Centre for Agricultural Strategy

Biotechnologies in agriculture and food-coming to the market

Edited by BJ Marshall & FA Miller

CAS Paper 34 July 1996

Marshall BJ & Miller FA (Eds)(1996) *Biotechnologies in agriculture and food - coming to the market.* CAS Paper 34.
Reading: Centre for Agricultural Strategy.

7 A European perspective on the development and application of biotechnologies

Bruno Hansen

INTRODUCTION

The European Commission (EC) has been involved in biotechnology since the mid-1970s and the Research Programmes began in a modest way with the Biomolecular Engineering Programme (BEP) of 1982-1986. Policy developments, including regulatory measures, have taken place in parallel with the growth of the Research Programmes. Since the publication of the Commission's Forecasting and Assessment in Science and Technology (FAST) report on Bio-Society (CEC, 1982), several Communications on this subject have been made to the European Parliament (EP) and the Council. I would draw your attention particularly,to the April 1991 Communication - *Promoting the competitive environment for the industrial activities based on biotechnology within the Community* (CEC, 1991) - which announced the Commission's Biotechnology Coordination Committee (BCC). Since that date, this Committee, on which I represent DG XII (Directorate-General XII), and which is chaired by the Commission's Secretary General, Mr David Williamson, has provided a powerful means of coordinating the different Directorate-Generals and of driving a European strategy for the development and application of biotechnology in all relevant industrial sectors including agriculture. This strategy was described in the 1993 White Paper on *Growth, competitiveness and employment* (CEC, 1993) and in the subsequent White Paper of June 1994 *Preparing the next stage* (CEC, 1994). The recommendations and conclusions of the latter report, which included research and development as a major aspect, were strongly endorsed by the European Councils of Corfu and Essen and further debated at

the 11 January 1996 Inter-Institutional Conference on Biotechnology held in Brussels and are as follows, to:

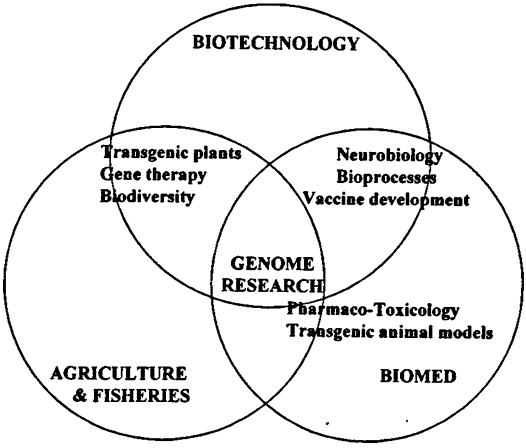
- review its regulatory framework, with a view to ensuring that advances in scientific knowledge are constantly taken into account and that regulatory oversight is based on potential risks;
- simplify procedures.....and reinforce scientific support for regulations;
- focus on most vigorous biotechnology research and development domains and increased coordination between the Community and Member States in order to avoid duplication;
- create a network of existing and new biotechnology science parks;
- improve further the investment climate for biotechnology;
- help public understanding;
- clarify further value laden issues in relation to some applications of biotechnology.

RESEARCH AND DEVELOPMENT

Perhaps more than any other emerging technology, commercial exploitation in this field is tightly coupled to research activities; for example, basic discoveries in molecular biology are rapidly turned into new drugs, new crop varieties and novel disease diagnostics. The promise of biotechnology for the 21st century rests on a vigorous and innovative science and engineering research base and a highly skilled workforce. A recent survey of some 400 new biotechnology companies indicated that, generally speaking, they have grown up around areas of academic excellence. This vital resource of innovation and skills, much of it funded by Member State governments, is readily available to meet the needs of industry and agriculture. However, experience has shown that Member States need to give greater recognition to the importance of the science base for biotechnology as has been done elsewhere. For example, the United States (US) may be spending as much as 7 billion ECU which is three times as much as the Member States and the Community research programmes spend in total. Furthermore, increased coordination is needed between and within Member States' research programmes to minimise wasteful duplication and to maximise collaboration of limited resources, with the overall aim of improving the efficiency of R & D expenditure. To these ends the Community Research Programmes in Life Sciences and Technologies under the 4th Framework Programme (FP4) from 1994 to 1998 have been expanded to 1674 million ECU, which is more than twice the size of earlier programmes.

There are three Life Sciences and Technologies research programmes under FP4 which are interactive and complementary (see Figure 1).

Figure 1
Fourth Framework Programme (FP4) - Life Sciences and Technologies



Source: European Commission

The BIOTECHNOLOGY programme of 588 million ECU provides the basic underpinning science that is exploited in the more mission-orientated BIOMEDICAL programme (358 million ECU) and the Agriculture and Fisheries (FAIR) programme (728 million ECU) covering agriculture, fisheries, agro-industry, food technologies, forestry, rural development and aquaculture. They have been designed to cross-fertilise one another bringing positive and synergistic benefits for exploitation of the results.

The technology-driven effort - the BIOTECHNOLOGY research programme

I would like to convey to you some significant achievements of the earlier Biotechnology programmes which have significantly expanded since their start in 1982. They demonstrate the trend towards applications of scientific results leading to innovative products and processes in the agriculture and food sector.

Firstly, successive biotechnology research programmes have supported research on lactic-acid bacteria which play a key role, particularly in the food industry. The value of products produced with their aid exceeds 100 billion ECU per annum in Europe and they are used in the production of over 200 million tonnes of silage. They are

thus by far the largest single group of micro-organisms exploited by industry and agriculture.

A targetted project on the physiology, biochemistry and genetics of lactic-acid bacteria was funded under the Biotechnology Research, Innovation, Development and Growth in Europe (BRIDGE) programme, with 34 participating groups (7 from industry), with a budget of close to 5 million ECU. The scientific productivity of this project was impressive - more than 250 joint and individual papers were published and 25 patents filed with 10 of them being granted. In addition, 31 bilateral contract agreements with European companies and the participating groups have been established. Since the industrial enterprises depending on lactic-acid bacteria (mostly in the food industry) are highly decentralised, the outcome of this project will have great significance for small as well as large multi-national companies.

In another group of projects known as Advanced Molecular Genetics Initiative for Community Agriculture (AMICA) there is a strong interest in engineering quantitative and qualitative changes in plant oils, carbohydrates and proteins. AMICA, which was set up under the 3rd Framework Programme (1990-1994) comprises 127 laboratories working collaboratively on 15 themes with 24 million ECU of support. One of the subthemes of this project studies the redirection of carbohydrate flow in plant cells. A molecular approach was taken to modify carbohydrate in interconversion processes in plant cells and to produce transgenic plants with new or modified carbohydrates. Transgenic plants were produced that accumulate fructan in different plant tissues. (Fructans are storage carbohydrates of which one example is inulin produced by around 15% of flowering plant species.) Inulin is beneficial to human health and can also provide increased drought tolerance for the plant. Three industrial companies participate in this project (from the United Kingdom, Denmark and Belgium) and are actively exploring the possibility of using this transgenic plant material as a new food and feed resource. At the same time they are very interested in investigating why plants which contain fructan are more resistant to stress. This demonstrates very nicely the reciprocal interplay between fundamental and applied research.

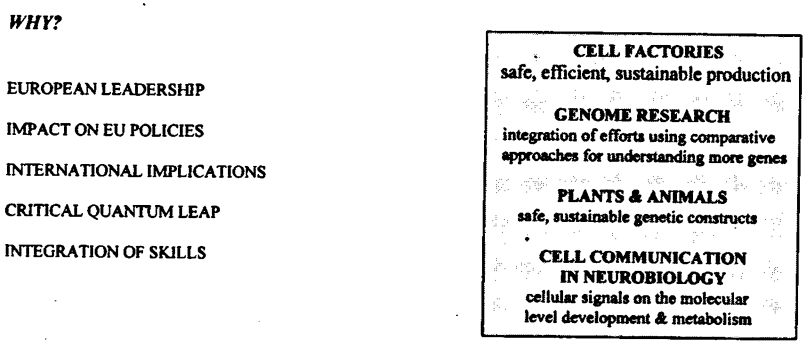
An enormous pool of information is being generated by the *Arabidopsis* genome sequencing and mapping and expressed sequence tag (EST) projects. From the 20 000 to 25 000 protein coding genes in *Arabidopsis* approximately half of the predicted genes have been identified with many previously unknown genes being discovered, which may be unique to higher plants. It is evident that this sequence databank represents the basis for future engineering of plants for commercial products and applications.

A group of Belgian and French laboratories were successful in constructing a recombinant vaccina-based vaccine expressing the surface glycoprotein of the rabies virus. This resulted in a highly

effective vaccine that was tested in a region of 2200 km² in Southern Belgium.

For the future, the BIOTECHNOLOGY Programme under FP4 is focusing on two broad areas of research - the 'cell factory' and 'biological materials'. A living cell can be regarded as a miniature biochemical factory, the function of which in certain circumstances can be influenced by man to produce high-value products such as hormones, vitamins, therapeutic proteins, etc. The research to be conducted under this specific programme will seek to develop these possibilities through a multidisciplinary approach to the living cell, combining biology (cell biology, microbiology, genetics, physiology, etc) and bioengineering (bioprocessing, fermentation, cell culture, downstream processing, etc). A proper exploitation of the cell factory requires an adequate knowledge of the genetic information of the different organisms (sequencing of model genomes), and a thorough understanding of plant and animal molecular and cell biology (see Figure 2).

Figure 2
Concentration of means



Source: European Commission

A second broad area of research will concern improvements in the production and use of biological materials in Europe, in particular in response to demands from industry. For example, research will be conducted into various biological materials important for health, agriculture and the chemical industry. The design of macromolecules with desired properties, the production of vaccines preventing major human or animal pathologies and the design of special organisms beneficial for the environment are some of the aims in this domain. Furthermore, the development of user-driven centres for bioinformatics, information infrastructures and resources as a service and support to wider scale research by the Community will be encouraged.

The application-driven effort - The FAIR Programme

An important task of the Agriculture and Fisheries programme (FAIR) of the FP4 is to support high quality research leading to specific applications of biotechnology in the agricultural and agro-industrial sectors (including food, non-food and forestry). Before describing this programme I would like to give some background on previous European Union (EU) agro-industrial programmes.

The ECLAIR, FLAIR and AIR Programmes

The European Collaborative Linkage of Agriculture and Industry through Research (ECLAIR) 1988-1993 programme (total budget 80 million ECU) was the first agro-industrial research programme implemented by the EC, and formed part of the 2nd Framework Programme. Almost in parallel with ECLAIR, the Commission launched the Food Linked Agro-Industrial Research (FLAIR) programme, 1989-1993 (with a total budget of 25 million ECU), which was more focused in the field of food science and technology. Both the ECLAIR and FLAIR programmes had close continuing links with the biotechnology programme BRIDGE, which looked at the fundamentals of plant and animal biotechnology. ECLAIR and FLAIR were succeeded by the Agriculture and Agro-Industry, including Fisheries (AIR) programme, 1991-1994, (total budget 378 million ECU), adopted on 23rd April 1990 as part ofthe 3rd Framework Programme, which was the first integrated programme put in place covering primary production, inputs, processing and consumer inputs.

Among the projects I would mention are several that have provided the basis for the development of new 'agribiotech' products, thus opening new market possibilities. In addition, these projects have increased the competitive position of European biotechnological research and have contributed to improving the strategic position of participating European companies.

A particularly good example is an ECLAIR project, which has generated new knowledge on the metabolism of lignin, including some key enzymes involved in the synthesis of this important cell-wall polymer and also their genes which have been cloned for the first time. This knowledge has led to the use of anti-sense gene technology in the development of transgenic trees with reduced lignin content of their wood. Genetic modification of wood in this way, as shown in a model system of tobacco, results in easier lignin extraction, reduced use of chemicals for removing lignin from cellulose during paper manufacture, and increased paper yield. Such developments may have dramatic effects on the economic and environmental performance of paper mills. The ultimate financial impact of these results could be very great, as paper is a $100 billion industry worldwide. One of the companies participating in this project is the UK's Zeneca Plant

Sciences, which is currently in the best international position to exploit the technology on the basis of worldwide patent protection. The prospects for commercialisation of modified poplar and of *Eucalyptus* trees are also considered to be good in the medium term.

Another important technology developed by ECLAIR is the control of fruit ripening through modification of ethylene metabolism. The application of antisense gene technology has been shown to reduce ethylene levels resulting in delayed fruit ripening. This provides a novel approach to increasing storage life and to improving the colour, texture, flavour, aroma, etc and thus fruit quality. By manipulating the expression of these genes, it becomes possible to control undesirable biochemical changes that impair quality, particularly in post-harvest storage. From a technical point of view, low-ethylene tomatoes or melons could be available for the European market within the next few years.

The ECLAIR programme has also included R & D on the production of pesticides in plant tissues as an alternative to chemical pesticide applications. The powerful insecticidal protein of *Bacillus thuringiensis* (Bt) can be expressed very effectively in plants and this technology, which was pioneered by European research in the 1980s, has been optimised under ECLAIR. Consumer safety and the agronomic and processing quality of transgenic food crops expressing insecticidal Bt proteins are being carefully analysed in FLAIR and AIR projects. Commercial exploitation of insect-resistant transgenic crop plants like tomato, potato or maize, is taking place for the first time this year in the US and may soon be available in Europe.

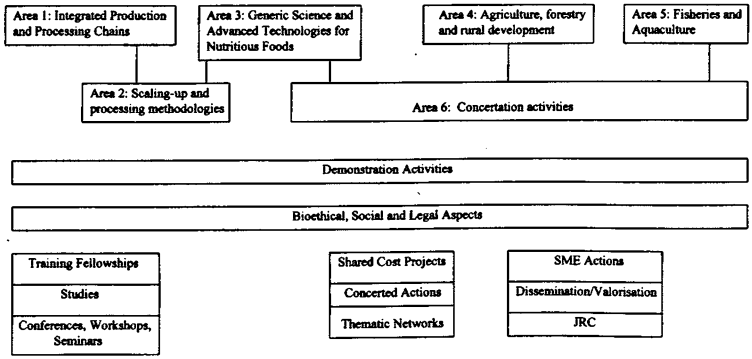
Other successful projects deal with new antifungal proteins obtained from plants, biocontrol agents based on micro-organisms and the development of molecular markers for assisted plant breeding.

The FAIR Programme (1994-1998)

The new FAIR programme - covering agriculture, fisheries, agro-industry, food technologies, forestry, rural development and aquaculture - forms part of the FP4, which was adopted by co-decision of Council and Parliament. It will run from 1994 to 1998, and has a total budget of 728 million ECU. The programme is extremely diverse (see Figure 3) including all aspects of the production and utilisation of biological raw materials, with the aim of developing new markets, products and processes for the raw materials coming from agriculture, forestry and fisheries.

Figure 3

Research, Technology and Development Programme on Agriculture and Fisheries (Including Agro-Industry, Food Technology, Forestry, Aquaculture and Rural Development) 1994-1998



Source: European Commission

All areas of the programme, except 5, take into consideration the applications of biotechnologies to agriculture and agro-industry. New food and non-food raw materials with desirable qualities will be developed, for instance, better tasting food from plants, with improved safety and nutritional value, freshness, storage quality, convenience and appearance.

The potential of food to influence human and animal health, not only through better nutrition, but also through prevention of conditions such as cancer and cardiovascular disease is addressed in the programme. The development of plant raw materials that may provide health benefits is an important objective of area 3. For example, foods with increased levels of antioxidants, vitamins or their precursors, and with fewer anti-nutritional and potentially toxic compounds, like nitrate, allergenic proteins, toxic secondary metabolites, etc.

A particularly promising aspect of plant biotechnology is the possibility of designing crops for the production of high-value-added compounds of industrial and pharmaceutical interest (eg, enzymes, antigens, antibodies, blood factors, nutriceuticals). This new field, known as molecular farming, is also covered by the FAIR programme under such topics as 'Application of Biotechnology to Food Materials', and the 'Green' Chemical and Polymer Chain'. A good example of this new technology is the production in plants of recombinant vaccines against human and animal diseases, a most interesting novel alternative methodology with advantages in terms of cost, safety, handling and also delivery. For example, edible vaccines can be produced in fruits and vegetables for fresh consumption.

During the first call for proposals (15 December 1994 to 15 March 1995) the FAIR programme received a large number of proposals on applied biotechnology and, following expert evaluation, several projects have been funded dealing with topics such as:

- edible vaccines produced in crop plants. This project links well with the objectives of the Task Force Vaccines and Viral Diseases of the EC;
- controlled ripening of fruits and vegetables;
- manipulation of source-sink relationships in legumes;
- proteins from pea plants as a source of functional properties;
- modification of lignin for tree improvement;
- a demonstration project to study the techno-economic feasibility of herbicide-tolerant transgenic oilseed rape plants.

Proposals submitted for the second call (15 June 1995 to 15 September 1995) are still under selection. The third call for proposals was launched on 15 December 1995 and the deadline for proposals is 15 March 1996. It is foreseen that the FAIR programme will have three additional calls for proposals during 1996 and 1997.

I have already described some of the achievements and objectives of the European Life Sciences and Technologies Research programmes. However, funding excellence in science and technology is not enough. If we wish to see the new and safer approaches of biotechnology brought to the market - in agriculture and food - **innovation** is necessary. The recently published Commission Green Paper on Innovation (CEC, 1995a) defines innovation as 'the successful production, assimilation and exploitation of novelty or new ideas'. In Europe we seem to have great difficulty in converting the assets of our scientific and technological strengths into sustainable economic performance. It is vital that we address those factors that may be breaking the link between creative technologies and their successful exploitation as new products, new crops or new foods. The June 1994 Communication (CEC, 1994) considered some of these factors, including regulation.

THE REGULATORY FRAMEWORK

In a recent report entitled *Biotechnology's economic impact in Europe,* produced by Ernst & Young in collaboration with the Senior Advisory Group on Biotechnology (SAGB) (Ernst & Young, 1994) a survey was carried out of those factors that influence a company's investment decisions. More than 80% of the companies questioned considered that 'the regulatory climate' was a major factor influencing their investments in Europe; some 70% considered that 'negative public perception' was the next most important factor.

The Commission has made a commitment on the Community's Biotechnology Regulatory Framework that was again repeated at the 11 January 1996 Inter-Institutional Conference on Biotechnology held in Brussels. The framework will be further developed by fully exploiting the inherent possibilities to adapt the horizontal biotechnology Directives to technical progress. At the same time amendments will be brought forward to incorporate changes that could not be introduced by technical adaptation alone, while leaving the basic structure of the framework intact. In fulfilment of that promise the Commission was able to adopt, in December 1995, a proposal to amend the Contained Use Directive (90/219/EEC) which regulates much research using recombinant DNA technology. Furthermore, at about the same time, the Commission adopted a new proposal on the patenting of biotechnological inventions that seeks to harmonise the relevant patent laws throughout the Union and ensure that European researchers can successfully protect intellectual property arising from their work. Both proposals have now been submitted to the Council and the EP, and are expected to have significant impacts on the competitiveness of industry and agriculture.

The Commission further promised to carry out a review of the implementation and functioning of the Deliberate Release Directive (90/220/EEC) which is continuing at the present time. The experience gained so far with this Directive has allowed us to adopt certain simplified procedures for certain cases of plant experimental releases. It is expected that further simplifications will be introduced in the near future.

The approval of products under this Directive has been more difficult than originally expected. The assessment carried out by one Member State has not so far satisfied all other Member States. This has meant that products have to be approved through Commission Decisions. However, the Commission is doing all that is possible to make this Directive function smoothly, especially in the case of products, while at the same time, of course, ensuring safety for human health and the environment.

PUBLIC PERCEPTIONS OF BIOTECHNOLOGY

The third topic covered by the Commission Communication relates to public perception. This may serve as a major constraint to private-sector investment and hence successful commercialisation of the technology. The introduction of any new technology (and biotechnology is no exception) raises critical reactions, even fear, from certain sectors of the public. Science is no longer perceived as being synonymous with progress as it was a few decades ago. The honeymoon with new technology is over. This subject has been fully

addressed in the recent EC White Paper *Teaching and learning. Towards a learning society* (CEC, 1995b). This has considered the growing public concerns about scientific and technical progress and concludes that the link must be demonstrated between science and the progress of mankind, by means of better information provision.

Experience with other subjects tells us that as long as there is **no knowledge** there is **no concern** but if there is **little** or **insufficient understanding** there is **great fear** and only an **adequate knowledge base** will allow **rational discussion**. That is why through the research programme we have helped a number of initiatives to provide information in a balanced and impartial way. But provision of information is not enough. It is important that dialogue is engaged to ensure that people see that their concerns are not being ignored, that their questions are being addressed and, if possible, answered. It is our intention to increasingly involve those groups of the public who are most affected by biotechnological developments, such as consumer and environmental groups, as well as farming organisations, in **open and informed dialogue**. A good example of the type of dialogue we have in mind is the Consensus Conference model which was held here on transgenic crop plants. A workshop on this topic was subsequently supported by the Commission.

In addition, a section of the research programmes specifically addresses ethical, social and legal aspects of biotechnology. I can provide you with information on the studies and workshops we have supported in this area to date. Ultimately, it is the public who must decide the 'desirability' of biotechnology and if a product serves no useful economic purpose, the public will make its own decision not to buy it.

CONCLUDING STATEMENT

In Europe we are now at a turning point in the exploitation of biotechnology. On the one hand we have the traditional approaches to agriculture, food, environment and even health-care. On the other hand, we have the rise of the new, more precise and powerful approaches of biotechnology. This turning point involves a cultural decision which is why we have the current debate on biotechnology in Europe. It is vital that this debate takes place with the participation of all the partners involved.

Biotechnology is here to stay, whether we like it or not. Inevitably, there will be a huge market for biotechnology products in Europe. I contend that it is our responsibility today to ensure that the ground is fertile for agricultural bioproduction in Europe and not just bioconsumption of course, taking into account safety and ethical considerations. European agriculture and European companies must

have the resources, including the knowledge base, to be as responsive, as flexible and as innovative as their competitors from other countries and other continents. Without this, future generations would be deprived of the benefits only technological progress can bring.

REFERENCES

CEC (1982) *FAST (Forecasting and Assessment in Science and Technology) Report on Bio-Society.* Brussels: CEC.

CEC (1991) *Promoting the competitive environment for industrial activities based on biotechnology within the Community.* Com. SEC. (91) 629. Brussels: CEC.

CEC (1993) *Growth, competitiveness, employment: the challenges and ways forward into the 21st Century.* White Paper. Luxembourg: EC.

CEC (1994) *Preparing the next stage.* COM (94) 219, Final. Brussels: CEC.

CEC (1995a) *Green Paper on Innovation.* COM (95) 688, Final. Brussels: CEC.

CEC (1995b) *Bulletin of the European Union.* Supplement 5/95.

CEC (1995c) *White Paper on Teaching and learning. Towards a learning society.* COM (95) 590, Final. Brussels: CEC.

Ernst & Young (1994) *Biotechnology's economic impact in Europe: a survey of its future role in competitiveness.* London: Ernst & Young.