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Review of GMOs under Research and Development and in the pipeline in Europe

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Review of GMOs under Research and Development and in the pipeline in Europe

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Foreword

Which agricultural GM plants are most likely to be developed up to the market level in the next decade? To address this question, the Directorate-General Agriculture (DG AGRI) requested the present study from the Joint Research Centre (DG-JRC). The expected outcome, a forecast of GM plants technically available, was considered useful for different policy areas for which the European Commission has responsibility (such as coexistence between production systems, agricultural markets, risk assessment, etc).

The various published "pipeline" lists for GM plants in agriculture were mostly based on scattered information released by industry and scientific institutes. In this report, the results were derived from an original survey of the situation of European R&D projects (the *research* phase) plus a statistical analysis of the database of experimental GM plants releases (field trials) conducted in the EU in the past 10 years (the *development* phase). The study was completed with desk research on the evolution of EU imports on certain crops and the specific situation of GM crops in Central and Eastern European Countries.

The study presented here has indeed produced GM plants "pipelines", divided into short- (next 5 years), medium- (next 5 to 10 years) and long-term perspectives (beyond 10 years). The information collected and analysed also illustrates (quite dramatically in some cases) the situation of the R&D activities on agricultural GM plants in Europe. The findings that field trial notifications have decreased 78% since 1998, or that the main reasons for cancelling research projects on agricultural GM plants are non-technical, are highlights from this report. The list of GM plants presented in this report reflect those findings, since the most innovative products seem to be displaced downstream towards the medium to long term horizon.

But there is much more interesting information in this study, for many different users. The results are presented here structured in a 34-page compilation report plus 14 annexes that may be of particular interest for different readers. Each annex can be considered a standing alone document and we recommend its reading.

The study has been co-ordinated by the Institute of Prospective Technological Studies (IPTS-JRC) and executed via the European Science and Technology Observatory. The work of our sister Institute for Health and Consumer Protection (IHCP-JRC) in maintaining the EU SNIF[1] database on experimental field trials of GMOs has been essential to this project.

1 The SNIF (Summary Notification Information Format) database contains notifications of all GMO field trials carried out within the EU from 1991 and onwards.

Contents

Chapter 1: Introduction

1.1 Background

The use of modern biotechnology in agriculture is at the heart of an intensive public and political debate. World-wide, in 2002, Genetically Modified Organisms (GMOs) were grown on an estimated global area of 58.7 million hectares (James 2002). However, in Europe the situation is static with only minor areas of genetically modified crops grown and a *de facto* moratorium in place since June 1999 on any new authorisations for marketing genetically modified organisms.

Whereas first generation GMOs focused on agronomic input traits, it is expected that second and third generation GMOs will embrace new products that better meet consumers expectations. To this aim, scientists are increasingly seeking to exploit the potential for biotechnology to improve food quality, to deliver new medicines, to contribute preventing diseases, to reduce health risks, and to improve environmental interactions.

In the Communication *Life Sciences and Biotechnology-A strategy for Europe* (COM(2002), 27 final), the European Commission has recognised the need to support decision-makers in issues related to the technological advances in life sciences. The action plan calls for the Joint Research Centre (JRC) and in particular its Institute for Prospective Technological Studies (IPTS), to "enhance technology foresight (...) for early identification of newly emerging issues and of elements of a policy response".

The European Commission (EC) has adopted Directive 2001/18/EC (repealing Directive 90/220/EEC) to govern the deliberate release of GMOs into the environment. The directive entered into force on 17 October 2002. In addition, the Commission also proposed a set of sector-based legislative proposals (for food, feed and seed). The process of adoption of rules on the traceability and labelling of GM-food, feed and seed throughout the entire production chain is well advanced.

A likely consequence of the new legislative framework is that the submission rate of new GMO dossiers[2] will accelerate. For European policy-makers, there is a need to know what GM products are under research and development (R&D), what the trends in research are, and what future potential agricultural biotechnology products might result. In view of all this, there seems to be a need to assess which agricultural GM products might request authorisation for commercialisation in Europe in the next decade.

The majority of current review studies on GMOs are based on information provided by research laboratories and/or released by industries. Most of them focus on the technological developments outside of Europe (i.e. in the US), with the consequence that very little work has been done on looking at the situation within Europe. Commissioner Busquin recently affirmed that new technologies might bring real benefits to citizens and improve the competitiveness of European agriculture and that research efforts should continue (European Commission 2002a). Therefore there is a need for studies which focus on the development of GMOs within the EU, and in particular which analyse any research undertaken, assess the European position, including also the activities conducted outside of the EU, and estimate the impact of these activities on the European market.

1.2 Objectives

The aim of this report is to flag-up GM plants in the pipeline; outlining those most likely to

2 Dossiers submitted for commercial authorisation in Europe

request authorisation for marketing[3] (to be grown or to be imported) in the EU in the next decade, and listing them in a structured way according to three different time-periods. The list is based on the scientific and technical availability/ development of the GMOs, not just in Europe but also outside Europe. Moreover, this report lists the main factors that influence the potential commercialisation of GMOs in the EU, from the point of view of those agents requesting commercialisation. The focus of the report is on cultivated GM plants, for all its possible applications (seed, food, feed, industrial use, and medicine).

1.3 Methodology

The methodology adopted in this study was to screen the different stages of development of GMOs; from the R&D design stage up to the request for market authorisation. It is based on original analyses carried out for this study (i.e. a survey of ongoing R&D projects in laboratories in Europe, analysis of the EU SNIF[4] database, EU import needs, and GMOs in Central and Eastern European Countries) and a thorough review of scientific literature and existing GMO databases outside of Europe. All the data were collected between February and May 2002. Additional details on the methodology are given in annex A of this report.

This report has classified GMOs under three different listed time-periods of potential commercialisation: short-, medium- and long-term. The lists are based only on the potential technological development of the GMOs. It was not the target of this study to integrate socio-economic considerations and implications.

Time-period

Depending on the crop species and the traits considered (onwards in this document the word trait is used to refer to a genetically modified characteristic), 8-12 years are needed to develop a new crop variety. This development can be broken down into three steps:

- Step 1: Construction of a new GMO in the laboratory (identifying the desired gene, isolating it, inserting or suppressing it and *in-vitro* tests), followed by greenhouse tests.
- Step 2: Testing of the GMOs in field trials. This step is essential to ensure the stability of the inserted gene(s) through several generations and to test for potential environmental/human health effects. This might require on average 5 to 6 years of field trials research until a variety is ready for commercialisation.
- Step 3: Submission of a dossier for commercialisation. After a dossier is submitted, it has to pass different assessment processes (of the competent Member State national authority and of the relevant Scientific Committees of the European Commission).

Trait categories

To harmonise the analysis, the traits (annex B) were grouped into a small number of categories, and these categories were used throughout the study:

- Input (agronomic) traits: Herbicide tolerance, insect resistance, resistance to other pathogens (including fungi, bacteria, virus, other species), abiotic stress/yield, male sterility, others input traits
- Output (quality) traits: Modified nutrients/ ingredients, industrial use, health-related compounds (molecular farming), others output traits
- Markers/other traits

3 In the report, "request authorisation for marketing" means GMO dossier which enters the submission process at EU level.
4 The SNIF (Summary Notification Information Format) database contains notifications of all GMO field trials carried out within the EU from 1991 and onwards.

So, when references are given in the text to *input traits* as a general term, it means all the different traits grouped within this category. The same applies for *output traits*, i.e. if used in general terms, it includes all the different traits - modified nutrients/ingredients, industrial use, health-related compounds (molecular farming), and others output traits.

Health-related compounds refer to molecular farming and to the production of antibodies, pharmaceutical proteins and/or (edible) vaccines. It does not include the production of enzymes for industrial processes.

If percentages are calculated for input or output traits, they include the percentage of each individual trait.

Chapter 2: Results

2.1 The short term perspective: next 5 years

This first list is based on GMOs that are pending authorisation in Europe or have already been approved for commercialisation (annex C). As GMOs might be grown in a country outside the EU and then authorised for import into the EU, GM plants approved for commercialisation in the main GMO growing countries (i.e. US, Canada, Argentina) have also been screened (annex D), as well as the import needs of Europe for these crops (annex E).

2.1.1 Situation in Europe

In the EU, 14 GM plants produced by different companies[5] have been approved for commercialisation so far. These are maize (4), oilseed rape (4), carnation (3), chicory (1), soybean (1) and tobacco (1). Depending on the particular plant, authorisations cover cultivation, import and processing for food and feed purposes, or just breeding activities. No further authorisations have been granted since October 1998.

Thirteen (13) applications that had been favourably informed by the Scientific Committee on Plants (SCP) were pending authorisation under the old Directive 90/220/EEC. These are maize/sweet maize (5), oilseed rape (3), cotton (2), chicory (1), fodder beet (1) and potato (1). This list includes one GMO with a modified starch metabolism (i.e. potato C/SE/96/3501 from Amylogene[6]) and one GMO with stacked traits (i.e. maize C/NL/98/08 from Pioneer, now Dupont). This indicates that GMOs with modified nutrient/ingredients and with stacked traits are likely to reach the market very soon.

Following the entry into force of the new Directive 2001/18/EC, some of these pending applications have been withdrawn by notifiers, others have been resubmitted, and new ones have been submitted. At the time of writing (March 2003), a total 19 applications have been submitted according to the provisions of the new Directive. These applications (see addendum in page 13) do not represent drastic changes (regarding species and traits) to the types of GM plants described above, but there is a significant increase in the presence of GM plants with stacked traits.

For a detailed list of all the GM plants pending now authorisation check annex C.

2.1.2 EU-15 Imports

The evolution of the EU-15 import needs of farm commodities has not changed since 1995, (highest import volumes being for soybeans and soybean meal) but the origins of these imports have changed.

Whilst in 1994, 80 % of the maize was imported from the US, in 2000, 92% of maize imports came from Argentina. The US administration has estimated the loss of exports of maize to Europe to US$ 300 million per year (US GAO 2001). But this shift from the US to Argentina can presumably be explained by economic factors, in addition to a GM factor, such as a more competitive market price from Argentina. Indeed, Argentina is one of the world's main GM maize growers and together with the US, Canada and China they have 99 % of the global area that is grown with GMOs (James 2001).

Soybeans are traditionally imported from the US, Brazil and Argentina. The main exporter to the EU is

5 In recent years significant changes have taken place among agrobiotechnology companies, such as company mergers. The most important mergers include the forming of Syngenta (by Novartis and Zeneca Agrochemicals) in 2000, the merger of Pioneer Hi-Bred International with DuPont in 2002, as well as the acquisition of Aventis Crop Science by Bayer in 2002. Details concerning the company structures are given in annex I.

6 GM high amylopectine potato (from Amylogene) has received positive opinion of the Scientific Opinion on Plants on 18 July 2002. http://europa.eu.int/comm/food/fs/sc/scp/out129_gmo_en.pdf

still the US, but import levels have recently decreased and stabilised at 1994 levels after relatively high increases during the 1990s up to 1998. A shift can be observed between imports from Brazil and Argentina (40 % increase from Brazil vs. a 75 % decrease from Argentina). This might be due to the GM situation, as Brazil is the main provider of GM-free soybeans[7] for the EU crushing industry (used for oil production – food), while the US and Argentina have larger growing surfaces of GM soybeans (1.5 and 2.5 million hectares respectively). Compare however, this result with that for soybean meal imports (used for feed), which are shared equally between Argentina and Brazil, thus indicating that the GM factor has little or no influence on the purchase decision of this type of commodity.

Oilseed rape was traditionally imported from Canada up to 1997, but since 1998 it has been almost completely substituted by Polish oilseed rape. Again the GM factor seems to be responsible for this shift, as in the case with soybeans, as Canada has been growing GM herbicide tolerant oilseed rape since 1995 whereas GM oilseed rape is not grown in Poland so far.

Small quantities of wheat are imported in the EU. Imports of soft wheat have doubled since 1994. The main exporters are Canada and the US.

2.1.3 Potential GM imports

The preceding section discussed how, over the last 5 years, the EU-15 maintained its import needs of farm commodities (e.g. maize, soybeans, soybean meal, oilseed rape). Looking at the GM crops already commercialised in the US, Argentina and Canada (annex D), it is possible to identify those which are most likely to request import authorisation into the EU.

In a way, a request for import approval for the EU (not for growing but for food and feed purpose) is faster to prepare than a full cultivation dossier. Also, some crops such as soybean are not cultivated in the EU to an extent that makes companies interested in requesting authorisation for cultivation. Moreover, a GM variety approved for import into the EU will have a larger threshold (for adventitious presence) than a non-authorised GM variety.

- In the next 5 years: GM herbicide tolerant soybean, GM herbicide tolerant oilseed rape, GM herbicide and/or insect-resistant maize and GM herbicide tolerant wheat.
- In the next 5 to 10 years: GM soybean with modified specific ingredients (mainly proteins) for animal feeding, GM soybeans with modified ingredients (mainly fatty acids) for nutrition and technical purposes, and GM maize with modified specific ingredients (mainly starch and proteins).

2.1.4 Pipeline GM products for the next 5 years

Based on the information collected, the following pipeline list is established:

Box 1: *Pipeline GM products for the next 5 years*

- Herbicide tolerant maize, oilseed rape, soybeans, wheat, sugar beet, fodder beet, cotton and chicory
- Insect-resistant maize, cotton and potatoes
- Modified starch or fatty acid content in potatoes, soybeans and oilseed rape
- Modified colour/form in flowers
- Modified fruit ripening in tomatoes
- Both herbicide tolerant and insect-resistant traits in maize and cotton

7 Brazil prohibits the growing and commercialisation of GMOs and defends its position as a GMO-free country. Government approval of GMOs has been put on hold, refereed to as a “judicial moratorium”, on the commercial release of GMOs, after a number of injunctions issued by Brazil’s Federal Court over recent years. Brazil is the only major agricultural exporter that does not use GM technology (mainly for soybean and corn). The country has officially banned any planting of Roundup Ready soybeans, however GM soybean is known to be produced in the southern part of the country using GM soybean varieties illegally imported from Argentina.

ADDENDUM

At the time of finalising this report (March 2003), there are 19 GM plants applications requesting the placing on the market under the new Directive 2001/18/EC. Some of these 19 applications are still in assessment phase by the lead Competent Authority, others have already been circulated to all EU Member States. These are recorded in the public web site managed by the JRC http://gmoinfo.jrc.it

The breakdown of these 19 notifications (see annex C for details) is as follows:

- *5 Herbicide tolerant rape*
- *2 Herbicide tolerant maize*
- *2 Herbicide tolerant sugar beet*
- *1 Herbicide tolerant fodder beet*
- *1 Herbicide tolerant soybean*
- *1 Herbicide tolerant cotton*
- *1 Insect resistant cotton*
- *5 Stacked herbicide tolerant/insect resistant maize*
- *1 Modified starch content potato*

These new notifications all belong to one of the categories forecasted above in the pipeline GM products for the next 5 years.

2.2 The medium term perspective: next 5 to 10 years

To establish the second list, the EU official SNIF database for GMO field trials (February 2002 version)[8] was analysed in detail (annex F). As previously mentioned, it might require an average of 5 to 6 years of field trials research before a GMO is ready to request authorisation for commercialisation. Therefore, analysis of a GMO being tested in field trials can be relevant for the future commercialisation of that GMO in the next 5 to 10 years. Traits that have only recently been tested in field trials are more likely to be ready for the market in this second time-period. Field trials that are almost finalised (for which submission in the process of commercialisation could be done in less than 5 years) are also included in this second list.

This analysis has also screened, but in less detail, GM plants under field trials in the US, as this might be indicative of GMOs to be imported into Europe in the medium term (annex H).

The CEECs also need to be considered as important stakeholders for European agriculture. Therefore, this investigation has also covered GMOs tested in laboratories and field trials in these countries (annex G).

2.2.1 Importance of the field trials

Field trials are a prerequisite step when applying for market approval. The aim of the field trials is to test, in small-scale experiments, the stability of the inserted gene, the characteristics of the GM crop compared to the conventional one (e.g. growth characteristics), and most importantly, to assess any potential risk to human health, animal health and the environment. The data obtained from field trials constitute a core part of the information submitted to regulators for the safety assessment. The field trial often represents a long and expensive stage in the development process (i.e. from laboratory design to the submission for marketing) of a GMO.

8 The SNIF database for GMO field trials conducted under Directive 90/220/EC is managed by the Joint Research Centre at the Institute for Health and Consumer Protection (IHCP) located in Ispra (Italy) (http://biotech.jrc.it/). GMO releases notified under Directive 2001/18/EC can be consulted in the new Web-site http://gmoinfo.jrc.it

2.2.2 General trends

Analysis of the annual number of field trial notifications of GMOs in the EU from 1991 to 2001 reveals a drastic drop between 1998 and 2001 (a 76 % decrease) (see Figure 1; provisional data for 2002 indicates a 87% decrease for the 1998-2002 period). The total number of plant field trial notifications in EU countries is 1687 (as of February 2002). In 2001, the Joint Research Centre received only 61[9] notifications for field

Figure 1: Annual number of field trial notifications in the EU between 1991 and 2001 (based on data from the SNIF database)

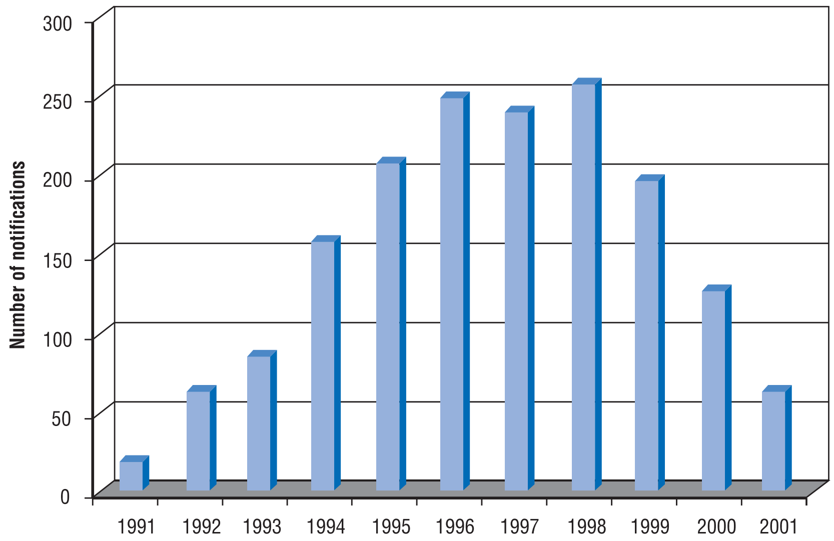
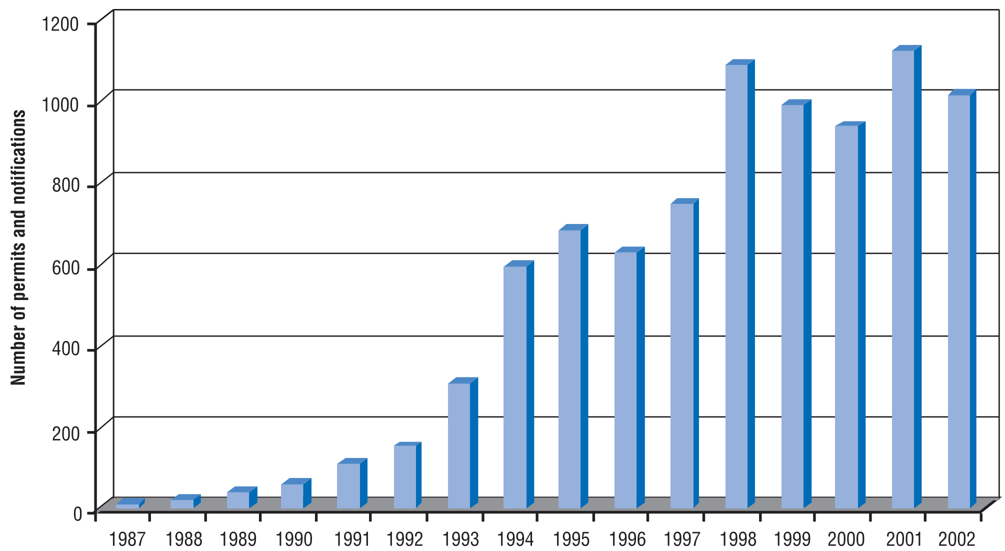


Figure 2: Total number of US permits and notifications approved by year



Source: USDA (2002)

9 This study refers exclusively to GM plants and does not include field trials with other organisms. This explains the difference in the number of field trial notifications estimated at 88 for the year 2001 in a recent communication of Commissioner Busquin (European Commission 2002b) as well as the total number of 1762 GMO field trial notifications which are expressed at the website of IHCP in July 2002 (http://food.jrc.it/gmo/index.htm).

trials with GM plants. This is generally regarded as an effect of the 1999 decision of the EU Council of Environment Ministers to block any new commercial release of GMOs[10], as well as the widespread tendency of the European public to reject GMOs.

In the US, over 8400 field trials have been registered since 1987 (APHIS 2002) (Figure 2). A direct comparison between the numbers of notifications in the EU (Figure 1) and the numbers of notifications in the US (Figure 2) is not feasible due to differences in how the data is collected. The US system requires a notification for every year while EU notifications can cover trials lasting more than 1 year. Nevertheless, when taking into account the average field trial duration in the EU of 2.6 years, it is still clear that the negative trend found in annual EU notifications since 1999 does not exist to the same extent in the US.

2.2.3 *Type of crops*

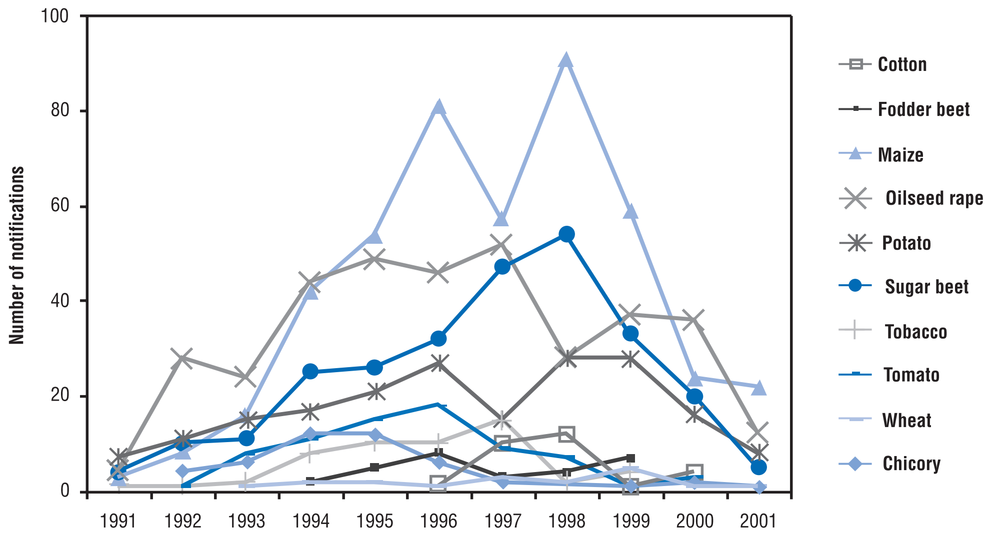
It emerges from the analysis that GMO field trials in the EU cover a large diversity of crops and traits, but that four crops dominate (maize, oilseed rape, potato, sugar beet) (Figure 3) and account for 75% of all field trials.

Figure 3 shows that maize, oilseed rape, potato and sugar beet were the dominant crops during the decade, while tomatoes, tobacco, fodder beet, and cotton were present but less represented between 1991 and 1998, and even almost completely disappeared between 1998 and 2001. On the other hand, wheat and chicory have had a limited but constant presence during the last 5 years.

2.2.4 *Type of traits*

- Input traits[12] are more prevalent in field trials than output traits[13] (77 % vs. 19 % respectively). This

Figure 3: Type of GM crops in EU field trials between 1991 – 2001[11] (based on data from the SNIF database)



10 In June 1999 a *de facto* moratorium was initiated by the EU Council of Environment Ministers: several ministers (from Denmark, Italy, Luxembourg, France, Greece, joined by Germany and Belgium in October 2001) agreed to suspend all approval applications for GMOs until the implementation of the revised directive 90/220/EEC, to provide a stricter legal framework covering not only safety, but also labelling and traceability of GMOs. The *de facto* moratorium is still in place.

11 Data for year 2002 are not included (as only 2 months data available).

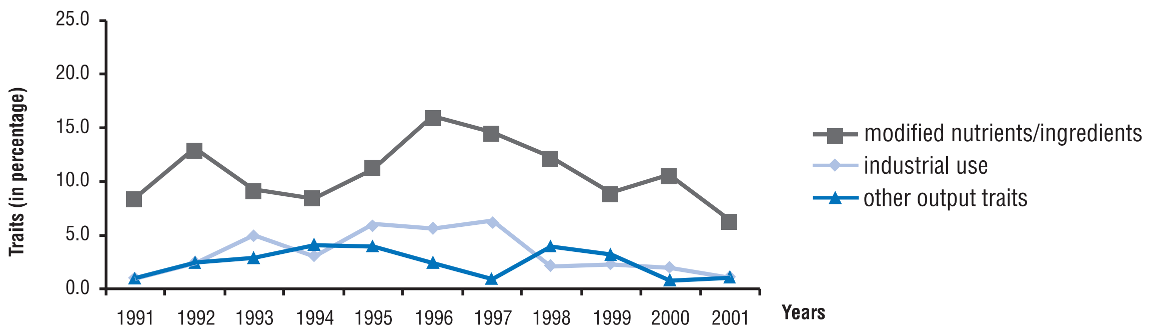
12 Input traits provide an agronomic advantage. Included in this set of traits are: Herbicide tolerance, Insect resistance, Resistance other pathogens, Abiotic stress/yield, Male sterility, Others

13 Output traits enhance the quality of the final GM product. Included in this set of traits are: Modified nutrients/ingredients, Industrial use, Health-related ingredients (molecular farming), Others

is a significant difference compared to GMOs in the laboratory R&D phase, where the numbers of current projects dealing with input and output traits are similar.

- "Resistance" traits, including herbicide (42 %), insect (11 %) and other pathogen resistance-tolerance (13 %) dominate field trial notifications (totalling 66 % of all traits tested). Some field testing activities on resistance traits are conducted for potential environmental implications. Crops with a high risk of gene flow, such as maize, oilseed rape and sugar beet (Bock et al 2002, Eastham and Sweet 2002), are targets of intensive safety research for evaluating environmental and agronomic risks (Kessler and Economidis 2001).
- Output traits account for 19 % of the total traits tested, which shows that the development of output traits is still in the early-phase of research. Other reasons to explain the low number of field trials might be technical and economic difficulties (due to the high cost of production and identity preservation) (Arundel 2002a). Crops with specific output traits (i.e. quality traits) have already been obtained through traditional breeding measures but are not widespread so far due to their high cost of production. GM technology provides a new tool to achieving the same goal more quickly, but might generate additional costs.
- Modified nutrients/ingredients (11.7 %) and male sterility (7.9 %) traits are tested in a variety of plants, therefore indicating the importance of these two traits for the future. Potential applications are modified starch composition in potatoes and modified fatty acid profiles in oilseed rape. Male sterility is important for plant breeders.
- Health-related compounds (molecular farming) are almost absent from EU field trials. This is a significant difference compared to GMOs in the laboratory R&D phase, where 11 % of projects involve traits with health-related compounds (molecular farming). Thus,

Figure 4: Share of GMO field trial notifications for certain output traits *in the period 1991-2001*[14] *(based on data from the SNIF database)*



14 Resistance traits are not represented. Values for 2002 are also excluded.

R&D activities in this field are limited to the early phase of development of GMOs and often to model "factory" plants (such as tobacco).

2.2.5 Evolution of some specific traits

Figures 4 and 5 show the number of field trial notifications for certain traits in the period 1991 - 2001. The percentages given are relative values. A percentage of 8.3% for modified nutrients/ingredients in 1991 means that among all the traits mentioned in field trial notifications in 1991, 8.3% relate to modified nutrients/ ingredients.

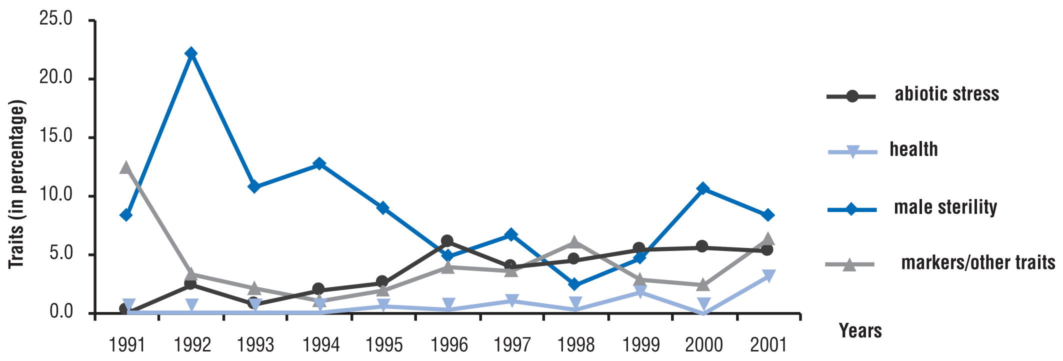
Figure 4 shows a general decrease in the number of field trials involving output traits. Modified nutrients/ingredients have dropped by more than half between 1996 and 2001 (16 % in 1996 vs. 6.5 % in 2001). Field trials involving traits for industrial use have dropped from 6.3 % in 1997 to 1.1 % in 2001. For the period 1991 - 2002, this trait has generally been applied to wheat , tobacco , oilseed rape and potato. The drop in the number of field trials might be explained by the fact that most of the research has already been finalised (e.g. the GM potato from Amylogene). Indeed, in the laboratory phase, GMOs modified for industrial use represent less than 4% of all the projects mentioned.

On the other hand, Figure 5 shows traits that have a small but constant rise over the period: abiotic stress/yield characteristics, markers/other traits and health-related compounds. Male sterility, on a decrease since 1992, has gained more interest since 1998. Male sterility is used by seed breeders to facilitate the process of hybrid seed generation and is also used as gene containment in forest tree production. Projects dealing with abiotic stress resistance (e. g. related to salinity) are particularly significant (not only for many EU areas but also for world agriculture). Projects dealing with directly improving the yield of crops (e.g. by nitrogen fixation, improving photosynthesis efficiency and modifying the energy metabolism of plants) might be of great impact in the future for some EU typical crops (maize, oilseed rape, sugar beet, potato).

Two elements can be observed from the analysis: the decrease in output traits (which includes modified nutrients/ingredients, industrial use, and other output traits) and the appearance (still very low presence) of plants producing health-related molecules (molecular farming) in Europe.

- General review papers discussing the future development of GMOs emphasise the importance of output traits and their promising developments (Müller and Rödiger 2001 - annex I). Despite this, this study has observed a decrease in the number of field trials involving output traits in Europe. This phenomenon is observed for both the US and Europe (Arundel 2002a). This means that the presence of GMOs with output traits in a pipeline list should be considered with reserve, as the trend for field trials for such plants in the last 5 years is not encouraging.
- The US is very active in the field of molecular farming. A current analysis of GMOs under R&D in Europe (almost 11 % in laboratory phase and less than 1 % in field trials) shows that GM plants for the production of pharmaceutical compounds might not be expected in the pipeline before the next 10 years (due to the R&D being in the early phase of development). Comparison with US data shows that the US is more advanced with higher number of field trials (see Box 2). The difference between Europe and the US is significant. Europe might engage more in this field as this emerging technology seems likely to have significant impacts on basic research as well as on the pharmaceutical, agricultural and biotechnology industries.

Figure 5: Share of GMO field trial notifications for certain input traits *in the period 1991-2001*[15] *(based on data from the SNIF database)*



Box 2: Development of GM plants for molecular farming

Molecular farming is the production of recombinant molecules in plants or animals for medicinal use. Molecular farming has the potential to provide diagnostic and therapeutic tools for health and other the life science applications. This is an emerging technology that seems likely to have a significant impact on basic research and the pharmaceutical, agricultural and biotechnology industries (Fischer et al. 1999). The field has raised a lot of expectations from the pharmaceutical industry which see a potential for a low cost production system, while for farmers it could develop into a niche-market with high added-value.

At least 18 proteins with applications for human or animal health have been expressed by transgenic plants (Daniell et al. 2001). The plants are used as an expression system. Successful expression has been reported in tobacco (e.g. heat-labile toxin B-subunit), potato (e.g. viral capsid protein), maize (e.g. glycoprotein S), lupin (e.g. envelope surface protein from hepatitis B virus), lettuce (e.g. envelope surface protein from hepatitis B virus), tomato (glycoprotein), *Arabidopsis* and alfalfa (both VP1 of foot-and-mouth disease virus).

On average, the time-lag between field trials and potential commercialisation is longer (more than the average 5 - 6 years) for GM plants used for molecular farming as the pharmaceutical products issued from the plant have still to undergo the pharmaceutical evaluation process (Kleter et. al. 2001).

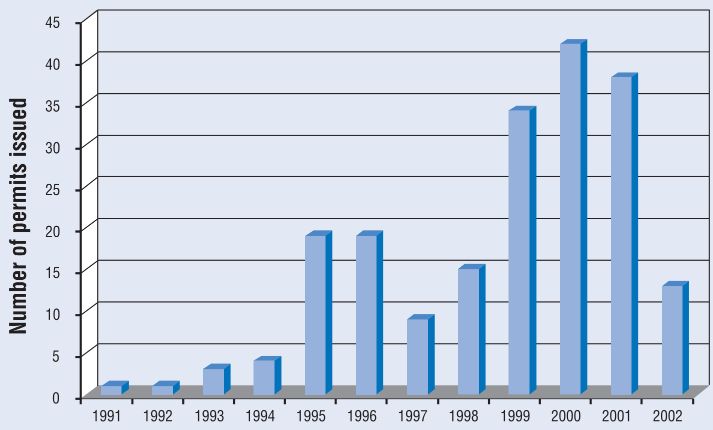
Situation in the US

Between January 1991 and June 2002, 198 permits/acknowledgements (corresponding to 315 out-door field trials with an average size of 2 hectares) were issued by the USDA on a case-by-case basis. These included pharmaceutical proteins, antibodies, novel proteins and industrial enzymes. The majority of the field trials were carried out between 1999 and 2002 (Figure 6) which indicates that interest has increased in the last three years (also annex H). FDA and USDA have already released draft documents[16] which provide a set of points to consider to demonstrate the safety, effectiveness but also the environmental issues and the confinement measures adopted for products produced by molecular farming. These guidance documents demonstrate the willingness of the US government to facilitate the development of this field into a commercial sector.

15 Resistance traits are not represented. Values for 2002 are also excluded.

16 Requirements for field trials, document from USDA (2002) "*Information of field testing of pharmaceutical plants in 2002*". May 2002 http://www.aphis.usda.gov/ppq/biotech/
Document from FDA (2002) "*Guidance for industry drugs, biologics and medical devices derived from bioengineered plants for use in humans and animals"*

Figure 6: Permits issued by USDA for molecular farming field trials



Source: Freese 2002 (period Jan.1991- June 2002)

Situation in the EU

In the EU SNIF database, only 16 field trials involving traits with health-related compounds were notified for the period 1991 - 2001. Traits included are the synthesis of albumin, antibodies, collagen, human alpha-1 antitrypsin, glucocerebrosidase protein, lactoferrin, putrescine methyl transferase, and rabies virus G glycoprotein cDNA synthesis. Industrial enzymes are not included, therefore the numbers of field trials cannot be directly compared between the US and Europe, but the general trend can be considered a good indication of the development.

The European Agency for the Evaluation of Medicinal Products (EMEA) is considering the new development of molecular farming and has recently issued a concept paper offering guidance on "quality-related points that should be considered by applicants proposing to market medicinal products with pharmacologically or immunologically active substances" produced in transgenic plants (EMEA 2001).

2.2.6 Stacked traits

Several traits can be "stacked" into a GM crop plant by genetic engineering or by conventional crosses between GM varieties (in this context, a trait used as marker gene is not regarded as a "stacked" trait). It is very probable that the presence of stacked traits in European field trials will increase in the future. World-wide, two crops (cotton and corn) with stacked traits for herbicide tolerance and insect resistance represented 8 % of the global GMO production area in 2001. This percentage has been regularly increasing over the last few years, being 6 % in 1999 and 7 % in 2000. This increasing trend is expected to continue in the coming years (James 2001).

Situation in Europe

In the EU, even if the parental GMO lines have been considered and approved for commercialisation, a GMO in which two traits are combined by traditional breeding is considered as a new GMO and thus needs a new authorisation process. The Scientific Committee on Plants of the EU released in 2000 a positive opinion on the cultivation in Europe of the first GM maize variety with stacked traits in the EU (T25 and MON810) (C/NL/98/08 from Pioneer (now Dupont), insect and herbicide tolerant). The application has been withdrawn but recently since the entry into force of Directive 2001/18/EC, applications for several GM maize lines with stacked insect and herbicide tolerance have been presented (see annex C).

When several traits are mentioned in one notification the SNIF database does not inform if these are stacked genes or refer to several independent GMOs. This report has assessed all notifications that refer to more than one trait. The analysis shows that 33.6 % of the notifications refer to two traits and 8.4% refer to three traits. From these numbers, some experts estimate that the share of field trials with stacked traits notified in the EU SNIF database does not exceed 15 % (Arundel 2002a). The most common combinations of traits are input traits, such as herbicide tolerance/insect resistance in maize, and herbicide tolerance/male sterility in oilseed rape. Sugar beet is mainly modified to include herbicide tolerance/virus resistance.

Situation in the US

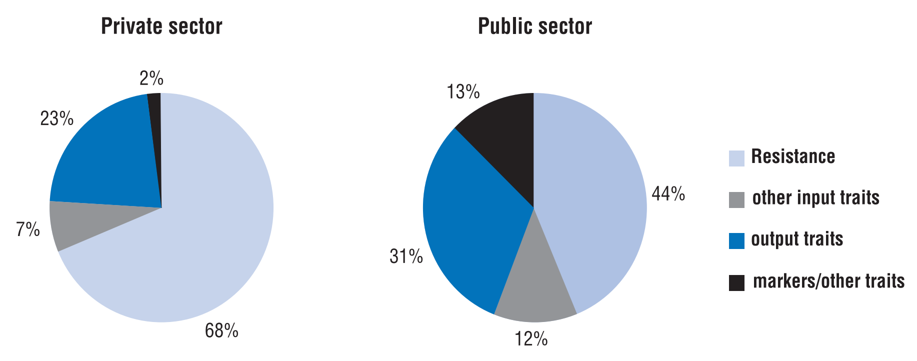
In the US, if each trait inserted in a specific plant has been proven safe by the regulatory bodies, then the GM Plant with the stacked genes does not need a new risk assessment. It can be submitted for commercialisation based on the information provided for each individual trait. The Agricultural Statistics Board of USDA gives the average percentage of biotechnology varieties planted for 2000 - 2001 (Agricultural Statistics Board USDA 2001). The crops covered were maize, soybeans and cotton. Stacked genes varieties include herbicide and insect resistance. For maize, 1 % of the biotech varieties planted have stacked genes. For cotton, 24 % of the biotech varieties planted have stacked genes and no planting of GM soybean with stacked genes was listed.

The APHIS database in GMO field trials gives little information on stacked genes. Field trials with two stacked genes are the most common (e.g. on maize herbicide/insect resistance), and only very few field trials were found with 3 or more traits. The most common combinations of traits are herbicide tolerance/insect resistance in maize, herbicide tolerance/modification of nutrients/ingredients (starch for maize, protein for oilseed rape), herbicide tolerance/male sterility in maize and oilseed rape. GMOs with two Bt genes are also being used (cry1AC and cry2Ab from Monsanto (Monsanto 2002)), GM cotton in Australia (Monsanto Biotech Knowledge Centre 2002). Potato for virus resistance/ insect resistance is a classical example.

2.2.7 Field trials: public and private sectors

The main actors in GMO field trials are large companies, accounting for 65 % of all notifications. SMEs, public research institutes and universities are less well represented with 6 %, 12 % and 4 % of all notifications, respectively (other actors 13%). The distribution of traits per group is presented in Figure 7.

Figure 7: Distribution of traits[17] tested in field trials by the public/private sectors for the period 1991- 2001 (based on data from the SNIF database)



17 Resistant traits: herbicide tolerance, insect resistance, other resistance (fungi). Other input traits: abiotic stress/yield characteristics, male sterility. Output traits: modified nutrients/ingredients, industrial use, health-related ingredients, other output traits

The private sector includes large companies and SMEs. Of all the field trials, 68 % involve resistance traits and 23 % output traits. SMEs present a broader spectrum of applications and give relatively more importance to output traits (16.2 % involving modified nutrients/ ingredients compared to 8.9 % for large companies). This can be explained by the business strategy adopted by SMEs in plant biotechnology in which they are looking for products with a potential niche-market, acting also as the gatekeeper between universities and large firms.

The public sector includes universities and public research institutes. Of all their field trials, 44 % involve resistance traits, 31 % output traits and 13 % markers/ other traits. In contrast to private companies, public research institutes and universities show less interest in field trials with herbicide tolerant and/or insect-resistant plants, while in particular trials related to resistance to pathogens and different types of output traits have specific relevance in these two actor groups. This is also the case for field trials related to abiotic stress/yield and genetic markers.

2.2.8 GMO field trials in the CEECs

GMOs in early-phase R&D and in field trials conducted in Central & Eastern European Countries (CEECs) (annex G) were included as part of this study. All CEEC governments are currently preparing regulations for GMOs to fulfil requirement laid down in EU regulations. The number of authorisations granted for field trials has decreased since 2000 and is likely to stay at this level until a regulatory framework in line with international obligations is in place.

GMOs are not authorised for commercialisation in CEECs, except in Romania (authorisation for growing) and the Czech Republic (authorisation for import and processing only). Most of the field trials are conducted by large companies, with the same companies conducting identical field trials in different countries. For example, Monsanto is conducting field trials on Roundup Ready GM maize in Bulgaria, Croatia and the Czech Republic; Du Pont is notifying field trials on GM Bt maize in Bulgaria, Croatia and the Czech Republic. Altogether, GMO field trials in the CEECs are characterised by a small number of notifiers (large companies), a small number of crops (maize, sugar beet, and potatoes) and a limited number of trait-crop combinations.

The most common combinations of crop/trait are herbicide tolerant GM maize, maize, insect resistant GM maize and herbicide tolerant GM sugar beet.

2.2.9 GMO field trials in the US

The situation of field trials in the US (annex H) is particularly relevant for the future pipeline of GMOs, as the US is strongly committed to using this new technology in agriculture. Requests for marketing approval in the EU are expected for most GMOs developed for the US market. In the US, three companies (Monsanto, DuPont and Bayer) accounted for 48 % of all trials and almost two thirds of the trials were carried out on maize, potato and soybean (Arundel 2002c).

Of the US field trials, 41.6 % involved pest and disease resistance, 27.5 % herbicide tolerance, 19.2 % output traits for food or industrial purposes, and the remaining 11.7 % other categories such as markers, fertility and agronomic traits (Arundel 2002b). Among the resistance traits, 63 % related to insect resistance (mostly using Bt genes), 21 % to virus resistance and around 12 % to fungi (Arundel 2002b). Around half of the industrial food quality traits were targeted at the modification of starch and sugar, including proteins. Other important categories of output traits were the modification of oils, fruit ripening and industrial purposes[18].

Concerning developments over time, it can be observed that between 25 % and 30 % of the field trials involved herbicide tolerance during the entire 1990s. Interest in pest and disease resistance traits has also stayed relevantly stable, accounting for around 40 % to 45 % of the total number of field trials. In Europe, the situation is reversed, with more field trials involving herbicide tolerance (42 %) than pest resistance (10.8 %). In contrast, there was a

18 Of the industrial purposes 50 % were pharmaceutical, around 20 % industrial enzymes or polymers and around 16 % related to fibre inputs.

considerable decline in the share of field trials for food industrial purposes, from around 30 % in 1995 to 17 % in 2001. The share of technical agronomic field trials increased from 5 % in 1993 to 16 % in 2001 (Arundel 2002b). The decline in food industrial applications is mainly due to the field trials for fruit ripening, since this research, in particular on tomatoes, has now been completed in the US.

Herbicide tolerant GM wheat may be submitted for commercial authorisation in the US between 2003-2005. The GM wheat is modified for herbicide tolerance (50 % of field trials), for resistance against viruses and fungi, and to increase yield-characteristics. Compared to the EU, the latter two traits are given greater importance in the US. Wheat varieties could request authorisation for marketing in Europe for consumption (food & feed only) over the next 5 years, and for growing in the next 5 to 10 years (Monsanto 2002).

2.2.10 Pipeline GM products for the next 5 to 10 years

Based on the information collected, the following pipeline list is established:

Box 3: Pipeline GM products for the next 5 to 10 years

- Fungi-resistant wheat, oilseed rape, sunflower and fruit trees
- Virus-resistant sugar beet, potato, tomato, melon and fruit trees
- Herbicide-tolerant wheat, barley and rice
- Modified starch content in potatoes and maize
- Modified fatty acid content in soybeans and oilseed rape
- Modified protein content in oilseed rape, maize and potatoes
- High erucic acid content in oilseed rape

2.3 The long term perspective: beyond 10 years

The list is based on GMOs currently under research and development in the laboratory. To identify these GMOs the analysis is based on the results of a questionnaire (plus personal interviews) sent to various European private companies (SMEs and large companies[19]) and public institutions (universities, public research institutions) involved in GMOs projects at the research-early development phase (annex J). The questionnaire-interview approach was complemented with a review of reports and scientific literature to cover other R&D developments in Europe and outside Europe (annex K). The results of these two approaches are used as an indication of the type of GMOs that might request authorisation for commercialisation 10 years from now.

2.3.1 The importance of GMO R&D projects in the laboratory phase

It is difficult to collect data on current R&D projects from the different parties involved in GMOs. The information is often difficult to find, incomplete and/or only partially released by private companies. To overcome this difficulty, a questionnaire was developed for the purpose of this study (see design in annex A) in which different institutions in Europe involved in GM work were asked about their current GMO projects under R&D. The average response rate was 29%, (27,8% for SMEs; 24.6% for large companies, 34,4% for universities, 26,2% of public research institutes and 16,9% for others institutions).

Depending on the species and the traits, eight to twelve years are needed to develop a new crop variety. The analysis of GMOs currently under R&D in the laboratory phase, in Europe, provides an indication of the crops and traits that are being tested, the type and direction of the research and ultimately of the type of GMOs that might request authorisation for commercialisation beyond 10 years.

19 SMEs: less than 500 employers, Large companies: more than 500 employers.

2.3.2 *Type of crops*

According to the questionnaire results, researchers in Europe are currently testing a variety of crops and traits (more than 15 plants mentioned) (annex J). The fields of applications are wide (for growing, for food and feed, for industrial uses) and the products tested are innovative (fruits, plants for molecular farming, marker genes).

Models plants (such as *Arabidopsis thaliana* and tobacco) and vegetables (such as tomatoes and potatoes, which are also used as model plants) are most often cited, confirming the *basic research* nature at this stage. Cereals[20] and field crops[21] are also frequently mentioned, while fruits, trees, grasses and flowers are less considered. Projects related to GM trees (4 %) and GM grasses (4 %) are comparable with projects related to GM maize (5 %) or GM sugar beet (3 %). Research with GM grasses is mainly mentioned by the private sector, while research with GM trees is exclusively mentioned by the public sector. R&D on GM trees implies a long-term investment that the private sector does not seem to be willing to undertake.

2.3.3 *Type of traits*

The analysis shows that a large variety of traits are under research. For input traits, the main ones are resistance (including herbicide, insect, pest and not specified resistance), abiotic stress or an improvement of yield characteristics and basic research activities. For output traits, the main traits are modified nutrients/ingredients and health-related compounds.

In particular, the analysis shows that input agronomic traits and output quality traits are equally covered. This observation is significant as it shows European researchers are increasingly interested in developing traits in line with final consumers' expectations. Indeed current declarations by large companies are that they will develop more GM products with output traits (annex I) (Tait et. al. 2001). This position is also backed up by recent scientific reports, which stipulate that the next waves of GMOs will be characterised by output quality traits (OECD 2000, Müller and Rödiger 2001).

2.3.4 *Combinations trait/crop*

Table 1 presents the most common combinations of trait/crop mentioned in GMO projects (the list is not presented in any order of importance). It can be observed that:

- Virus resistance is inserted into a great diversity of crops, indicating the increasing importance in Europe of research into virus resistance in GM crops.
- The abiotic stress/yield characteristic is mainly tested in model plants, indicating that these traits are still in the early phase of development. Nevertheless, the increasing appearance of field trials related to abiotic stress/yield characteristic indicates a growing interest for this group.
- The modification of fatty acids, protein content and modified starch metabolisms are mainly tested in crops with large markets, indicating the high interest and potential profits of seed producing companies and opportunities available for European agriculture.
- Health-related compounds are introduced into model crops. Health-related compounds refer to molecular farming and the production of recombinant antibodies, "functional" food ingredients (i.e. antioxidants), pharmaceutical proteins and/or (edible) vaccines. For manipulating "functional" ingredients content, due to the complexity of most of the relevant metabolic pathways, more research is needed in this field before commercialisation can be expected.
- Outside the EU there are examples of hypoallergenic crops that being developed. One interesting case is the development of a hypoallergenic GM soybean (USDA ARS 2002) (in the laboratory phase).

20 Cereals include maize, wheat, barley, oat, rice, rye
21 Field crops include oilseed rape, sugar beet, alfalfa, cotton, flax, fodder beet, soybean, sunflower

Table 1: Most important trait-crop combinations of GMOs in the laboratory R&D phase, based on survey carried out by Fraunhofer ISI, 2002.

Traits	Crops
Herbicide tolerance	Cereals
Insect resistance	Potato
Virus resistance	Sugar beet, tomato, melon, fruit trees
Fungi resistance	Cereals, oilseed rape
Nematode resistance	Potato, sugar beet
Abiotic stress/yield	*Arabidopsis*, tobacco, cereals, grasses, potato
Modification of protein content	Oilseed rape, maize, potato
Modification of fatty acids	Oilseed rape, soybean
Modification of starch metabolism	Potato, maize, sugar beet
Industrial use	Potato, maize
Modification of fruit ripening	Tomato
Modification of colour/form	Flowers
Health-related compounds	Tobacco, *arabidopsis*, potato, tomato[22]

2.3.5 Activities of public and private sectors

The public and private sectors differ in their GMO R&D activities. The public sector works on a broad range of plants while the private sector focuses on a limited number of crops. In general, the public sector is involved in basic research and on areas that are far from commercialisation. The private sector, especially large companies, is working on products that have large potential markets and a high expectation of commercialisation.

The public sector is working on many different plants (such as cereals, potatoes, tomatoes, fruits, trees) but mainly *Arabidopsis thaliana* and tobacco. The tested traits are very diverse, but mainly involve abiotic stress/yield characteristics, modified nutrients and health-related compounds, often in projects addressing new technical or methodological approaches. Research projects on abiotic stress are more frequent compared to those influencing the yield capabilities of plants and carried out in various crops while yield-influencing factors are exclusively mentioned for *Arabidopsis*. Most of the projects with modified nutrients/ ingredients are dealing with enhancement of nutritional value (wheat, rice, potato, *Arabidopsis*, tomato) and modified oligosaccharides metabolism. Health-related compounds is tested in tobacco, *Arabidopsis*, tomato, potato indicating that different crops are tested as production system.

The private sector meanwhile mentions research activities into crops with large markets (maize, wheat, oilseed rape, sugar beet, vegetables and grasses), and the most common traits introduced are resistance traits, modified ingredients (especially enhancement of nutritional value, starch, protein and fatty acid), and health-related compounds (molecular farming). The involvement of the private sector in seeking quality products (output traits) is confirmed both by the answers of the survey and the screening of the

22 only one project mentioned for respectively maize, barley and oilseed rape

annual reports of large companies (annex I). Interestingly, GM projects dealing with health-related compounds were exclusively mentioned by SMEs. GM projects with health-related compounds are still in early phase development and mainly the public sector (for the basic research) and SMEs (for potential niche market with high added value) are involved.

2.3.6 Funding of GM projects

The questionnaire did not investigate the source or the amount of funding of the research projects on GM plants. Funding is available at EU and Member State level. Between 1994 and 1998, Enzing et al. 1999 estimated that 17 % of the public research funds devoted to biotechnology by the national governments of the 15 EU Member States and Switzerland were targeted towards plant and animal biotechnology. For eight countries analysed in detail (Austria, Finland, France, Germany, Italy, Spain, Switzerland, United Kingdom) which represented 83 % of the total funds spent for biotechnology in the 16 countries, this equalled around EUR 712 million for plant biotechnology and EUR 674 million for animal biotechnology (Enzing et al. 1999). The availability of public research funds for agrobiotechnology significantly differs between Member States of the EU.

A considerable number of agrobiotechnology research projects are funded within the framework of existing research programmes of the EU. For example over a 15-year period, 81 projects on GMO safety research have been supported, representing a total EU funding of about EUR 70 million (Kessler and Economidis 2001), corresponding to 10% of the national investments.

However, several experts stressed during the interviews that the forthcoming EU Sixth Framework Programme makes no specific provision for funding plant biotechnology research projects. This is interpreted as a lack of clear commitment to research on GM plants that could potentially cause a further slowing down of future research on GM plants.

2.3.7 Pipeline GM products beyond 10 years

Based on the information collected, the following pipeline list was established:

Box 4: *Pipeline GM products beyond 10 years*

- GM plants resistant against abiotic stress factors (cold, salinity, drought)
- GM plants with enhanced yield (all crops)
- GM plants for molecular farming (tobacco, maize, potato, tomato)
- GM plants with an enhanced content of "functional" ingredients (rice, vegetables)
- GM trees with modified lignin content
- GM hypoallergenic crops

2.4 Constraints for commercialisation

The results presented here are based on the answers to questions 3 and 5 of the survey of ongoing R&D projects in laboratories in Europe (annex L). Factors which might influence the potential commercialisation of GMOs in the EU were already predefined in the questionnaire, with participants being presented with a tick list of factors.

Among the institutions that participated in the survey (of which there was 165 responses), it was found that overall 39 % have cancelled at least one R&D projects on GMOs in the last four years (from all phases of development) (see Table 2). The frequency of cancelling R&D projects is lower for the public sector (23 %) and higher in the private sector (61 %).

The main reasons for cancelling GMO R&D projects are the unclear regulatory framework and an uncertain market situation (Figure 8). Major differences can be observed between the public and private sectors. The reasons for cancelling R&D projects in the private sector are mainly the unclear legal situation, difficulties in handling existing regulations (e.g. unclear or high requirements for safety testing, length of the notification process), uncertain market situations and high costs. The public sector reasons include: limited financial resources, scientific feasibility of the projects and, to a lesser extent, uncertain market situations and low consumer acceptance. This difference in rationale is probably explained by the fact that the public sector is more involved in basic research (research projects on laboratory level) and once funds have been obtained for the research, the main element that might stop a project are scientific or technical limitations that arise. On the other hand, private industry more closely monitors the development of R&D projects and cancels project if the opportunity/cost ratio decreases significantly – which was the case for the development of agricultural GMOs in the EU in recent years.

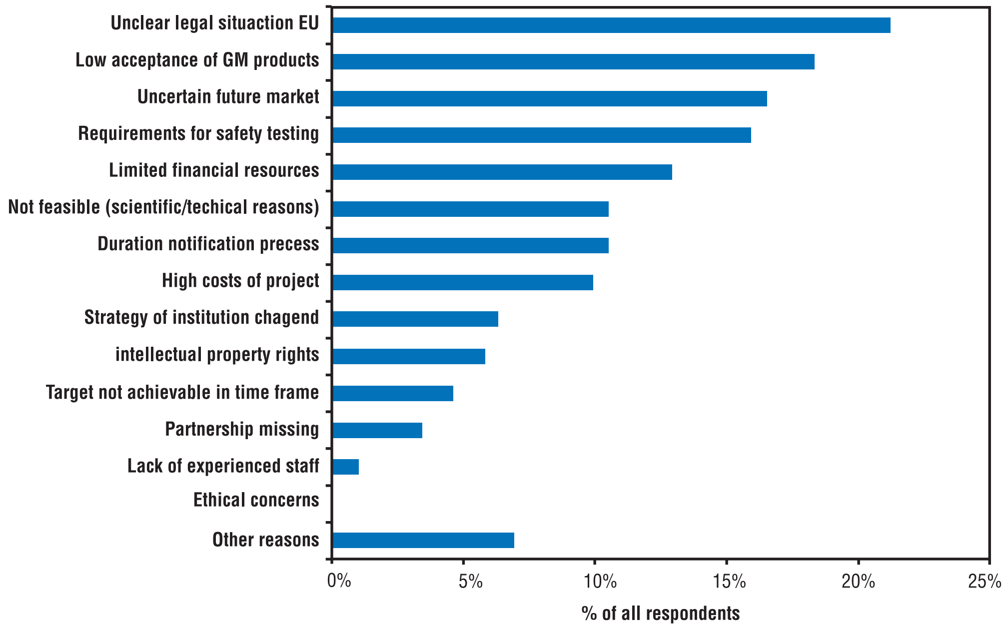
When asked about the constraints to the future commercialisation of GMOs in the EU, all groups raised the same issues, i.e. low consumer acceptance, the unclear legal situation in the EU and difficulties in the practical handling of the regulation processes. To a lesser extent other issues were raised but given lower weighting by the respondents, i.e. market situations, the financing of GMO projects, ethical concerns, and intellectual property rights issues.

Table 2: Respondents cancelling GMO R&D projects in the last four years, based on survey carried out by Fraunhofer ISI, 2002.

Institution	Number of respondents	% of respondents who have cancelled GMO projects
SME	33	54.5
Large company	28	67.5
University institutes	44	25.0
Public research institutes	37[1)]	21.6
Total	165[2)]	38.8

1) One respondent answered "Don't know"
2) Includes 3 who did not answer the question

Figure 8: Reasons for cancelling GMO R&D projects, based on survey carried out by Fraunhofer ISI, 2002 (164 respondents).



Chapter 3: Summary of GMOs in the Pipeline

This last section presents a compilation of the information screened during this study, where tentative lists of GMOs-pipelines were established for three different time-periods. The lists have an advantage over other review papers of GM products in the pipeline is that they are based on the strongest background information possible. The lists are specifically based on technological development of the GMOs. It was not the target of this study to include socio-economic considerations or implications.

Broadly, the short-term pipeline list summarised in Figure 9 includes few novel applications. The slowing down in field trial activities in the EU in the last 5 years will lead to a slower introduction of innovative GMOs crops on the future market. The group of GMOs covering the next 5 years period is characterised by input agronomic traits (herbicide tolerant and insect resistant GMOs), while few GMOs with output traits are expected. The second group, which covers the next 5 to 10 years, is more diverse, with input traits still dominating the market but it also includes GMOs for output quality product and industrial use applications. However, some of the output-traits GMOs may enter the EU market via imports only. The third group is non-exhaustive, as any GMOs currently under early-stage development could be a potential candidate. In particular, great expectations are given to the development of GM plants for molecular farming, of crops resistant to abiotic stress and of functional GM food (including hypoallergenic foods).

These lists of GMOs in the pipeline are coherent with other recent review reports. Müller & Rödiger (2001) present three wave steps for the development of green biotechnology (giving very general trends) following the 3-scale time-period defined in this study. The first wave (between 1985 and 2005) is characterised by input traits, the second wave (between 2000 and 2010) is characterised by output traits and the introduction of GM products in food and animal feeds, and the third wave (between 2010 and 2020) is characterised by the development of molecular farming, industrial raw material and bioenergies (Müller & Rödiger 2001).

In their report on Economic Issues in Agricultural Biotechnology, the Economic Research Service of USDA analysed the economic aspects of several key areas (such as agricultural research policy, production and marketing). They do not list pipeline products for different time horizons but propose examples of GM products in the pipeline. Their non-exhaustive list is categorised by input traits (e.g. herbicide tolerance in sugar beet, wheat, alfalfa, fruits and vegetables, insect resistance and the introduction of other Bt-toxins with different specificity and the increased combination of genes) and output traits (e.g. low-phytate corn, altered nutritional characteristics in soybeans and corn, coloured cotton or cotton with improved fibre properties, delayed-ripening in fruits and vegetables, altered gluten levels in wheat for improved baking quality, naturally decaffeinated coffee) (ERS 2001).

The Science and Technology Foresight Centre (Japan) proposed a list of pipeline GM plants to be commercialised between 2011-2019 in Japan. Widespread proliferation of GM crops with improved yields, disease resistance and freeze resistance is expected in 2013. Functional ingredients and food are expected during the period 2013-2015. The commercialisation of breeding technology for drought-resistant and salt-resistant plants and GM crops with yield characteristics is expected between 2018-2019 (Shoji et. al. 2002).

Figure 9: *GMOs in the pipeline for three different time-periods*

Period 2002- 2007

Group 1: next 5 years

- Herbicide tolerant maize, oilseed rape, soybeans, wheat, sugar beet, fodder beet, cotton and chicory
- Insect-resistant maize, cotton and potatoes
- Modified starch or fatty acid content in potatoes, soybeans and oilseed rape
- Modified colour/form in flowers
- Modified fruit ripening in tomatoes
- Both herbicide tolerant and insect-resistant traits in maize and cotton

Period 2007- 2011

Group 2: next 5 to 10 years

- Fungi-resistant wheat, oilseed rape, sunflower and fruit trees
- Virus-resistant sugar beet, potato, tomato, melon and fruit trees
- Herbicide-tolerant wheat, barley and rice
- Modified starch content in potatoes and maize
- Modified fatty acid content in soybeans and oilseed rape
- Modified protein content in oilseed rape, maize and potatoes
- High erucic acid content in oilseed rape

Period after 2011

Group 3: more than 10 years

- GM plants resistant against abiotic stress factors (cold, salinity, drought)
- GM plants with enhanced yield (all crops)
- GM plants for molecular farming (tobacco, maize, potato, tomato)
- GM plants with an enhanced content of “functional” ingredients (rice, vegetables)
- GM trees with modified lignin content
- GM hypoallergenic crops

Source: IPTS- Fraunhofer ISI

Chapter 4: Conclusions

- The *development* phase of GMOs: The annual number of GMO field trial notifications being registered in the EU has dropped by 76 % since 1998. This is the effect to the 1999's decision of the EU Council of Environment Ministers to block any new commercial release of GMOs as well as the widespread tendency of the European public to reject GMOs. This drop shows a lack of confidence from the notifiers to test GMO in field trials with the expectation of future commercialisation.

- The *research* phase of GMOs: According to the respondents of the survey, the single most important reasons for cancelling R&D projects within agricultural biotechnology in the EU are *the unclear legal situation in the EU*, the second and third *being low consumer acceptance* and *uncertain future markets*, respectively (see Fig. 8).

- What could be the significance of a prolonged slowdown of the research and development phases for agricultural GMOs in the EU?.

  - Novel GM varieties and applications appear "delayed" in the pipeline lists of GM crops likely to request authorisations for cultivation. Indeed the short therm predictions in the study contain little innovative applications.

  - SMEs, who already have scaled down their R&D programmes, will stay in stand-by mode for this new technology and might not engage in new innovative plant biotechnology research. There is limit in the capacity of "recovery" of research activities after a prolonged slow down.

  - In this context of uncertainties, large biotech companies may continue relocating research, conducting GMO field trials and commercialising new GMOs outside of the EU. Without field trials being carried out in the EU, many GMOs may request authorisation in the EU for import and processing only.

- Outside Europe, the interest for GM technology has not abated and many applications of this new technology in agriculture can be found in research (The Pew Initiative 2001), and being followed-up by field trials experiments.

- This study looks at scientific/technical developments to arrive to pipelines of new commercial GM varieties. It is clear that other factors might significantly influence the pipeline proposed (changes in the regulatory framework, acceptance of GMOs by consumers, market opportunities)

- The study shows that in the next decade, the range and quality of genetic modifications in crops and the numbers of new products likely to be seeking regulatory approval will be greater than those already considered. Anticipating GMOs that might request authorisation in the future might be useful for all risk assessors.

- The European Commission is studying mechanisms for the co-existence of GM and non-GM crops (European Commission 2002c). The pipeline lists shows that the crops most likely to request authorisation for marketing in Europe in the short-term are maize, oilseed rape, potatoes, tomatoes, sugar beet and cotton. This information is useful for focusing priorities for coexistence research projects.

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Annexes

A: Methodology

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Annex A: Methodology

During the study a set of different methodological approaches was used in order to analyse information on GMOs in the different phases of development: R&D in laboratory phase, field trials and pending or commercialised GMOs. The following methodologies were used during the project:

- Review of scientific literature and reports
- Analysis of GMO field trial databases and GM products approved for commercialisation
- Questionnaire-based survey among companies and research institutions involved in GMO Research and Development
- Expert interviews

The survey provides information on the crops, traits and actors involved in research and development (R&D) projects in the laboratory and greenhouse phase in Europe, as well as the most relevant factors influencing commercialisation of GMOs and the most promising areas of development. It creates a first picture of the basic and applied research carried out in Europe on GMOs. The expert interviews are used to substantiate the findings of the survey. In this section, we will refer to *GMO projects in laboratory phase,* including experiments conducted in small-scale greenhouse and in confined conditions. The analysis of the *GMO field trials* database gives a picture of the GMOs under evaluation for risk assessment under field conditions and constitute a group of GMOs a step closer to commercialisation. The analysis of the *GMOs pending or approved for commercialisation* gives insight in GM products that have started/passed so far the process for commercialisation. Altogether, the use of these different methodologies gives a unique picture of GMOs in R&D in Europe, from laboratory up to requesting authorisation for commercialisation.

Review of scientific literature

In the starting phase of the project, the project team identified and collected relevant scientific articles and reports by screening relevant databases and the internet. This literature and information search aimed to collect data on scientifically and technically available GMOs as well as their status of development and the most decisive factors for commercialisation of GMOs.

Database analysis

An important source of information for the study are databases of GMO field trials or GM products approved for commercialisation. According to Directive 90/220/EC (amended by directive 2001/18/EC), Part B, information on the applications of field trials with GMOs is collected for all EU Member States. In 1992 the European Commission established a procedure to record information on the release of GMOs into the environment in form of summaries (SNIF = Summary Notification Information Format) in order to ensure the exchange of information between responsible authorities in the countries of the EU. This information is gathered in the SNIF database managed by the Joint Research Centre at the Institute of Health and Consumer Protection (IHCP) located in Ispra (Italy). A version of this database (version of February 2002) was put at the disposal of the project team by IHCP. In order to homogenise and combine information included in the database, classification for different data have been developed by the project team in close co-operation with staff from IPTS. This relates in particular to the type of plants, GM traits and type of notifiers. The classification scheme developed for the plants included in the SNIF database is shown in annex B.

The project team defined the following trait categories for the SNIF database:

- Herbicide tolerance
- Insect resistance
- Resistance to other pathogens (e. g. fungi, bacteria, virus, nematode resistance)
- Abiotic stress/yield (e. g. drought, frost, salinity tolerance, modification of energy metabolism, photosynthetic activity, nitrogen fixation)

- Male sterility (male sterility/fertility restauration/ restoration)
- Modified nutrients/ingredients (e. g. removal of antinutritive ingredients, enhancement of nutritional value, modification of fatty acid, protein, oligosaccharides or starch metabolism)
- Industrial use (e. g. enzyme production, genetic modification for improving food processing, non-food applications)
- Health-related compounds (e. g. albumine synthesis, collagen synthesis, pharmaceutical compounds, human albumin synthesis, human lactoferrin synthesis)
- Other output traits (e. g. modification of colour/ form, ripening processes of plants)
- Marker/other traits (e. g. GFP, hemygrocin tolerance)

In addition, the project team including staff from IPTS updated the classification schemes for marker genes, size of the field trials as well as the type of notifiers. Afterwards, the information contained in the SNIF database was re-classified by the project team and staff of IPTS and a statistical analysis was performed using the programme SPSS[23].

The SNIF database is based on notifications of EU field trials with GMOs. A notification may include several locations over a period of several years. The number of locations and notifications for the whole time-period is therefore higher than the current number of notifications (1,687 notifications in February 2002). Furthermore, a notification may include several crops *or* several traits. For our analyses, crops and traits were counted separately, therefore, their number exceeds the number of notifications. For the statistical analysis, the assumption was made that all field trials are carried out for the time-period for which the notification document is valid[24]. In case of several traits or several plants covered in one single notification document, each single trait or plant was counted separately in the statistical analysis since there is no information available which traits or plants (or combinations of them) are really used in the respective field trials. Thus, when a notification covers several traits it is not possible to tell whether it refers to one single GMO with stacked genes, or several individual GMOs of the same crops. Information derived from the analysis of the SNIF database basically refers to notifications of field trials, but does not completely reflect the trials that are actually carried out by the notifiers each year.

GM products approved for commercialisation as well as information related to pending or withdrawn applications for market approvals in the EU were analysed on the basis of European Commission MEMO (European Commission 2002a) and the Robert Koch Institute (RKI) database, which was downloaded in March 2002[25]. For GM field trials and GM products approved for commercialisation in the CEECs a review was made based on information available on Internet and direct contact with national experts.

As GMOs developed outside the EU might be imported in the EU, GM field trials for the most important crops (maize, wheat, soybean, oilseed rape, cotton, tobacco) conducted under regulations of the US Department of Agriculture were analysed, using the data supplied by the US Animal and Plant Health Inspection Service (APHIS)[26]. For this purpose, the classifications developed for the SNIF database (e. g. for traits or type of notifiers) were used as well. Information on the global status of GM plants approved for commercialisation was obtained from the AGBIOS database which is run by Agriculture and Biotechnology Strategies Inc. (Canada)[27]. A brief statistical analysis of the databases on GM field trials and GMOs approved for commercialisation in USA was performed filtering out the type of traits, notifiers and crops.

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24 Several company representatives reported during the personal or telephone interviews that in particular in the last five years companies often do not realise a field trial each year, although they have the permission for carrying out the respective trials. In this sense, the underlying assumption might overestimate the extent of field trials which are carried out in reality.

25 This database is available on the Internet under http://www.rki.de.gentec/inverkehr/invklist.htm.

26 This database is available on the Internet: http://www.nbiap.vt.edu/biomon/datacat.htm.

27 This database is available on the Internet: http://www.64.26.172.90/agbios.

Survey

A survey among private companies and research institutes active in the field of GMOs was conducted within the project in order to get an overview about basic and applied research activities on GMOs. For this purpose a questionnaire (in English) was developed in a form of six questions related to R&D projects on GMOs currently carried out in Europe at the respective institution (open question), reasons for cancelling R&D projects related to GMOs (pick up question with up to five answers), commercially interesting areas for the coming five to ten years (open question) as well as major constraints for commercialisation of GMOs in the EU (pick up question). In addition, the location (country), the position and the type of the respondents were asked. The developed questionnaire as well as the contacting letter are attached in this annex. The importance of each project, in terms of budget allocated, was not requested from the interviewees.

Table A1: Universe and response rate of the survey

Country	Questionnaires Sent (total)	"Returned"[1]	Corrected[2]	No. of valid Responses	Response rate (%)
Austria	8		8	3	37.5
Belgium[3]	30	4	26	7	26.9
Czech Republic	6	1	5	2	40.0
Denmark	25	3	22	8	36.4
Finland	25	4	21	6	28.6
France	76	6	70	12	17.1
Germany	161	17	144	43	29.9
Greece	15	4	11	2	18.2
Ireland	7	1	6	0	0.0
Italy	55	9	46	9	19.6
Luxembourg	1		1	0	0.0
The Netherlands	60	10	50	27	54.0
Norway	3		3	0	0.0
Poland	5	1	4	1	25.0
Portugal	22	1	21	3	14.3
Serbia	2		2	1	50.0
Slovakia	2		2	0	0.0
Slovenia	2		2	0	0.0
Spain	61	8	53	13	24.5
Sweden	19	2	17	4	23.5
Switzerland	9		9	1	11.1
United Kingdom	63	7	56	13	23.2
Anonymous				12	
Total	658	78	580	168	29.0

1) This column includes the number of responses of institutions which were „returned" e. g. due to a wrong mail/postal address, institution is out of business or it does not belong to the target group (i. e. not active in genetic engineering in the agricultural field).

2) This column includes the number of questionnaire sent out minus the „returned" questionnaires, so that it includes the net universe of the survey.

3) Explanation for reading the table (case of Belgium): Among 30 questionnaires sent out, 4 didn't belong to the target group (returned), the actual number of addresses was corrected to 26 (corrected). Among the 26 questionnaires sent out, 7 answers were received (number of valid response) so the percentage of answers is 26.9 % (response rate).

Source: Fraunhofer ISI 2002

The universe of companies and research institutes eligible for participating in the survey are the ones which are or have been involved in the notification of GMO field trials registered in the European SNIF database, participants in national programmes of R&D on GMOs, or laboratories involved in basic research on GMOs. The addresses of the notifiers of the SNIF database (version February 2002) were used and complemented by lists of EU and national programmes in the GMO area and lists of industrial association members (e. g. seed associations, associations of agri-chemical companies). A total of 639 addresses of companies, co-operatives, research institutions, industrial associations and other actors in Europe were collected to which a questionnaire was sent in February/March 2002[28]. 70 % of the questionnaires were sent directly to a person and 30 % to an institution. Several contacted persons forwarded the questionnaire to colleagues or to company's member of an industrial association resulting in 19 additional questionnaires. In case an e-mail address was available, the questionnaire was transferred electronically to the respective contact person or institution. Around three-quarters of the questionnaires were mailed electronically, the rest was sent by mail. In total, 78 questionnaires had either an unknown address or did not belong to the target group[29]. The "net universe" of 580 institutions forms the basis of the survey (table A1). Almost one quarter of these institutions is located in Germany (144) followed by France (70), the United Kingdom (56), Spain (53), the Netherlands (50) and Italy (46) (table A1). A small number of institutions were also contacted in accession countries (Bulgaria, Czech Republic, Poland, Slovakia, Slovenia).

In order to facilitate the filling-in of the questionnaire, an electronic version was put on the Internet and made available to the interviewees (restricted access with password). If desired, the interviewees could mail or fax the questionnaire as well. One third of answers (32 %) were received via Internet and 68 % by mail or fax (people addressed by mail answered also via Internet). In March 26th, 2002 a reminding letter or e-mail was sent to those institutions which had not responded until then. A total of 168 filled-in questionnaires were received until the final closing date of the survey on April 8th, 2002. The total response rate is 29 %[30] which is in the range of recent surveys in comparable universes of companies and research institutions (Wörner et al. 2000). A high response rate of 54 % can be registered in the Netherlands, which is due to the fact that one industrial association motivated their member-companies to fill in the questionnaire. No filled-in questionnaire was received from Ireland (table A1). The information of the filled-in questionnaire was collected in an Access database and statistically analysed with SPSS[31].

In all important subgroups of notifiers, a good coverage could be achieved since 35 SMEs, 28 large companies, 44 university institutes and 37 public research institutes participated in the survey. The response rate per actor group is presented in table A2. Results allow a statistical analysis for each single subgroup. All major seed producing companies answered the questionnaire[32], as well as main

28 The questionnaire was sent in two lots: first lot was sent on 25th February and a second lot was sent on beginning of March 2002. The second lot was smaller and corresponded to institutions which coordinates were not yet collected at the date of 25th Febraury 2002. This mailing in two lots had no influence on the response rate as the institutions contacted with the reminding letter were belonging to both lots.

29 Not in the target group includes all actors that are not active in the field of biotechnology /GMOs, are not in the agriculture field and have never been working in the field.

30 The response rate is calculated on the basis of the number of filled-in questionnaires valid for statistical analysis and the number of the "corrected" universe i. e. institutions which e. g. could not be contacted or did not belong to the target group are excluded from the universe. In case an "adjusted response rate" should be considered in which the number of all returns (246 answers) is related to the number of sent out questionnaires (658 questionnaires), the corresponding figure would amount to 37 % in the survey. Several explanations might be given to argue on the 71 % of non-repondents: the hight sensitivity of the subject and also the fact that a lot of surveys were carried out within the last two or three years in the field of biotechnology.

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32 It is important to note that all major seed producing companies participated to the survey and answered centrally in the survey. This means that a lot of answers received from all subsidaries of the respective company were integrated in the "central" answer. In this sense the large companies answered the survey very satisfactory but this is not totally reflected in the response rate of this group.

research team in universities and public research institutes. The response rate per actor group is given in table A2. The median number of GM plant projects mentioned by each actor group is given in table A3.

It is assumed that the weight of each actor group is the same. This assumption could be further exploited.

The degree of representativity of the sample depends on the relationship between the agents who answered to the survey and the population. This coverage ratio should take into account some quantitative variable such as the number of employees or the sales of the agent category (for the case of the private firms). Unfortunately, those figures referred to the population for the public and private agents considered in this study are not available. Given that the response rate to the questionnaires is almost thirty percent, one would argue that the degree of representativity of the sample is relatively satisfactory.

Table A2: Response rate of the survey per actor group

Actor group	Questionnaires				
	Sent (total)	"Returned"[1]	Corrected[2]	No. of valid Responses	Response rate (%)
SME	141	15	126	35	27.8
Large companies	139	25	114	28	24.6
Universities	137	9	128	44	34.4
Public Research Institutes	159	18	141	37	26.2
Others	82	11	71	12	16.9
Anonymous				12	
Total	658	78	580	168	29.0

1) This column includes the number of responses of institutions which were "returned" e. g. due to awrong mail/postal address, institution is out of business or it does not belong to the target group (i. e. not active in genetic engineering in the agricultural field).

2) This column includes the number of questionnaire sent out minus the „returned" questionnaires, so that it includes the net universe of the survey.

Source: Fraunhofer ISI 2002

Table A3: Median of the number of projects per actor group (GM plants in the laboratory phase only)

Actor group	Number of projects	Median (of the number of projects)
SMEs	46	1
Large companies	34	2
Universities	95	3
Public research institutes	74	3
Others	20	1

Source: Fraunhofer ISI 2002

The information collected in the survey is mainly used to get insight in the character of GMO projects in laboratory phase in the EU, the relevance of different influential factors for the commercialisation of new GMOs as well as promising areas for commercialisation of GMOs. It was never the target of the project team to collect all research projects with GMOs, which are carried out in the EU since this would be a very costly and time-consuming activity, which cannot be realised within the time frame of this project. However, it was intended to get a picture as clear as possible in this area, taking into account the very short time available for the survey.

The results obtained in the survey are limited by the fact that around two thirds of the contacted institutions did not fill in the questionnaire and the differing answering rates between the involved countries. In this respect in particular research activities located in Mediterranean countries, France or Ireland might be underrepresented in the sample. In addition, institutions which are very familiar with e-mail and the Internetinstitutions, which are very familiar with e-mail and the Internet, might be over-represented in the survey. The fact that an English version of the questionnaire was sent to the respondents should not have influenced the willingness and ability to answer the questionnaire substantially, since most of the scientific and commercial information in agrobiotechnology is communicated and disseminated in English language.

Some limitations in the information obtained might arise by the design of the questionnaire as well. Due to practical reasons, the reference to projects related to GMOs was surveyed using an "open question" (see question 2 of the questionnaire). This resulted in a limited number of filled-in questionnaires in which the respondents did not precisely describe the project (e. g. they did not mention which type of resistance was the target of the genetic modification). Moreover, the respondents might have mentioned only the most interesting projects, or the ones most likely to be accepted by general public. But again, the aim of the project was not to screen all research projects in Europe but to give a first picture. Altogether it can be stated that the survey allows to givegiving a first picture concerning the GMO projects in laboratory phase in the EU and the factors influencing their potential commercialisation from a notifier point of view.

Expert interviews

In order to substantiate the findings of the written surveys and get more insight in the underlying reasons for the achieved results, 16 personal and telephone interviews were carried out with experts from companies and research institutions in April 2002. The experts were selected on the one hand based on the answers given in the written survey, on the other hand the views of additional persons and institutions who have not participated in the survey were taken into account. 5 of the 16 interviewed experts come from large companies, 5 from SMEs, 2 from university institutes and 4 from public research institutes. In order to get a most complete picture of the differing situation in the different Member States of the EU, experts from France, the United Kingdom, Germany, the Netherlands, Belgium, Italy, Spain, Austria and Switzerland were interviewed. The interviews were based on an interview guide (see in this annex) which included questions related to the company/institute and interviewed person, the process of R&D and commercialisation of GMOs, the framework conditions for R&D and commercialisation of GMOs in the EU as well as the characteristics of future GMOs. Minutes were taken of the information given by the experts and incorporated in the overall analysis of the project. A quantitative statistical analysis was not performed (and never intended) based on the interview results due to the limited number of interviewees and the short time frame available for this task. Instead the information stated by the experts was used in a qualitative way to substantiate the findings of the written survey, database and literature analyses.

Questionnaire on commercialisation of GMOs in the EU

1. Does your institution use genetic engineering approaches or methods in R&D projects related to plants, animals or microorganisms?

Yes ☐ No ☐ Do not know ☐

2. Which R&D projects on GMOs are currently carried out in your institution? Please characterise the relevant R&D projects in the following table using a separate line for each project.

Organisms	Target of genetic modification (traits)	Phase of development (e. g. laboratory, field trials)

3.1 Has your institution cancelled R&D projects aimed to genetically modify plants, animals or microorganisms in recent 4 years?

Yes ☐ No ☐ Do not know ☐

3.2 What have been the main reasons for cancelling the respective R&D projects? Please select up to 5 factors of the following list.

☐ Not feasible from a scientific/technical point of view.

☐ The target could not be achieved within the scheduled duration of the project.

☐ High costs of the projects.

☐ Modification of the strategy of the institution.

☐ Limited financial resources.

☐ Lack of experienced staff.

☐ Appropriate (cooperation) partnership is missing.

☐ Problems with intellectual property rights.

☐ Unclear or high requirements for safety testing of products.

☐ Duration of the notification process.

☐ Unclear legal situation in the EU.

☐ Low acceptance of users/consumers of GM products.

☐ Uncertainties about future market situation.

☐ Ethical concerns.

☐ Other reasons (please specify):

4. **Which GMOs currently developed in the EU are the most promising from a commercial perspective in the coming 5 to 10 years?**

5. **In which areas do you see major constraints for commercialisation of GMOs or products produced with the help of GMOs in the coming 5 to 10 years in the EU? Please assess the relevance of each factor of the following list.**

Constraints are:	Very high	High	Average	Low	Do not know
Public R&D infrastructure	☐	☐	☐	☐	☐
Technology transfer mechanisms	☐	☐	☐	☐	☐
Financing	☐	☐	☐	☐	☐
Personnel (availability, skills etc.)	☐	☐	☐	☐	☐
Intellectual property rights	☐	☐	☐	☐	☐
Practical handling of regulation processes	☐	☐	☐	☐	☐
Legal situation	☐	☐	☐	☐	☐
Market opportunities	☐	☐	☐	☐	☐
Industry structure	☐	☐	☐	☐	☐
Acceptance of consumers/users	☐	☐	☐	☐	☐
Ethical considerations	☐	☐	☐	☐	☐
Other fields (please specify):	☐	☐	☐	☐	☐

6. **Some information related to your institution and yourself:**

Location (country):

Your position:

Type:

☐ Large company (>500 employees)

☐ Small and medium-sized company (<500 employees)

☐ University institute

☐ Non-university public research institute

☐ Other (please specify):

If you wish to receive a summary of the results of the survey, please specify your e-mail address:

Please return the questionnaire before April 5, 2002

to Dr. Martina Menrad, Fraunhofer ISI, Breslauer Str. 48, 76139 Karlsruhe (Germany),

E-Mail: gmo@isi.fhg.de, Fax: +49-721-6809-476

Thank you for the time invested and your cooperation!

Letter / Questionnaire on commercialisation of GMOs in the EU

Dear (Name of Director, contact person),

Modern biotechnology and genetic engineering is expected to be one of the key technologies in agriculture in the future. A wide variety of genetically modified organisms (GMOs) are being developed in R & D projects in and outside the EU. Little is known, however, about how many of these are likely to request introduction for commercialisation in the EU in coming years.

The European Commission has therefore commissioned a study which aims to anticipate which GMOs and derived products, in the agricultural field, will request authorisation for commercialisation in the EU over the next decade. This study is being carried out by the Fraunhofer Institute for Systems and Innovation Research (ISI), Karlsruhe (Germany) in co-operation with the Institute for Prospective Technological Studies (IPTS), Seville (Spain) from the European Commission Joint Research Centre.

We would like to include your institution in this study as it has been identified as a significant research performer in the agricultural field. As part of the study a questionnaire has been developed in order to collect data on relevant R & D projects, as well as factors influencing commercialisation of GMOs in the EU. We would be very grateful if you could complete the attached questionnaire. Alternatively, you may prefer to go to the web site below and follow the link to an electronic questionnaire. Please open it using the user ID "gmo" and the password "tomato".

http://www.isi.fhg.de/bt/survey

The questionnaire should not require any search for information since it refers to basic data. Where this is not the case, estimated values will be sufficient. Please return the questionnaire by **22 March, 2002**. You may return your filled in questionnaire anonymously, if you wish. Completed questionnaires will be treated as strictly confidential and only aggregated results will be presented. If you would like a summary of the results, we would be happy to provide it. Please contact Dr. Martina Menrad if you have any further questions about the survey.

We would be very grateful if you could take a few moments to fill in the questionnaire. We would like to thank you for your kind co-operation on behalf of the European Commission in advance.

Yours sincerely

Dr. Martina Menrad

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Interview guide to expert interviews

1. Information on the company/institute and interviewed person

1. Name, function within the company/institute
2. General areas of business and research activities of the company/institute

In case the institution has not filled in a written questionnaire:

3. Does your institution use genetic engineering approaches or methods in R&D projects related to plants, animals or microorganismsmicro-organisms?
4. Which R&D projects on GMOs are currently carried out in your institution?

In case the institution has already filled in the questionnaire:

3. Can you give us some details about the research projects (e. g. duration, which targets, which milestones have been already achieved, difficulties, when will the projects be finished)?
4. What have been the reasons for initiating and carrying out the respective projects?

2. Process of R&D and commercialisation of GMOs

1. What are typical steps in the process of R&D and commercialisation of GMOs? How long is an average duration necessary for the single steps?
2. How is this process organized in your institution?
3. Who decides about the R&D portfolio related to GMOs and the commercialisation of the respective products? According to which criteria? Are there specific consultation bodies for such decisions?
4. Which factors influence the decision whether to cancel or continue a project related to GMOs? *(In case a questionnaire has been filled in, please take the answer in the questionnaire as starting point for this question)*
   - Relevance of different factors
   - Has the relevance of single factors changed in recent years?
   - In which way does the relevance of single factors depend on the character of the different projects?

3. Framework conditions for R&D and commercialisation of GMOs in the EU

1. What is your opinion of the general framework conditions for R&D activities and commercialisation of GMO's in the EU?
   - Is it necessary to differentiate between R&D activities and commercialisation? In which respect?
   - Has the situation changed in recent four years?
   - In which way?
2. Which influential factors relevant for R&D activities and commercialisation of GMOs can be judged as favourable and unfavourable in the EU? What are the mains reasons for your assessment? *(In case a questionnaire has been filled in, please use the answer in the questionnaire as starting point for this question)*

3. Does the situation in your country differ substantially from the global situation in the EU?
   - Concerning which factors?
   - In which way?

4. In which fields substantial changes are necessary to improve R&D activities and commercialisation of GMOs in the EU?
   - What kind of changes/improvements would you suggest?
   - What about the implementation of your suggestions: How probable do you assess the realisation within the coming five years?
   - Which actors should become active and in which way to realise your suggestions

5. What kind of consequences do you expect if your suggestions are not realized?

4. Character of future GMOs

1. Which developments related to GMOs are the most promising in a five to ten years perspective?
   - from a scientific/technical point of view
   - from a business perspective
2. How do you assess the position of EU scientists/companies in these areas?
3. GMOs of the so-called second generation aim at improvement of quality characteristics of plants and modification of output traits. What is the actual state of development in this area? What might be feasible from a scientific/technical point of view within the next five to ten years?
4. How do you assess the market opportunities for GMOs with modified output traits in the EU?
5. Do you think such products are able to overcome the acceptance barriers of many EU consumers related to genetic engineering approaches in the food and nutrition area?

Annex B: Trait categories

Table B1: *Classification scheme for traits mentioned in the SNIF database*

Trait category	Traits	Specified traits in SNIF database
Herbicide tolerance	Herbicide tolerance	asulam tolerance
		bromoxynil tolerance
		broomrape control
		dalapon tolerance
		glufosinate tolerance
		glyphosate tolerance
		herbicide tolerance
		imidazolglyc erol phosphate dehydratase synthesis
		isoxaflutole tol erance
		isoxazole tolerance
		oxynil tolerance
		sulfonamide tolerance
		sulphonylurea tolerance
Insect resistance	Insect resistance	Bt-derived insect resistance
		chymotrypsin protease inhibitor synthesis
		cowpea trypsin inhibitor synthesis
		insect resistance
		kunitz gene protease inhibitor
		lectin-encoded insect resistance
		mannose specific lectin protein synthesis
		pea derived insect resistance
		pea lectin inhibitor synthesis
		potato trypsin protease inhibitor synthesis
		serine protease inhibitor
		Vicia faba derived insect resistance
Resistance to pathogens	Fungi resistance	chitinase synthesis
		expression of cf9 resistance gene
		expression of hordothionin gene
		fungal resistance
		fungal resistance (Fusarium spp.)
		fungal resistance (Phytophtora infestans)
		fungal resistance (Sclerotina sclerotiorum)
		fungal resistance (soft rot and blackleg: Erwinia carotovora spp.)
		glucanase synthesis
		lysozyme synthesis
		osmotin synthesis
		oxalate decarboxylase synthesis
		oxalate oxidase synthesis
		pathogenesis-related proteins synthesis
		reduction of blackspot
		resveratrol synthesis
		ribosomal inactivating protein synthesis

Trait category	Traits	Specified traits in SNIF database
		stilbene synthesis
		stimulation hypersensitivity response
	Bacteria resistance	bacterial resistance
		bacterial resistance (expression of T4 lysozyme)
		bacterial resistance (Pseudomonas marginalis)
		expression of anti-microbial proteins
		oligogalacturonate lyase synthesis
		pectate lyase synthesis
	Virus resistance	virus resistance
		virus resistance (alfalfa mosaic virus)
		virus resistance (beet mild yellow virus)
		virus resistance (beet western yellow virus)
		virus resistance (cucumber mosaic virus)
		virus resistance (grapevine fanleaf nepovirus)
		virus resistance (lettuce mosaic potyvirus)
		virus resistance (lily symptomless virus)
		virus resistance (maize dwarf mosaic virus)
		virus resistance (plum pox potyvirus)
		virus resistance (potato leafroll virus)
		virus resistance (potato mop-top virus)
		virus resistance (potato virus X)
		virus resistance (potato virus Y)
		virus resistance (rhizomania - beet necrotic yellow vein virus)
		virus resistance (tobacco rattle virus)
		virus resistance (tomato spotted wilt virus)
		virus resistance (tomato yellow leaf curl virus)
		virus resistance (watermelon mosaic virus)
		virus resistance (zucchini yellow mosaic virus)
	Resistance against other species	cystein proteinase inhibitor synthesis
		disease resistance (not specified)
		nematode resistance
Abiotic stress/yield	Resistance to abiotic stress	bruising resistance
		cyanamide tolerance
		drought tolerance
		frost tolerance
		increased fitness
		metallothionein synthesis
		reduced shattering of mature pods
		stress tolerance
		suppression of shade avoidance
		tryptophan-2-monoxygenase synthesis
	Yield influencing factors	alteration of phosphate metabolism
		arginine decarboxylase expression
		cytokinin synthesis
		downregulation of the photorespiration rate
		dwarf phenotype introduction

Trait category	Traits	Specified traits in SNIF database
		expression of S-Adenosylmethionine decarboxylase
		expression of tryptophan-2-monoxygenase
		glutamine synthetase synthesis
		improved rooting ability
		increased yield
		inhibition of photosynthetic proteins
		nitrate reductase synthesis
		nitrite reductase synthesis
		overexpression of nitrate reductase
		overexpression of photosynthetic proteins
		polyphosphate kinase synthesis
		pyrophosphate synthesis
		S-adenosyl methionin decarboxylase synthesis
		stimulation of growth rate
		sucrose phosphate synthesis
		sucrose transporter protein synthesis
		superoxide dismutase synthesis
Male sterility	Male sterility	citrate synthesis
		male sterility/fertility restoration
Modified nutrients/ingredients	Antinutritive ingredients	downregulation of glucosinolate
		glucosinolate reduction
		low nitrate level
		low nitrite level
		phytic acid conversion
		reduction of antinutritional effect of phytic acid
	Enhancement of nutritional value	alteration of forage quality
		downregulation of cinnamoyl CoA reductase
		improvement of digestibility
		increased nutritional value
		phytase synthesis
		reduction of phosphate pollution
	Fatty acid metabolism	alteration of oil composition
		high stearate content
		reduction of stearic acid content
	Protein metabolism	alteration of amino acid metabolism
		asparagine synthesis
		downregulation of amino acid permease
		improved storage proteins
		increased amino acid content in seed
		inhibition threonine synthase
		lysine synthesis
		methionine/lysine rich protein synthesis
		threonine synthesis
	Oligosaccharides metabolism	downregulation of fructose-1,6-bisphosphatase
		downregulation of invertase
		downregulation of sucrose

Trait category	Traits	Specified traits in SNIF database
		fructan production
		fructan synthesis
		Fructosyltransferase synthesis
		inhibition phosphoglucomutase
		invertase synthesis
		kestose biosynthesis
		levan sucrase synthesis
		nystose biosynthesis
		sucrose:sucrose fructosyltransferase synthesis
		trehalose synthesis
		trehalose-6-phosphate synthesis
	Starch metabolism	ADP glucose pyrophosphorylase synthesis
		alteration of carbohydrate composition
		alteration of starch biosynthesis
		branching enzyme synthesis
		downregulation of amylose synthesis
		downregulation of endoglucanase
		downregulation of granule bound starch synthase
		expression of hexokinase II
		expression of maltose binding protein
		glucogene biosynthesis
		glycogen branching enzyme synthesis
		improvement of starch quality
		inhibition of NAD-malic enzyme
		production of starch, consisting of pure amylopectine
Industrial use	Food processing	High Molecular Weight glutenin synthesis
		improvement of baking quality
		improvement of malting quality
		improvement of processing quality
		increased storage
	Non-food applications	alteration of lignin biosynthesis
		downregulation of o-methyl transferase
		high erucic acid content
		high laurate content
	Enzyme production	alpha-amylase secretion
		conversion of xylan into xylose
		dog gastric lipase cDNA synthesis
		expression of yeast lipase gene
		glucose isomerase synthesis
		use as bioreactors
Health	Health-related compounds	albumin synthesis
		antibody synthesis
		collagen synthesis
		expression of pharmaceutical compounds
		human albumin synthesis
		human alpha-1 antitrypsin synthesis

Trait category	Traits	Specified traits in SNIF database
		human collagen synthesis human glucocerebrosidase protein synthesis human lactoferrin synthesis putrescine methyl transferase synthesis rabies virus G glycoprotein cDNA synthesis
Other output traits	Modification of colour/form	alteration of leaf morphology alteration of pigment production chalcone synthesis delphinidin synthesis dihydroflavonol reductase synthesis improvement of flowering characteristics optimisation of the production of athocyanins phytochrome A synthesis phytochrome B synthesis
	Modification of ripening	ACC synthase synthesis alteration of ethylene biosynthesis alteration of keeping qualities alteration of ripening characteristics alteration of the distribution of storage metabolites auxin synthesis controlled cell division downregulation of acid invertase downregulation of pectin esterase downregulation of polyphenol oxydase improvement of vase-life increased cell wall thickness inhibition of flowering inorganic pyrophosphatase synthesis polygalacturonase synthesis
Marker/other traits	Marker	2-Deoxyglucose-6-phosphate resistance Ac/Ds two components transposon system chlorsulphuron tolerance expression of green fluorescent protein from jellyfish expression of tetracyclin repressor hygromycin tolerance mannose isomerase synthesis marker system methotrexate tolerance rol gene product(s) synthesis
	Other traits	cytoplasmatic exclusion protein synthesis expression of activator of EtOH utilisation gene expression testing gene stability testing gene tagging increase the endogenous hormone level monitoring transgene flow

Source: Fraunhofer ISI and IPTS 2002

Annex C: GMO commercialised and pending authorisations in Europe

Table C1: *GMO products approved under Directive 90/220/EEC (only GM plants) as of March 2001*

Organism	Trait	Event	Application	Country	Company	Year [1)]
Carnation C/ NL/96/14	Modification of colour	lines 4,11,15,16	Marketing	Netherlands	Florigene	01/121997 MS consent
Carnation C/ NL/97/12	Prolonged vase life	line 66	Marketing	Netherlands	Florigene	20/10/1998 MS consent
Carnation C/ NL/97/13	Modification of colour	lines 959A, 988A, 1226A, 1351A, 1363A, 1400A	Marketing	Netherlands	Florigene	20/10/1998 MS consent
Chicory C/NL/ 94/25	Male sterility, herbicide tolerance (Glufosinate)	RM3-3, RM3-4, RM3-6	Breeding activities	Netherlands	Bejo-Zaden BV	20/05/1996
Maize C/F/94/ 11-03	Herbicide tolerance (Glufosinate), insect resistance	Bt 176	As any other maize	France	Ciba Geigy (now Syngenta)	23/01/1997
Maize C/F/95/ 12-07	Herbicide tolerance (Glufosinate)	T25	As any other maize	France	AgrEvo GmbH / Aventis Crop Science	22/04/1998
Maize C/F/95/ 12-02	Insect resistance	MON 810	As any other maize	France	Monsanto	22/04/1998
Maize C/UK/96/ M4/1	Insect resistance, herbicide tolerance (Glufosinate)	Bt 11	Import and processing	United Kingdom	Northrup King (Syngenta)	22/04/1998
Oilseed rape C/UK/94/M1/1	Male sterility, herbicide tolerance (Glufosinate)	MS1 x RF1	Breeding activities	United Kingdom	Plant Genetic Systems/Aventis Crop Science	06/02/1996
Oilseed rape C/ F/95/05-01/A	Male sterility, herbicide tolerance (Glufosinate)	MS1 x RF1	As any other oilseed rape	France	Plant Genetic Systems/Aventis Crop Science	06/06/1997
Oilseed rape C/ F/95/05-01/B	Male sterility, herbicide tolerance (Glufosinate)	MS1 x RF2	As any other oilseed rape	France	Plant Genetic Systems/Aventis Crop Science	06/06/1997
Oilseed rape C/ UK/95/M15/1	Herbicide tolerance (Glufosinate)	HCN92 Topas 19/2	Import and processing	United Kingdom	AgrEvo GmbH / Aventis Crop Science	22/04/1998
Soybean C/UK/ 94/M3/1	Herbicide tolerance (Glyphosate)	GTS40-3-2	import and processing	United Kingdom	Monsanto	03/04/1996
Tobacco C/F/ 93/08/02	Herbicide tolerance (Bromoxynil)	PBD6-238-2		France	Seita	08/06/1994

1) Date of commission decision/ Member State consent

Sources: European Commission 2002a, RKI 2002, Transgen 2002,

Table C2: GMO plantsroducts that were pending approval under the old Directive 90/220/EEC when it was repealed and the new Directive 2001/18/EC entered into force.

Organism File No.	Trait	Event	Application	Country	Company	Year[1]
Chicory C/NL/ 94/25/A	Male sterility, Herbicide tolerance (Glufosinate)	RM3-3, RM3-4, RM3-6	Food, feed	Netherlands	Bejo-Zaden BV	18/12/1998
Cotton C/ES/ 97/01	Herbicide tolerance (Glyphosate)	RRC1445	As any other cotton	Spain	Monsanto	14/07/1998
Cotton C/ES/ 96/02	Insect resistance (Bt cryIA (c) gene)	IPC531	As any other cotton	Spain	Monsanto	14/07/1998
Fodder beet C/DK/97/01	Herbicide tolerance (Glyphosate)	A5/15	As any other fodder beet	Denmark	DLF-Trifolium, Monsanto, Danisco Seed	23/06/1998
Maize C/ES/ 98/01	Herbicide tolerance (Glyphosate)	GA21	As any other maize	Spain	Monsanto	22/09/2000
Maize C/F/95/ 12.01B	Insect resistance (Bt cryIA (b) gene)	MON 809	As any other maize	France	Pioneer	15/05/1998
Maize C/F/96/ 05-10	Herbicide tolerance (Glufosinate), insect resistance Bt cryIA (b) Gene	Bt 11	As any other maize	France	Novartis (now Syngenta)	30/11/2000
Maize C/NL/ 98/08	Herbicide tolerance (Glufosinate), insect resistance, Bt cryIA (b) Gene	T25 + MON 810	As any other maize	Netherlands	Pioneer	06/06/2000
Oilseed rape C/DE/96/5	Herbicide tolerance (Glufosinate)	Falcon GS40/90 pHoe6/Ac	As any other swede rape	Germany	AgrEvo GmbH / Aventis Crop Science	14/07/1998
Oilseed rape C/BE/96/01	Male sterility and herbicide tolerance (Glufosinate)	MS8 x RF3	As any other swede rape	Belgium	Plant Genetic Systems/Aventis Crop Science	19/05/1998
Oilseed rape C/DE/98/6	Herbicide tolerance (Glufosinate)	Liberator pHoe6/ Ac	As any other swede rape	Germany	AgrEvo GmbH / Aventis Crop Science	30/11/2000
Potato C/SE/ 96/3501	Starch modification (amylose-free)	IEH 92-527-1	As any other starch potato	Sweden	Amylogene	18/07/2002

1) Year of release of the favourable opinion of EU scientific committee

Sources: European Commission 2002a, RKI 2002, Transgen 2002,

Table C3: GM Plants – Notifications received by the Commission under Directive 2001/18/EC As of 26 February 2003

Product notification details	Company
1. Oil seed rape – herbicide resistant GT 73 **Received by the Netherlands** (C/NL/98/11) under Dir 90/220/EC. **Received by the Commission** under Dir 2001/18 : **16/1/03** Uses: import and uses in feed and industrial processing, not for cultivation.	**Monsanto**
2. Maize Roundup Ready NK603, **tolerant to glyphosate herbicide** **Received by Spain** (C/ES/00/01) under Dir 90/220 : 21/12/2000 **Received by the Commission** under Dir 2001/18 : **17/01/03** Uses: import and use in feed and industrial processing, not for cultivation.	**Monsanto**
3. Maize hybrid MON810 x NK603 (glyphosate-tolerant and containing Bt toxin) **Received by UK** under Dir 90/220/EC. (C/GB/02/M3/03) **Received by the Commission** under Dir 2001/18 : **15/01/03** Uses: import and use in feed and industrial processing, not for cultivation.	**Monsanto**
4. Potato with altered starch composition from Sweden (C/SE/96/3501) **Received by the Commission** under Dir 90/220: 20.05.98 Favourable opinion of EU Scientific Committee 18.07.02 **Received by the Commission** under Dir 2001/18/EC: **24/01/03** Uses: for cultivation and production of starch, not for use as human food.	**AMYLOGENE HB**
5. Oilseed rape (Ms8, Rf3) from Belgium (C/BE/96/01) **Received by the Commission**: under Dir 90/220 16.01.97 Favourable opinion of EU Scientific Committee 19.05.98 **Received by the Commission** under Dir 2001/18: **5/02/03** Uses: import and cultivation in the EU, uses in feed and industrial processing.	**Bayer CropScience**
6. Soybeans Glufosinate tolerant (Events A 2704-12 and A 5547-127) from Belgium (C/BE/98/01) **Received by the Commission** under Dir 2001/18: 5/02/03 Uses: import only	**Bayer CropScience**
7. Roundup Ready sugar beet (event T9100152), glyphosate tolerant from Belgium C/BE/99/01 **Received by the Commission** under Dir 2001/18: **5/02/03** Uses: for cultivation and use in animal feed, processing of sugar and other products.	**Monsanto/ Syngenta**

Product notification details	Company
8. Oilseed rape tolerant for glufosinate-ammonium herbicides. (FALCON GS40/90pHoe6/Ac) from Germany (C/DE/96/5) **Received by the Commission** under Dir 90/220: 25.11.96 Opinion of EU Scientific Committee 27.07.98 **Received by the Commission** under Dir 2001/18: **7/02/03** Uses: for import and cultivation	**Bayer CropScience**
9. Oilseed rape tolerant for glufosinate-ammonium (Liberator pHoe6/Ac) from Germany (C/DE/98/6) **Received by the Commission** under Dir 90/220: 29.10.98 Favourable opinion of EU Scientific Committee 30.11.00 **Received by the Commission** under Dir 2001/18: **7/02/03** Uses: for import and cultivation	**Bayer CropScience**
10. Roundup Ready Sugar Beet event H7-1 (tolerant to glyphosate) from Germany C/DE/00/8 **Received by the Commission** under Dir 2001/18**: 7/02/03** Uses: for cultivation and use in processing of sugar and other processed products.	**KWS SAAT AG/Monsanto**
11. Maize MON 863 X MON 810 (protection against certain insect pests) from Germany C/DE/02/9 (6788-01-09) **Received by the Commission** under Dir 2001/18**: 7/02/03** Uses:, for import and use of grain and grain products.	**Monsanto**
12. Oilseed rape (event T45) tolerant for glufosinate-ammonium herbicide from UK C/GB/99/M5/2 **Received by the Commission** under Dir 2001/18**: 10/02/03** Uses: import and use in feed and industrial processing.	**Bayer CropScience**
13. Maize herbicide and insect resistant (line 1507 — CRY1F) **Received by** the Netherlands (C/NL/00/10) under Dir 90/220/EC. **Received by the Commission** under Dir 2001/18 : **12/02/03** Uses: import and processing, not for cultivation	**Pioneer/ Mycogen Seeds**
14. Insect-protected Cotton expressing the Bt *cryIA(c)* gene (line 531) from Spain (C/ES/96/02) **(Received by the Commission under Dir 90/220: 24.11.97** Favourable opinion of EU Scientific Committee 14.07.98) **Received by the Commission** under Dir 2001/18**: 12/2/03** Uses: for import, processing and cultivation	**Monsanto**

Product notification details	Company
15. Roundup Ready Cotton tolerant to herbicide (line 1445) from Spain (C/ES/97/01) **(Received by the Commission under Dir 90/220: 24.11.97** Favourable opinion of EU Scientific Committee 14.07.98) **Received by the Commission** under Dir 2001/18**: 12/2/03** Uses: for import, processing and cultivation	**Monsanto**
16. Roundup Ready Maize tolerant to glyphosate (GA21) from Spain (C/ES/98/01) **Received by the Commission under Dir 90/220: 20.05.99** Favourable opinion of EU Scientific Committee 22.09.00 **Received by the Commission** under Dir 2001/18**: 13/2/03** Uses: use in feed and industrial processing	**Monsanto**
17. Maize MaisGard/Roundup Ready (derived from MON 810 and GA21). **Tolerance to glyphosate and Cry1Ab protein derived from Bt.** **Received by** Spain (C/ES/99/02) 3/9/1999 under Dir 90/220/EC. **Received by the Commission** under Dir 2001/18**: 13/2/03** Uses: import and use in feed and industrial processing, not for cultivation.	**Monsanto**
18. Maize 1507 (or Bt Cry1F 1507) **Received by** Spain (C/ES/01/01) 11/7/2001 under Dir 90/220/EC. **Received by the Commission** under Dir 2001/18**: 13/2/03** Uses: import, feed and industrial processing, and cultivation	**Pioneer Hi-Bred / Mycogen Seeds**
19. Roundup Ready Fodder beet (line A5/15) from Denmark (C/DK/97/01) **Received by the Commission under Dir 90/220:** 09.10.97 Favourable opinion of EU Scientific Committee 23.06.98 **Received by the Commission under Dir 2001/18/EC**: 26/02/03 Uses: for cultivation and animal feed.	**DLF-Trifolium, Monsanto and Danisco Seed**

Annex D: GMOs commercialised outside Europe

Table D1: GM maize approved for commercialisation outside the EU

Company	Trait	Event	Product approval				
			Country	Plant-ing	Food/ Feed	Food	Feed
Aventis Crop Science	Insect resistance, herbicide tolerance (Glufosinate)	CBH-351	USA	1998			1998
Aventis Crop Science	Male sterility, herbicide tolerance (Glufosinate)	MS3	Canada	1996		1997	1998
		MS3	USA	1996	1996		
Aventis Crop Science	Male sterility, herbicide tolerance (Glufosinate)	MS6	USA	1999	2000		
Aventis Crop Science	Herbicide tolerance (Glufosinate)	T14, T25	Argentina	1998		1998	1998
			Australia		2002		
			Canada	1996		1997	1996
			Japan	1997		1997	1997
			USA	1995	1995		
BASF Canada	Herbicide tolerance (Cyclohexa-none)	DK404SR	Canada	1996		1997	1996
De Kalb Corporation	Herbicide tolerance (Glufosinate)	B16 (DLL25)	Canada	1996		1996	1996
			Japan	1999		1999	2000
			USA	1995	1996		
De Kalb Corporation	Insect resistance, herbicide tolerance (Glufosinate)	DBT418	Argentina	1998			
		DBT418	Canada	1997		1997	1997
		DBT418	Japan	1999		1999	
		DBT418	USA	1997	1997		
Dow Agro Sciences, Pioneer Hi Bred	Insect resistance, herbicide tolerance (Glufosinate)	TC1507	USA	2001	2001		
Monsanto	Herbicide tolerance (Glyphosate)	GA21	Argentina	1998			
			Australia			2000	
			Canada	1998		1999	1998
			Japan	1998		1999	1999
			USA	1997	1996		
Monsanto	Insect resistance	MON80100	USA	1995	1996		
Monsanto	Insect resistance, herbicide tolerance (Glyphosate)	MON802	Canada	1997		1997	1997
			Japan	1997			
			USA	1997	1996		
Monsanto	Insect resistance, herbicide tolerance (Glyphosate)	MON809	Canada	1996		1996	1996
			Japan	1997		1998	
			USA	1996	1996		
Monsanto	Insect resistance	MON810	Argentina	1998		1998	1998
			Australia	2000			
			Canada	1997		1997	1997
			Japan	1996		1997	1997
			South Africa	1997		1997	1997
			USA	1995	1996		

Company	Trait	Event	Product approval				
			Country	Plant-ing	Food/ Feed	Food	Feed
Monsanto	Herbicide tolerance (Glyphosate)	MON832	Canada	1997			
Monsanto	Insect resistance	MON863	USA			2001	
Monsanto	Herbicide tolerance (Glyphosate)	NK603	Canada	2001		2001	2001
			Japan	2001			
			USA	2000	2000		
Pioneer Hi Bred	Herbicide tolerance (Imidazolinone)	3751IR	Canada	1996		1994	1996
Pioneer Hi Bred	Male sterility, herbicide tolerance (Glufosinate)	676, 678, 680	USA	1998		1998	
Pioneer Hi Bred	Herbicide tolerance (Imidazolinone)	IT	Canada	1998			
Syngenta Seeds	Insect resistance, herbicide tolerance (Glufosinate)	176	Argentina	1996		1998	1998
			Australia		2001		
			Canada	1996		1995	1996
			Japan	1996		1996	1996
			USA	1995	1995		
Syngenta Seeds	Insect resistance, herbicide tolerance (Glufosinate)	BT11 (X4334CBR, X4734CBR)	Argentina	2001		2001	2001
			Australia	2001			
			Canada	1996		1996	1996
			Japan	1996		1996	1996
			USA	1996	1996		
Syngenta Seeds	Herbicide tolerance (Imidazolinone)	EXP1910IT	Canada	1996		1997	1996

Source: AGBIOS 2002

Table D2: GM oilseed rape approved for commercialisation outside the EU

Company	Trait	Event	Product approval				
			Country	Plant-ing	Food/ Feed	Food	Feed
Aventis Crop Science	Herbicide tolerance (Glufosinate)	HCN10	Canada	1995		1995	1995
			Japan	1997		1997	1998
			USA	1995	1995		
Aventis Crop Science	Herbicide tolerance (Glufosinate)	HCN92	Canada	1995		1995	1995
			Japan	1996		1996	1996
Aventis Crop Science	Male sterility, herbicide tolerance (Glufosinate)	MS1, RF1=>PGS1	Canada	1995		1995	1995
			Japan	1996		1996	1996
Aventis Crop Science	Male sterility, herbicide tolerance (Glufosinate)	MS1, RF2=>PGS2	Canada	1995		1995	1995
			Japan	1997		1997	1997
Aventis Crop Science	Male sterility, herbicide tolerance (Glufosinate)	MS8xRF3	Canada	1996		1997	1996
			Japan	1998		1997	1998
			USA	1999	1996		
Aventis Crop Science	Herbicide tolerance (Oxynil)	OXY-235	Canada	1997		1997	1997
			Japan	1998		1999	1999
Aventis Crop Science	Male sterility, herbicide tolerance (Glufosinate)	PHY14, PHY35	Japan	1997		1997	1998
Aventis Crop Science	Male sterility, herbicide tolerance (Glufosinate)	PHY36	Japan	1997		1997	1997
Aventis Crop Science	Herbicide tolerance (Glufosinate)	T45, (HCN28)	Australia		2002		
			Canada	1996		1997	1995
			Japan	1997		1997	1997
			USA	1998	1998		
Calgene	High content of laurate and myristate oil	23-18-17, 23-198	Canada	1996		1996	1996
		23-18-17, 23-198	USA	1994	1994		
Monsanto	Herbicide tolerance (Glyphosate)	GT200	Canada	1996		1997	
Monsanto	Herbicide tolerance (Glyphosate)	GT73, RT73	Australia			2000	
			Canada	1995		1994	1995
			Japan	1996		1996	1996
			USA	1999	1995		
Monsanto	Herbicide tolerance (Glyphosate)	ZSR500/502	Canada	1997			1997
Pioneer Hi Bred	High content of oleic acid	45A37, 46A40	Canada	1996			
Pioneer Hi Bred	High content of oleic acid	46A12, 46A16	Canada	1996			
Pioneer Hi Bred	Herbicide tolerance (Imidazolinone)	NS738, NS1471, NS1473	Canada	1995		1995	1995

Source: AGBIOS 2002

Table D3: *GM cotton approved for commercialisation outside the EU*

Company	Trait	Event	Product approval				
			Country	Planting	Food/Feed	Food	Feed
Calgene	Insect resistance, herbicide tolerance (Oxynil)	31807/31808	Japan	1998		1999	1999
			USA	1997	1998		
Calgene	Herbicide tolerance (Oxynil)	BXN	Australia		2002		
			Canada	1996		1996	
			Japan	1997		1997	1998
			USA	1994	1994		
DuPont Canada	Herbicide tolerance (Sulfonylurea)	19-51A	USA	1996	1996		
Monsanto	Herbicide tolerance (Glyphosate)	MON1445/1698	Argentina	1999		2001	2001
			Australia	2000		2000	
			Canada	1996			
			Japan	1997		1997	1998
			USA	1995	1995		
Monsanto	Insect resistance	MON531/757/1076	Argentina	1998		1998	1998
			Australia	1996		1996	1996
			Canada	1996		1996	
			China	1997		1997	1997
			India	2002			
			Japan	1997		1997	1997
			Mexico	1997		1997	1997
			South Africa	1997		1997	1997
			USA	1995	1995		

Source: AGBIOS 2002

Table D4: *GM potatoes approved for commercialisation outside the EU*

Company	Trait	Event	Product approval				
			Country	Planting	Food/Feed	Food	Feed
Monsanto	Insect resistance	ATBT04-6, ATBT04-27, ATBT04-30, ATBT04-31, ATBT04-36, SPBT02-5, SPBT02-7	Australia		2001		
			Canada	1997		1996	1997
			Japan			1997	
			USA	1996	1996		
Monsanto	Insect resistance	BT6, BT10, BT12, BT16, BT17, BT18, BT23	Canada	1995		1995	1995
			Japan			1996	
			USA	1995	1994		
Monsanto	Insect resistance, virus resistance	RBMT15-101, SEMT15-02, SEMT15-15	Australia		2001		
			Canada	1999		1999	1999
			USA	1999	1998		
Monsanto	Insect resistance, virus resistance	RBMT21-129, RBMT21-350, RBMT22-082	Australia		2001		
			Canada	1999		1999	1999
			USA	1998	1998		

Source: AGBIOS 2002

Table D5: GM soybeans approved for commercialisation outside the EU

Company	Trait	Event	Product approval				
			Country	Plant-ing	Food/ Feed	Food	Feed
Agriculture and Agri Food Canada	High content of linolenic acid	OT96-15	Canada			2001	
Aventis Crop Science	Herbicide tolerance (Glufosinate)	A2704-12, A2704-21, A5547-35	Canada	1999		2000	
			Japan	1999			
			USA	1996	1998		
Aventis Crop Science	Herbicide tolerance (Glufosinate)	A5547-127	USA	1998	1998		
Aventis Crop Science	Herbicide tolerance (Glufosinate)	GU262	USA	1998	1998		
Aventis Crop Science	Herbicide tolerance (Glufosinate)	W62, W98	USA	1996	1998		
DuPont	High content of oleic acid	G94-1, G94-19, G168	Australia			2000	
			Canada	2000		2000	2000
			Japan	1999		2001	2000
			USA	1997	1997		
DuPont	High content of oleic acid	G94-1, G94-19, G168	Australia			2000	
			Canada	2000		2000	2000
			Japan	1999		2001	2000
			USA	1997	1997		
Monsanto	Herbicide tolerance (Glyphosate)	GTS 40-3-2	Argentina	1996		1996	1996
			Australia			2000	
			Brazil	1998		1998	1998
			Canada	1995		1996	1995
			Japan	1996		1996	1996
			Korea			2000	
			Mexico	1998		1998	1998
			South Africa	2001		2001	2001
			USA	1994	1994		
			Uruguay	1997		1997	1997

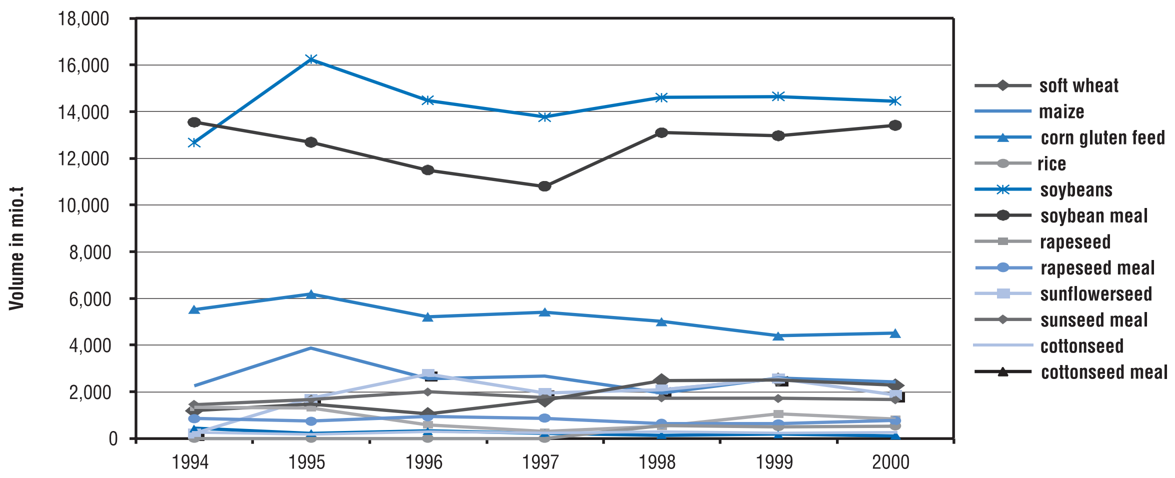
Source: AGBIOS 2002

Annex E: Imports of crops in the EU

In order to assess the future potential impact of GMOs grown outside the EU, a short overview is given on the import situation of the EU for the main commodities likely to include genetically modified varieties.

Apart from a few exceptions, the imports in the EU of the main farm commodities between 1994 and 2000 remain more or less unchanged, with the exception of corn gluten feed and soft wheat.

Figure E1: *Development of the imports of farm commodities in the EU-15*



Source: Toepfer International, edition 2000/01

Table E1: *Extract of the supply balance for the main farm commodities in the EU-15*

Product	Production mio. t			Imports mio. t			Consumption mio. t			Imports vs consumption %		
	1994/95	1999/2000	%	1994/95	1999/2000	%	1994/95	1999/2000	%	1994/95	1999/2000	%
CEREALS												
soft wheat	78.6	95.7	21.8	1.5	2.3	51.4	68.9	82.2	19.3	2.2	2.8	27.0
maize	29.6	38.6	30.4	3.4	2.5	-25.5	31.5	39.0	23.8	10.7	6.4	-39.8
corn gluten feed	0.0	1.7	-	6.2	4.9	-20.6	-	6.6	####	-	74.2	####
rice	1.25	1.44	15.6	0.49	0.62	26.3	1.59	1.86	17.2	30.9	33.3	7.7
OILSEEDS												
soybeans	0.9	1.2	28.8	15.2	15.9	4.2	16.1	17.0	5.6	94.5	93.3	-1.2
soybean meal	0.7	0.9	28.2	24.5	27.8	13.4	24.5	26.9	9.9	100.2	103.4	3.2
rapeseed	7.5	9.4	25.3	0.9	1.0	14.7	8.3	9.9	20.4	10.7	10.2	-4.7
rapeseed meal	4.1	5.0	21.1	1.3	1.1	-17.3	5.4	6.0	11.8	23.8	17.6	-26.0
sunflowerseed	3.6	2.7	-24.9	2.3	2.1	-8.8	5.8	4.8	-18.2	40.0	44.6	11.4
sunseed meal	2.0	1.5	-24.4	3.3	2.9	-12.5	5.3	4.4	-17.1	63.0	66.5	5.5

Source: Eurostat

Cereals and corn

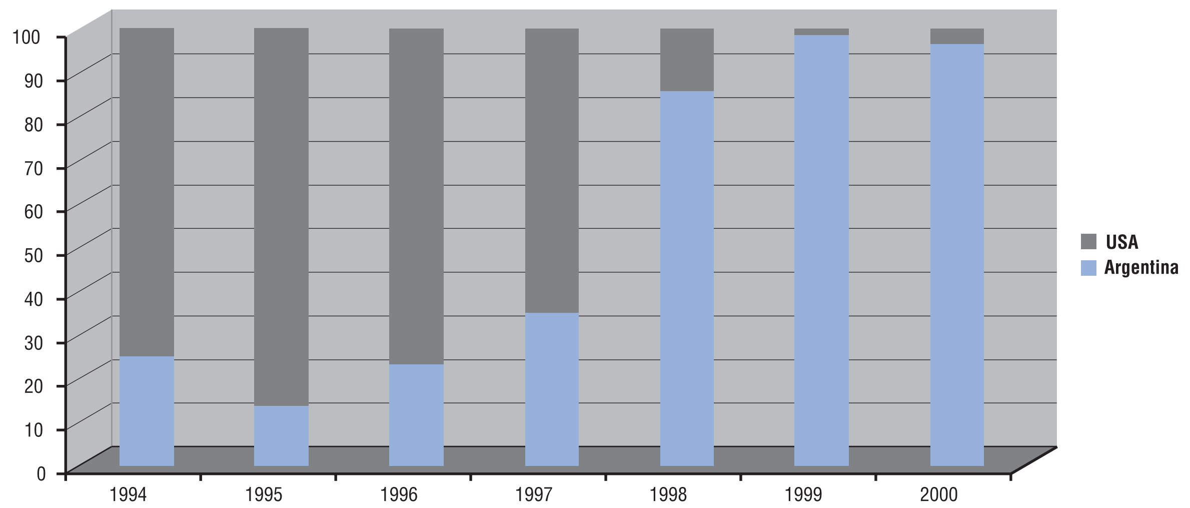
The main imported commodities in this category during the crop year 1999/2000 are soft wheat with 2.3 mio.t, maize with 2.5 mio.t and rice with 0.6 mio.t.

The imports of soft wheat have increased by 50% since 1994, this is partly explained by an increase in the demand of the milling industry for high quality milling wheat originating from North America. The two main importing countries (Canada, the US) both profited from this trend. In both countries no GM wheat varieties have been grown in recent years, but Monsanto has announced to introduce and launch a herbicide tolerant wheat variety on the US market as from 2005 (AgraFood Biotech 2002), so that this situation might change in the second half of the coming decade. However, imports of soft wheat amounted only to around 2.8 % of the soft wheat internal use in the EU in 2000 (Eurostat) and the self-sufficiency is now around 115%.

In maize production the EU is slightly under a level of self-sufficiency of 100 %. Imports of maize contribute to around 4 % to 8 % of the total consumption in the EU (DG Agri 2001) and are strictly under the WTO tariff quotas agreed for 2 mio. t to be imported into Spain and 0.5 mio.t to be imported into Portugal. While in 1994, 80% of the maize was imported from the US, 92% of 2000 maize imports are coming from Argentina. The US already complained that the loss of potential export of maize to Europe is estimated at 303 mio. euros per year (Alden and Man 2002). Both in Argentina and the US transgenic maize varieties play a significant role in agriculture: In the US the area grown with transgenic maize increased from 2.27 mio. ha in 1997 to 9.55 mio. ha in 2000. In Argentina 0.74 mio. ha were grown with transgenic maize in 2000 (DG Agri 2001). This equals to more than one quarter of the area grown with maize in the US (James 2002) and around 10 % in Argentina (DG Agri 2000). Therefore the shift from the US to Argentina is probably explained by more competitive market price for ArgentinianArgentinean maize since the opening to other third countries of the maize import quotas that were previously reserved for the US.

In addition to maize the EU imports corn-processing products, in particular corn-gluten feed. In 2000 these imports amounted to around 4.5 million tonnes which came to more than 98 % from the US. The imports of corn gluten feed show a steady slight decrease following the Agenda 2000 reduction of the common prices for cereals that makes them more competitive for feed compounders.

Figure E2: Imports of maize in the EU-15



Source: Toepfer International, edition 2000/01

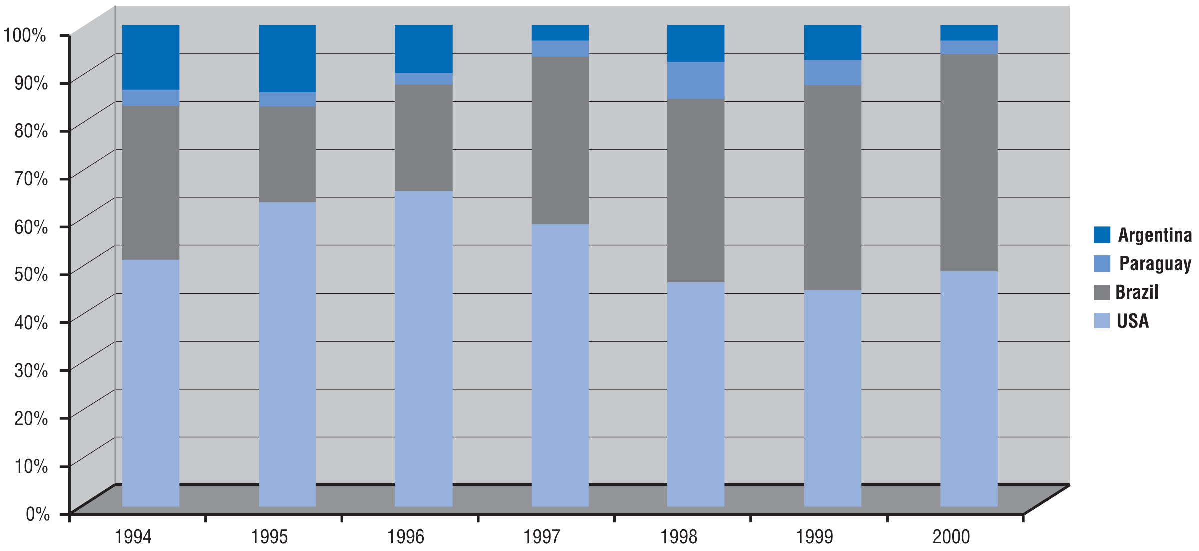
Oilseed products

The imports of soya, whether beans or meals and cakes, after a decrease between 1994 and 1997, have recovered their previous level or even increased as from 1998.

In contrast to cereals, the EU has a strong vegetable protein deficit and its degree of self-sufficiency is much lower for oilseeds used for food, feed and industrial purposes. Indeed, self-sufficiency is only 5% for soya and the EU is worldwide the most important importer of soybeans and derived products with annual imports of around 14.5 mio. t of soybeans 30 mio. t of soybean meal. The most important EU trade partners for soybeans and derived products are Brazil, Argentina and the US, with respectively 12.5 mio.t, 7.3 mio.t and 7.1 mio.t imported in 2000. In particular for Argentina and Brazil the EU market has a specific relevance, since around one half of the soybean production of these countries is sold in the EU. The world leading exporting nation of soybeans and derived products, the US, delivers around 10 % to 15 % of its production to the EU. This equals to around one third of the US soybean exports (DG Agri 2000).

When considering separately the import figures for soybeans and for soybean meals, distinct purchase behaviours can be observed. Indeed soybeans are traditionally imported from the US, Brazil and Argentina. The main exporter is still the US that have decreased and stabilised at the level of 1994 after relatively high increases until 1998. Nevertheless a shift can be observed between Brazil and Argentina who respectively increased by 40% and decreased by 75%. Here comes the GM factor as Brazil is the main provider of GM-free soybeans[33] for the EU crushing industry (use for oil production – food + meals for feed), while the US and Argentina are growing the largest surfaces of GM soybeans (respectively 1.5 and 2.5 million hectares).

Figure E3: Imports of soya beans in the EU-15



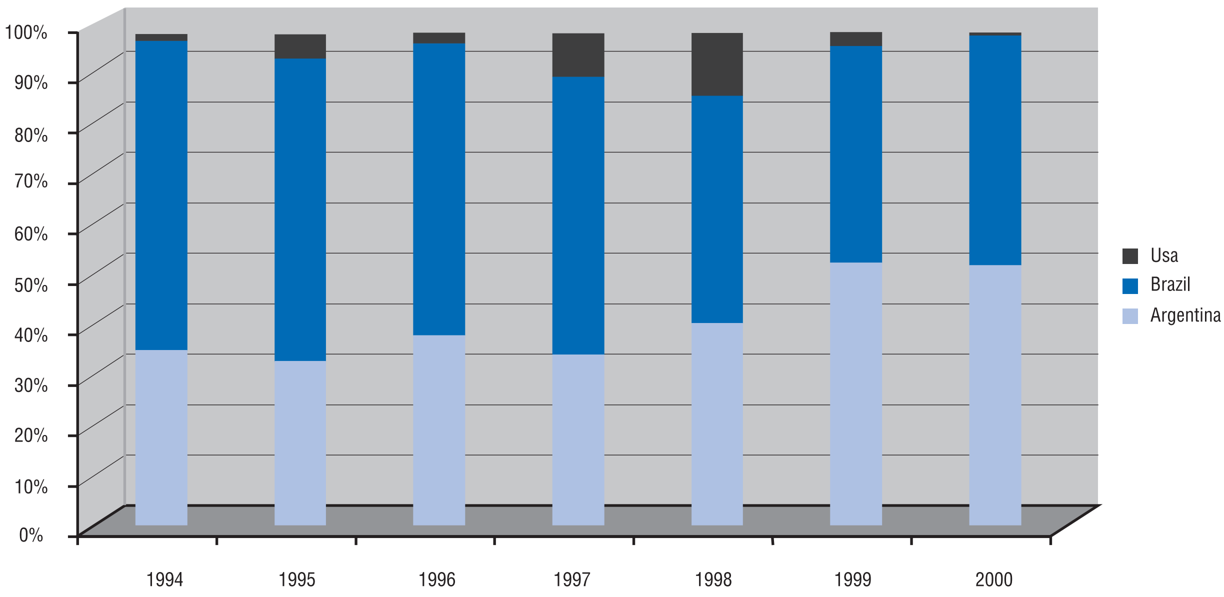
Source: Toepfer International, edition 2000/01

33 Brazil excludes growing and commercialisation of GMO and defends a position of GMO-free country. Government approval of GMOs has been put on hold, refereed as a "judicial moratorium" on the commercial release of GMOs, after a number of injunctions issued by the Brazil's Federal Court over the last years. Brazil is the only major agricultural exporter that does not use GM technology (mainly for soybean and corn). The country has officially banned any planting of Roundup Ready soybeans, however GM soybean is known to be produced in the southern part of the country using GM soybean varieties illegally imported from Argentina.

Nevertheless, this result should be compared with the soybean meal imports (used for feed), which are equally shared between Argentina and Brazil thus indicating that the GM factor has no or little influence on the purchase decision of this type of commodity.

Soybean usage in the EU can be broadly broken down into food, industrial and animal feed purposes. Within the EU, animal feed dominates total usage of soybean meal since around 25.5 to 26.5 million tonnes of soybean meal are annually used in animal feed (about 95 % of the total soya protein usage). In the feed industry of the EU, soya meal account to around half of all proteins used in EU feed manufacturing (Task Group on Public Perceptions of Biotechnology 2002). In addition to differing nutritional values of different oilseed meals, the price relationships between the different sources of protein in animal feeding play a decisive role for the use of a specific oilseed meal in animal feeding. Soya oil is mostly processed in a wide range of foods (e. g. margarine, salad dressings). The EU uses annually about 1.9 to 2.0 million tonnes of soya oil mostly derived from imported beans crushed in the EU (Task Group on Public Perceptions of Biotechnology 2002). Altogether the Task Group of Public Perceptions of Biotechnology 2002 estimates that the market for non-GM soybeans, meal and oil in the EU food and feed sectors account for up to a quarter of total Soybeans and meal used. In recent years this market

Figure E4: *Imports of soybean meals in the EU-15*



Source: Toepfer International, edition 2000/01

The area grown with transgenic soybeans in the US significantly increased from 0.4 million hectares in 1996 to 16.28 million hectares in 2000. During the same period the corresponding figures for Argentina rose from 0.05 million hectares in 1996 to 7.16 million hectares in 2000 (DG Agri 2001). This equals to around 54 % of the area grown with soybeans in the US in 2000 and to an adoption rate of around 90 % in Argentina (James 2000). In Brazil GM varieties have to date not yet officially been permitted for planting, but there is evidence of a significant volume of illegal planting in recent years which was estimated between 15 % and 40 % of all soybean plantings in this country (DG Agri 2001, Task Group on Public Perceptions of Biotechnology 2002). This means that the majority of globally traded soybeans and meals may be derived from GM seeds.

could be covered by using "soft IP" systems. For the coming years increasing difficulties are expected to cover the non-GM demand of soybeans and derived products in the EU, in particular if mainstream food retailers claim for "non-GM" livestock products (Task Group on Public Perceptions of Biotechnology 2002).

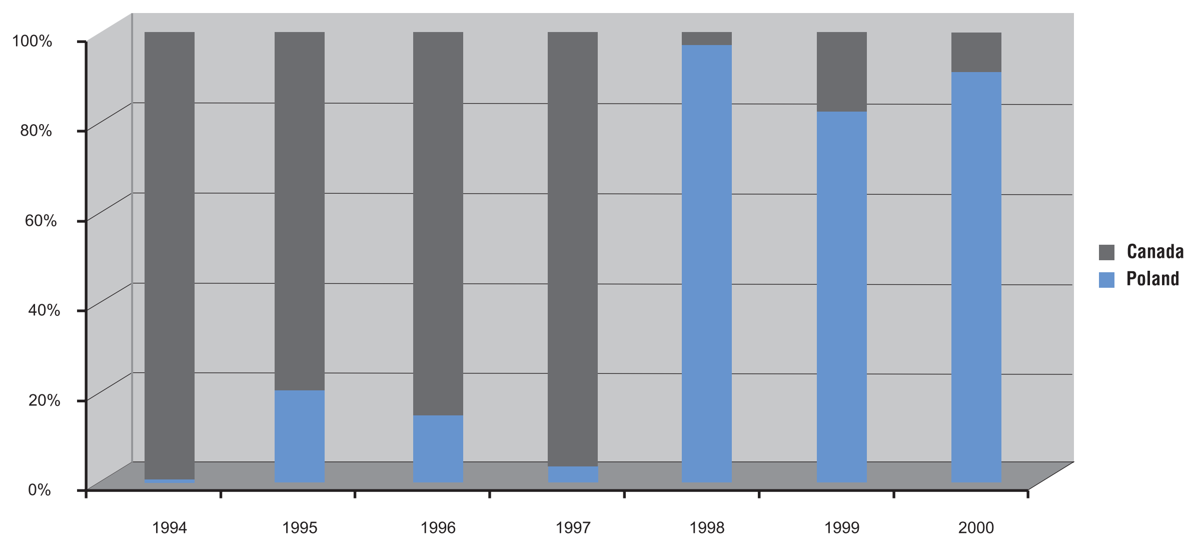
In contrast to soybeans and derived products, the EU has a high level of self-sufficiency in the production of oilseed rape and derived products. In 2000 around 0.8 million tonnes rapeseed and 0.75 million tonnes rapeseed meal were imported in the EU compared to a total production of around 9 million tonnes (European Commission 2001c). Both imports of rapeseed and rapeseed meal showed a slightly declining trend since the mid 1990s (table E2). The relevance of Canada which was the main importing country for soybeans in the mid 1990s of the EU has almost vanished. This development goes in line with a strong increase of the area of grown GM canola in Canada, which reached 2.5 million hectares (55 % of the total acreage grown with oilseed rape) in 2000 (James 2000, Canola Council of Canada 2001).

In 2000 imports of sunflower seed amounted to 1.85 million tonnes and those of sunseed meal to 1.65 million tonnes (table E2). In this year the imports of sunflower seed and derived products exceeded the EU production of 3.3 million tonnes (European Commission 2001c) slightly. The most important country for imports of sunflower seeds and derived products is Argentina. So far no transgenic sunflower variety has been approved for commercial growing (AGBIOS 2002).

Other products

Imports of other products with relevance for genetic modification are of little significance for the EU. Cottonseed and cottonseed meal were both imported to 0.2 or 0.1 million tonnes respectively in 2000 (table E2). The same relates to potatoes for which between 0.5 and 0.9 million tonnes were imported in the EU annually since 1997 (table E2). This equalled to less than 2 % of the EU potato production. Annual imports of raw tobacco in the EU amounted to around 0.5 million tonnes.

Figure E5: Imports of rapeseed in the EU-15



Source: Toepfer International, edition 2000/01

Table E2: *Imports of major crops in the EU from 1994 to 2000 (1,000 tonnes)*

Product	Import region	1994	1995	1996	1997	1998	1999	2000
Soft wheat	Total	1,181	1,452	1,033	1,625	2,466	2,501	2,266
	Canada	377	375	433	623	788	984	979
	US	286	615	420	575	1,015	988	975
Maize	Total	2,246	3,817	2,564	2,661	1,950	2,589	2,413
	Argentina	533	528	586	918	1,434	2,031	1,905
	US	1,656	3,325	1,939	1,708	238	30	69
Corn gluten feed	Total	5,519	6,175	5,200	5,400	5,000	4,384	4,498
	US	5,360	6,010	5,100	5,275	4,852	4,318	4,441
	Brazil	63	50	30	35	36	14	50
	Argentina	76	57	32	37	49	29	20
Rice	Total	n.a.	n.a.	n.a.	n.a.	556	489	519
Soybeans	Total	12,670	16,230	14,480	14,603	14,603	14,641	14,449
	US	6,318	9,812	9,159	7,805	6,627	6,469	6,908
	Brazil	3,921	3,073	3,102	4,637	5,414	6,106	6,376
	Paraguay	421	467	650	448	4,083	762	397
	Argentina	1,583	2,082	1,307	350	1,010	961	381
Soybean meal	Total	13,539	12,680	11,490	10,800	13,099	12,958	13,403
	Argentina	4,727	4,165	4,318	3,687	5,242	6,713	6,914
	Brazil	8,292	7,617	6,597	5,955	5,900	5,554	6,131
	US	282	695	328	999	1,699	446	183
Rapeseed	Total	1,325	1,303	579	280	520	1,038	836
	Canada	1,183	887	226	70	1	10	2
Rapeseed meal	Total	839	731	923	865	630	613	758
	PR China	305	0	202	188	0	37	304
	India	202	240	236	262	191	24	0
Sunflowerseed	Total	210	1,705	2,755	1,952	2,089	2,567	1,857
	Argentina	47	611	483	19	403	67	258
	Hungary	51	224	89	120	57	99	193
	US	32	322	252	68	205	157	14
Sunseed meal	Total	1,444	1,660	1,985	1,750	1,726	1,700	1,657
	Argentina	1,216	1,520	1,640	1,495	1,521	1,465	1,374
Cottonseed	Total	180	110	170	185	207	147	173
Cottonseed meal	Total	422	222	316	220	133	168	112
	Argentina	98	92	89	71	24	69	10
Potato	Total	n.a.	n.a.	n.a.	491	527	876	598
Raw tobacco	Total	n.a.	n.a.	n.a.	536	541	523	512

Source: Eurostat

Annex F: Results of derived from the SNIF database

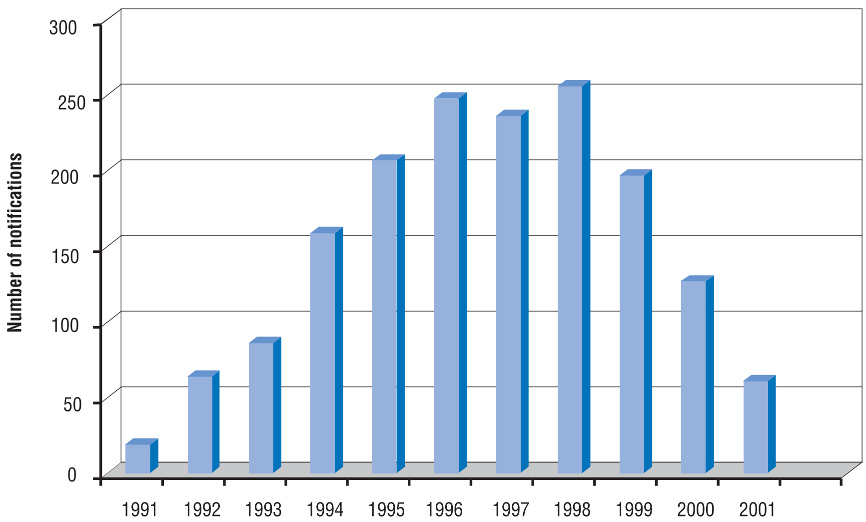
General development of field trial notifications

The SNIF database was analysed for the period 1991 to 2002 on the basis of the 1,687 notifications registered in February 2002. The number of notifications for GMO field trials increased rapidly between 1991 and 1997 to reach a peak in 1998 and declined rapidly afterwards to the level at the beginning of the decade (Figure F1). In 2001, the Joint Research Center received no more than 61[34] notifications for field trials with GM plants. This strong decrease in the number of GMO field trials in the EU has not taken place to this extent outside Europe (e. g. USA) (APHIS 2002). There is an obvious response effect to the 1999's decision of the EU Council of Environment Ministers to block any new commercial release of GMOs[35] as well as the widespread tendency of the European public to reject GMOs.

With more than 500 notifications, France accounted for almost one third of the total number of notifications followed by Italy (272), UK (209) and Spain (180). The average duration of a notification is 2.6 years with 80 % of the notifications having a durationduration of less than four years (except Austria, Germany, Ireland and the Netherlands with average duration of more than four years). Almost 60 % of the notifications refered to one single location (site where field trials are carried out) and references to more than five locations in average were found in notifications originating from France, Ireland and the Netherlands.

There is a balanced distribution of the size of the field trials. Sizes of the field trials are ranking from less than 500 m^2 (16 % of notifications), comprised between 1,000 m^2 and 2,000 m^2 (11.8 %), comprised between 3,000 m^2 and 5000 m^2 (10.4 %), up to

Figure F1: Number of field trials notifications in the EU between 1991 and 2001



Source: Calculations of Fraunhofer ISI on the basis of SNIF database (version Feb. 2002)[36]

34 In this study we refer exclusively to GM plants and did not include field trials with other organisms in the analysis. This explains the difference in the number of field trials estimated to 88 for the year 2001 in a recent communication of Commissioner Busquin (European Commission 2002b) as well as the total number of 1,762 GMO field trial notifications which are expressed at the website of IHCP in July 2002 (http://food.jrc.it/gmo/index.htm).

35 In June 1999 a de-facto-moratorium was initiated by the EU Council of Environment Ministers: several ministers (from Denmark, Italy, Luxembourg, France, Greece, joined by Germany and Belgium in October 2001) agreed to suspend all approval applications for GMOs until the implementation of a stricter legal framework covering not only safety, but also labeling and traceability of GMOs.

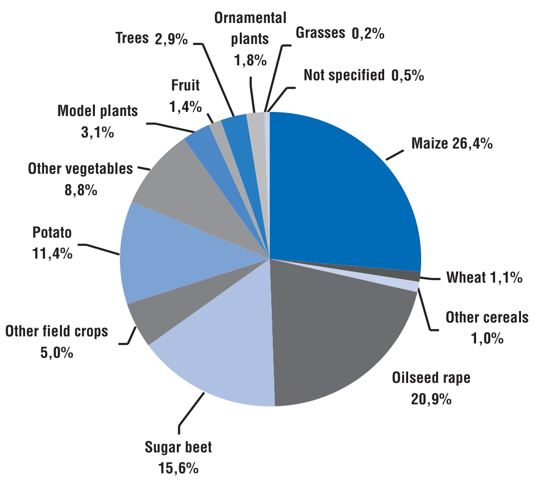
36 Data for year 2002 were excluded (as only 2 months data available)

40,000 m^2 and 100,000 m^2 (7.9 %) and superior to 100.000m^2 (4.4 %). This result indicates that 41 % of the GMO field trials are conducted on fields of a size superior than 5,000 m^2.

Type of crops

The majority of the notifications refered to four crops: maize (26.4 %), oilseed rape (20.9 %), sugar beet (15.6 %) and potato (11.4 %) (figure F2), while other crops like tomatoes, tobacco, chicory, vegetables, cotton, fodder beet and wheat ranked between 4.2 % and 1.1 %. A broad range of GM plants including fruit, grasses, flowers and trees are slightly represented and together they account for around 6 % of all notifications registered between 1991 and 2001. The proportions of the main crops have not changed significantly between 1993 and 2001, but the total number of notifications has decreased dramatically, showing a decline in all major crops since 1999. This result is in agreement with other analyses found in scientific literature (Arundel 2002b, Müller & Rödiger 2001).

Figure F2: Distribution of crops in GMO field trial notifications (1991 to 2001)



Total number of crops: 1,748[37]

Source: Calculations of Fraunhofer ISI on the basis of SNIF database 2002

When considering the evolution during the last ten years, maize, oilseed rape, potato and sugar beet were dominant crops during the whole decade while tomatoes, tobacco, fodder beet, and cotton were present but less represented between 1991and 1998 and have almost completely disappeared between 1998 and 2001. On the other hand, wheat and chicory had a limited but relatively constant importance during the entire time-period.

The review of the SNIF database shows few projects on GM cotton (1.7 % of all notifications, mainly in Spain). This is mainly due to climatic conditions that do not favour the growing of cotton (except in south of Spain and in Greece) in Europe. An important development of GM cotton is taking place in USA and elsewhere in the world[38].

Type of traits

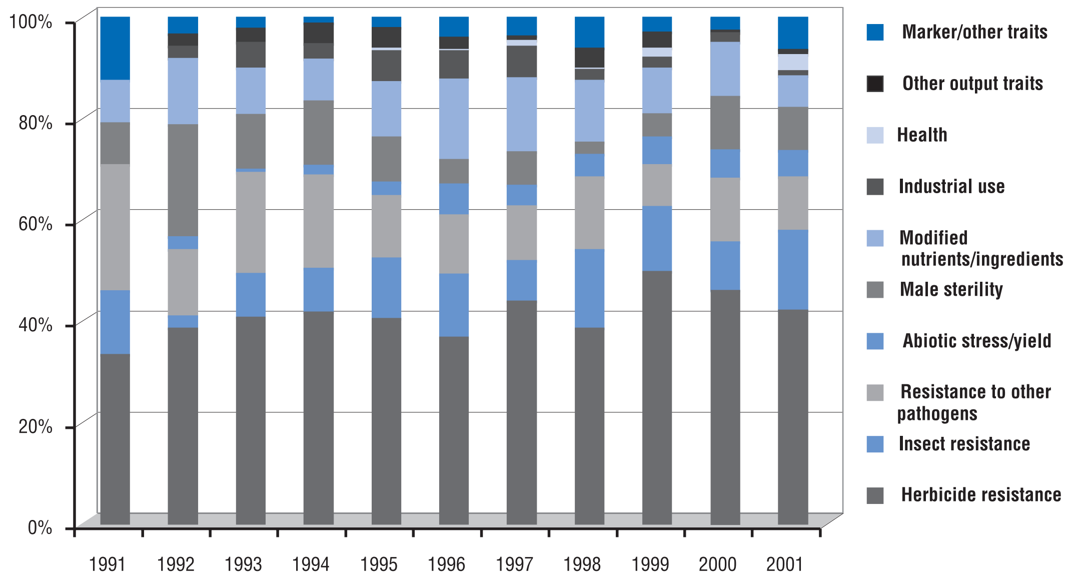
Over the whole period between 1991 and 2001, resistance traits against pathogens, insects and herbicides were predominant in field trial notifications (66 % of all notifications). Herbicide tolerance accounted for 42 % of all notifications followed by insect resistance with 11 % and resistance against other pathogens with 13 %. Output traits like modification of nutrients/ ingredients, change in colour/form and ripening, changing characteristics for industrial uses and GM plants for the production of health-related compounds accounted for 19 % altogether (figure F3). Both male sterility and yield enhancing factors/resistance against abiotic stress increased their proportion since 1996 but remained on a very small scale (figure F3)

Until the mid 1990s an increase in the importance of output traits was observed reaching their highest level in 1996 with almost one quarter

37 - Some notifications include more than one crop so the total number of crops is higher than the total number of notifications of 1,687.
- Other cereals include barley, buckwheat, rice, rye.
- Other field crops include cotton, coffee, cowpea, flax, fodder beet, mustard, peanut, soybean, sunflower.
- Other vegetables include asparagus, aubergine, bean, broccoli, cabbage, carrots, cauliflower, celery, chicory, cucumber, fennel, horseradish, lettuce, mint, olive, pea, pepper, radish, squash, tomatoes, yam, winged bean.
- Model plants include tobacco, *Arabidopsis thaliana*

38 India approved commercialisation of GM cotton in March 2002 (GENET 2002a) and China is already growing 1.5 millions hectares of GM cotton (ISAAA 2001).

Figure F3: *Share of traits in GMO field trial notifications*



Source: Calculations of Fraunhofer ISI on the basis of SNIF database 2002

of all field trial notifications. Afterwards a relatively steady decline of the percentage of output traits was registered reaching a level of 12 % of all field trial notifications in 2001 (figure F3). The sharp decline in the number of field trials with output traits since 1996 referedreferred to almost all categories, especially to modification in starch and fatty acid metabolism and modifications for non-food industrial uses. Since 1995 few field trials on health-related compounds (mostly carried out in tobacco and maize) emerged in the EU.

Trait-crop combinations

The distribution of trait categories of important crops in EU field trial notifications is

Table F1: *Distribution of traits for selected GM plants in EU field trials notifications (1991 to 2001)*

Traits	Maize	Wheat	Oilseed rape	Sugar beet	Potato	Tobacco	All crops
Herbicide tolerance	55.8 %	46.4 %	54.3 %	67.8 %	1.4 %	16.9 %	42.0 %
Insect resistance	31.2 %	0.0 %	0.7 %	0.0 %	7.2 %	0.0 %	10.8 %
Resistance against other pathogens	1.3 %	7.1 %	6.3 %	19.5 %	26.0 %	14.3 %	12.8 %
Abiotic stress/yield	1.8 %	0.0 %	2.3 %	2.9 %	5.5 %	18.2 %	3.8 %
Male sterility	4.6 %	3.6 %	20.8 %	1.3 %	0.6 %	1.3 %	7.9 %
Modified ingredients/ nutrients	2.8 %	17.9 %	8.7 %	6.8 %	47.8 %	13.0 %	11.7 %
Industrial use	0.9 %	10.7 %	5.2 %	0.0 %	5.2 %	15.6 %	3.8 %
Health	0.9 %	0.0 %	0.0 %	0.0 %	0.0 %	11.7 %	0.6 %
Other output traits	0.4 %	3.6 %	0.3 %	0.0 %	2.8 %	3.9 %	2.6 %
Marker/other traits	0.3 %	10.7 %	1.4 %	1.8 %	3.6 %	5.2 %	3.9 %
Number number of traits	677	28	573	385	362	77	2,678[1)]

1) Several notifications have more than one trait. Therefore, the number of traits in this analysis is higher than the total number of notification

Source: Calculations of Fraunhofer ISI based on SNIF database 2002

Table F2: Traits of main crops in the field trial phase 1991 to 2001

Trait category	Traits	Maize	Wheat	Oilseed rape	Sugar beet	Potato	Tobacco	All crops
Herbicide tolerance	Herbicide tolerance	378	13	311	261	5	13	1124
Insect resistance	Insect resistance	211		4		26		289
Resistance to other pathogens	Fungi resistance	5	2	34	6	45	5	145
	Bacteria resistance			1	1	10		14
	Virus resistance	4			68	33	4	175
	Resistance to other species			1		6	2	10
Abiotic stress/yield	Resistance to abiotic stress	6		10	5	5	5	39
	Yield influencing factors	6		3	6	15	9	64
Male sterility	Male sterility	31	1	119	5	2	1	212
Modified nutrients/ ingredients	Antinutritive ingredients	1		4			8	17
	Enhancement of nutritional value	7		4	1	2	2	25
	Fatty acid metabolism			32				35
	Protein metabolism	2		6	3	3		22
	Oligosaccharides metabolism	2		2	14	22		45
	Starch metabolism	7	5	2	8	146		169
Industrial use	Food processing		3			17		41
	Non-food applications	2		28			2	43
	Enzyme production	4		2		2	10	19
Health	Health-related compounds	6					9	16
Other output traits	Modification of colour/form	3				3	3	21
	Modification of ripening		1	2		7		49
Marker/other traits	Marker	1	2	4	5	11	2	77
	Other traits	1	1	4	2	2	2	27
	Total	677	28	573	385	362	77	2678[1)]

Source: Calculation of Fraunhofer ISI on the basis of the SNIF database 1991 to 2001

shown in table F1 (and in more detail in table F2). This analysis reveals that herbicide tolerance was strongly focused on crops with a high grown area in the EU (e. g. maize, wheat, oilseed rape, sugar beet), while it was of lower importance in crops with limited acreage (and the corresponding volume of the seed market). Insect resistance was mainly used in maize and to a smaller extent in potatoes. Resistance against other pathogens showed a relatively broad range of plants with a relevancerelevance above average in potatoes (fungi, virus resistance), sugar beet (virus resistance) and tobacco (fungi, virus resistance). Abiotic stress factors and yield improvement were covered in all plants (excluding wheat) with a relatively high share in tobacco, indicating again the "feasibility status" of these activities. Male sterility as a tool to facilitate plant-breeding programmes was of particular interest in oilseed rape and maize.

Table F3: *Trait-crop combinations in GMO field trials*

Trait	Crop[1)]
Herbicide tolerance	Maize, oilseed rape, sugar beet (fodder beet, soybean, cotton, cereals)
Insect resistance	Maize, cotton, potato
Virus resistance	Sugar beet, potato, tomato (melon, fruit trees)
Fungi resistance	Oilseed rape, potato (sunflower, fruit trees)
Bacteria resistance	Potato
Abiotic stress/yield	Tobacco
Male sterility	Oilseed rape, maize
Modification of protein content	Oilseed rape (maize, potato)
Modification of fatty acids	Oilseed rape
Modification of starch metabolism	Potato
Industrial use	Potato, oilseed rape (tobacco, tomato, wood trees)
Modification of fruit ripening	Tomato
Modification of colour/form	Flowers
Health	(Tobacco, maize)
Marker	(Flowers, wood trees)

1) Only a limited number of field trails has been carried out in crops within brackets.

Source: Fraunhofer ISI based on SNIF database (version Feb. 2002)

The modification of specific ingredients (for use in the food industry or for non-food purposes) was tested in all covered plants. Almost all notifications on starch modification were done in potato, whereas modifications of fatty acid profiles and traits for non-food industrial uses were predominant in oilseed rape. The other categories of output traits were tested in wheat (changing characteristics for improved flour quality), oilseed rape (changing oil content for technical purposes), potatoes (improving food processing abilities) and tobacco (enzyme production). An overview on the most important trait-crop combinations in the field trials carried out in the EU is given in table F3.

Stacked genes

As an indication for the importance of stacked genes in field trials with GM plants, the project team analysed the notifications that refer to more than one trait. From the SNIF database, no valid information is available which genes are actually combined in field trials carried out in reality. When a notification covers several traits it is not possible to tell whether it refers to one single GMO with stacked genes, or several individual GMOs of the same crops. In order to get information on potential combinations of traits in GM plants, we analysed the notifications that refer to multiple traits.

The distribution of the number of traits in EU field trials with GM plants is shown in table F4. Altogether more than one trait is mentioned in 42 % of the field trial notifications. Most of the combined traits are introduced in oilseed rape, wheat, potatoes and maize, and to a smaller extend tobacco and sugar beet (table F4). The most common combinations of traits for the main crops maize, oilseed rape, sugarbeet and potatoes are shown in table F5. In maize 69 % of the field trial notifications with more than one trait refer to a combination of herbicide and insect resistance, while in oilseed rape herbicide tolerance and male sterility are by far the two most important traits combined. No dominating combination of traits can be found in potatoes since in this crop traits of all categories are combined with each other with very limited numbers of field trials for each combination. No combination of traits are filtered out for wheat and tobacco, due to the very low number of field trial notifications with more than one trait in these crops.

Activities of different actor groups

Between 1991 and 2001 around 65 % of all field trial notifications were submitted by large companies[39], while SMEs (6 %), public research institutes (12 %) and universities (4 %) show a limited relevance in this respect. Among the large companies, Monsanto, Pioneer and Aventis Crop Science account for around one quarter of all field trials in the EU (Arundel 2002b). The different actor groups concentrate their activities on different plants.

Large companies focus their field trials on crops with a high grown area in the EU, while publicly financed research institutes and

Table F4: *Distribution of different number of traits in GMO field trial notifications (1991 to 2001)*

Plant	Maize	Wheat	Oilseed rape	Sugar beet	Potato	Tobacco	All crops
1 trait	58.6 %	50.0 %	49.3 %	82.7 %	48.3 %	65.5 %	58.0 %
2 traits	40.3 %	50.0 %	50.4 %	14.7 %	44.2 %	32.7 %	33.6 %
3 and more traits	1.1 %	0 %	0.3 %	2.6 %	7.5 %	1.8 %	8.4 %
Number of field trial notifications with more than one trait	191	10	185	47	103	19	709
Total number of field trial notifications	462	20	365	272	199	55	1,687

Source: Calculations of Fraunhofer ISI based on SNIF database 2002

Table F5: *Combinations of traits in GMO field trial notifications for main crops (1991 to 2001)*

Crop	Combined traits	No. of field trial notifications
Maize (total 191 notifications)	Herbicide + insect resistance	132
	Herbicide tolerance + male sterility	29
Oilseed rape (total 185 notifications)	Herbicide tolerance + male sterility	114
	Herbicide + fungi resistance	8
	Modification of fatty acid composition + industrial use	22
Sugar beet (total 47 notifications)	Herbicide + virus resistance	24
Potatoes (total 103 notifications)	No dominating combination of traits	

Source: Calculations of Fraunhofer ISI based on SNIF database 2002

39 Large companies: more than 500 employees. SME: less than 500 employees

universities show more interest in "exotic" crops or model plants. This finding can be substantiated in particular in large companies in which 73 % of all field trials are carried out in three crops (maize, oilseed rape, sugar beet) (table F6). SMEs are mainly conducting field trials with potatoes, tomatoes, other vegetables and flowers. Public research institutes show the broadest range of activities in field trials with GM crops, thereby specifically focusing on potatoes, tomatoes, other vegetables, oilseed rape, flowers, trees and fruit. Universities often conduct field trials with GM oilseed rape and potatoes. In addition, this actor group shows a specific interest in fruit, model plants and trees (table F6). Field trials on wheat and other cereals which have a high relevance for EU agriculturecereals that have a high relevance for EU agriculture are mainly carried out by public research institutes, but have a limited significance in each actor group.

The different actor groups also show specific interest in singular trait categories in field trials with GM plants. This relates in particular to large companies in which half of the field trials refer to herbicide tolerance. In addition, field trials related to insect resistance (13.3 %) or male sterility (10.8 %) show a relevance above average in this actor group (table F7). Field trials of SMEs are focused on resistance against insects and other pathogens (in particular fungi, viruses), while herbicide tolerance account for less than one quarter (23.4 %) of all field trial notifications of SMEs (table F7). The focus of SMEs on fungi and viruses could be due to the types of crops in which they were active (often horticulture) and the creation of new companies like Mogen[40] which were working on specific niche market. Another focus of SMEs are output traits of which all categories show a relevance above average for this actor group. In contrast to private

Table F6: Distribution of different crops per actor group in GMO field trials in the EU (1991 to 2001)

Plants	SME	Large company	Public research institute	University	Total
Maize	17.9 %	30.0 %	5.8 %	5.7 %	26.5 %
Wheat	0.0 %	0.5 %	3.3 %	0.0 %	1.1 %
Other cereals	3.6 %	0.2 %	5.4 %	2.3 %	1.1 %
Oilseed rape	13.4 %	22.6 %	14.2 %	24.1 %	20.8 %
Sugar beet	7.1 %	20.8 %	3.8 %	9.2 %	15.3 %
Other field crops	4.5 %	10.7 %	1.7 %	0.0 %	7.5 %
Potato	25.0 %	6.7 %	21.3 %	16.1 %	10.1 %
Tomato	8.9 %	3.1 %	11.3 %	1.1 %	4.4 %
Other vegetables	8.9 %	1.7 %	10.8 %	5.7 %	4.7 %
Model plants	2.7 %	2.5 %	1.3 %	11.5 %	3.2 %
Fruit	0.0 %	0.5 %	5.0 %	19.5 %	2.0 %
Trees	0.9 %	0.5 %	7.1 %	3.4 %	1.4 %
Flowers	7.1 %	0.2 %	9.2 %	1.1 %	1.7 %
Grasses	0.0 %	0.2 %	0.0 %	0.0 %	0.1 %
Total number of notifications	112	1,276	240	87	1,972[1)]

1) Several notifications have more than one notifier. Therefore, the number of plants in this analysis is higher than in figure F2.

Source: Calculations of Fraunhofer ISI on the basis of SNIF database 2002

40 http://www.hollandbiotechnology.nl/FIRM/ZenecaMogen/Zeneca.html

Table F7: Distribution of different traits in GMO field trials in the EU 1991 to 2001

Trait category	SME	Large company	Public research institute	University	Total
Herbicide tolerance	23.4 %	50.0 %	22.8 %	14.4 %	42.6 %
Insect resistance	18.0 %	13.3 %	6.9 %	2.9 %	12.1 %
Resistance to other pathogens	21.6 %	10.8 %	20.1 %	20.1 %	12.4 %
Abiotic stress/yield	0.6 %	2.8 %	8.4 %	8.6 %	3.7 %
Male sterility	2.4 %	8.6 %	3.9 %	3.6 %	8.0 %
Modified nutrients/ingredients	16.2 %	8.9 %	15.6 %	18.7 %	11.0 %
Industrial use	6.6 %	2.2 %	6.3 %	9.4 %	3.8 %
Health	1.2 %	0.2 %	0.0 %	1.4 %	0.7 %
Other output traits	7.8 %	1.7 %	4.2 %	7.2 %	2.6 %
Marker/other traits	2.4 %	1.4 %	12.0 %	13.7 %	3.2 %
Total number of traits	167	1,871	334	139	2,905[1)]

[1)] Several notifications have more than one notifier. In these cases the respective traits are calculated for each notifier. Therefore, the number of traits in this analysis is higher than in table F1.

Source: Calculations of Fraunhofer ISI on the basis of SNIF database 2002

companies, public research institutes and universities show less interest in field trials with herbicide tolerant and/or insect-resistant plants, while in particular trials related to resistance to other pathogens (e. g. fungi, viruses) and different types of output traits have specific relevance in these two actor groups. This is also the case for field trials related to abiotic stress/ yield and genetic markers which show a relevance in these two actor groups which is by factor 2 or 3 higher than the general average (table F7).

Annex G: GMOs in CEECs

In addition to the situation in the EU, GMOs under R&D in the Central & Eastern European countries are taken into account within this project as it is possible that GMOs will be grown in those countries and request commercialisation in the EU in the coming ten years.

The project team has collected information (from Internet Web pages and personal interviews) on GMO (commercialised and field trials) conducted in Central and Eastern European Countries (CEEC), identifying when possible the type of plants used, the type of traits tested, category of notifier as well as on-going research activities. It is not always easy to distinguish between an authorisation for large field trials (e. g. 12,000 ha) and an authorisation given for commercial production. In general, information on commercialised GMOs and field trials conducted in CEEC is difficult to collect, as certain governments or responsible ministries does not always maintain a publicly available register of all GMOs released. Therefore, part of the information presented in this section of the report has been gathered through personal interviews with national representatives and in direct contact with ministries.

GMOs are not authorised for commercialisation in any of the Central and Eastern European Countries (CEEC), except Romania where GM crops are commercially grown, and in the Czech Republic where one authorisation for the import and processing of Monsanto Roundup Ready soybeans has been issued. Ukraine was growing GM crops in 1999 but has not confirmed any areas grown with transgenic crops for 2000 (James 2000).

From a regulatory point of view, CEEC are seeking to get in line with EU legislation. They are working to put in place legal framework for biotechnology to comply with the requirement of the EU Directives implemented with the assistance of international organisations as the Organisation for Economic Co-operation and Development (OECD) and the United Nation Environment Programme. Since 1999, each country of Central and Eastern Europe is assisted, in the context of the project “Implementation of national Biosafety frameworks in pre-accession countries of Central and Eastern Europe”, to establish a workable and transparent national Biosafety framework. Each country is encouraged to establish a regulatory framework with administrative systems, systems and methodologies for risk assessment and management and mechanisms for public communication, comparable to those of the EU.

Bulgaria

In 1991 and 1993, Bulgaria conducted several field trials with GM tobacco (local variety) modified to be virus and bacteria resistant. The field trials stopped in 1998 after recommendations from the major tobacco buyers to avoid testing GM tobacco in Bulgaria. In 1995, field trials with GM alfalfa were conducted to test the development of a marker system (kanamycin resistance). These three field trials were requested by the Institute of Genetic Engineering (BINAS 2002). In 1998, the council for biosafety of GM higher plants granted permission for field trials in order to cover local diversity of soil and climatic conditions, fauna and flora. The field trials were extended up to 12,000 hectares in 1999, 20,000 hectares in 2000 and 19,000 hectares in 2001. In 2002, the total surface with GM plants (mainly corn) do not exceed 20,000 hectares (Atanassov 2002). Among the trials are GM maize (resistant to roundup Ready, or corn borer), GM potatoes (Superior New Leaf Bt resistant) and GM sunflowers (fungi resistant).

Notifiers are large companies, like Monsanto, Pioneer Hi-Bred International (now DuPont) and Syngenta Seeds, the company “GAB” and a research institute, the Institute of Genetic Engineering. The traits tested in GM maize field trials are herbicide tolerant (Roundup Ready or Liberty), Bt resistant or a combination of herbicide and insect resistance. It should be noted that in the Pioneer’s 2000 seed catalogue, farmers had the possibility to buy several varieties of GM maize (LibertyLink maize, Maisgard Bt maize, combined Maisgard and LibertyLink maize hybrid) (ANPED 2002a).

R&D in plant biotechnology (laboratory phase) in Bulgaria is mainly performed on (i) tobacco, potato (local varieties) and sugar beet for agronomic traits (virus-resistant TSWV and BNYWV), (ii) tobacco for improved abiotic stress tolerance (increased production of osmoprotectant compounds proline, fructan and glycine betaine and expression of metalothionine (mMTF1) for heavy metal resistance, (iii) potatoes for enhanced nutritional value and pathogen resistance, (iv) tomato for higher content of beta-carotene, v) alfalfa for reduced lignin content and improved digestibility, vi) grape for cold resistance, virus resistance, bacteria resistance and tree growth regulation vii) ornamental flowers (carnation, dahlias, rose) for higher yields and disease resistance and viii) barley for herbicide tolerance (GMP 2002, Atanassov 2002).

Croatia

Between 1997 and 1999, field trials of GM maize hybrids were conducted in Croatia. GM maize was modified to be herbicide tolerant: LibertyLink (Aventis Crop Science), Roundup Ready maize (Monsanto) and Bt and gluphosinate tolerant maize (Pioneer). Several NGOs in Croatia have claimed the use of GM microorganisms to produce antibiotics and their release into the environment without any control. In November 1998, the Parliament recommended the government to introduce a moratorium on any release of GMOs. In June 2001, the Croatia government started drafting legislation to ban the production of GMOs and restricted imports of food containing GMOs until an international Biosafety Protocol is introduced. Croatia is now having a campaign "Croatia GM-free" and might become an exporter of GMO-free soybean seeds (ANPED 2002b).

Czech Republic

In the Czech Republic, Roundup Ready GM Soybean from Monsanto is approved for commercialisation for import and processing only (not for growing). Over the last three years, a number of small-scale field trials with GM plants were conducted in the Czech Republic (approved under the Variety Act national law) (ENV 2002). A total of 38 approvals for field trials were issued by the Ministry of Environment: 1 authorisation for field trial was given in 1997, 3 in 1998, 19 in 1999, 9 in 2000, 4 in 2001 and 2 in 2002. Since 2000, there is a clear decrease in the number of authorisations given. GM crops were tested for future variety registration, herbicide registration tests, experimental and breeding purposes. Field trials were conducted with GM herbicide tolerant sugar beet, maize, winter oilseed rape, wheat and insect-resistant (Bt) maize. Approvals for field trials were also given for GM flax, potatoes and plum tree virus-resistant for research purposes (Demnerova 2002).

Notifiers for field trials are mainly large companies: Monsanto (sugar beet Roundup Ready, maize Roundup Ready NK 603, Bt maize MON810), Aventis Crop Science (Liberty & male sterility winter oilseed rape, maize resistant to herbicide), Syngenta Seeds (Roundup Ready sugar beet), Liberty Pioneer Hi Bred (Bt maize, herbicide tolerant maize), KWS (sugar beet resistant to herbicide Liberty), Novum Seeds (oilseed rape resistant to herbicide Liberty), Force Limagrain (maize resistant to herbicide Liberty). The Institute for Plant Molecular Biology is responsible for the field trials on flax and the private company Agritec in collaboration with the Institute of Biology of the Czechoslovak Academy of Sciences carried out field trials on potatoes (ANPED 2002c).

R&D in laboratory phase focuses on the development of plants for scientific purposes (e. g. plant hormone activities in *Arabidopsis*, tobacco) and on modification of the characteristics of the plant: potatoes with reduced sweetening during storage, potatoes with higher regeneration ability, potatoes with increased resistance towards abiotic stress, health related compounds (vaccines against pappiloma adenovirus), barley and wheat with improved feeding qualities, ornamental plant species with changed morphological characters.

Basic research (not specified) is also conducted on local varieties of cauliflower, oilseed rape, flax and pea (Ovesna 2002).

Estonia

No field trial of GM plants has been allowed in Estonia so far.

Hungary

A database with GMO field trials conducted in Hungary is publicly available[41]. Over the last four years, Hungary has given a total of 69 authorisations for field trials, 14 authorisations were given in 1999, 22 in 2000, 24 in 2001 and 9 in 2002. Among these 69 authorisations, GM maize counted for 70 %, sugar beet 11.7 %, wheat 5.8 %, potatoes 5.8 % and tobacco 5.8 % of the trials. One field trial was conducted on turnip. The traits tested were herbicide tolerance (glufosinate, glyphosate), insect resistance (Bt or non specified), modification of gluten content and virus resistance.

The notifiers for field trials were mainly large companies: Pioneer Hi-Bred (herbicide tolerant maize, insect-resistant maize), Monsanto (insect-resistant maize, herbicide tolerant maize, herbicide tolerant sugar beet), Syngenta Seeds (herbicide tolerant maize, herbicide tolerant sugar beet, male sterility combined with herbicide tolerance in turnip), Aventis Crop Science (Bt-resistant maize, glyphosate tolerant sugar beet), KWS (glufosinate tolerant sugar beet). Public Research Institute and SMEs were involved in field trials with wheat (modified gluten content, glufosinate ammonium tolerant), potato and tobacco (virus resistant) and maize (insect resistant, glufosinate tolerant).

Hungarian institutes working in R&D projects in the laboratory phase in agrobiotechnology (laboratory work) are mainly involved in (i) tobacco to study light-regulated gene expression, (ii) alfalfa to study plant development control, (iii) wheat and maize with improved metal tolerance, (iv) several plants with coat protein-mediated virus resistance (v) potatoes pesticide resistant and (vi) basic research in mycotoxin-producing fungi in genus *Fusarium* (GMP 2002).

Poland

Over the last five years, a number of small-scale field trials with GM plants were conducted in Poland (ANPED 2002d). In 1997, authorisations were given for field trials on GM potatoes, corn and sugar beet, 10 to 20 authorisations were given in 1998, 10 in 1999 and 9 in 2000. Crops tested were maize, potatoes, winter oilseed rape, spring rape, sugar beet and fodder beet. In the list of field trials for 2000, the traits tested were mainly herbicide tolerance (sugar beet, maize) and virus resistance (potatoes). The notifiers for field trials were large companies: Monsanto (sugar beet Roundup Ready), Aventis Crop Science (winter oilseed rape resistant to herbicide ammonium glufosinate), Syngenta Seeds (sugar beet Roundup Ready), KWS (glufosinate tolerant sugar beet). One research institute, the Institute for Biochemistry and Molecular Biology, notified the field trial on GM potatoe. It should also be noted that in the mid 1990s, Poland tested a GM animal: a GM carp modified with human growth hormone genes to induce quicker growth.

Romania

In Romania, 2,000 hectares of commercial growing of GM soybean herbicide tolerant and 1,000 hectares of GM potatoes (virus or insect resistance) have been reported in 1999 (DG Agri 2000). In 1999, the Ministry of Agriculture gave approvals for field trials of GM soybean, potatoes, maize and sunflower seeds. Large companies involved in the field trials were Monsanto and Pioneer Hi-Bred. No more information on the traits has been made available.

Slovenia

No field trial of GM plants has been allowed in Slovenia.

41 http://www.biosafety.hu/databases.php3

Research and development in laboratory phase in plant biotechnology in Slovenia is performed on (i) virus-resistant plants, (ii) fungal-resistant potato, (iii) flax with modified deposition of lignin and cellulose, (iv) plants with improved nutritional quality for feed, (v) plants producing interesting pharmaceutical substances, (vi) alfalfa ovalbumine gene. Many research projects are conducted in laboratories to better understand the plant metabolism as the production of protein inhibitors in potato, plant growth regulators, their role in organogenesis and in plants' response to stress conditions, and the metabolism of reserve substances and their role in seed dormancy of conifers. Research are also conducted in the centre PLANTA, founded in collaboration with the pharmaceutical factory KRKA, Novo Mesto and the seed company Semenarna. They are involved in research activities on plant physiology, tissue culture (virus free) and plant virology for agricultural and pharmaceutical applications (GMP 2002).

Ukraine

Over the last years, Ukraine has given seven authorisations for field trials. The crops modified were GM oilseed rape, maize, sugar beet and potatoes. The modified traits were herbicide (Liberty Link) resistance and Bt resistance. The major notifiers were large companies: Aventis Crop Science (herbicide tolerant oilseed rape, herbicide tolerant sugar beet), Monsanto (Bt-resistant potato), Syngenta Seeds (Bt-resistant potato) and DeKalb (now monsanto) (herbicide tolerant maize) (BINAS 2002). Between 1997 and 1999, Ukraine conducted field trials on genetically modified Bt potatoes from Monsanto ("NewLeaf" potatoes) on an estimated surface of 1,000 hectares. The products of the field trials, 1,300 tons of GM Bt potatoes, were destroyed by crushing and composting after a decision of the Ministry of Health, in 1998, not authorised transgenic potatoes for human consumption in Ukraine (ANPED 2002e). At the end of 1999, Ukraine did not confirm any transgenic hectares for the year 2000 (James 2001).

Annex H: USA GMO field trials

The situation in the US is of particular relevance for the future pipeline of GMOs as this country is strongly engaged in using this new technology in agriculture. Therefore, the project team analysed the GMO field trials conducted under USDA regulations for the most important crops which might have relevance for imports to the EU. The respective data on GMO field trials are supplied by the Animal and Plant Health Inspection Service (APHIS) which is available on the Internet (APHIS 2002)[42].

With more than 9,100 field trials the United States were considerably more active in R&D on GMOs than the EU. Like in the EU, field trials with GM plants are concentrated among a small number of firms and a limited number of crops in the USA. Three companies (Monsanto, DuPont and Aventis Crop Science) accounted for 48 % of all trials and almost two third of the trials were carried out in maize, potato and soybean (Arundel 2002b). According to an analysis, 27.5 % of the US trials related to herbicide tolerance, 41.6 % to pest resistance, 19.2 % to output traits for food or industrial purpose and the remaining 11.7 % to other categories like markers, fertility and agronomic traits (Arundel 2002a). Among pest resistance 63 % related to insect resistance (mostly using the Bt gene), 21 % to virus resistance and around 12 % to fungi (Arundel 2002b). Around half of the industrial food quality traits were targeted to the modification of starch and sugar as well as proteins. Other important categories of output traits were modification of oils, fruit ripening and industrial purposes[43]. Concerning the development over time, it can be observed that herbicide tolerance had the dominant position with a proportion between 25 % and 30 % during the entire 1990s. Pest resistance traits also did not change their relevance significantly and had a share of around 40 % to 45 % of the total number of field trials. In contrast, there was a considerable decline in the share of field trials for food industrial purposes from around 30 % in 1995 to 17 % in 2001, while the share of technical agronomic field trials increased from 5 % in 1993 to 16 % in 2001 (Arundel 2002a). The decline in food industrial applications is mainly due to field trials for fruit ripening, since this research, in particular on tomatoes, has been completed in the USA.

In order to get more insight in the GM product pipeline in the USA, a more detailed analysis was carried out for the most important crops with relevance for US imports to Europe. An overview about the most relevant traits for maize, wheat, soybeans, oilseed rape, cotton and tobacco which have been used in US field trials from 1991 to 2002 is given in table H1.

Maize

The field trials in maize which is by far the most important GM crop in US field trials concentrated on insect resistance (39 %), herbicide tolerance (27 %) and modified ingredients (almost 13 %) (table H1). Compared to the EU, field trials with herbicide tolerant maize play a significantly lower role in the US, while on the other hand field trials with modified ingredients and markers have a higher relevance in the USA. In the last five years, herbicide tolerant maize has lost importance in US field trials in favour of insect resistance. The modification of specific ingredients (in particular starch and proteins) has not significantly changed its position. In addition, a few field trials related to substances interesting for pharmaceutical purposes emerged during this period.

Wheat

More than half of the field trials with transgenic wheat in the USA referred to herbicide tolerance.

42 The analysis of the APHIS database includes both notifications and applications. In addition, field trials which were denied or withdrawn are also included, since these trials will indicate the direction of research interests as well.

43 From the industrial purposes 50 % were pharmaceuticals, around 20 % industrial enzymes or polymers and around 16 % related to fibre inputs.

In addition, resistance against other pathogens (mainly viruses and fungi) as well as yield-influencing factors play a significant role in the US trials (table H1). Compared to the EU, the latter two traits have a higher relevance in the USA. During the last five years herbicide tolerance is by far the most important trait in US field trials with transgenic wheat. During this period protein modification as well as modification of yield-influencing factors gained increasing importance.

Soybeans

US field trials on soybeans which are often imported to the EU concentrated on herbicide tolerance, modification of specific ingredients (in particular proteins and fatty acids) and improvement of soybeans for animal feed purposes (table H1). Since 1997 herbicide tolerance significantly lost relevance in US field trials with soybeans, while animal feed improvement, enhancing the yield of the crop as well as insect resistance gained weight.

Oilseed rape

US field trials on transgenic oilseed rape showed almost similar targets like those of soybeans and concentrated on herbicide tolerance, modified ingredients (mainly modification of the fatty acid composition of rapeseed) and male sterility (table H1). Compared to the situation in the EU, herbicide tolerance and male sterility have a significantly lower relevance in the USA, while in particular modification of the fatty acid composition is a more important target of genetic modification of rapeseed in the USA. It seems noteworthy as well that the number of field trials with rapeseed significantly decreased in the last five years in the USA from around 50 in the year 1998 to only 8 trials in 2001.

Cotton and tobacco

Both in the USA and the EU, field trials on cotton concentrated on herbicide tolerance and insect resistance (table H1). There was no significant change in the relevance of these two dominating traits in the US during the last five years. US field trials on tobacco focused very much on resistance against other pathogens (in particular virus resistance), which had a much lower relevance in the corresponding EU trials. In addition, there was a broad range of other targets of genetic modification of tobacco both in the EU and the US (table H1), which again indicates that tobacco is often used as model plant in early stages of the development of a transgenic crop. Field trials on GM tobacco are also conducted to improve the tobacco variety or to modify its composition. In the USA the dominant traits in tobacco (virus resistance) lost relevance in the last five years, while on the other hand the number of field trials with output traits like removal of allergens or enhancement of health-related compounds has increased.

Molecular farming in USA

USA is already very active in the field of molecular farming as this emerging technology seems likely to have significant impact on basic research and the pharmaceutical, agricultural and biotechnology industries. Molecular farming is defined as the production of antibodies, biopharmaceuticals and edible vaccines in plants using genetic engineered modifications (Fischer et al. 1999). In June 2002 the FDA and USDA have released a draft document "*Guidance for industry drugs, biologics and medical devices derived from bioengineered plants for use in humans and animals*" (FDA 2002). In this document, they provide a set of points to consider to demonstrate the safety, effectiveness but also the environmental issues and the confinement measures adopted for products produced by molecular farming (e. g. host and source plants characterisation, environmental considerations, manufacturing and process-related considerations and pre-clinical considerations).

APHIS/BRS regulates the importation, interstate movement and release into the environment (field trials) of all GM plants for molecular farming. APHIS prohibits the commercial sale of GM plants for

Table H1: Distribution of different traits in US field trials with selected GM plants between 1991 and 2002

Traits	Maize	Wheat	Soybean	Oilseed rape	Cotton	Tobacco
Herbicide tolerance	27.4 %	56.0 %	46.3 %	33.5 %	41.7 %	8.2 %
Insect resistance	39.0 %	0.0 %	6.6 %	9.2 %	46.0 %	7.7 %
Resistance to other pathogens	3.7 %	21.6 %	6.7 %	1.9 %	0.5 %	43.2 %
Abiotic stress/yield	3.8 %	10.8 %	2.1 %	2.9 %	3.9 %	4.5 %
Male sterility	4.2 %	0.0 %	0.1 %	8.7 %	0.5 %	0.5 %
Modified ingredients/nutrients	12.6 %	7.7 %	23.2 %	35.4 %	1.7 %	13.2 %
Industrial use	0.6 %	1.9 %	8.8 %	3.9 %	3.5 %	0.9 %
Health	1.3 %	0.0 %	1.8 %	0.5 %	0.0 %	3.6 %
Other output traits	0.6 %	0.0 %	1.5 %	0.0 %	2.0 %	4.1 %
Marker/other traits	6.9 %	1.9 %	2.8 %	3.9 %	0.2 %	14.1 %
Number of traits	4,625	259	668	206	635	220

1) Several notifications have more than one notifier. In these cases the respective traits are calculated for each notifier. Therefore, the number of traits in this analysis is higher than in table F1.

Source: Analysis of Fraunhofer ISI based on APHIS 2002

molecular farming but allows some permits for commercialisation of products produced from GMO field trials[44]. In USA, between 1991 and June 2002, 198 permits/acknowledgements (corresponding to 315 out-doors field trials with average size of 2 hectares) have been issued by USDA on a case-by-case basis[45]. Interest has increased in the last three years with the majority of field trials carried out from 1999 to 2002 (Figure H1). Corn is by far the most popular crops used with more than two third of the field trials in molecular farming (Figure H2). Other crops modified for molecular farming include soybeans, rice, barley, wheat, canola and tobacco (GE Food Alert 2002). The main actors for requesting field trials are ProdiGene of College Station with 85 permits (43 % of the total permits) mainly for GM maize hybrids. Monsanto and Agracetus requested 44 permits for growing GM maize and soybeans, Applied Phytologics requested 13 permits exclusively in GM rice, CropTech requested 7 permits in GM tobacco and Large Scale Biology, with 10 permits, focused on viral-vectored tobacco (GE Food Alert 2002, Powledge 2001).

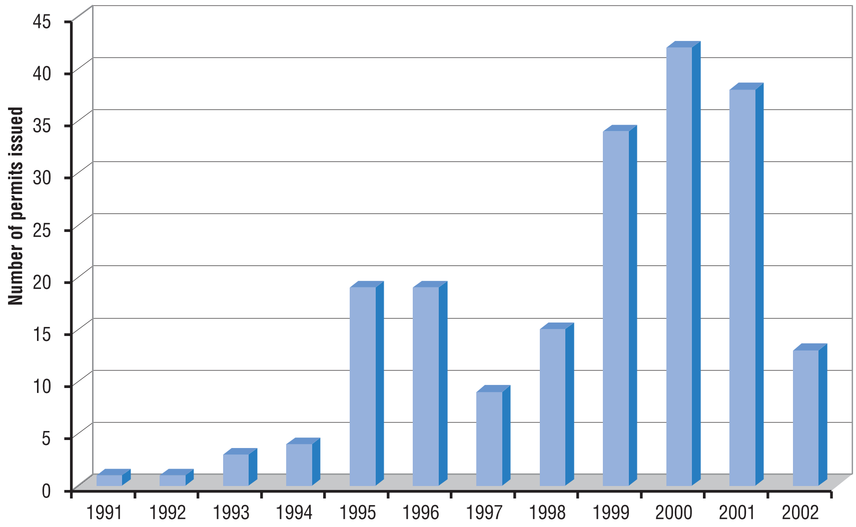
Despite the concerns raised on possible contamination of human food due to outcrossing of transgenic pollen from GMO field trials on molecular farming and on the lack of adequate regulatory framework in USA[46], commercialisation of GM plants for molecular farming is expected for the next 10 to 15 years. The “guidance for industry” document distributed for comments demonstrate the willingness of the US government to further development. Nevertheless, as in the rest of the pharmaceuticals industry, the high costs of bringing a drug through the approval process (at least 500 millions US$) may slow down the arrival of green pharmaceuticals which might not be expected before the next decade (Fischer et al. 2001)

44 In this context, ProdiGene marketed avidin and -glucuronidase produced by GM maize through Sigma Chemical Company, and Genencor International marketed an industrial enzymes produced by GM maize. ProdiGene already planned to market trypsin produced through GM maize.

45 Requirements for field trials detailed in the recent document from USDA “*Information of field testing of pharmaceutical plants in 2002*”. May 2002 http://www.aphis.usda.gov/ppq/biotech/

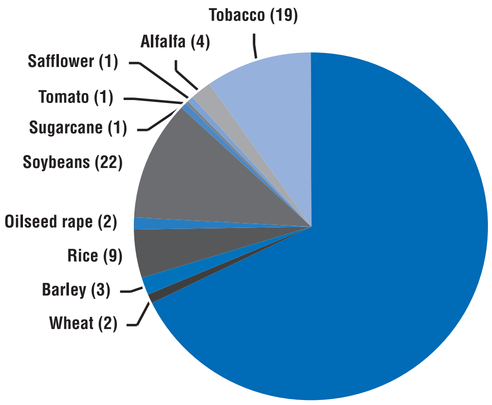
46 Genetic Engineering Food Alert recently expressed their concerns that USDA does not adequately evaluate and supervise field trials for production of pharmaceutical compounds. They recommend, for GM crops modified for molecular farming, to avoid the use of crops used in human food, to avoid outdoor releases and advocate the use of gene containment techniques (GE Food Alert 2002).

Figure H1: Permits issued by USDA for molecular farming field trials between 1991 and June 2002[47]



Source: Freeze 2002

Figure H2: Distribution of crops used for molecular farming field trials in USA (1991 to June 2002)



Total: 198 permits

Source: Freeze 2002

Stacked genes

The relevance of the stacked genes in US field trials with the selected GM plants was analysed on the basis of the APHIS data as well. As shown in table H2 the combination of two traits had a certain importance in US field trials during the last decade, while three or more traits were hardly modified in GM plants. Concerning the different plants, stacked genes had the highest importance in maize, oilseed rape and cotton while they were of minor importance in soybeans, tobacco and wheat (table H2). The most important trait combinations in the GM plants analysed are shown in table H3.

Due to a very low number of US field trials with stacked genes with tobacco and wheat, no trait combinations are filtered out for these crops. In maize the combination of herbicide and insect resistance was realised in almost 69 % of all US field trials, while the combination of herbicide tolerance with male sterility, modification of starch or protein metabolism was less frequent (table H3). In soybeans specific output traits (modification of fatty acid or protein metabolism) were combined with each other or herbicide tolerance. Almost 72 % of the US field trials with stacked genes in oilseed rape referred to herbicide tolerance and male sterility, while in cotton all of these trials were carried out with herbicide- and insect-resistant plants (table H3).

47 Data for 2002 were collected between January 2002 until June 2002

Table H2: *Relevance of stacked genes in US field trials with selected GM plants between 1991 and 2002*

Plant	Maize	Wheat	Soybean	Oilseed rape	Cotton	Tobacco
1 trait	85.0 %	98.8 %	96.3 %	88.0 %	91.8 %	98.1 %
2 traits	14.8 %	1.2 %	3.7 %	12.0 %	8.2 %	1.9 %
3 and more traits	0.2 %	0 %	0 %	0 %	0 %	0 %
Number of field trials with stacked genes	601	3	24	22	48	4
Total number of field trial notifications	4,018	256	644	184	587	212

[1)] Several notifications have more than one notifier. In these cases the respective traits are calculated for each notifier. Therefore, the number of traits in this analysis is higher than in table F1.

Source: Analysis of Fraunhofer ISI based on APHIS 2002

Table H3: *Important combinations of traits in US field trials with GM plants between 1991 and 2002*

Crop	Traits	No. of field trail notifications
Maize	Herbicide + insect resistance	414
	Herbicide tolerance + male sterility	78
	Herbicide tolerance + modification of starch metabolism	36
	Herbicide tolerance + modification of protein metabolism	26
Soybean	Herbicide + fungi resistance	7
	Herbicide tolerance + modification of protein metabolism	5
	Modification of fatty acid metabolism + modification of protein metabolism	11
Oilseed rape	Herbicide tolerance + male sterility	16
Cotton	Herbicide + insect resistance	48

Source: Analysis of Fraunhofer ISI based on APHIS 2002

Annex I: Large companies' pipeline lists

For most multinational agrochemical companies, strategic plans do involve the construction of new agro-biotechnology orientations that integrate a combination of both chemical and biotechnology development. Multinational agrochemical large companies did envisage a future with biotechnology that might be through two different ways: products based on biotechnology and using biotechnology to develop better products (Tait et al. 2001).

In this section, we are presenting the pipeline products for main large companies in biotechnology, based on information available in annual reports (not exhaustive list).

Monsanto (Monsanto 2001)

Monsanto is divided into Monsanto-AgChem, Monsanto-Seeds, Monsanto-Pharma, and their full-lines brands include Asgrow, DeKalb, Holdens, Cargill-Seeds International, Calgene, Monsoy, Agracetus, Holden's Foundation Seeds Inc., Plant Breeding International Cambridge Limited. In 2000, Monsanto and Pharmacia & Upjohn merge the two companies. The new company is called Pharmacia Corporation. The agricultural operations will retain under Monsanto name.

Global acreage of Monsanto biotech products has increased, from 2 million hectares in 1996 to 42 million hectares in 2001 and 48 million hectares in 2001. In 2001, Monsanto tends to develop higher-value products and focus its research and development activities on seeds and traits, using new technology (genomics) to increase the speed of R&D activities.

For products with agronomic traits (with on-farm productivity improvement), Monsanto plans to develop plants with: increase grain yield, better environment stress tolerance, insect control and Roundup Ready resistance. Products under field trials include enhanced Roundup Ready cotton, higher-yielding soybeans, Roundup Ready and insect-resistant soybeans. Products close to the market include Roundup Ready/YieldGard rootworm-resistant maize, Roundup Ready wheat, hybrid Roundup Ready oilseed rape. Two requests for authorisation in the USA are under way (under regulatory processes) with expected commercialisation by 2003: *YieldGard* rootworm-resistant maize and *Bollgard II* insect-resistant cotton. Monsanto plans to expand commercialisation of *Bollgard II* cotton in Australia by 2002 and in Mexico by 2003. Field trials on Roundup Ready wheat are carried out and request for commercialisation is expected between 2003 – 2005 (ENDS Daily 2002).

For products with output traits (with clear consumer benefits), Monsanto R&D focuses on enhancing plants compounds and plants with higher nutritional value, such as proteins, lipids and carbohydrates. They are also screening bioactive compounds in plants – substances with therapeutic value – that can be developed as dietary supplements or used to produce more nutritious foods. Among the crops and traits that are tested for probable interest are: improved oil and proteins content in soybeans for feed, improved energy maize III for feed and healthier oil for food uses. Products under advanced development (close to commercialisation) include high starch/ethanol maize and improved energy II maize for feed. Products under regulatory submission are *processor preferred* soybeans and improved energy maize I for feed.

Bayer (Bayer 2002)

Aventis CropScience was acquired by Bayer AG (Germany) in 2002. On June 4, 2002, the launch of the new Bayer CropScience, an independent operating subsidiary formed through the merger of Bayer's Crop Protection Business Group with Aventis CropScience SA, was announced (Bayer News 2002). The new company have three autonomous business line: Crop Protection, BioScience and Environmental Science. The section BioScience from Bayer CropScience will comprises the seed and biotechnology business (Bayer CropScience 2002).

Bayer CropScience considers biotechnology as an essential factor for the future and will benefit from Aventis CropScience's expertise. A focus in BioScience (section of Bayer CropScience) is currently to develop crop improvement technology covering both the genetic/seeds, the agronomic in-put traits and the out-put traits of plants used for food, feed as well as other industrial applications.

Aventis CropScience' flagship product is LibertyLink that combines broad spectrum herbicide Liberty and glufosinate resistance. Other products, that were under pipeline for Aventis CropScience and which expertise will be transmitted to the new Bayer CropScience include: Seed Link, a pollination control technology to achieve higher-yielding oilseed rape hybrids, FiberMax a GM cotton seed varieties with superior fiber quality, a high-yielding rice hybrids in India (Aventis 2002).

DuPont (DuPont 2002)

In 2002, Pioneer Hi-Bred International, Inc., has merged with Du Pont Company. The products listed below include products from both companies. Pioneer Hi-Bred International has already commercialising GM products, including insect-resistant corn and herbicide tolerant soybeans, corn and oilseed rape. Two GM maize (insect-resistant MON809 and mixed insect-herbicide tolerant T25 + MON810) are pending authorisation in the EU.

Products in the pipeline include soybeans with healthier oil composition, animal feed with improved nutritional quality (higher digestibility, decrease content of phosphorus in livestock manure), insect-resistant crops (protection against black cutworm, corn rootworm), higher quality grain (lower probability of mycotoxins development), corn with more efficient processing (higher level of oil), biotechnology-produced fiber alternatives identical to the silk of spiders. DuPont (through Pioneer Hi-Bred International activities) is also involved in the production of bio-based clothes and plastics (new processes that allow fully recyclable fibers, clothes and plastics from renewable resources), as well as sustainable fuels, lubricants and other industrial products developed through agriculture (Pioneer 2001).

DuPont, through Pioneer Hi-Bred International activities, has several products under research and development, with agronomic traits (abiotic stress condition) and also products with clear consumer benefit (oilseed with different oil composition, allergenicity, flavor). Among the products under development are (Pioneer 2001)

- plants with better environment stress tolerance (corn with improved tolerance to heat, draught, acid or saline soils),
- plants as factory (plants producing blocks for polymer, ingredients for plastics, paints, new protein as a based silk-like fibers, cosmetics and adhesives),
- corn with more efficient processing (higher level of starch and oil, better texture, longer shelf-life, improved thickeners and better water-holding capacity) and food quality (higher iron absorption),
- soybean with improved quality (increased fatty acid composition, higher levels of isoflavones, and reduced allergenicity (recent development of a new hypoallergenic soybean) (USDA 2002),
- grain for feed that improved meat-egg-milk quality (shelf life, nutritional composition, flavor, cholesterol content),
- papaya virus resistant (ringspot)

Seminis (Seminis 2002)

Seminis was established in 1994 and is the largest developer, grower and marketer of fruit and vegetable seeds in the world. Their full-lines brands include Asgrow Vegetable Seeds, Petoseed, Royal Sluis and Bruinsma, and they offer more than 4,000 distinct seed varieties representing nearly 60 species, under granted or pending 160 patents.

Seminis has a line of commercially available squash hybrids with virus production developed through biotechnology. Sales here account for less than 0.5 % of their annual revenue. Very few elements on the biotech strategy of the company are available from public information. Seminis is very careful and states that it is developing traits for the markets in North America and Europe mostly through traditional plant breeding. Nothing is indicated as regards developing countries. When reading the general business strategy, it could be assumed that the company would use the experience gained with virus-resistant squash and produce other virus-resistant species. The market for developed countries is primarily driven by a demand for foods with enhanced nutritive qualities and increased awareness of the health benefits of fruits and vegetables, and the rapidly growing fresh, pre-cut and processing industries have unique requirements for specialised varieties that offer improved quality, recovery rates and less spoilage, while increasing flavour, nutrition and convenience. Biotechnology has an important paper to play in the issue of output traits for the enhancement of nutritional value and it could be assumed that R&D would aim at producing this new transgene category.

Syngenta (Syngenta 2002)

Syngenta was formed in 2000 by the merger of two leading agribusiness companies, Novartis and Zeneca Agrochemicals. Among full-line brands are Ciba-Geigy, Sandoz. The company's strategy is to create, using new technologies and genomics, products with "*value for the grower through delivery of better yields and healthier, higher quality food for humans and feed for animals*". Syngenta is highly involved in the sequencing genomes of important crop cereals. Syngenta sequenced first the entire genome of rice (47,000 genes), had virtual map for cereals as maize, wheat and barley, and in 2001, had sequenced the genome of a fungal pathogen. This knowledge is used to assist the invention process for new chemicals and to improve traditional crop varieties as well as GM plants. This gives Syngenta a leader position in crop protection and crop genetic research. Currently, GM seeds products account for 2 % of Syngenta's sales.

For products with agronomic traits, Syngenta will maintain its leader position in biotechnology by continuing developing insect, fungi and herbicide tolerant crops, on GM wheat (resistant to Fusarium fungus and reduce level of mycotoxin in the grain) and GM barley. Research will continue on GM maize resistant to Western corn rootworm, resistant to insect and nematode with the identification of new genes encoding for novel proteins and GM oilseed rape with high-yield top cross hybrids. Concerning disease resistance, Syngenta will follow its efforts in the development of rice protected against rice blast, tomatoes with significant level of tolerance to late blight and vegetables and flowers (tomatoes, lettuce, melons, cucumbers) with viral and fungal disease resistance.

For products with output traits, advancement are on plants with higher oil or vitamin content or higher health beneficial dietary components, on the development of Vitamin A enhanced "golden rice", on GM maize with increasing starch processing and poultry feeding efficiencies. Syngenta is also involved in the development of new marker gene system, Positech™, as an efficient alternative to antibiotic marker genes.

Annex J: Results of the survey: R&D projects in laboratory phase

In this chapter an overview on GMOs in the R&D phase in the EU is given. Within this report the activities in research and development (R&D) for laboratory phase of GMOs include all projects which are still in laboratory or in greenhouse, i. e. no field trials or a deliberate release of the GMOs in the environment has been carried out with these GMOs so far.

Several assumptions have been considered for this analysis. The 658 institutions in Europe contacted for the survey might not be representative of the totality of actors in the field of GMO in Europe. For the analysis, they are considered as ana homogenous representative sample.

It is assumed that the weight of each actor group is the same. These assumptions could be further explored.

GMO under R&D in laboratory phase in the EU

GMO in laboratory phase in the EU are analysed on the basis of the written survey among research institutes and companies[48] as well as an intense literature review. In total 458 projects on GMOs have been mentioned by the interviewers among them 336 projects are in the R&D laboratory phase (laboratory and glasshouse). The projects include all organisms, with GM plants being predominant (80 %), GM microorganisms (14 %) and GM animals (6 %) being of minor importance. In the following an overview is given on R&D laboratory activities related to GM plants.

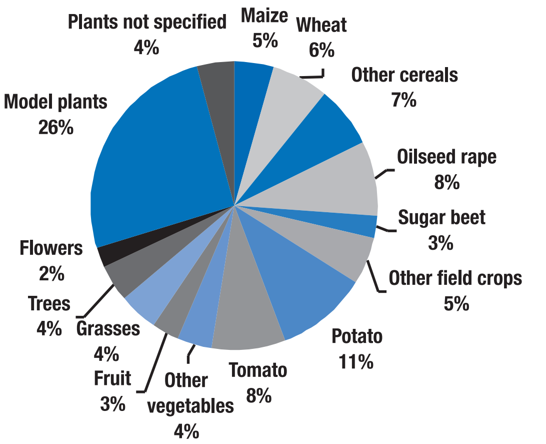
Type of crops

When analysing the total number of projects mentioned by companies and research institutions, we can observe a broad variety of more than 15 plants (figure J1). Four different groups have been identified for their relative importance. The first group which accounts for more than a quarter of all GM plants mentioned is model plants[49] (*Arabidopsis thaliana* and tobacco). The second important group is vegetable (including potatoes (11 %)) and tomatoes (8 %) which accounts for 23 % of the projects. It should be noticed that potatoes and tomatoes are partly used as model plants as well. The two other relevant groups are cereals (maize, wheat, other cereals (including barley, oat, rice, rye) and specific field crops (oilseed rape, sugar beet but also e. g. alfalfa, cotton, flax, fodder beet, soybean, sunflower) (details in annex B). Altogether, these four groups account for more than 80 % of all GM projects in the laboratory phase. Other crop categories like fruits, (wood) trees, grasses or flowers are of minor importance in the EU (figure J1). Still, it should be stressed that trees and grasses raise quite a lot of interest in R&D as the percentage of current projects with trees (4 %) and grasses (4 %) is comparable with the percentage of current projects with maize (5 %) or sugar beet (3 %). We will see in a later section (activities of different actor group) that research with GM grasses is mainly mentioned by SMEs and large companies while research involving GM trees is exclusively mentioned by universities and public research institutes. R&D at laboratory phase on GM trees implicates long-term investment that private sector does not seem to be ready to take currently.

48 For this purpose the interviewees were asked to characterise the currently running projects on GMOs with regard to organism, target of genetic modifications (trait) and phase of development (see question 2 of A3 in the annex A).

49 Model plants serve to investigate the biochemical and physiological mechanisms of certain plant traits and to develop and test new biotechnological tools and methods. Usually they are not intended for direct commercialisation. The most important model plant is *Arabidopsis thaliana* which genome has been totally sequenced in 2000, and is therefore often used to analyse the structure and function of genes in plants. Another important model plant is tobacco which is frequently used as a standard plant in the laboratory phase of the development of GMOs since most genetic engineering techniques are well established in tobacco. In some research project related to GMOs tomatoes or potatoes might serve as model plants as well. For the purpose of this project we limit the definition of model plants to *Arabidopsis thaliana* and tobacco since these two plants are most frequently used for this purpose.

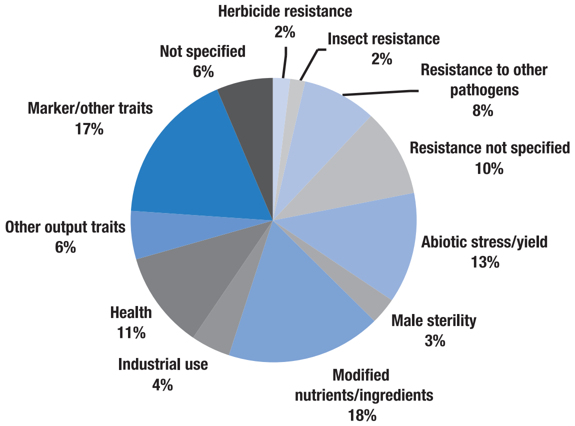
Figure J1: Distribution of GM plants under R&D in laboratory phase



Total: 269 projects

Source: Survey of Fraunhofer ISI 2002

Figure J2: Distribution of traits under R&D in laboratory phase



Total: 269 projects

Source: Survey of Fraunhofer ISI 2002

Type of traits

The traits mentioned by the interviewees in the survey have been classified by the project team according to the trait categories developed for the SNIF database and adopted for the purpose of this survey (annex B).

Input agronomic traits account for 38 % of all projects mentioned. Resistance against herbicides, insects and other plant pathogens are investigated in 21 % of all projects (figure J2). Around 13 % of all identified projects deal with abiotic stress or the improvement of yield characteristics of plants (figure J2). Some of the R&D projects in laboratory phase dealing with abiotic stress resistance (e. g. related to salinity) might be oriented to developing countries, while other projects dealing with improvement of yield characteristics of plants (nitrogen fixation, improving photosynthesis efficiency and modifying energy metabolism of plants) might be of higher interest for European agriculture.

Output traits[50] account for 39 % of all traits with half of the projects referring to modification of specific nutrients or ingredients (figure J2). Within this category main emphasis lies on the trait "enhanced nutritional value" with a share of 9 % of all projects related to GM plants and being basically realised in tomatoes, potatoes, carrots and rice as well as maize and grass for feed purposes. The output trait category "health-related compounds" plays an important role as well, since it accounts for 11 % of all projects related to GM plants in the laboratory phase (figure J2). These projects aim at the production of monoclonal antibodies, phytopharmacies, pharmaceutical proteins or (edible) vaccines. This high proportion of output traits in GMOs projects in R&D laboratory phase is an indication of the interest on the development of GM products with consumer benefits.

17 % of all projects are classified in the "marker/other traits" category. Most of these projects relate to basic research activities in GM plants (*Arabidopsis thaliana*, tobacco, tomatoes or potatoes) which include research on genetic modification methods, genetic markers as well as scientific studies on plant metabolism, plant growth and plant development. Therefore, this category includes projects in a very early phase of the development of a GMO.

Crop-trait combinations

The distribution of traits for the most important crops is shown in table J1 (and in more detail in table J2). The most important nine crops have been represented in this table, which correspond to 180 projects out of a total of 269.

50 Output traits include modified nutrients/ingredients, health-related ingredients, industrial use and other output traits.

Arabidopsis thaliana and tobacco are mainly modified for abiotic stress/yield, health-related compounds as well as basic research activities (table J1). This indicates again that such projects are still in an early stage of development – a finding which is supported by scientific literature as well. This relates in particular to the stabilisation of the water household of plants under abiotic stress conditions (like e. g. drought, salinity or cold temperatures) (DFG 2001, PEW 2001, Kempken & Kempken 2000, Hoshida et al. 2000). The modification of photosynthesis pathways, regulation of photorespiration as well as nitrogen fixation are important mechanisms to influence the yield capabilities of plants. The metabolic pathways of these mechanisms are very complex and mostly the molecular principles and structures are not yet totally understood (DFG 2001, Kempken & Kempken 2000, Hoffmann 1997), so that only in selected cases such mechanisms can be genetically modified in crops used for agricultural production.

Arabidopsis thaliana and tobacco play the dominant role in research projects in laboratory phase on health-related compounds as well (table J1). These projects aim at the production of monoclonal antibodies, phytopharmacies, pharmaceutical proteins or (edible) vaccines. A review of the relevant scientific literature reveals that the targets which are mentioned by the interviewees of the survey are in line with the global activities in this field (Daniell et al. 2001, De Kathen 2001). With respect to agricultural crops, production of pharmaceutical substances is planned in tobacco, potato, tomato, maize and rice worldwide (Daniell et al. 2001, De Kathen 2001, Düring 2001). With the exception of rice (which is of limited relevance for EU agriculture) laboratory research activities on health-related compounds are carried out in all of these plants in the EU as well (table J1).

A significant role is given to develop genetic modification methods and markers as well as to realise general research projects on plant metabolism, plant growth and plant development which are included in the trait category "markers/other traits" (table J1). Model plants like *Arabidopsis thaliana* and tobacco as well as wheat and barley play an important role in these projects (table J1). This observation underlines on the one hand the specific difficulties to establish genetic modification methods in these monocotyledonous plants, but on the other hand is triggered by the high importance of cereals for EU agriculture. Other important targets of laboratory research projects in cereals in the EU are herbicide tolerance, fungi resistance, enhancing the yield capabilities as well as modification of protein content (table J1).

The modification of specific ingredients or nutrients for nutrition purposes or industrial use plays a specific role in research projects in maize, oilseed rape, potatoes, tomatoes as well as specific vegetables (like carrots), rice and grasses. In maize research activities aim at modifying the protein content as well as the starch metabolism (often for industrial purposes). In oilseed rape main emphasis is put on modification of protein content (often for animal feeding purposes) as well as changing fatty acid profiles partly with respect to enhancement of nutritional value for use in human consumption. Research activities in potatoes mainly concern modification of the carbohydrate metabolism (e. g. modified starches, production of oligosaccharids) sometimes also for industrial purposes. Modification of the carbohydrate metabolism is also a target in research activities in sugar beets.

An overview on the scientific literature concerning modification of nutrients and ingredients for the improvement of product quality for food or feed purposes as well as for industrial use support the results obtained in our survey. On a global basis, maize, soybeans, potatoes and oilseed rape are major crops concerning genetic modification of specific nutrients or ingredients. In oilseed rape global research activities concentrate on changing fatty acid profiles both for food and non-food purposes as well as enhancing the production of specific aminoacids in this crop (Wenzel & Mohler 2001, Hoffmann 1997). In potatoes the modification

Table J1: Distribution of traits in most important GM crops in laboratory phase

Trait categories	Arabi-dopsis	Tobacco	Cereals[1]	Maize	Oilseed rape	Sugar beet	Potato	Tomato
Herbicide tolerance	0 %	0 %	7 %	8 %	0 %	0 %	0 %	10 %
Insect resistance	0 %	3 %	0 %	8 %	0 %	0 %	8 %	0 %
Resistance to other pathogens	6 %	0 %	11 %	0 %	5 %	71 %	15 %	5 %
Resistance not specified	3 %	7 %	25 %	17 %	18 %	0 %	15 %	10 %
Abiotic stress/yield	26 %	17 %	11 %	8 %	5 %	14 %	8 %	5 %
Male sterility	3 %	7 %	4 %	0 %	5 %	0 %	0 %	10 %
Modified ingredients/ nutrients	9 %	7 %	11 %	25 %	55 %	0 %	27 %	15 %
Industrial use	3 %	3 %	0 %	17 %	0 %	14 %	8 %	10 %
Health	14 %	37 %	4 %	8 %	5 %	0 %	8 %	15 %
Other output traits	6 %	3 %	7 %	0 %	0 %	0 %	0 %	10 %
Markers/other traits	31 %	17 %	21 %	8 %	9 %	0 %	12 %	10 %
Number of projects	35	30	28	12	22	7	26	20

1) Cereals include barley and wheat

Total: 180 projects

Source: Survey of Fraunhofer ISI 2002

of the carbohydrate metabolism is predominant, but emphasis is put on the enhancement of the total protein content as well (Hoffmann 1997). In maize quality improvements basically refer to the enhancement of aminoacids essential for feed purposes (Dingermann 1999, Krebbers et al. 1999, Dixon 1999, Hoffmann 1997) as well as modification of the carbohydrate metabolism. Work on the improvement of vitamin and mineral content in plants is mainly carried out in rice and tomatoes so far.

A literature survey for fruit, forest trees and flowers reveals that a broad range of species is covered in research projects in fruits with main emphasis put on resistance traits (e. g. against bacteria, fungi and viruses) and control of growth and ripening. Most of the laboratory research activities related to genetic modification of forest trees are carried out in poplar and aim at herbicide tolerance, tolerance to abiotic stress factors or development of resistances against pathogens. Global research activities on flowers are mostly dedicated to the modification of colour or form (B11 in the annex).

An overview on the most important trait-crop combinations of GMO projects in laboratory phase mentioned by the interviewees of the survey is given in table J3 and reveals the high diversity in research activities related to GM crops in the EU.

Stacked genes

The relevance of stacked genes in R&D activities in the laboratory phase related to GM crops in the EU cannot be analysed on the basis of the data collected within the survey since the interviewees did not mention specific information on trait combinations in the single crops.

Activities of different actor groups

Table J4 represents the distribution of plants per type of actors. The numbers are expressed as percentage of all projects mentioned. For example, maize is mentioned in 4.5 % of all the projects and among the projects mentioned by the different actor group, SMEs have 6,5 % of its projects on maize, large companies 14.7 %, public research

Table J2: Traits of main crops in R&D laboratory phase

Trait category	Traits	Arabidopsis	Tobacco	Barley	Wheat	Maize	Oilseed rape	Sugar beet	Potato	Tomato
Herbicide tolerance	Herbicide tolerance			2		1				2
Insect resistance	Insect resistance		1			1			2	
Resistance to other pathogens	Fungi resistance			1	1		1	1	1	
	Bacteria resistance								1	
	Nematode resistance	2						3	1	
	Virus resistance			1				1	1	1
Resistance (not specified)	Resistance (not specified)	1	2	3	4	2	4		4	2
Abiotic stress/yield	Resistance to abiotic stress	5	5	1	2		1		2	
	Yield influencing factors	4				1		1		1
Male sterility	Male sterility	1	2		1		1			2
Modified nutrients/ ingredients	Enhancement of nutritional value	1	1		1	2	4		2	3
	Fatty acid metabolism	1					5			
	Protein metabolism						3			
	Oligosaccharides metabolism	1	1			1			2	
	Starch metabolism				2				3	
Industrial use	Food processing					1			1	2
	Non-food applications							1	1	
	Enzyme production	1	1			1				
Health	Health-related compounds	5	11	1		1	1		2	3
Other output traits	Modification of colour/form				1					
	Modification of ripening	2	1		1					2
Marker/other traits	Marker	3		1	1					
	Other traits	8	5	1	3	1	2		3	2
	Total number of projects	35	30	11	17	12	22	7	26	20

Source: Survey of Fraunhofer ISI 2002

institutes 1.4 % and universities 2.1 %. By comparing the distribution per actor, it is possible to draw general trends of interest for laboratory research on GM plants.

Large companies concentrate their research activities on maize, wheat, oilseed rape, sugar beet, vegetables and grasses, while SMEs focus on oilseed rape, potatoes, grasses, other field crops and model plants (table J4). In contrast, universities and public research institutes carry out most of their research activities in *Arabidopsis thaliana* and tobacco indicating the basic research character of many GM-related laboratory R&D activities of these institutions. In addition, these publically financed institutions work on a broad range of different plants without such a strong focus than private companies (table J4).

Table J3: *Most important trait-crop combinations of GMOs under R&D in the laboratory phase*

Traits	Crops
Herbicide tolerance	Cereals
Insect resistance	Potato
Virus resistance	Sugar beet, tomato, melon, fruit trees
Fungi resistance	Cereals, oilseed rape
Nematode resistance	Potato, sugar beet
Abiotic stress/yield	*Arabidopsis*, tobacco, cereals, grasses, potato
Modification of protein content	Oilseed rape, maize, potato
Modification of fatty acids	Oilseed rape, soybean
Modification of starch metabolism	Potato, maize, sugar beet
Industrial use	Potato, maize
Modification of fruit ripening	Tomato
Modification of colour/form	Flowers
Health-related compounds	Tobacco, *arabidopsis*, potato, tomato

Source: Survey of Fraunhofer ISI 2002

Table J4: *Distribution of different crops per actor group in the R&D laboratory phase*

Plants	SME	Large company	University	Public research institute	All actors[1)]
Maize	6.5 %	14.7 %	2.1 %	1.4 %	4.5 %
Wheat	2.2 %	14.7 %	5.3 %	8.1 %	6.3 %
Other cereals	4.3 %	8.8 %	5.3 %	10.8 %	7.1 %
Oilseed rape	23.9 %	14.7 %	4.2 %	1.4 %	8.2 %
Sugar beet	0.0 %	14.7 %	2.1 %	0.0 %	2.6 %
Other field crops	10.9 %	2.9 %	3.2 %	5.4 %	5.2 %
Potato	15.2 %	0.0 %	7.4 %	9.5 %	10.4 %
Tomato	8.7 %	2.9 %	5.3 %	14.9 %	8.2 %
Other vegetables	0.0 %	11.8 %	6.3 %	1.4 %	4.1 %
Fruit	0.0 %	0.0 %	1.1 %	6.8 %	3.0 %
Grasses	10.9 %	11.8 %	1.1 %	2.7 %	4.5 %
Trees	0.0 %	0.0 %	3.2 %	10.8 %	4.1 %
Flowers	0.0 %	2.9 %	2.1 %	4.1 %	2.2 %
Model plants	10.9 %	0.0 %	45.3 %	21.6 %	25.7 %
Plants not specified	6.5 %	0.0 %	6.3 %	1.4 %	4.1 %
Total number of projects	46	34	95	74	269

1) 20 projects are carried out by other actors than the ones listed in this table.

Source: Survey of Fraunhofer ISI 2002

Table J5: Distribution of different traits per actor groups in the R&D laboratory phase

Traits	SME	Large company	University	Public research institute	All Sectors
Herbicide tolerance	0.0 %	0.0 %	1.1 %	4.1 %	1.9 %
Insect resistance	0.0 %	2.9 %	1.1 %	2.7 %	1.9 %
Resistance to other pathogens	6.5 %	14.7 %	5.3 %	6.8 %	8.2 %
Resistance not specified	17.4 %	20.6 %	7.4 %	4.1 %	10.0 %
Abiotic stress/yield	6.5 %	8.8 %	12.6 %	20.3 %	12.6 %
Male sterility	2.2 %	0.0 %	3.2 %	5.4 %	3.0 %
Modified nutrients/ingredients	23.9 %	23.5 %	17.9 %	6.8 %	17.5 %
Industrial use	4.3 %	8.8 %	3.2 %	5.4 %	4.5 %
Health-related compounds	19.6 %	0.0 %	13.7 %	6.8 %	11.2 %
Other output traits	2.2 %	2.9 %	4.2 %	12.2 %	5.6 %
Marker/other traits	17.4 %	5.9 %	18.9 %	24.3 %	17.5 %
Traits not specified	0.0 %	11.8 %	11.6 %	1.4 %	6.3 %
Total number of projects	46	34	95	74	269

Source: Survey of Fraunhofer ISI 2002

Concerning genetically modified traits, large companies concentrate their research activities on resistance traits as well as modified ingredients (especially starch and fatty acid metabolism) (table J5). The latter field is also the target of SMEs which show additional interest in health-related compounds, research projects related to plant growth and development, while resistance traits have a lower relevance in SMEs compared to large companies. In contrast to the research profile of large companies, universities and public research institutes put certain emphasis on R&D activities on abiotic stress tolerance and yield improvement, GM plants which health-related compounds as well as basic studies on plant metabolism and improvement of genetic engineering techniques (table J5).

SMEs focus their laboratory research projects in oilseed rape and potatoes on the modification of specific ingredients (e. g. fatty acids, proteins) for nutrition purposes or industrial use as well as fungi resistance, while GM grasses are modified to develop abiotic stress factors. In the laboratory research projects of large companies resistance traits play an important role in all major plants (maize, wheat, oilseed rape, sugar beet), complemented by modification of starch metabolism in wheat as well as fatty acid metabolism in oilseed rape.

Research projects in laboratory phase of universities in *Arabidopsis thaliana* and tobacco mainly focus on abiotic stress factors, enhancing the yield capabilities of plants, improvement of genetic engineering methodologies and production of health-related compounds. The latter trait category is an important target in projects in tomatoes as well, while research projects in potatoes are often targeted to the modification of the starch or oligosaccharide metabolism.

Laboratory research projects of public research institutes in *Arabidopsis thaliana* and tobacco have the same focus like those of universities, while the laboratory R&D activities of public research insitutes in wheat are mainly targeted to improve genetic engineering tools – an aim which is also covered in projects with rice, potatoes and tomatoes. In potatoes research towards resistance against pathogens (e. g. insects, bacteria) plays a certain role at public research institutes as well, while projects in tomatoes mainly focus on improving the quality characteristics of this crop for food processing purposes.

Annex K: Review GMOs under R&D worldwide

Table K1: *Examples for modification of product quality in GM plants*

Quality feature or substance	Origin of the applied genes	Transgenic plants
Proteins		
Content enhancement of different amino acids (e. g. lysin, methionine, tryptophan)	Overproduction of feed-back insensitive bacterial genes for aspartokinase and dihydropicoline acid synthase (lysin) or overproduction of a heterologeous expressed mutant of a biosynthesis enzyme (tryptophan); overexpression of a methionine-rich, corn-own protein (methionine)	Oilseed rape, soybean, maize
Enhancement of the total protein content	Transformation of a non-allergenic albumin gene, expression in seeds	Potato, cassava
Lipides		
Reduction of fatty acid strings, enhancement of laurine acid content (margarine production)	Transfer of a gene for a specific acetyl-ACP thioesterase from Umbellularia californica	Oilseed rape
Modification of fatty acid profiles, enhancement of unsaturated fatty acids (oil acid 18:1, linoleic acid 18:2, linolenic acid 18:3)	Cloning of FAD 3 and FAD 2 gene. Coding for desaturases adding additional doublebindings (18:1, 18:2, 18:3)	Soybean, oilseed rape, sunflower
Carbohydrates		
Amylose- or amylopectin- free starch or saccharose accumulation	Antisense-repression of plant-own enzymes (e. g. GBSS, Q-enzyme, AGPase)	Potato, maize
Cyclodextrin expression	Transfer of the CTG gene from Klebsiella pneunmoniae	Potato
Increased starch accumulation (reduced fat adsorption during frying)	Transfer of the mutated AGPase gene (glgC16) from E. coli	Potato
Vitamins and minerals		
Formation of ß-carotene (enzymatic transformation of geranylg eranylpyrophosphate into ß-carotene)	Transfer of genes encoding key enzymes of the terpenoid metabolic pathway from narcissus or bacterium Erwinia uredovora	Rice
Enhancement of iron content (increase of ferritin) and –availability (reduction of phytic acid, increase of absorption by cysteine)	Transfer of a ferritin gene from Phaseolus vulgaris, a phytase gene from Aspergillus fumigatus; overexpression of the cysteine-rich metallothionein-like protein	Rice
Increased contents of carotenes (e. g. lycopine and lutein)	Transfer of a bacterial gene for changing phytoen into lycopine	Tomato

Source: Completed according to Hoffmann 1997

Table K2: *Examples for genetic modifications in fruit*

Aim	Genetic modification	Product	Status
Resistance to bacteria (fire blight)	Transfer of a gene for the lytic enzyme from "giant silk moth"	Apple, pear	Field trials
Resistance to insect pests (coddling moth/apple cutworm)	Transfer of a Bt gene (apple) Transfer of lectin genes from snowdrop (goilseed rapefruit)	Apple, goilseed rapefruit	Greenhouses and limited field trials
Resistance to viruses			
plum pox virus, (transmitted by aphids)	Transformation with the gene of the virus coat protein	Pear, banana, goilseed rapefruit, melon	Laboratory, field trials
		Stone fruit (plum, peach, nectarine, apricot, cherry)	Field trials
Papaya ringspot virus	Transfer of the coat protein gene of the disease-causing virus	Papaya	Market introduction
Resistance to fungi	Mostly by transfer of genes for cell wall decomposing substances like chitinase or lysozyme	Apple, pear, strawberry, kiwi	Field trials
Control of the flowering period in order to attain that all fruits are ripe at the same time	Temperature-sensitive pineapple genes, which control flowering, shall be changed respectively	Pineapple, strawberry	Development
Control of the ripening process	Blocking of a gene, which causes the decomposition of cell walls by an enzyme	Raspberry	Field trials
Delay in ripening	Suppression of ethylene production	Pineapple, pear, strawberry, kiwi, mango, plum, melon	Development
Prevention of browning	Blocking of polyphenoloxidase genes	Banana	Laboraroty, greenhouse
Shortening of the juvenile phase	Expression of the genes LFY and AP1 from arabidopsis thaliana under control of CaMV 35S promoter	Citrus fruit	Field trials

Sources: PEW 2001, Transgen 2001a

Table K3: *Examples of GM plants for industrial use*

Quality feature or substance	Origin of the applied genes	Usage	Transgenic plants
Proteins			
Expression of enzymes like -amylase, phytase, xylanase	Genes from bacillus lichniformis (-amylase), aspergillus niger (phytase), clostridium thermocellum (xylanase)	Food industry	Tobacco, alfalfa
Lipides			
Desaturation of fatty acids	Antisense-repression of plant-derived genes or genes from umbelliferae for expression of petroselin acid	Polymer production, detergents	Oilseed rape
Extension of fatty acid strings	Transfer of the LPAAT-gene from limanthes douglasii (increase of eruca acid content)	Lubricants, solvents, softener and others	Oilseed rape
Modified models of fatty acids(increase of lauric acid content)	Transfer of the gene for a specific acety-ACP-thioesterase from umbellularia californica	Detergents	Oilseed rape
Carbohydrates			
Amylose- or amylopectine-free starch or sucrose accumulation	Antisense-repression of plant enzymes (e. g. GBSS, Q-enzyme, AGP)	Adhesive, paper (amylopectin) films (amylose)	Potato, maize
Fructans	Transfer of CTG-genes from klebsiella pneunmoniae		Potato
Synthetic Polymers			
Accumulation of polyhydroxy butyric acid (PHB)	Transfer of genes for enzyme 3-ketothiolase, acetoacetyl-CoA reductase, PHA synthasis from ralstonia eutropha	polymeres which can be decomposed biologically	Arabidopsis thaliana, oilseed rape, soybean
Accumulation of Polyhydroxybutyrate-covalerate co-polymer (PHB/V)	Transfer of 4 genes (ilvA466, BktB, phbB, phbC) from e. coli and ralstonia eutropha	polymeres which can be decomposed biologically	Arabidopsis thaliana, oilseed rape
Protein-based polymer (PBP)		similar elastin	

Source: Completed according to Hoffmann 1997

Table K4: Examples for research activities related to genetic modification of forest trees

Breeding aim	Type	Genetic modification/ transferred genes
Control of development		
Improved taking roots of cuttings or in-vitro shoots	Juglans nigra x Juglans regia (walnut hybrid)	Inhibition of chalcone synthase activity
Generation of sterility in order to prevent spreading of foreign gene	Populus spp. (poplar types); Liquidambar styraciflua (ambergris); Pinus taeda (pine)	mutated homeotic gene of bloom building
Enhanced growing	Populus tremula x Polulus alba	Overexpression of a glutamate synthase gene fom Pinus (umbrella pine?)
Improving of product quality		
Enhancement of cellulose synthesis; Reduction or/and modification of lignin composition	Populus spp. Picea glauca, Picea abies Eukalyptus spp.	Genes for coniferin-specific -glucosidase and 4-coumarat-CoA-ligase
Development of resistances to pathogens and insect pests		
Resistance to insect pests	Populus spp. (poplar types and hybrids); Liquidamber styraciflua (ambergris); Larix decidua (European larch)	Genes for insecticided bacillus-thuringiensis proteins and proteinase inhibitors
Resistance to bacteria in order to prevent root collar tumours	Populus seiboldii x Populus grandidenta (poplar hybrid)	Antisense onco-genes from agrobacterium tumefaciens
Resistance to fungi	Populus-hybrids; Ulmus spp. (elm types); Castanea sativa (European chestnut)	Chitinase genes; -1,3-Glucanase genes
Resistance to herbicides		
Resistance to total herbicides like glyphosphate, phosphinotricin, chlorosulfuron	Populus spp. and hybrids	Genes of herbicide-decomposing enzymes most often with bacterial origin
Tolerance of abiotic stress factors		
Tolerance of oxidative stress	Populus spp. (poplar types)	Glutathione reductase gene (gor) or glutathione synthetase gene (gsh II)
Tolerance of drought stress	Populus tremula (aspen tree) Pinus halepensi (aleppo pine)	Genes for water stress-induced proteins
Tolerance of quicksilver	Liriodendron tulipifera (tulip tree)	Hg2+ -reductase gene merA

Sources: Zoglauer et al. 2000, Foyer et al. 1995

Table K5: Examples for transgenic plants with modified bloom colour

Plant	Colour	Genetic modification	New colour
Chrysanthemum	pink	Chalcon synthase	white
Gerbera	red	Antisense-chalcone synthase; Dihydroflavonol-4-reductase	pink
Carnation	pink	Chalcon synthase	pale pink
	white	Flavonone-3',5'-hydroxylase	blue
	red	Antisense- flavonone-3-hydroxylase	white
Petunia	violet	Antisense- chalcon synthase	white
	white	Dihydroflavonol-4-reductase	salmon pink

Source: Kempken & Kempken 2000

Table K6: Examples for the production of pharmaceutical substances in GM plants

Product	Application (cause/pathogen)	Transgenic plant
Pharmaceutical proteins		
Human serum albumin	Blood protein	Potato, tobacco
Human haemoglobin , ß	Blood substitute, emergency medicine	Tobacco
Human -1-antitrypsin	Cystic fibrosis, diseases of the liver	Rice
Human encephalin	Neurotransmitter for pain control	Arabidopsis thaliana
Human hirudin	Thrombin inhibition	Canola
Human somatotropin	Dwarfism, Tuner Syndrome	Tobacco
Glucocerebrosidase	Morbus Gaucher	Tobacco
pEGF	Epidermal growing factor in pigs (pEGF)	Tobacco
Human lactoferrin	Improvement of iron availability	Potato, tomato, rice
Vaccines (human)		
Cholera toxin B	Cholera (vibrio cholerae)	Potato
Hepatitis B – surface antigene	Hepatitis B (hepatitis B virus)	Tobacco, potato, lupine
Norwalk virus capsid protein	Diarrhoea (Norwalk virus)	Potato, tobacco
Glykoprotein	Rabies (rabies virus)	Tomato, tobacco, spinach
Glykoprotein B	Cytomegalic disease (cytomegalovirus)	Tobacco
Vaccines (animal)		
VP 1 FMDV	Food and mouth disease (FMD-Virus)	Alfalfa, arabidopsis thaliana
Glykoprotein S	Diarrhoea in piglets (transmissible gastroenteritis corona virus)	Maize, tobacco
VP 60 HDV	Haemorrhagig fever in rabbits (haemorrhagic disease virus, HDV)	Potatoes
Antibodies		
Guy's 13 MAK, secreted	Caries (streptococcus mutans)	Tobacco
MAK: Anti-HSV (IgG)	Herpes simplex (herpes simplex virus 1 und 2)	Maize, soybean
Chimeric antibody	Cancer treatment (carcinoembryogenic antigen)	Rice
human scFv	Cancer treatment (carcinoembryogenic antigen)	Rice, wheat

Sources: Daniell et al. 2001, de Kathen 2001

Table K7: Pharmaceutical substances from genetically modified animals in development and in clinical testing[1)]

Human protein	Planned application in diseases	Enterprise	Reached status in development
MDX-CD4-mAB (monoclonal antibody against CD 4)	Rheumatoid arthritis	Medarex	Phase I
ABX-IL8 mAB (monoclonal antibody against interleukin 8)	Psoriasis, rheumatoid arthritis	Abgenix	Phase I/II phase II
α-1-antitrypsin	Cystic fibrosis, emphysema, acute respiratory distress syndrome (RDS)	PPL Therapeutics	Phase II phase I research status
α-glucosidase	Pompe's disease (cardiac glycogen storage)		Phase II (project given up)
Antithrombin III	Transplantation in the area of the coronary vessels	Genzyme Transgenics	Phase III
ABX-EGF mAB (monoclonal antibody against epidermal growth factor)	EGF-depending types of cancer	Abgenix	Preclinical
ABX-RB2 mAB (monklonaler antibody against RB2)	Autoimmune diseases, transplant rejection	Abgenix	Preclinical preclinical
Bite salt stimulated lipase	Cystic fibrosis	PPL Therapeutics	Preclinical
C-1-esterase inhibitor	Cystic fibrosis	Pharming	Preclinical
Collagen typ I	Tissue repairing	Pharming	Preclinical
Collagen typ II	Rheumatoid arthritis	Pharming	Preclinical
Extra cellular superoxid dismutase	Reperfusion injury, acute respiratory distress syndrome (RDS)	PPL Therapeutics	Preclinical
Factor VIII	Haemophilia B	PPL Therapeutics	Preclinical
Factor IX	Haemophilia B	PPL Therapeutics, Pharming	Preclinical
Fibrinogen	Tissue adhesive for trauma and operations	PPL Therapeutics, Pharming	Preclinical
Lactoferrin	Gastro-intestinal protection	Pharming	Preclinical
Protein C	Prevention of deep phlebothromboses	PPL Therapeutics	Preclinical
Calcitonin (from salmon)	Osteoporosis	PPL Therapeutics	Preclinical
α-1-proteinase inhibitor	hereditary lack of α-1-proteinase inhibitor	Genzyme Transgenics	Research status
D2E7 antibody	Arthritis	Genzyme Transgenics	Research status
CTKA41G antibody	Psoriasis, rheumatoid arthritis	Genzyme Transgenics	Research status
PRO 542 antibody	HIV/AIDS	Genzyme Transgenics	Research status
Antegren antibody	Neurological diseases	Genzyme Transgenics	Research status
β-interferon	Multiple sclerosis	Genzyme Transgenics	Research status
Collagen	Biological glue	PPL Therapeutics	Research status
Glucagon-similar peptide 1	Typ-2 diabetes	PPL Therapeutics	Research status
Glutamine acid decarboxylase	Typ-1 diabetes	Genzyme Transgenics	Research status
Human growth factor	Growing deficiency	Genzyme Transgenics	Research status
Human serum albumin	Plasma substitute	Genzyme Transgenics, PPL Therapeutics	Research status
Insulin	Typ-1 diabetes	Genzyme Transgenics	Research status
Interferon alpha	Cancer	Genzyme Transgenics	Research status
MSP-1 (malaria vaccine)	Malaria	Genzyme Transgenics	Research status
Tissue plasminogen activator (tPA)	Heart attack and pulmonary embolism	Genzyme Transgenics	Research status

1) If there are no other remarks, the transferred gene is from human.

Source: Das 2001

Annex L: Results of the survey: constraints for commercialisation

Within the EU only limited knowledge was available concerning the importance of influential factors which shape the decision of research institutions or companies, whether to develop a GMO up to the commercialisation status or whether to stop the project in an earlier phase. Therefore, this aspect was covered in the survey among companies and research institutions in two ways. In a first step the factual behaviour of the institutions in the past was checked and asked, whether the institution has cancelled R&D projects[51] aimed to genetically modify plants, animals or microorganisms in the last four years as well as for the main reasons for this decision[52]. In a second step the interviewees were asked to assess important factors which influence the potential commercialisation of GMOs in the EU in the coming five to ten years[53].

Cancelling of R&D projects on GMOs per actor group

As outlined in table L1 almost 39 % of the responding institutions have cancelled at least one R&D projects related to GMOs in the last four years. This results does not mean that the institutions are not working anymore in this field but that they have cancelled at least one project within the last four years There are significant differences between commercial companies and research institutions in this respect. While less than one quarter of the universities or public research institutes have

Table L1: Cancelling of R&D projects related to GMOs in the last four years

Institution	Number of respondents	GMO projects cancelled	
		Yes	No
SME	33[1)]	54.5 %	45.5 %
Large company	28	67.5 %	32.5 %
University institutes	44	25.0 %	75.0 %
Public research institutes	37[2)]	21.6 %	75.1 %
Total	165[3)]	38.8 %	60.6 %

1) 35 SMEs answered the survey but 2 SMEs did not answered the related question
2) One respondent answered "Don't know"
3) Other institutions are included, 3 questionnaires without an answer to this question.

Source: Survey of Fraunhofer ISI 2002

51 See question 3.1 of the questionnaire (in the annex).

52 See question 3.2 of the questionnaire (in the annex). The interviewees were asked to select up to five reasons for cancelling R&D projects on GMOs out of the following list: Not feasible from a scientific/technical point of view / The target could not be achieved within the scheduled duration of the project / High costs of the projects / Modification of the strategy of the institution / Limited financial resources / Lack of experienced staff / Appropriate (cooperation) partnership is missing / Problems with intellectual property rights / Unclear or high requirements for safety testing of products / Duration of the notification process / Unclear legal situation in the EU / Low acceptance of users/consumers of GM products / Uncertainties about future market situation / Ethical concerns / Other reasons

53 See question 5 of the questionnaire (in the annex). The interviewees were asked to assess the relevance of the constraints for commercialisation in the following areas: Public R&D infrastructure / Technology transfer mechanisms / Financing / Personnel (availability, skills etc.) / Intellectual property rights / Practical handling of regulation processes / Legal situation / Market opportunities / Industry structure / Acceptance of consumers/users / Ethical considerations / Other fields.

cancelled GMO projects, more than half of the SMEs and two third of the large companies reported such activities (table L1). Public research institutes have difficulties to find funding for starting a new project but when funds have been acquired, most of them conduct the research and do not have tendency to cancel a project (only 23 % have cancelled projects). On the other hand, the private sector needs more rapid results and revenue return to maintain their activities (61 % have cancelled projects).

In addition, a relatively high importance was given to financing and cost aspects as well as the feasibility of the planned R&D projects, while intellectual property right issues, an appropriate co-operation partner or partnership as well as experienced staff was only for a small group of respondents a reason for cancelling R&D laboratory projects related to GMOs (figure L1). No institution mentioned ethical concerns in this respect (figure L1).

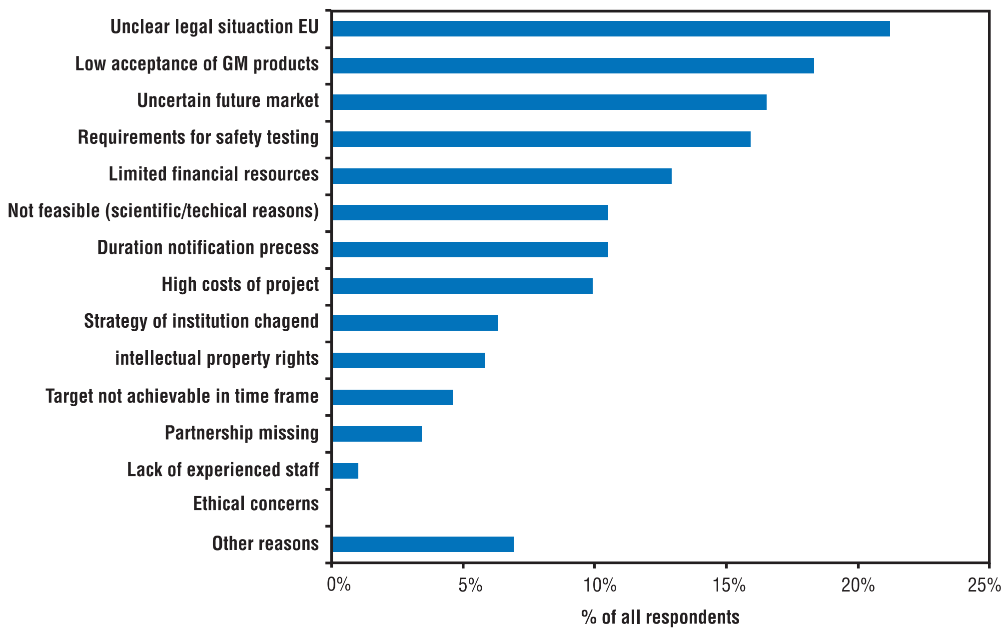
Reasons for cancelling R&D projects on GMOs

A broad range of different reasons was mentioned by the respondents for cancelling R&D projects related to GMOs in the agricultural field. The highest importance was given to the regulatory field (e. g. unclear legal situation in the EU, unclear or high requirements for safety testing of products), and the uncertain market situation due to low consumer and user acceptance of GM products (figure L1). Between 16 % and 21 % of all respondents marked these two aspects.

Reasons for cancelling R&D projects on GMOs by actor groups

There are significant differences in the underlying motives for cancelling R&D projects between commercial companies on the one hand and research institutions on the other. Both university institutes and public research institutes highlighted limited financial resources as main reason in this respect (table L2). All the other reasons were relatively scattered among research institutions without giving a totally clear picture. While universities put some emphasis on the

Figure L1: Reasons for cancelling R&D projects related to GMOs



Total: 164 respondents

Source: Survey of Fraunhofer ISI 2002

unclear legal situation and high requirements for safety testing of products as well as technical or scientific feasibility of the planned projects, public research institutions underlined the uncertain market situation and low consumer acceptance of GM products (table L2). The assessment of the different reasons for cancelling GMO projects goes in line with their major activities, since universities and public research institutes have a strong focus on projects in the laboratory phase. Therefore, most of them are not directly affected by all factors that deal with the notification and market approval process of GMOs as well as the market of such products, while on the other hand acquisition of research funds is one of the most important targets of such institutions in order to continue already running projects or to start new ones.

In contrast to research institutions, a higher number and broader set of influential factors were mentioned by commercial companies as reasons for cancelling projects related to GMOs (table L2). Both SMEs and large companies put a focus on the unclear legal situation in the EU as well as the handling of existing regulations (e. g. unclear or high requirements for safety testing of products, duration of the notification process) as well as market-related issues, like e. g. uncertainties about the future market situation as well as low consumer acceptance

Table L2: Assessment of reasons for cancelling GMO projects by different actors

	SME	Large company	University institute	Public research institute
Total number of institutions	33	28	44	37
Number of institutions which cancelled GMO projects	18	19	11	8
Total number of reasons[1)]	80	85	29	23
Average number of reasons per institution	4.4	4.5	2.6	3.1
Reasons for cancelling projects related to GMOs				
Not feasible from a scientific/ technical point of view	5.0 %	9.4 %	13.8 %	8.0 %
The target could not be achieved within the scheduled duration of the project	2.5 %	3.5 %	3.4 %	8.0 %
High costs of the projects	10.0 %	8.2 %	3.4 %	4.0 %
Modification of the strategy of the institution	5.0 %	5.9 %	3.4 %	4.0 %
Limited financial resources	6.3 %	2.4 %	24.1 %	24.0 %
Lack of experienced staff	1.3 %	0.0 %	0.0 %	4.0 %
Appropriate (co-operation) partnership is missing	2.5 %	1.2 %	3.4 %	8.0 %
Problems with intellectual property rights	7.5 %	2.4 %	3.4 %	4.0 %
Unclear or high requirements for safety testing of products	10.0 %	11.8 %	13.8 %	4.0 %
Duration of the notification process	7.5 %	9.4 %	0.0 %	0.0 %
Unclear legal situation in the EU	17.5 %	12.9 %	13.8 %	4.0 %
Low acceptance of users/consumers of GM products	11.3 %	12.9 %	6.9 %	12.0 %
Uncertainties about future market situation	10.0 %	14.1 %	6.9 %	8.0 %
Other reasons	3.8 %	5.9 %	3.4 %	8.0 %
Total	100 %	100 %	100 %	100 %

1) Multiple answers (up to 5) were possible in this question.

Total: 56 respondents

Source: Survey of Fraunhofer ISI 2002

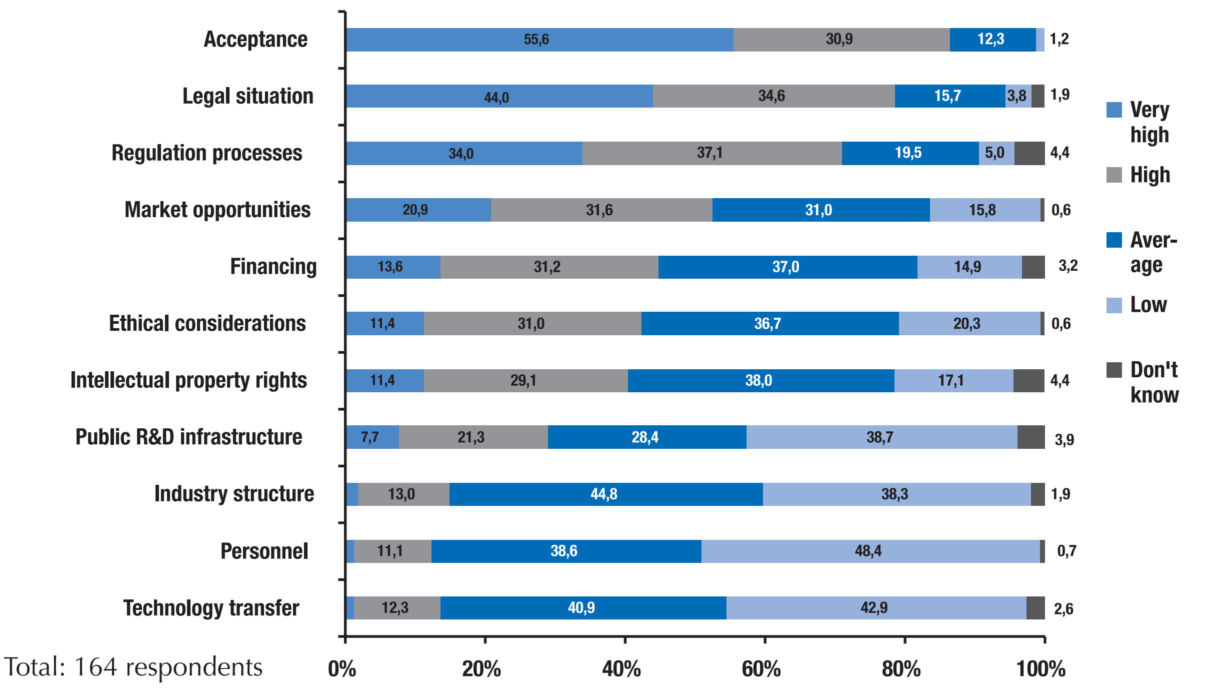
(table L2). In addition, the companies complained about the high costs of GMO projects, while financing of the activities seems not to be a major problem.

Constraints for potential commercialisation of GMOs in the EU

In addition to the behaviour of the institutions in recent years, the interviewees were asked to assess the constraints for potential commercialisation of GMOs in the EU in the coming five to ten years. The big majority of the respondents identified low consumer acceptance of GM products, the unclear legal situation in the EU and the practical handling of the regulation processes as major constraints for future commercialisation of GMOs in the EU (figure L2). Market opportunities, financing, ethical concerns and intellectual property rights followed in the constraint list created by the respondents, but those factors was given significantly lower weight than consumer acceptance and the regulatory situation. In contrast, industry structure, availability of trained personnel as well as technology transfer mechanisms were not regarded as an important constraint for commercialisation of GMOs (figure L2). All in all, the estimations of the respondents about the future perspectives of GMOs underline their decisions and reasons for cancelling R&D projects related to GMOs in the last four years. Only ethical concerns were ranked higher related to the future estimations since they did not influence the cancelling of R&D projects at all.

In contrast to the reasons raised for cancelling R&D projects related to GMOs, only slight differences in the future assessment of the situation in the EU occurred between the different actor groups, i. e. all institutions active in the GMO area in the EU share a critical view, in particular related to the regulatory situation, consumer acceptance and market uncertainties, independently if the institution focuses on basic research or intents to launch GM products on the market. Compared to the other actor groups, SMEs gave slightly more weight to intellectual property rights and the unclear legal situation in the EU as major constraint, while large companies highlighted the uncertain market opportunities and the practical handling of the regulation processes. Both types of industrial companies did not regard the R&D infrastructure as a major constraint which was mainly emphasised by university institutes.

Figure L2: Constraints for commercialisation of GMOs in coming ten years



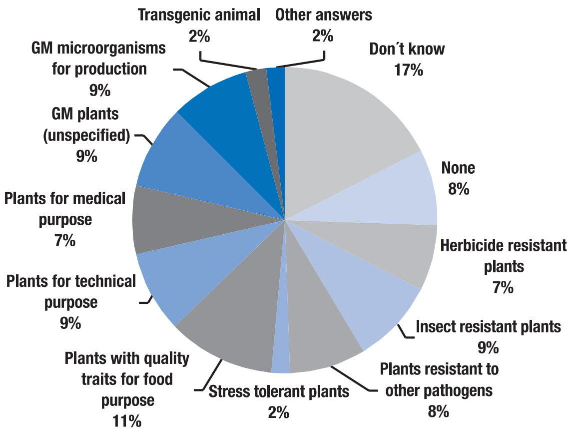
Source: Survey of Fraunhofer ISI 2002

Annex M: GMOs in the pipeline in Europe

Promising areas for commercialisation (based on survey results)

A high level of uncertainty about future perspectives of commercialisation of GM products in the EU emerged in the survey as well as during the expert interviews indicated by 17 % of the experts (in particular from SMEs) who were not able to answer such a question in the questionnaire (figure M1). Another 8 % of the participants of the survey answered that there will be no promising area for commercialisation of GMOs in the EU in the coming years. Taken these two groups together means that one quarter of the institutions active in GMO R&D has considerable doubts about the future commercial opportunities in this field in the EU.

Figure M1: Most promising areas of GMOs in the coming ten years



Source: Survey of Fraunhofer ISI 2002

In case there will be a commercially interesting area in agrobiotechnology in the EU in the coming years, the high majority of the respondents of the survey as well as the experts in the personal or telephone interviews agreed that this will relate to GM plants since only 2 % of the survey participants mentioned transgenic animals as an interesting field and another 9 % referred to GM microorganisms for production purposes (figure M1). Both the interviewed experts and the respondents of the survey expressed high expectations in output traits for different purposes in the coming ten years. In total 27 % of the survey participants mentioned such plants as commercially interesting areas thereby giving highest priority to output traits for human consumption (11 %), followed by technical (9 %) and medical purposes (7 %). Compared to their high importance in GMO field trials (and products already approved for commercialisation) in the EU, the survey participants expressed rather moderate expectations with regards to input and agronomic traits since only 24 % of them considered pathogen or herbicide tolerant plants as the most interesting area in the coming decade (figure M1). Only a small minority (2 %) assessed stress tolerant GM plants as a promising commercial future option. This is probably due to the limited relevance of such traits in the European climate.

The findings of the survey were underlined during the expert interviews. Input traits (in particular herbicide and/or insect-resistant crops like e. g. maize, soybeans, oilseed rape, cotton, sugar beets) were regarded as short-term option whose realisation will mainly depend on political decisions, the shaping of the respective regulations, their implementation and practical handling as well as acceptance of users (e. g. farmers), food processing companies, food retailers and the final consumer in the EU. Due to the current situation and environment for GMOs in the EU, several experts expressed considerable doubts if there will be a realistic possibility to introduce herbicide tolerant and/or insect-resistant crops in the European market in the near future.

Transgenic plants resistant against pathogens like viruses, fungi or nematodes as well as GM plants with modified output traits (with a few exceptions like e. g. the "Golden rice", maize/potatoes with modified starch content, oilseed rape with modified oil content) were mostly regarded as mid- to long-term options whose realisation will depend on a variety of influential factors. In particular for modification of complex metabolic pathways of plants (which are often necessary for the development of GMOs with "functional properties" aiming to prevent nutrition-related diseases in humans) or for the development of health-related compounds a time horizon from at least ten years until commercialisation was regarded as the minimum range from several experts. In addition, some experts expressed doubts concerning the expected high market potentials of such products.

Time horizons of GMOs in the EU

As outlined in the subsequent analyses, GMOs which most probable will request commercialisation in the coming decade in the EU mainly refer to GM plants. Therefore the detailed analysis of the future pipeline of GMOs will be concentrated on plants. In order to assess the probability of specific GMOs to request authorisation for commercialisation in the coming decade, it is important to know which GM plants with which traits are in the different phases of development. Therefore an overview is given in table M1 which intends to summarise the main findings of previous chapters concerning the GMOs under R&D in the EU. The following different groups of trait-crop combinations can be

Table M1: Overview on distribution of trait-crop combinations in the EU in different phases of development

Trait	R&D laboratory phase	Field trials	GMO commercialised or pending approval
	Main plants	***Main plants***	***Main plants***
Herbicide tolerance	Cereals[1]	Maize, oilseed rape, sugar beet, wheat, fodder beet[3] soybean[2], cotton[2], cereals[1,2]	Maize, oilseed rape, soybean, cotton, sugar beet, fodder beet, tobacco, chicory
Insect resistance	Potato	Maize, potato, cotton[2]	Maize, cotton
Resistance to other pathogens	Cereals[1], potato, sugar beet, oilseed rape, tobacco, fruits	Sugar beet, potato, tomato, oilseed rape, sunflower[2], melon[2], fruits[2]	-
Abiotic stress/yield	Arabidopsis, tobacco, cereals[1], grasses, potato	Tobacco	-
Male sterility		Oilseed rape, maize, chicory[2]	Oilseed rape, chicory
Modified ingredients/ nutrients	Oilseed rape, potato, maize, cereals[1], sugar beet, soybean, arabidopsis, tobacco	Potato, oilseed rape, maize[3], wheat[3]	Oilseed rape, soybean, potato
Industrial use	Potato, maize, tomato, tree	Potato, oilseed rape, tobacco[2], tomato[2], wood trees[2]	-
Health	Tobacco, arabidopsis, potato, tomato	Tobacco[3],	
maize[3]	-		
Other output traits	Arabidopsis, tomato, wheat, flowers	Tomato, flowers	Tomato, flowers
Marker	Cereals[1], arabidopsis, wood trees	Marigold[2], wood trees[2], cereals[1,2]	-

1) Cereals include wheat and barley.
2) High relevance in field trials of the respective crop, but limited number of field trials had been carried out in the respective crop in the EU.
3) Very limited number of trials.

Source: Fraunhofer ISI 2002

distinguished in the EU which have differing time horizons for further development and potential commercialisation.

GMOs in the EU in the coming five years

The first group consists of GMOs already approved for commercialisation in the EU or which are waiting for approval for commercialisation. In this group, the GMOs have already been submitted to evaluation for their commercial introduction in Europe. In addition, some GMOs are also included in this group of which field trials have been carried out in the last decade in order to form the basis for an application for market approval. In general, the technical problems for developing such products are solved (i. e. there are established standard techniques to genetically modify the plants) and it does not require too extensive efforts, long time and large amounts of money to introduce them in the process of requesting authorisation for commercialisation. These GMOs have the potential to be commercialised within the coming five years given the de facto moratorium in the EU will be released and there will be a market for such products. This result is in agreement with a recent review on GM biotechnology which expects input traits to continue to determine the overall picture in biotechnology in the next few years (Müller & Rödiger 2001). During this time-period it can be expected as well, that different genes will be combined in one plant to a higher extent.

The following GMOs are part of this group:

- Herbicide tolerant maize, oilseed rape, sugar beet, fodder beet, soybean, cotton, chicory
- Insect resistant maize, sweet maize, cotton, potato
- Fruit ripening in particular in tomatoes
- Modification of colour/form in flowers
- Modification of specific ingredients: fatty acid content in oilseed rape or soybeans; starch content in potatoes

GMOs in the EU in six to ten years

The second group of GMOs consists of trait-crop combinations whichcombinations, which are basically in the field trial phase, but no products have been approved or are pending approval in the EU so far. For these crops, the notifiers have not yet decided to start the process of commercialisation's request. Often scientific approaches have been developed which allow the genetic modification of the respective plants but these approaches need to be adopted or fine-tuned for specific purposes. In addition, it needs prove of these approaches in the environment of an open field as well as the development of a plant variety whichvariety that fulfils the expectations of the farmers/growers and subsequent members of the process chain. Therefore often a combination of field trials and additional research is characteristic for this group. Depending on the specific trait-crop combination most GMOs in this group will have a time horizon for potential commercialisation whichcommercialisation that might exceed five years. During this time-period stacked genes will be increasingly used in GM plants. The following GMOs are part of the second group:

- Herbicide tolerance in cereals like wheat, barley, rice
- Resistance against other pathogens:
  - virus resistance in sugar beet, potato, tomato, melon and fruit trees
  - fungi and virus resistance in potatoes and fruits
  - fungi resistance in wheat, oilseed rape and sunflower
- Modified ingredients/technical use:

- enhancement/modification of protein content in oilseed rape, maize, potato
- enhancement of erucic acid content in oilseed rape (for technical purposes)
- modification of fatty acid content in oilseed rape, soybean (for technical and nutritional purposes)
- modification of starch/oligosaccharides in maize, potato, sugar beet

GMOs in the EU after more than ten years

A third group of GMOs can be selected which are mainly in the R&D laboratory phase. In most of these projects scientists in research institutions (and to a lower extent in companies) have discovered interesting molecular characteristics, metabolic pathways or genes for a specific target and try to bring forward these discoveries in order to develop a commercially interesting product. Often these projects are carried out on model plants[54] which have either a totally sequenced genome or established techniques for genetic modification. In some cases preliminary field trials are carried out as well demonstrating the basic principle and effects on the environment. Since the targets of these projects generally require the modification of complex metabolic pathways of plants, most of them will have a rather long-term time horizon which might exceed the ten years period according to estimations given by experts in the interviews[55]. Müller & Rödiger (2001) estimated that in the long term (time-period 2010-2015) it is likely that output traits will gain a greater significance in the market compared to input trait products.

The following trait-crop combinations have been selected for this group:

- Resistance against abiotic stress factors/ enhancing yield: broad variety of plants, in particular cereals, grasses, potatoes
- Health-related compounds: tobacco, maize, potatoes and tomatoes are often used in laboratory R&D projects for this purpose or in the few field trials carried out in the EU
- Enhancing of "functional" ingredients in plants which intend to prevent nutrition-related diseases in humans: rice or vegetables (e. g. carrots, tomatoes) are mostly used in laboratory R&D projects for this purpose
- Use of plants as bioreactors for the production of a broad range of (high-value) substances: it is not clear at this stage of development in which plants they might be preferably developed
- Modification of lignin content: trees

Müller & Rödiger (2001) present three wave steps for the development of green biotechnology (general trends) that follow the three time-period defined presently. The first wave (between 1985 and 2005) is characterized by input traits, the second wave (between 2000 and 2010) is characterized by output traits and the introduction of GM products in food and animal feeds, and the third wave (between 2010 and 2020) is branded by the development of molecular farming, industrial raw material and bioenergies (Müller & Rödiger 2001).

In their report on Economic issues in Agricultural Biotechnology, the Economic Research Service of USDA analyses the economic aspects of several key areas (such as agricultural research policy, production and marketing). They do not provide pipeline products with different time horizons but propose examples of GM products in the pipeline. The non-exhaustive list is categorized by input traits (herbicide tolerance in sugar beet, wheat, alfalfa, fruits and vegetables, insect resistance and the introduction of other Bt-toxins with different specificities and the increased combination of genes) and output traits (low-phytate corn, altered nutritional characteristics in soybeans and corn, coloured cotton or cotton with improved fiber properties, delayed-ripening in fruits and vegetables, altered gluten levels in wheat for improved baking quality, naturally decaffeinated coffee) (ERS 2001).

GMOs in the CEEs

In the accession countries mainly large multinational companies (like e. g. Monsanto, Du Pont, Aventis Crop Science) were active in field trials with GMOs in recent years. The most common trait/crop combinations were herbicide tolerant GM

54 *Arabidopsis thaliana* or tobacco are frequently used, sometimes also potato or tomato.
55 An illustrative example in this context is the development of the "Golden Rice" which took more than ten years.

maize, insect-resistant GM maize as well as herbicide tolerant GM sugar beets or soybeans. This indicates that the large companies mainly test their most important products developed in the EU and outside Europe but do not develop peculiar GMOs for accession countries. The overview on GMOs in the R&D phase in accession countries revealed some research activities in these countries but the impression arises that these are often stand-alone activities of single research institutes or companies which will not result in a broad pipeline of GMO products in the coming decade.

GMOs commercialized wordwide

Worldwide (mainly USA, Canada, Japan, Argentina, Australia) GMOs approved for commercialisation concentrated on herbicide and/ or insect-resistant maize (sometimes combined with male sterility), herbicide tolerant oilseed rape (sometimes combined with male sterility), herbicide tolerant soybeans, herbicide and/or insect-resistant cotton as well as insect and/or virus-resistant potatoes. In terms of output traits relatively few products have been commercialised so far, namely three varieties of oilseed rape with modified oil content (e. g. high content of oleic acids or laurate oil), three varieties of soybeans with modified oil content (e. g. high content of linolenic acid or oleic acid) as well as delayed-ripening tomatoes and some form or colour-modified flowers. With regards to other major agricultural crops, herbicide tolerance is the dominating trait in approved GMOs in rice, wheat and sugar beet as well but for these plants only one or two products have been approved in the last years which are hardly cultivated (James 2001).

Field trials with GMOs in the USA

An analysis of the field trials of major crops in the USA revealed that herbicide tolerance was the most important trait in US field trials in the 1990s and had a high relevance e. g. in wheat, soybeans, cotton, oilseed rape and maize, but it lost relevance in particular in soybeans and maize in the last five years. In addition to herbicide tolerance, US field trials in GM maize concentrated on insect resistance with an increasing trend in the last five years as well as modification of specific ingredients (mainly starch and proteins). The modification of specific ingredients (mainly proteins and fatty acids), partly for improving animal feeding, partly for technical purposes, insect resistance and enhancing the yield of the crop gained increasing relevance in field trials with GM soybeans in the USA in the last five years. Both in the USA and the EU field trials on cotton concentrated on herbicide tolerance and insect resistance with no significant change in the relevance of these two dominating traits in the US during the last five years. In wheat[56], herbicide tolerance is by far the most important trait, but protein modification as well as modification of yield-influencing factors gained increasing relevance in the last five years.

56 It should be considered that in wheat a low number of field trials has been carried out in the USA during the recent decade indicating again the specific difficulties to establish genetic engineering techniques in this crop.

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