange of genes between related species (Darmency, 1997).

The possibility of isolating fields where GM plants are grown by allowing for a sufficiently large area of land around them (refuge area) appears as impossible in practice, with negative economic consequences for farmers : as pesticides cannot be applied on refuge areas, a fall in production is expected.

Insect resistance and the utilisation of plants integrating the Bt gene

1 Between different species.

Biopesticides based on Bacillus Thurengiensis (Bt) have been largely used in agriculture prior to the development of the techniques of genetic modification (Lambert and Peferon, 1992).
Discovered in 1902 in Japan, isolated and identified in 1911 by a German researcher, Bt is a bacteria of the Gram+ family capable of synthetising endotoxins which kill specific lepidopterus (100 species are concerned). Biopesticides based on Bt were first marketed in France in 1938. The discovery of the resistance of certain caterpillars to a Bt based biopesticide in 1979 prompted the creation of a "Management Working Group" by the main companies marketing Bt biopesticides in 1988.

The genes coding for these endotoxins (so-called *cry* genes) have been directly integrated in the plant through genetic modification techniques. This continuous production of toxins in the plant causes however a constant selection pressure, with the development of insect resistance.

Managing resistance

Creating refuge areas around GM crops is one of the solutions proposed for those GM plants expressing high doses of toxins, enabling a dilution of the resistance factor by crossing between toxin sensitive and toxin resistant populations. According to a report by the Union of Concerned Scientists, non-Bt refuge areas should represent 20 to 50% of the cultivated areas, depending on the crop and the insect concerned.

Another strategy would be to include several *cry* genes in a plant, since it has been found that pests such as the diamondback moth (*P. Xyltosella*) is resistant to 4 different toxins (Tabashnik et al, 1997). However, this is very difficult to achieve and the possibility of concentrating on crop rotations expressing different toxins in order to reduce insect resistance to Bt is currently being explored.

In view of further reducing the selection pressure, research has been carried out on the joint introduction in a plant of a gene expressing the toxin and a promoter1 limiting its expression in time and space.

A reduction in the quantity of toxins produced is another aim (Royal Society, 1998), but would reintroduce the use of pesticides.

In France, several research institutes are working on a joint biosafety project on the environement inititated by the government and having the followng aims : ensuring the traceability of GM products, collecting information on their behaviour and non-intended effects, following the theoretical possibilities of the occurence of unfavourable impacts on the environment when used on a large scale.

2.2 Risk assessment

Field trials in the USA and in Europe are essentially centered on testing for herbicide and pest tolerance (so-called "input traits", representing 53% of tested traits) and quality ("output") traits.

Field trials are part of the monitoring scheme set up for any new GMO aimed at the evaluation of

1 A promoter regulates gene expression.

environmental risks : after the laboratory, plants are grown in glasshouses, small plots (1m x 1 m) and finally larger plots up to 1 ha. In practice, the results of these field trials are finally used for assessing the management of GM crops on a large scale.

In France, these tests have been carried out through a programme managed jointly by several research institutes since 1995 and focusing on oilseed rape, maize and sugarbeet. The parameters studied include : pollen dispersion, the appearance of European corn borers resistant to Bt, the crossing between the different varieties of each crop and related species, and the relevance for the current weeding practices. Similar tests are carried out by private companies.

It remains however questionable whether tests on small-scale areas can provide a reliable evaluation of gene flow. Given the irreversible contamination likely to affect the environment, how can the ecological risk in the field be evaluated? The interinstitutional tests in France have been reconducted for three years and more information should be available in the future, for instance, on the distance needed between GM and non GM crops. First results indicate that the pollen dispersion is dependent upon a series of parameters (plot area and orientation, wind and insects, the more or less isolated situation of the plant,...) and that the frequency at which interspecific hybrids occur is low, how can such results be extrapolated to larger areas? Simulations indicate that even if the frequency of crossings between cultivated and wild plants is very low, the gene conferring resistance will be transferred (Gouyon, 1994).
Complementary evaluations should also take into account the impact of the introduction of GM crops on the surrounding insect fauna, conducting trials not only on those insects the new GM crop should kill (basis of current tests carried out for market authorisation), but also on non-target insects.

The main criticism made by opponents to the application of GMO technologies to plants is that these plants do not have an evolutionary past, i.e. they have not developed in a given ecosystem, amongst natural predators. The natural evolutionary mechanisms have influenced the development of each species in a specific ecosystem, interacting with the existing flora and fauna, in a given geological and climatic context.

The conservation of biodiversity is also questioned : would the introduction of GMOs favour the elimination of cultivated species which do not adapt to the productivist ideal of modern industrial agriculture? Furthermore, adapted varieties are in this case highly dependent upon the use of inputs to compensate for their uniformity (the uniformity of large areas bringing about the vulnerability of cultures).

3 Risk-benefit assessment of GM food[1]

The evaluation of the risks and benefits of GM food has been based on the concept of "substantial equivalence"[2], whereby a comparison (nutritional and toxic substances) is made between the composition of a novel food and a current « reference » food. The concept of "substantial equivalence" is problematical since a GMO recognized as such under one circumstance would no

1 The focus on two food crops (tomato and maize) and animals, to see the implications for food security of the introduction of GMO in food, is developed in Annex IV.

2 Under this principle, the labelling of food derived from GM plants or animals is not compulsory and it is not envisaged to evaluate, label or trace the animal which will have been fed with transgenic maize (Hermitte, 1997).

longer be equivalent for a different crop, environment or other specific conditions which may have caused a deregulation of the gene.

3.1 For human health

The importance of taking into account health aspects of the introduction of GM food has been reflected by the creation of specific national agencies aimed at issuing recommendations concerning possible risks for human health. In the UK, for instance, a Food Standards Agency has recently been created and a similar body has been set up in France (Agence Française de Sécurité Sanitaire des Aliments) (Philipon, 1999).

Several consequences resulting from the introduction of foreign genes in a genome are unpredictable, as well as the effects on the composition of the food concerned. Besides desirable (primary) effects, the introduction of foreign genes may thus produce undesirable (secondary) effects.

The risks for human health are twofold : toxic and allergic. One potential danger is the intake of new, unknown pathogens together with modified plants, which may have appeared due to the modification which has made plant species resistant to viral infections.1

It has been shown that inactivated viruses, inserted in GM plants, are capable of recombining with the host genome and be « reactivated » (Martinez, 1997). Inserted genes may activate oncogenes and cause certain cancers (Pimbert, 1997).

Toxicological risks can be associated with the addition of one new gene in a plant. Secondary metabolic changes may cause undesirable effects, such as the production of new toxic substances or stimulating the production of toxins normally present in the plant, even if only at very low level (see solanine in potato, tomatine in tomato or erucic acid in oilseed rape) (Le Déaut, 1998).

The evaluation of allergenic risks is complicated by the uncertainties linked to the prediction and future of the behaviour of transferred genes. The effect of a gene's genetic and cellular environment on the characteristics of amino-acids produced may have been underestimated. The behaviour of proteins is thus not fully known and it is currently impossible to say whether these changes will bring about an increased sensitivity to allergenic substances (Le Déaut, 1998).

If we consider that a GM plant only produces an expected protein, the exact sequence of its amino-acids can be known. This can be compared to the sequences of known allergenes contained in gene banks and look for homologies in order to predict the risk of allergenicity. However, the proteins expressed by transgenes and derived from bacteria often contain no recognized allergene and historical, clinical and epidemiological comparisons are difficult (Wal, 1997). Furthermore, allergenicity in food is rarely due to one single component, but to a large number of proteins (glycoproteins). Experiments on animals (90-day feeding tests on rats) do not currently provide a valid extrapolation to humans.

1 In order to do this, genes derived from viruses are inserted in the plant's genome. This method cannot exclude the risk of creating new viruses with potential negative effects.

3.2 For the environment

The new genetic combinations arising from modern genetic engineering have never been tested as part of an evolutionary process (Hindar, 1998).The unpredictable stability of the introduction of new genes in a genome imply that the performance of GMO in the long-term is equally difficult to predict. The phenotype1 in particular may vary according to the events occuring in the environment of the GM organism. As a result, reaching a clear understanding of the potential ecological hazards is difficult.

A useful example to illustrate these difficulties is the application of genetic engineering to acquaculture, with the aim of producing animal proteins. Confined fish breeding cannot ensure that no accidental disseminations occur.

Apart from direct effects on the performance of the fish itself, ecological and/or population imbalances occur. Through the introduction of the breeding of transgenic atlantic salmon tolerant to frost, acquaculture would expand to the North, with inevitable direct consequences on the existing fauna and biological diversity in those areas (Hindar, 1998).

It seems therefore that there are potential hazards for biodiversity associated with the (uncontrolled) dissemination of GMO in the environment, sometimes compared to the introduction of a species in a new area in the past. Other arguments are in favour of an increase in biological diversity precisely through the creation of "genetically new" living organisms. The difficulty is that *a priori* estimates on the effects of these disseminations cannot be made.

3.3 For the economy and society

Consumer perception and public opinion

Since 1991, large surveys on the opinions of Europeans on biotechnology and genetic engineering have been carried out (Eurobarometer surveys). In general, the results have predominantly shown a reticence towards these technologies, for both the priniciple of genetic modification of foods, plants and animals, and the mechanisms with which they are regulated (POST, 1998).

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1 Phenotype : term used to refer to morphological or functional characteristics of an individual derived from the interaction of its genotype with the environment in which it is found (Marabini, 1993).

These reactions vary according to country : in 1996, favourable reactions towards biotechnology were found in Portugal, Spain, Italy and Ireland, while there was little confidence in The Netherlands, Germany, Luxembourg and Denmark. France, the UK, Belgium and Greece were in an intermediary position (Bonny, 1996).

There have been several factors contributing to the negative reactions by consumers in Europe to the introduction of the first transgenic plants : the presence of marker genes causing antibiotic resistance, the production of products without direct benefits for the consumers, developed by multinational agro-chemical companies and concerning mainly animal feed. GMO have been asssimilated to the results of productivism associated with public health accidents. Initially, a clear labelling of GMO foods such as tomato paste in the UK did not cause much fuss (POST, 1998) since consumers had a choice to buy GM foods or not. What has fuelled adverse reactions is however the incorporation of GM soya, maize and other bulk crops into many processed foods.1

Further contradictions on the initial authorization of Bt maize for animal feed in France - which has then been banned from cultivation - have questioned the legitimity of the national competent authority (the CGB) and doubts have arisen on the transparency of decisions and the importance given to the evaluation of risks associated with GMO in food (Joly, 1998a).

GM products are felt as something inevitable and at the same time consumers are unable to see the direct benefits which they could derive from GMOs and their widespread usage, which is felt as being more often spurred by the expected profits which the industry might derive from it (IFN, 1998).

Farmers and agricultural practices

Arguments in favour of biotechnology for farmers include the provision of means for the simplification of agricultural practices, yield increases, lowering production costs and the reduction in chemical applications for crop protection, contibuting to the conservation of the environment (Rouvillois and Le Fur, 1999).

Several authors (Jeremy Rifkin, A. Messean), however, consider that the introduction of GMO in agriculture enables the continuation of the productivist model of agriculture, to the detriment of other, more sustainable modes of production. Few research teams study the environment in its own dimension, considering the multiple factors which make up the ecosystem.

As far as trade is concerned, the French FNSEA deplores the fact that nothing has been decided concerning imports of GM agricultural produce, while its production has been banned in the EU.2

Benefits are essentially measured in terms of expected returns. However, the objectives of a qualitative type of agriculture are not based on an increase in returns. Other production methods might be as competitive as those using GM varieties, particularly if the negative externalities of

1 This lack of segregation is to due to the fact that producers believe that there is no significant difference beteen GM and non-GM plants (see the concept of "substantial equivalence"). This has repercussions on food processors and retailers (several EU retailers excluding GM products in their own brand products).
2 Agra Presse, July 1999.

intensive agricultural production methods are taken into account (Terraux, 1997).

Ethical issues

With the development of biotechnology, Nature has become a resource with a high commercial value for its genetic components, the basis of new products, above all for the pharmaceutical and agro-chemical industry (Haynes, 1999). Patents giving intellectual property rights have extended to live organisms and its genetic material. Nature has thus become an object of private property and the Convention on Biodiversity has mentioned the need for compensation for countries giving access to their natural resources.

Due to the very nature of the subject studied (genes, their variation, transmission and organisation in the genome), research on GMOs concentrates many questions on human values and the relationship between science and ethics. The genetic modification of living organisms raises philosophical and ethical questions, the definition of "species", their appropriation by man through patents and also the status of animals and plants compared to man.

The introduction of GMOs can have a negative impact for developing countries if the production of molecules previously derived from local plant varieties becomes possible in laboratories (e.g. vanilla) or other plants grown in the North 1. Moral values should have priority above commercial considerations, especially if it is claimed that development and solidarity between poor and wealthy countries are fundamental. To this end, financial means should be allocated to research into the applications of biotechnology which are interesting for developing countries, adapting to their traditions and taking into consideration their way of life (FAO Seminar, Paris 1999).

Given that the prevailing model today is intensive agriculture, the debate on biotechnology has concentrated on a restricted definition of risk : global risk (social, economic, environmental) deriving from an industrial type of agriculture has not been taken into account, as well as other methods which can respond to the real problems encountered in the field (Levidow, 1999).

Further issues raised include the impact on the environment : on the loss of biodiversity and the ecosystem's equilibrium, with the fear that new plants and animals are created, crossing the species barrier, simply in response to the socio-economic plans of man.

1 Example of the gene for laurate (a fatty acid present in palm oil) which, introduced in oilseed rape, will influence the economy of those countries producing palm oil (Biofutur n° 164, February 1997, pp.23-24).

4 Utilisation of antibiotics resistance factors

Today, at least half of GM plants which are cultivated, tested or awaiting authorisation in the world, contain antibiotic marker genes. The risks associated with these genes concern the spread of human and animal resistance to antibiotics. This is because the inserted genes could integrate bacteria present in the digestive tract and the guts or bacteria in the soil, with effects on humans and animals (Le Déaut, 1998).

Bacterial resistance to antibiotics is a phenomenon induced by the fact that antibiotics are widely used in sectors ranging from human medicine to animal breeding and crop production. Resistance is not only dependent upon individual consumption but also global use, for all sectors and countries. For some companies, the need to use antibiotics resistance factors as marker genes in gene transfer is no longer technically necessary, since other systems have been introduced. For others (company interviews), they are still widely used in transgenic plants commercialized for food purposes precisely since no viable alternatives are available yet.

The current transgenic plants contain one or two antibiotic resistance genes (examples: AmpR and *npt*II). TPS technology, well known as "Terminator", uses the antibiotic tetracyclin.

NGOs such as Friends of the Earth1 believe that it is irresponsible to take a risk, even if minimal, of contributing to the build up of antibiotic resistance and affecting the main tool for fighting against bacterial infections.

5 Objectives of current research outside Europe

The International Agricultural Research Centres (IARCs)2, which were formed to "benefit the countries of the South" and as custodians of Third World germplasm, are today adapting to the rapid transformation of agricultural sciences through genetic engineering by developing links with private sector research (Bialy, 1991).

The major changes which the CGIAR has had to face include (Manicad and Lehmann, 1997): a shift from original crop specific research to the integration with the concepts of sustainability and eco-regionality, which is yet to be achieved; and a change in scientific paradigm, from conventional plant breeding towards biotechnology. In practice, this has meant a shift to the characterization of germplasm for particular agronomic traits.

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1 Antibiotiques : alerte aux abus !, July 1999.

2 Financially supported by the Consultative Group on International Agricultural Research (CGIAR), which inititated the green revolution.

The property of the IARCs genebank collections were to be used for the benefit of global research, developing public good technologies which contrast with the proprietary nature of technologies developed by the private sector (Manicad, G., 1999). Since the 1980's, due to internal and external pressures, the legal status of the collections held by these centres has been questioned. The implications of the partnerships developed with commercial industries must be assessed, as the genetic material owned by private sector research plays an increasingly important role in research done in the CGIAR centres.

Can current research remain competitive if it is conducted by small public research teams? It seems that, to this end, industrial types of patents should be avoided, in favour of the protection envisaged by UPOV, compatible with the aims of biodiversity conservation. Public research could guarantee access to poor farmers through free access to licences (Griffon, 1998).

PART C - TECHNICAL FILE

1 Genetic engineering

There is no universally accepted definition of **biotechnology**, even though many attempts have been made to find an exhaustive definition. It entails a number of techniques using micro-organisms, plant and animal cells or their constituents in order to produce substances useful to man (Kahn, 1998). Another definition would be, according to the OECD : "the utilisation of biological organisms, systems and processes for the production of goods and services". Biotechnology doesn't have an end as such, but provides a certain amount of tools which can be applied to many sectors, from agri-food to health.

Modern biotechnology, which has developed over the last 20 years, allows the manipulation of genetic material in a precise and controlled way (Rogers, 1995), compared to conventional breeding techniques.

Genetic engineering, (also referred to as genetic modification, genetic manipulation and gene technology), can be thought of as a subset of biotechnology and is a set of techniques where individual genes1 can be copied and transferred to another living organism to alter its genetic make up and thus incorporate or delete specific characteristics into or from the organism.

The development of genetic engineering techniques has enabled a considerable increase in the range of applications. It is today possible to transfer a specific gene from any live cell to a plant or animal, crossing the species barrier. This represents an innovation from traditional breeding techniques for the selection of new varieties.

Its success in recent years can be partly explained by the major advances which have been made in different domains such as molecular biology and tools such as bio-informatics, gene sequencing and image analysis. However, it has been recognised that the role of genes is much more complex than initially thought.

A better knowledge of the functioning of cells was essential. Gene sequencing techniques have been developed in order to locate the genes for the expression of the agronomic traits of plants on the chromosomes2 and to study the interaction between genes and their environment. It is presupposed that successful manipulation of genes brings real insights into the underlying effects of the manipulation. However, many fundamental questions remain unresolved. Gene expression, for instance, is not fixed but may vary according to the environment. Identical genes inserted in different genomes will not be expressed in the same way. Genomes are fluid, changing, adaptable, and this nature makes the outcome of a transformation intrinsically unpredicatble (Martinez, 1997).

1 A gene is the so-called biological unit of inheritance; a segment of DNA which provides the genetic information necessary to make one protein (International Forum for Genetic Engineering).
2 A microscopic particle containing thousands of genes (DNA) found in the nucleus of the cell.

1.1 Modification of plant genome

Gene transfer involves the introduction of a DNA sequence in the genome1 of a plant cell. The aim is to produce plants with improved and stable traits for biotechnological applications.

When an interesting trait has to be introduced into plants, (such as pest resistance provided by certain strains of the bacteria *Bacillus thurengiensis* (Bt), toxic for a number of larvae damaging crops), the proteins involved are identified and the gene coding for this protein is isolated. The gene, through different techniques (using, e.g., a micro-organism called *Agrobacterium* or a virus), is transferred to another biological organism.

Genetic modification implies a horizontal transfer of genes between species which do not ususally cross. Viruses may cause a horizontal transfer of genes but remain limited by the species barriers and by the fact that all cells have mechanisms degrading or desactivating foreign genes. Through genetic engineering, foreign genes have been equipped with powerful promoters having their origin in viruses which will force the expression of these genes in the host organism at a higher rate (10 to 100 times). Artificial vectors may in particular migrate horizontally to a large number of species and combine with other genes in order to generate new bacterial or virus-derived pathogens (Ho, 1998).

Inserted genes seem to lack stability (research has shown that they may even «misteriously disappear » after a few generations 2) and may move and multiply within the genome (Pimbert, 1997). The lack of stability of genetic insertions makes comparisons with plants bred by conventional techniques difficult (Rogers, 1995).

1.2 Modification of animal genome

The objectives pursued in the modification of the animal genome are essentially the improvement in animal performance and rearing conditions and the improvement in the characteristics of food derived from animals. Modifications of the animal genome are less frequent compared to plant modifications due to a number of technical difficulties involved.

Examples of current research include changing milk composition such as increasing its protein content for the optimisation of cheese production or the production of milk without lactose (some consumers being allergic to lactose).

Improving the nutritional value of milk in order to produce medicines or food supplements has been done, for instance, through an increase in the amount of phosphorous-rich proteins. These modifications are however well mastered only in mice.

Another aim of the modification of the animal genome is to achieve leaner animal carcasses (e.g. 5 to 7% fat instead of 26 to 33% in sheep in an australian experiment). The consequences of the latter tests have nevertheless shown that animals often had physiological anomalies (such as diabetes) due to an uncontrolled expression of the transgene involved.

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1 The totality of genes in an organism.
2 Sinclair Mantell, Wye College, personal communication.

Other experiments on animals involving transgenes having an impact on food production have been aimed at seeking resistance to frost in salmons, raising fertility in sheep (Booroola gene), improving the digestion of cellulose (enzyme secretions) to improve food intake1, pigs and chickens capable of synthetising essential amino-acids (which would no longer be brought by the food ration), chickens genetically programmed for their leanness (Bonny, 1998).

2 Possible applications

2.1 Optimisation of culture yields

Resistance to pests

Genetic engineering claims that it can slow down the build-up of pest resistance to commonly used pesticides since transgenic plants are made to produce toxins, fighting plagues.

Disease resistance

Transgenic plants resistant to viruses have alreay been developed (potatoes, melons, cucumbers, sugarbeet, tomato). The aim is to minimize crop losses.

Herbicide tolerance

A crop which is tolerant to an herbicide allows it to be sprayed to eliminate weeds without damaging the plant itself. This technique has been used for several crops such as soyabeans, sugarbeet, lettuce, melon, potato, wheat, oilseed rape and sunflower.

Two herbicides, glyphosate (Roundup) and ammonium gluphosinate (Basta) are increasingly used in GM plants producing food. In order to avoid that the plant’s growth be negatively influenced by the herbicide in its tissues, another gene from bacterial origin had to be inserted, able to metabolize the active substance.

2.2 Optimisation of nutritional properties

One example of the optimisation of nutritional properties is an experiment of a genetic modification of soyabeans enabling the creation of a plant with an oleic acid content of 85%, against the usual 15% : an increased proportion of oleic acid has curative effects on cardio-vascular diseases in humans and the nutritional properties of soya are thus enhanced. This has been achieved through the identification of genes controlling the plant's fatty acid metabolism, whereby the enzyme2 changing from oelic acid to linoleic acid has been inactivated.

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1 L-M. Houdebine, personal comm.

2 A protein which speeds up the rate of a chemical reaction.

However, doubts subsist on whether the nutritional properties of soya are improved when it is enriched in oleic acid, given that this plant is a particularly well balanced source of essential fatty acids. Furthermore, the origin of cardio-vascular diseases is to be found in a number of factors (age, sex, overweight, diabetes,...) and the food parameter is but one factor among many others. Increasing the intake of oleic acid would not be a global approach and the need for a balanced diet would be undersestimated.

Further research examples have concentrated on wheat (improvement of bread-making characteristics), potatoes (improvement of organoleptic qualities) and rice (decrease in allergenic effects).

2.3 Adaptation of plants to stress conditions

The creation of new plant species resistant to frost, drought or soil salinity is of great interest for those regions (particularly developing countries) where these conditions bring about a reduction in crop yields. Very little information is available on the subject. The recent Agbiotech conference, organised by Nature Biotechnology in London in November 1999, has examined the most recent research on biotechnology in agriculture. The recent experiments concerned : the development of plant resistance to certain metals, techniques for the transformation of plants to fight pollution, the production of immonuglobuline A and oils.

3 Possible developments in research needs and scenarios in the next 20 years

Plants and Animals

No scientific consenus exists at the moment on the risks involved in the use of GMO in food, but several experts have underlined possible hazards justifying the development of more reliable and precise evaluation methods.

Even if the probability of the occurence of potential risks remains small, it is likely to grow as the use of GM plants spreads in the long-term. When examining the tests which have been carried out to date, certain important aspects concerning the composition of novel foods may have not been sufficiently taken into account.

As far as GM animals are concerned, none of the companies interviewed is involved in research on their development. Major technical difficulties remain, with high costs and low success rates. Research will thus very probably remain limited in the foreseeable future.

Multinational companies hold their own views as to the future of genetic engineering :

While Monsanto doesn't believe in a rapid development of quality GMOs, (essentially due to the difficulties of inducing the expression of a character when it is dependent on several genes, often non identified and to the fact that quality crachteristics will remain imperceptible by the consumer), other firms are planning to invest in this sector. Looking back, many promises have been made in the 80's as far as the problems transgenic plants would be able to solve, but commercial developments to date have concentrated on insect-resistant plants or tolerant to herbicides (Seralini, 1997a, 1997b).

Du Pont is well placed in the development of highly selective herbicidal molecules and has no particular interest in the development of herbicide resistance through genetic engineering. It also holds the best know-how worldwide on the metabolism of fatty acids and has concentrated on the enrichment of soya in oleic acid and the production of a soya protein called "Supro" supposed to lower the cholesterol level1. Work is also carried out on the improvement of the taste of soya milk through an increase in the sucrose content.

Zeneca is taking advantage of the important returns from the pesticides market and has faith in the development of "second generation" GMOs, producing improved food quality crops for human consumption and nutritional traits for livestock feeding (value-enhanced crops). In the food sector, research is mainly focused on nutraceuticals (also called functional foods), whereby crops are designed to produce medicines or food supplements within the plant. Zeneca holds the technology for the multiplication of the lycopene level in tomato (an anti-oxidizing pigment mainly used in cancer prevention). Research is also ongoing on a wheat enriched with carotenoids (anti-oxidizing agents) and increasing micro-nutrient content in general. Other projects include, at an experimental stage, fungus resistance for maize and bananas and the production of lectins ("anti-insect" proteins).

Rhône-Poulenc considers that many more years of research will be needed to develop products which would meet consumer expectations. For the moment, agronomic applications of GMOs are

1 "Supro" is currently awating the USA's FDA marketing authorisation.

essentially carried out in the USA. Pest resistance in-built in plants should be achieved by 2005 and 2008 should see the development of qualitative applications for human and animal food (production of essential amino-acids). The research carried out on quality GMOs concerns : starch content, increase in the oil content (maize and soya), enriched oils (oleic, stearic and lauric acids).

Limagrain continues to focus on its basic business : seed production. Biotechnology and genetic engineering in particular are considered as essential tools in order to achieve variety improvement.

Several research areas can be identified as being particularly important for the future :

1. A better knowledge of the genome : many genes are still unkown. Major advances have been made in understanding how the genome is organized, but there is a lack of knowledge when it comes to explain why it is so perfect and able to ensure an ordered development of living organisms. Research on the structure of genes has revealed that nucleic acid molecules composing them are chemically inert and that their activity is dependent upon the presence of active molecules1.

2. Heredity laws and the evolution of the species : more research is needed in order to understand the chemical mechanisms involved in the process of heredity and the interactions between the genome and its environment, in order to explain why some genes are "inactivated" and are not expressed.

3. The laws of embryo development : research has shown that embryo development is not simply the realisation of a genetic programme, but that other modifications of its environment and interactions within it also contribute2 (epigenetics)3.

4. A better understanding of the "ecology" of genes in order to know whether genetic engineering can take place without risks. The DNA molecule is organized in a particular way (the "supra-code") and gene transfer may alter this organisation4

The biotechnology sector is today facing financial difficulties (laying off people, fall in shares), but multinationals still keep to their plans for future research.

The improvement of the evaluation methods for food risks, through the definition of "global" methods to determine the exact composition of GM varieties should be able to contribute to the assessment of the impact of GMO in food (Philipon, 1999).

1 See R. Lewontin (1992). The dream of the human genome. New York.
2 See D. Johnston and C. Nusslein-Volhard (1992). The origin of pattern and polarity in the Drosophila embryo. Cell n° 68. pp. 201-219.
3 See H. Atlan (1999). La fin du tout génétique. Vers de nouveaux paradigmes en biologie. Sciences en question. INRA editions.
4 Research conducted by Dr. J.-C. Perez in France on the genomes of the AIDS viruses, in association with Prof.J.-C. Chermann (INSERM) and Pr. L. Montagnier (Intitut Pasteur).

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ANNEX I - Experts and companies interviewed

Experts

Pierre Besançon
Nutritionist, President of the Biotechnology group
of the French Council for Public Health
University of Montpellier II
Genetics and food science laboratory

Sylvie Bonny
Researcher
INRA Economie et Sociologie Rurale, Grignon, France

Josette Chausaux
Ingénieur de Recherche, Unité Lutte biologique, La Minière INRA

Denis Bourguet
Chargé de Recherche, INRA, La Minière

Yves Chupeau
Molecular biology dept.
INRA Versailles, France

Catherine Pannetier
Molecular biology dept.
Researcher INRA Versailles and CIRAD, France

Yves Bertheau
Phytopathology and detection methodology, GMO detection methodology team
INRA Versailles, France

Louis Houdebine
Molecular biology dept.
INRA Jouy-en-Josas, France

Stéphane Lemarié
INRA ESR, Grenoble, France

Antoine Messean
CETIOM (Centre technique interprofessionnel des oléagineux métropolitains), Grignon, France

Gilles-Eric Seralini
Molecular biology professor
Caen University, France

Anne Castelain
GMO Campaigner
Amis de la Terre (Friends of the Earth)

Yves Manguy
Spokesperson of the National Coordination for the defence of farm seeds
Russec, France

Jan Diek van Mansvelt
Biological Farming Systems Group
Wageningen Agricultural University, NL

Marielle Matthee
T.M.C. Asser Instituut
Institute for Private and Public International Law
International Commercial Arbitration and European Law, Den Haag, NL

Birgit Loos
Centre for Substances and Risk Assessment
Bureau CGO
National Institute of Public Health and the Environment, Bilthoven, NL

Frans W.A. Brom
Centre for Bio-Ethics
University of Utrecht, NL

Jos van Damme
Head Department Plant Population Biology
Dutch Institute for Ecological Research, Heteren, NL

Miriam van Gool
Biodiversity Campaigner
Greenpeace, Amsterdam, NL

Louise Luttikholt
Biologica
Dutch Platform for Organic Farming and Food, Utrecht, NL

G. Wensvoort
Vereenigde Octrooibureaux, Amersfoort, NL

Lorna Haynes
Escuela de Ingenieria de Sistemas
Universidad de los Andes, Venezuela

Mark Cantley
Adviser
Life Sciences & Technologies

European Commission, DG Research

Bernhard Zechendorf
Documentalist
European Commission, DG Research

Richard Hardwick
Senior Administrator
European Commission, DG Agriculture

Companies interviewed

Dupont de Nemours France SA
M. de Trogoff
General Manager for France, Crop Protection Manager for Europe, the Middle-East and Africa, World Manager for wheat biotechnologies, Paris, France

Zeneca Sopra
Gérard Sutra
Research Station Manager, National Coordinator for biotechnologies, Grisolles, France

Rhône-Poulenc Agro
Alain Dini, Director, RPA Biotech
and Georges Santini, Ethics, Environment and Communication
Lyon, France

Monsanto
M. Pasteau, External relations
Bron (Lyon), France

Limagrain
Jean-Claude Guillon
Director Strategy and Communication, Chappes, France

Novartis Seeds SA
Christian Morin
Head of Communication, Saint Sauveur, France

Participation to scientific seminars

21-24.09.99 - PhD course on Social Aspects of Biotechnology. Wageningen Agricultural University, The Netherlands.

29.09.99 - Agence Française de Sécurité Sanitaire des Aliments (AFSSA). Séminaire sur les biotechnologies de la reproduction animale et sécurité sanitaire des aliments, Paris.

07.10.99 - Association Française pour la FAO. Colloque "Les Sciences au Service de la Sécurité Alimentaire Mondiale". Palais du Luxembourg, Paris.

26-29.10.99 - Ecole Chercheur "Ethique Economique et Sociale", INRA, La Londe les Maures, France.

ANNEX II - Chronological overview of the development of industrial groups in the Life Sciences sector

Multinationals	Acquisitions/mergers/alliances	Date	New entity	Seed business turnover (billionFF)
Astra Zeneca	Suiker Unie (alliance)	1996	Avanta	3
Ciba Geigy	Sandoz (merger)	1996	Novartis	6,5
	Maïsadour (alliance)			
	Benoist (alliance)			
Dow Elanco	Mycogen (100%)	1998	Dow	1,5
	Agrigenetics	1993		
	United Agriseeds	1996		
	Morgan Seeds	1996		
Dow	Eli Lilly	1998		
AgroSciences	Semences Verneuil (alliance)	1998		
	Dinamilho Carol Agricol	1988		
	Biosource Technologies	1998		
	Illinois Fundation Seeds	1999		
Dupont	Pioneer Hi-Bred (joint-venture)	1997	Optimum	8,5
	PTI Protein Technology International	1998	Quality	
	Pioneer Hi-Bred (100%)	1999		
Hoechst AgrEvo	Schering (alliance 40%)	1994	AgrEvo	9,1
	Plant Genetic System (maize)	1996		
	Sun Seeds	1997		
	Genetic Logic (3 year alliance)			
	Cargill (USA , Canada and GB)	1998		
	Rhône Poulenc	1998	Aventis	
	Limagrain Pau Euralis (alliance)	1998		
	Rhobio (created with Biogemma)	1998		
Monsanto	Agracetus	1996		5
	Asgrow Agronomics (maize)	1997		
	Agripo's wheat seed business (wheat)	1996		
	Monsoy (soya)	1996		
	Mendel	1996		
	Holden's Foundation Seed (maize)	1997		
	Calgène	1997		
	Stoneville Pedigree Seed (cotton)	1997		
	Ecogen	1998		
	Dekalb	1998		
	Delta Pipeline Land (cotton) (brevet GPS)	1998	Renessen	
		1998		
	Cargill Europe	1998		
	PlantBreeding International Cambridge			

Source : Dupont-Fauville, 1999

ANNEX III - Private and public agricultural research in the USA

The creation of numerous links existing between private and public sector research in the USA today has been influenced by the diminishing public funds available for research in the 80's and 90's as well as the possibility for the private sector to acquire the ownership of biotechnological inventions. Universities have created Biotechnology Centers favouring start-ups initiatied by researchers. These have linked with State Agricultural Experiment Stations (SAES) and work closely with private companies.

Several regulations and programmes have been introduced since 1980, such as the Technology Transfer Act (1986), whereby Cooperative Research and Development Agreements have been signed between an Agricultural Research Service (ARS, i.e. a federal laboratory) and one or more private or university partner. Private companies could thus have access to the ARS's laboratories and personnel, developing new products and processes and benefit from an exclusive property right over the invention. The ARS benefited from a better knowledge of the difficulties linked to the marketing of new biotechnology products and better information on research and industry information needs.

At the beginning of the 90's, the USDA developed new tools for the improvement of partnerships between the private and public sector. Biotechnology Research and Development Corporations were created, aimed at the development of new technologies, making the link between the government and private companies.

Links with farmers have also been favoured, universities testing new crops and processes on-farm and farmers having access to the universities' projects (transfer of information between farmers, private companies and researchers). Producers' associations collect "checkoffs" (a tax on sales) from farmers and these are invested into research in transgenic plants.1

1 The United Soybean Association has signed a research contract with DuPont at the beginning of this year, financing projects on soyabeans conducted by ARS already working with the biotechnology firm.

ANNEX IV - Risk-benefit assessment of GM foods - case studies

Case study 1 : TOMATO

The examples used for this case study are the FlavSavr tomato, developed by Calgene in the US, and the tomato developed by Zeneca, used as puree in the UK.

Both tomatoes have been genetically modified in order to inhibit the production of an enzyme which is naturally produced by the fruit, the polygalacturonase (PG) and which is involved in the degradation of the cell walls, conducing to fruit ripening. PG also causes the degradation of pectines contained in tomatoes when these are processed. On the whole, a GM tomato contains more solids and less water than its conventional relatives,which means that there is less waste at harvesting and processing costs are lower, resulting in a slightly cheaper product for the consumer (POST, 1998).

The FlavSavr Tomato has been developed in 1992 for the trait of "delayed ripening", the fruit being able to ripen on the plant, achieveing thus a better taste while remaining firm up to the shelves. However, the effects of transport were badly evaluated and the ripe tomato did not arrive in the shops in the conditions expected. The organoleptic characteristics of parent plants were insufficient and the application of genetic engineering techniques could not result in a satisfactory taste. Consumers disliked the product due to the high price compared to quality1.

Yields and disease resistance were not up to expectations either. Calgene conducted eight field trials on FlavSavr between 1989 and 1992. The US Animal and Plant Health Inspection Service (APHIS) held the view that there was a low risk of transgenic plants intercrossing with relatives and that they were not going to alter current agricultural practices nor have an impact on wildlife and insects. In the end, Calgene increasingly doubted on the possibility of developing a tomato which would have the necessary agronomic traits for a commercial production.

It can be see how traditional breeding methods and genetic engineering are complementary, with the main role which germplasm plays in order to achieve good agronomic performances in the new variety2. Furthermore, a quality GMO can only pretend to generate added value if the agronomic characteristics are kept from A to Z (company interviews).Traditional breeding methods have the adavantage of obliging the breeder to seek genes of interest in wild varieties, contributing to the conservation of the diversity of the genetic make-up and will as such remain one of the basic tools for genetic improvement.

Transgenic tomatoes can produce tomato purees and sauces which are viscous without the need for a process of inactivation of PG through heat ("hot-break"). The result is a reduction in the costs of energy, avoiding additives and, through the reduction in time needed for processing, a better taste can be achieved. Tomato purees have been successfully marketed by Zeneca in the UK in 1996. A communication campaign in partnership with two retailers (Sainsbury's and Safeway Stores) included product labelling, a 4-page prospectus on the advantages of the product, and an attractive sales price (-20%), proving that transparency could be a major asset in the development of a new

1 Genetic engineering : too good to go wrong? Case study n° 12.
2 Vallat, O. and Pech, J-C. (1997) Fruits et légumes scientifiques. La lettre scientifique de l'IFN, n° 52, November.

product.1

Current developments have however shown that influences from NGOs conducting anti-GMO campaigns and adverse consumer reactions, particularly in the UK, changed the 1996 situation. The Zeneca tomato repesented a major advantage for the processor who made energy savings linked to a reduced processing time (company interviews).

As far as health is concerned, GM tomatoes are seen as presenting a potential risk due to the presence, in their genetic make-up, of a gene resistant to kanamycine (*npt*II gene). Kanamycine is an antibiotic which is hardly used in human and animal treatments today. However, a specific mutation of one pair of bases in the *npt*II gene can result in resistance to amikacine, an antibiotic which is used in intensive care units for the treatment of hospital-borne infections and which is used in the treatment of tuberculosis (Le Déaut, 1998).

1 Best, S.G.(1997) Stratégie pour convaincre les consomateurs. Biofutur n° 172, November, pp. 29-31.

Case study 2 : MAIZE

Bt1 maize, developed in order to fight against the European Corn Borer, will be used as example.

The most evident ecological impact of a Bt crop consists in a significant reduction in the application of insecticides. The gene providing resistance, however, is only efficient for a limited number of insects. As a result, a Bt crop must continue to be sprayed against those insects which are not sensitive to the genetically transferred toxin (Hokkanen, 1998). This innovation is attractive because, apart from the cost savings on chemical products, their reduction is also positive for the reduction of health risks for those applying the product.

In order to assess the advantages of Bt maize compared to the use of pesticides, their potential impact on ecosystems must be studied. One negative impact is the persistence in time and the dissemination in the environment. For the Bt toxin, produced by GM maize, persistance is rather long and dissemination wide-ranging, compared to all other modern pesticides (Hokkanen, 1998). From an ecological point of view, it corresponds to the utilisation of a conventional pesticide with high persistence on large areas.

In order to ensure the continuity of the economic interest due to savings in plant protection applications, there is a need to control the development of resistance in target insects. A fundamental rule in the fight against plagues states that relying on more that one arm is capital. The more an insect is exposed to Bt, the greater the selection pressure which is exerted on it, favouring the development of resistance to Bt2 .

The utilisation of Bt as biopesticide is to be differenciated from the expression of the toxin by the plant. Spraying biopesticide based on Bt delivers a given amount over a limited period of time, then the toxin is inactivated by UVs3. The selection pressure is thus greatly reduced compred to a plant producing the Bt toxin over an entire growth period. Further studies have shown that some Bt maize cultivars do not secrete a sufficient amount of Bt toxin to fight against the European Corn Borer all through the season and particularly in Southern Europe.
Field observations have highlighted that the quantity of Bt secreted by transgenic plants is not so high nor constant as the theory suggests and might have a negative impact on minor pests.

The possible adverse effects of Bt crops on the environment, such as non target insect fauna feeding on Bt plants, reduces the range of benefits which can be achieved from their use.

An risk/benefit assessment of GM maize should also take into account the possible alternatives, such as the introduction of different agricultural practices and the use of integrated pest management (IPM). Agro-chemical companies are undertaking research on new molecules for phytosanitary products which are more targeted towards specific insects and which are eliminated in the environment at a faster rate. Genetic engineering seeks to select molecules whose action is focused on a gene of parasites which is not present in humans (company interviews).

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1 *Bacillus thuringiensis* (see also Part B, Chapter 2.1.2)
2 Courrier de l'Environnement, INRA n° 35, pp. 25-32, November 1998.
3 Ibid.

Case study 3 : ANIMALS

95% of transgenic animals are today mice, since the application of genetic engineering to farm animals it still very rare due to the technical difficulties encountered and the fact that genes with a net positive effect and no negative effect must be available. In order to tackle all the aspects (health, environment and economic) of this case study, several examples will used.

Health1

Animal products derived from the application of new technologies are related to the European Novel Food regulation. The safety of their use in food destined to humans is based on a preliminary evaluation of the toxicological risks and nutritional qualities. For a more reliable and complete risk assessment, the concept of "substantial equvalence" should be extended to cover knowledge of : the transgenes used (analysis of genetic constructions), the products expressed (new proteins, metabolic derivatives, expression sites, residual levels in processed products, toxicity, allergenicity), "non intentional" effects resulting from the action of genetic modification (pleiotropic effects).

Case by case answers are needed given the various objectives pursued with the application of genetic engineering techniques to animals. Quality improvement (animal carcass improvement, nutraceuticals) demands a nutritional evaluation. Stimulating the production of the growth hormone (GH) in pigs, sheep, bovines and fish results in muscular growth through the reduction of body fat. The production of GH could interfere with the animal's metabolism, which would tend to store a higher amount of chemical residues in its organs. The fat/muscle relationship being higher, these animals could accumulate more dioxine and pollutants depending on the chemical sanitary quality of their feed. Hormonal residues in meat and meat products can have endocrinous, immunological and immunotoxic, neurobiological and cancerigenous effects for humans. Developement can also be affected. Exposure to even small quantities of these residues implies risks, in particular for children, but no threshold has been determined to date.

Environment2

The example of genetic engineering applied to aquaculture enables the evaluation of the impact on the environment due to the difficulty of confining fish on a specific area. Modern aquaculture shows that accidental disseminations are current. There is thus a need to know the effects of the introduction of a foreign gene into a fish in order to evaluate the impact of the introduction of the same fish species in wild populations. This is becasue of the specific reproduction patterns of certain fish species : high fertility, possibility of high interspecific hybridisation resulting in fertile hybrids.

At present, knowledge is limited to the impact of the introduction of new species for which it has been shown that, in terms of population desequilibrium, observations could only be made long-term.

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1 Interviews; Besançon, P. - Communication at AFSSA Scientific Seminar, 1999; Houdebine, L-M (1998).
2 Hindar, K. (1998); Prunet, P. Communication at AFSSA Scientific seminar 1999; Prunet, P. and Breton, B. (1998).

In Norway, between 5 and 15% of salmon populations are derived from farmed fish : "farmed genes" can thus replace "wild genes" in 6 to 20 generations and less than 3 for the most affected populations. This "contamination" of wild populations is problematical since they may casue ecological and/or population desequilibriums according to the effects of the trangeneon the animals' physiology. For example, the utilisation of an transgenic Atlantic salmon tolerant to low temperatures would result in : an expansion of aquaculture towards the North, endangering the populations which are currently preserved from the effects of escaped fish; to a loss of biodiversity caused by the introduction of a new predator fish in the Northern water ecosystems.

Economy and society1

In 1993, Eurobarometer was already showing a strong negative reaction to genetic engineering applied to farm animals. The belief that there are traditional alternative solutions which do not bring about irreversible changes in the genetic characteristics of animals contribute to reject biotechnological research in this domain.

Research on milk composition, in response to a number of consumer demands, still hasn't brought about the solutions expected : the drop in lactose content in order to avoid allergenic problems can lead to other types of allergies, due to a change in protein configuration; lactoferrin or lysozyme enrichment (for the protection of the consumer's digestive system) is dependent upon the conservation of the properties of these molecules after pasteurisation. Other alternatives to genetic engineering can often be found in order to achieve the same objectives.

A project carried out at INRA can shed light on the evaluation of the costs and benefits of the introduction of GM in animals for farmers. Experiments were conducted on sows expressing the transferrine gene of rabbits in their milk in order to suppress iron deficiency in piglets. As a result, piglets would no longer need an iron injection at birth and a number of pathologies of sows and piglets would be reduced.

The techniques employed remain heavy and expensive and results are not up to expectations. This is due to the mutagenic effect of the DNA introduced which causes a high number of embryo deaths. Amongts the GM animals obtained, a large proportion doesn't express the transgene fully and many contributing factors are still not understood.

It seems that investment in the GM of animals would thus only be economically viable if it was able to lower the costs linked to the treatment of a pathology by 10% or if it would increase production by 10%. Furthermore, the elimination of iron injections is not of great interest for pig breeders since its cost is quite low. It is also not very clear whether transferrine can cure iron deficiency (it might rather optimise an additional intake). A better sow lactation due to the reduction of pathologies is a viable argument, with an improvement in piglet growth as a result.

Other alterantives, such as breeding pigs according to the principles of organic agriculture should also be considered before making a choice (the incidence of sow pathologies are greatly reduced in this type of farming system due to open air breeding and preventive treatments and piglets do not suffer iron deficiency due to the good health of their mothers).

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1 Interviews; Research carried out by L.-M. Houdebine at INRA Jouy-en-Josas; Technoscope de Biofutur n° 190, June 1999, p. 2-14.

ANNEX V - A review of recent regulatory initiatives for GMOs concerning health, the environment, agriculture and ethics

USA

Date	*Initiator*	*Domain*	*Initiative/Proposal*
May 1998	Alliance for Biointegrity (NGO)	Health	A complaint has been lodged against the FDA, the agency in charge of authorising GMOs.
Summer 1999	US Academy of Science	Health and environment	In order to respond to the above complaint, it has been charged with the preparation of a positional paper on the effects of GMOs for health and the environment.
June 1999	Ecologists	Environment	Letter to Bill Clinton to ask for a ban on GM maize following the publication in May 1999 of the results of the study of Cornell University on the Monarc butterfly.
18/10/99	FDA	Health	It announced that it was going to re-examine the innocuity of food containing GMOs and is organising public meetings since 18/11 oin order to gather the opinion of the American people on GMOs.
28/10/99	Representatives of civil organisations (CSOs) (1)	Agriculture	They met Dan Glickman to ask that the USDA abandons its research on "Terminator" technology. Several recommendations were made.
30/11 - 03/12/99.	USA and Canada	WTO	GMOs should be included in negotiations in order to impose a revision of the European decisions in terms of authorisation and labelling of GM products.

GB

Date	*Initiator*	*Domain*	*Initiative/Proposal*
18/05/99	BMA (British Medical Association)	Health and environment	Advises in a report ("The Impact of Genetic Modification on Agriculture, Food and Health"), not to market GMOs in the UK before their innocuity can be proven. It states that current knowledge on the dangers of GMOs are insufficient and that potential risks are linked to the consumption of these products and their dissemination in the environment. The use of antibiotic marker genes should be avoided due to the build-up of resistance. Vivienne Nathanson, Research director at the BMA, says that GM food may cause unexpected allergies and a number of experiments on animals have suggested that GM food can be toxic..
21/05/99	British Government	Biosafety	It announced a series of measures destined to reinforce "human and environmental safety". GM food will be under the responsability of the new Food Standards Agency.
October 1999	British Government	Biosafety	It declared a 1-year moratorium seeds of herbicide-tolerant plants and 3 years on insect-resistant plants. It created a scientific committee in order to study the negative effects of GMOs in humans, their impact on biodiversity and ecology.
06/10/99	Erik Millestone, Sussex University and British scientists	Health	They have asked that tests of a higher quality than those using the concept of "substantial equivalence" be adopted in order to study the effects of the consumption of GMO in humans.

FRANCE

Date	*Initiator*	*Domain*	*Initiative/Proposal*
March 1999	35 organisations (seed producers, retailers, industries, consumer associations).	Agric. Sectors	Study of the "technical feasability" and "economic pertinence" of the setting up of a GM-free food chain.
Summer 1999	French Government.	Health	Asks AFSSA (Agence française pour la sécurité sanitaire des aliments) to undertake an evaluation the sanitary risks of food containing GMOs.
July 1999	Trade Secretary	Labelling	"Until the Commission hasn't adopted a position banning the imports of GMOs, we should fight against the US to claim the labelling of these products…the consumer must choose and needs to be clearly informed".

BELGIUM

1999	Ministry of Health and Consumer protection	Health	Creation of a Federal Agency for Food Safety which should carry out controls from the field to the consumer, as from 1/1/ 2000.

(1) CSOs present : American Corn Growers Association ; Consumer Union ; National Family Farm ; Coalition Ralph Nader ; International Center for Technology Assessment ; Mothers and Others for a Livable Planet ; Consumer Federation ; Sustainable Agriculture Coalition ; North Dakota farmer Fred Kirschenmann ; RAFI (the Rural Advancement Foundation International).

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