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## BIOTECHNOLOGY IN THE COMMUNITY

(Communication from the Commission to the Council)

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# THE SCOPE AND SIGNIFICANCE OF BIOTECHNOLOGY

# 1. THE SCOPE AND SIGNIFICANCE OF BIOTECHNOLOGY

## 1.1. THE SCOPE OF BIOTECHNOLOGY

Biological science is now very diversified and boasts a large number of sub-disciplines (biochemistry, genetics, microbiology, physiology, morphogenesis, systematics, plant and animal anatomy, ecology, bio-physics, bio-informatics ...). The practical applications of these sciences, building on the pragmatic successes of the preceding centuries, are fundamental to modern standards of food supply, health care, and more generally to man's ability to control his environment and exploit living organisms to produce useful goods and services. Yet in the light of the developments of the past two decades, it is clear that biological science still contains vast further potential to contribute to human welfare.

The sum total of these applications, which directly support the promotion of health care, of bio-industries and of agriculture, may be considered to constitute the field of biotechnology. The definition is however unsatisfactory because it lacks specificity and because it fails to distinguish between traditional and modern approaches to the domestication and transformation of life on this planet. For this reason, the Commission has suggested (*) that the biotechnology which is relevant to the removal of current scientific and technical barriers to the promotion of health and the development of industry and agriculture be designated as "new biotechnology"; it can be characterized in terms of the scientific breakthroughs which are expected to contribute significantly to the solution of contemporary problems.

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(*) Framework Programme for Community S/T Activities 1984-1987 (COM(83) 260 final), and supporting paper : Plan by Objective : Biotechnology (doc. XII-37/83).

These breakthroughs are numerous and include the following :

- the development of cell and enzyme technology, that is to say the creation of new bio-industrial methods based upon the use of the catalytic properties of enzymes for the transformation of raw materials and agricultural products.

- the recently acquired capacities of man to transfer geretic information between distantly related organisms and to insert purely "synthetic" information into organisms, thereby obtaining new useful living entities.

- the promotion of molecular and cellular approaches for the detection and treatment of pathological conditions in living organisms.

- the improvement of techniques for the selection and cultivation of microorganisms, animal cells and plant cells and for the manipulation of their behaviour under controlled conditions.

- the elaboration of methods for the regeneration into fertile and differentiated individuals of individual axenically-cultured plant cells (i.e. grown and isolated on sterile media).

- the development of downstream processing techniques for treatment, extraction, purification and conversion of useful materials following the stage of bio-mass production.

## 1.2. SIGNIFICANCE OF THE NEW BIOTECHNOLOGY

### 1.2.1. The applications in sight

The importance of the new biotechnology has been stressed and discussed at length in a profusion of documents prepared, since 1975 by the services of the Commission, and, more recently, by national governments and international agencies (for a detailed and comprehensive appraisal see COM(83) 328/2 (Background note on biotechnology national initiatives presented at Stuttgart). In brief, it can be stated that some important industrial applications (production of monoclonal antibodies, preparation of new vaccines, synthesis of high value products including antibiotics, amino acids, and proteins such as insulin and interferon, and detoxification, microbial leaching for the mining of metal...) exist worldwide, with the focus of current

developments particularly in the USA and to a lesser extent in Japan and Europe. Many significant achievements may be expected before the end of the present century. The areas principally concerned are outlined in figure 1. The advances in sight have been described in 1980 and 1982 by the Commission services in the proposal for a Community programme in Biomolecular Engineering and in the FAST report. They will undoubtedly include :

- the creation, through the use of recombinant DNA techniques, of cell lines and strains of organisms displaying new properties (increased symbiotic capacities, disease resistance, high protein yields ...) or able to accomplish functions (synthesis, conversion, concentration, fixation, degradation) essential for the production of food, feeds, pharmaceuticals, chemicals and energy.

- the construction of new types of reactors for bio-mass processing, the treatment of wastes, the recycling of useful materials and the large-scale transformation of raw materials into classes of compounds that can be exploited by industry. Many of the new developments in fermentation will depend upon the availability of enzymes and cells isolated or produced by biochemical or genetic engineering techniques and upon basic knowledge acquired in microbiology, informatics and robotics.

- development of methods, more reliable and less expensive than those used presently, for toxicological testing and the evaluation of pharmaceutical properties; and the development of new products through the use of "rational" and computer-assisted design techniques.

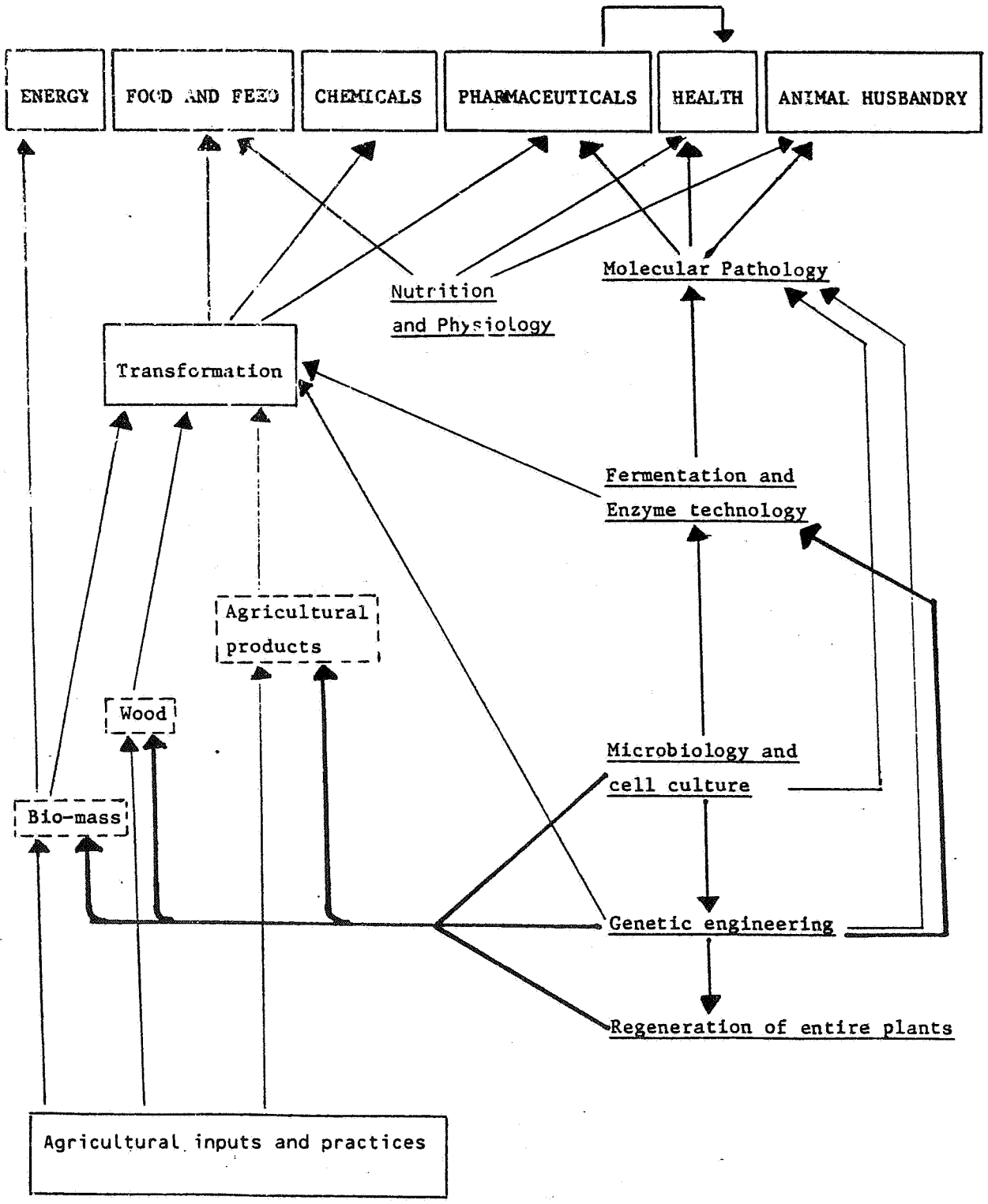


Figure 1 : Biotechnology : a multidisciplinary approach to the domestication of biological organisms. Research in molecular pathology, fermentation and enzyme technology, microbiology and cell culture, genetic engineering and plant cell differentiation contributes to the development of new approaches, processes and products essential to some of the requirements of man.

### 1.2.2. Market potential

Many widely varying estimates have been made of the market potential of biotechnology in the coming decades, questions of definition being a major cause of the discrepancies shown below ; but both these estimates, and the R&D and investment behaviour of major companies, reflect forecasts of an increasing proportion of GNP attributable to products and services of "biotechnological" nature. A rough calculation indicates that over 40 % of manufacturing output in a developed industrial country is biological in nature or origin, and therefore likely to be influenced or transformed by developments in biotechnology.

Some estimates ($) of world market potential for biotechnology.

| Source | current market | 1990 | 2000 |
|---|---|---|---|
| T.A. Sheets | 25 m | | 64.8 bn(*) |
| Business Communications Co.Inc. | 60 m | 13bn | |
| IMSWORLD | | 27bn (US only) | |
| Information Services (London) | 10 m | 500 m | |
| OTA Report : products based on r-DNA technology | (food and pharmaceuticals | | 7.4 bn |
| | (chemicals | | $ 50-100 bn |
| Policy Research Corp., cumulative 1980-2000, | agriculture | | $ 5- 10 bn |
| Products made by genetic engineering techniques | medical | | |
| MITI, Japan : "Japan's biotechnology market" (Japan Economic Journal, 28 Dec. '82) | | | ¥ 4-6trillion = $ 16-24 bn |

(*) Breakdown by sectors of T.A. Sheets estimate : Alternative energy products 16.3 ; new foodstuffs 12.6 ; health care products 9.1 ; industrial chemicals by biotechnology 10.5 ; agricultural chemicals 8.5 ; copper and nickel leaching 4.5. Note that this omits potentially major new sectors such as microbial enhancement of oil recovery.

### 1.2.3. Company responses

The mushrooming of biotechnology companies has been most evident and widely reported in the U.S.A. : by April 1981 well over 100 companies had been launched, with share offerings exceeding $ 1.1. billion. Best known are Cetus (market capitalisation $ 400 m in mid-1981, $ 370 m. In June 1983), and Genentech ($ 280 m in mid-1980, $ 563 m. in June 1983) of the specifically biotechnology companies ; Hybritech is of similar magnitude. The "Biofutur" listing of 25 U.S. companies specialised in biotechnology totals market capitalisation $ 3.2. bn in June 1983. But the major financial driving forces are the oil, chemical and pharmaceutical groups, who are investing heavily (see box).

Some examples of biotechnology related R&D expenditures and investments

- Dupont : $ 150 m capital expenditure commitment in life sciences, 1982-84, 1981 R&D expenditure in life sciences, over $ 180 m.
- $ 67 m. (inflation-indexed) 10-year contract between Hoechst and Massachusetts General Hospital, for molecular biology research.
- $ 6 m agreement between Dupont and Harvard Medical School, for research on molecular genetics.
- $ 5 m funding by Shell of Cetus' work on human interferons ; $ 40 m R&D agreement also reported.
- $ 70 m investment by International Nickel, Schering-Plough, Grand Metropolitan and Monsanto in a new private company : Biogen ; originally Geneva-based.
- $ 5 m participation by Dow in Collaborative Genetics.
- $ 29.4 m acquisition by Schering-Plough of DNAX Ltd., a small Californian biotechnology firm.
- $ 120 m. investment by Schering Plough for interferon production in Ireland.

Multinational companies such as Monsanto or Hoffmann La Roche are strongly represented in Europe, and typically pursuing a long-term oriented strategy based on four elements :

- development of in-house capabilities at key centres (e.g. Monsanto : St.Louis ; Dupont : Wilmington ; Hoffmann La Roche : New Jersey - i.e. mainly U.S., even for firms of European origin).
- research contracts with specialist biotechnology companies (examples in box).
- research contracts with key individuals and teams in universities.
- sharing of risks and costs of long-term research and "venture" activities with firms not directly competitive in their major sectors, by "joint research companies" - e.g. Biogen ; or note that Cetus, although publicly quoted, is controlled (5 out of 9 directors) by the major companies ; French example is Transgène, created by Paribas, Assurances Générales, Elf Aquitaine, BSN and L'Air Liquide.

Europe's major oil, chemical and pharmaceutical firms have been active in the development of biotechnology - e.g. ICI, BP and Hoechst have all invested significantly, but so far unprofitably, in single-cell protein R&D and production facilities. Food firms have been active, where organised on an adequate scale ; cf. the investments by Tunnel and Amylum in the isoglucose process ; or Unilever's development of plant tissue culture and propagation techniques for oil palms. In pharmaceuticals, many of Europe's companies are world leaders ; and two of these, NOVO (Denmark) and Gist-Brocades (Netherlands) dominate the world market for industrial enzymes, with shares of some 50 and 25 %, respectively.

Faced with the challenges of biotechnology, and with their particular breadth in terms of the multi-disciplinary skills required and the many market sectors potentially affected, most companies react nervously : they do not have all the skills in-house, and they realise that their established areas of strength may come under attack from an unexpected direction.

There is therefore a strong readiness to look outside for expertise, to buy knowledge from elsewhere, or to seek an alliance with, or a share in, some competent centre of knowhow in biotechnology.

Even for the European companies, the "elsewhere" and the "competent centres" have been sought in the U.S. (cf. Hoechst - MGH agreement, Dutch discussions with IPRI California, U.K. - Japanese collaboration) while the major U.S. companies with customary thoroughness do not neglect the centres of expertise in Europe (cf. Biogen, and many direct university contacts).

It is difficult to obtain precise, reliable or comprehensive figures, but from the reports and data available it appears probable that the U.S. is substantially exceeding total European Community activity :

a) in the number and scale of investment in small, new, "venture capital" companies in biotechnology (even a 90% "failure rate" may be less important than a 10% "success rate")
b) in the development of medium-sized specialist biotechnology companies such as Cetus, Genentech, Genex, Hybritech, IPRI, Collaborative Genetics....
c) in the capital investment and recurrent expenditure on R&D in biotechnology by the major oil, chemical and pharmaceutical firms ; it is possible that in agro-food, the major European firms are being more innovative, although it has been claimed that certain specific developments have not been sufficiently encouraged by national regulations or Community market regimes.

The gap is narrower if the important biotechnology capabilities of Switzerland and the Scandinavian countries are included. In basic research and technological capabilities, the situation is much more evenly balanced : collaboration with Europe, and with research centres in Europe, is therefore still of major interest to the U.S. and Japan.

### 1.2.4. Strategic significance

Biotechnology has engendered enormous enthusiasm shown for it in recent years(*), the importance attached to it by industrial investors and the public authorities (less by Trade Unions and consumer associations), being based upon the following reasoning :

- it constitutes a fundamental tool of socio-economic development.

  Theorists of "long-wave" economic cycles see biotechnology (after the new technologies of automation, information and communication), as the driving force of basic innovation for the next long cycle which the economy of the West is entering. Whether or not one accepts such a theory, it is clear that the scale of potential application (current and long-term) within most fields of human activity makes biotechnology a powerful tool for renewal and innovation of the economic base of contemporary society. In sector-specific terms, biotechnology, and in particular the new chemistry awaiting discovery and exploitation within the cell, is one of the few major sources of innovation so desperately needed to restore the prospects of the chemical industry in the industrial world. It provides an incentive and a direction for the new accumulation of investment capital needed to re-establish a phase of economic growth.

- Biotechnology is altering certain aspects of the international division of labour, through increased

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(*) There have been countless special numbers on biotechnology by the specialist scientific press, the popular science reviews, and the mass circulation press. Scientific reviews or newsletters exclusively devoted to biotechnology have also appeared : e.g. Biofutur, Biotech Quarterly, Biomass, Biotech News, Bio/technology, Biotechnology Bulletin, Biotechnology, Industrial Biotechnology, Biotechnology Newswatch, Telegen Reporter, Practical Biotechnology, Biotechnology News, Bio-Engineering News, Bio-Sciences, Genetic Technology News, Swiss Biotechnology,....

competition between the industries to which it is relevant (agro-food, petrochemicals, pharmaceuticals, environment industry, water treatment and distribution...), and through restructuring and re-grouping at both national level and amongst the multinational firms ; the evidence is clear in the patent applications, licence agreements and R&D investments. Intense competition is taking place between Community countries to capture both the expanding domestic markets and the export markets. It would be misleading to mention only the competition between Europe and the U.S. and Europe and Japan, the more so since it is noticeable that Europeans often appear to prefer to collaborate with Japan and the U.S. rather than with one another.

- Biotechnology may contribute to the easing of certain strategic constraints at world scale, which weigh particularly upon the countries of the Third World ; basic health, food production and storage, nutrition, energy, environmental problems.

The strategic significance of biotechnology (and similarly "knowledge-based" industries) is underlined by the current debate in U.S. government circles on the modification of anti-trust law as applied to collaborative efforts in industrial research.

## 2. BIOTECHNOLOGY IN THE MEMBER STATES : THE NEED FOR A COMMUNITY APPROACH

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### 2.1. BIOTECHNOLOGY IN THE COMMUNITY

#### 2.1.1. The relative weight and importance of current efforts in the Member States

The efforts carried out throughout the world and within the Community for the promotion of modern biotechnology have been assessed by the FAST-group of DG XII and are outlined in detail, country by country, in the Plan by Objective "Biotechnology" (doc. XII-37/83), which was prepared as a supporting document for the First Framework Programme for Community S/T Activities 1984-1987, and more recently, in the background note "National initiatives for the support of biotechnology R & D" (COM(83) 328 final/2), prepared to accompany document COM(83)328, "Biotechnology : the Community's role" at the Stuttgart Council, 17 June 1983. From the information available, the following conclusions can be derived on the scope and nature of biotechnological R&D in the Member States :

#### 2.1.2. The slow emergence of modern biotechnology in European countries

With the exception of the Federal Republic, where industrial strength in several applied fields of molecular biology began to be built, as early as 1974, on the basis of a major report prepared by DECHEMA, the signal to the Member States that modern biological research was central to the evolution of agriculture and industry was issued in 1975 in the preparatory documents for a Community programme in biomolecular engineering. These documents were complemented, in 1977, by the studies of D. THOMAS and A. RORSCH on enzyme technology and genetic engineering. National reports which served as platforms for the elaboration of strategies in biotechnological R&D in

Member States appeared in 1979 in France ("Sciences de la vie et société" by GROS, JACOB and ROYER), in 1980 in the United Kingdom (SPINKS report) and increasingly thereafter : over 10 national reports were published in 1981. It is therefore not surprising, in view of the late entry of the Member States in the so-called biotechnology race, to note that the impact of European R&D in bio-sciences and in key areas of applied biology has been relatively weak during the period 1975-1980. The lack of competitiveness in both basic and applied research is illustrated by surveys on patent distribution in the important area of enzyme immobilization (data provided, for the period 1977-1979, by the patent department of the society SMITH KLINE-RIT).

### 2.1.3. A substantial but incomplete effort in the Member States

Detailed appraisal of current R&D spending by governments and private firms throughout the world indicates that in the Member States of the Community, Public Authorities invested in recent years for biotechnology approximately $ 150-350 million per year as compared to 200-550 in the USA and at least 50 in Japan (The wide ranges reflect the divergent definitions of biotechnology, e.g. covering greater or lesser proportions of agricultural or biomedical research). Funding by private industries was very much larger. Community firms, although outspent on average by US and Japanese enterprises, display very substantial strength in several instances. Illustrative examples of this strength are to be found in the annual R&D budgets of companies such as Unilever (mainly agro-food), Hoechst (chemicals and pharmaceuticals), and other European-based giants, with R & D budgets exceeding 200 MioECU p.a. ; significant elements of this R & D being at least "biotechnology-relevant" (see also 1.2.3. above and COM (83)-328 final/2 : "National initiatives for the support of biotechnology R&D").

## 2.2. EUROPEAN EFFORTS : IMPORTANT BUT FRAGMENTED

As evidenced by current deficits in trade and in patents and by the continual emigration of competent scientists, the efforts of the Member States, in spite of their magnitude in financial

terms, remain insufficiently productive. The lack of commercial competitiveness in modern Europe has recently been examined in two U.S. studies, which independently arrived at similar conclusions. One recently "leaked" report was prepared for the Office of Science and Technology Policy of the White House by a working group drawn from several federal agencies. Its assessment of the competitive situation in biotechnology bluntly concluded :

"The U.S. faces the stiffest challenge from Japan".

On Western Europe's biotechnology :

"... In general, the lack of qualified scientists and engineers (particularly in process and purification technologies), inadequate industry/university cooperation, and belated and insufficient R&D funding by industry and government, are probably the biggest barriers to commercial competitiveness in these countries. In addition, the West German and British Governments are concerned over the emigration of scientists from their countries, many of whom are working in the U.S."...

(Competitive and Transfer Aspects of Biotechnology; Commercial Aspects of Biotechnology ; Policy Option Papers. Report delivered to George A. Keyworth, Science Adviser to the President, 27th May 1983).

The two-year assessment by the U.S. Office of Technology Assessment to be published in October 1983, "Biotechnology : Commercialization and International Competitiveness" states (in the draft version of May '83) :

"Japan will be the most serious competitor to the United States in biotechnology. It has a very strong bioprocess technology base upon which to build, and the Japanese Government has specified biotechnology as a national priority...
The European countries trail the United States and Japan in the commercialization of biotechnology. They are generally not as aggressive, either industrially or through government laws and policies."

The lack of European competitiveness results from serious deficiencies and weaknesses affecting the entire

TRAINING-RESEARCH-DEVELOPMENT-PRODUCTION-DISTRIBUTION network upon which modern technologies need to be based.

These deficiencies and weaknesses, which create barriers to innovation and the development of a large unified market for biotechnology products in Europe, have been identified in the FAST report and in the Plan by Objective : Biotechnology. They can be ascribed to scale and structural factors which are, themselves, the direct consequences of fragmentation into isolated national policies.

### 2.2.1. Scale factors : the failure to achieve "critical mass"

The traditional applications of biology to industry and to agriculture have been developed over long periods of time, through sporadic progress within isolated disciplines.

The connections between basic science and technology were not, in the past, as intimate as they are now, and the R&D requirements for significant progress were relatively limited, remaining within the scope of individual nations ; at the limit, restricted to the work of a few imaginative scientists able to reproduce at industrial scale the experimental conditions under which they had controlled transformation processes in the laboratory. It was during this period that European countries, exploiting a research base built up slowly over a long period of time, and developed more rapidly over recent decades, organized strong national capacities for the processing of foods, chemicals and pharmaceuticals.

The sudden advent of modern biotechnology, with its multidisciplinary complexity, its relatively high investment costs and the rapidity of its evolution in the USA and Japan now demands a scale of effort at all stages from applied research through development to industrial exploitation, which is beyond the resources typically available within individual Member States within the European Community. This weakness, less salient in the case of fundamental research, where Europe maintains a firm traditional strength through the coordination work of EMBO, ESF and other scientific organizations, is more pronounced in basic biotechnology and in industrial development.

In basic biotechnology, that is to say in the portion of research located half-way between the fundamental study of life and the industrial exploitation of its properties and mechanisms, the insufficiencies of the Community derive in part from the dispersion and isolation of national efforts.

The problems being tackled are, in many cases, at the stage where we are sure we can solve them soon - in one way or another. But we must, as a community, keep in play many parallel but different attempts at a solution until one gains in competition over the rest. (The classic example is the European Organisation for Research on the Treatment of Cancer : EORTC).

This can only be done by organised concertation across a very wide technology base - i.e. that of the whole Community (and this implies organised Euro-wide groups of needers, potential clients, as well as concertation on the supply side of problem-solving).

Even the larger Member States, if they work in isolation, may have difficulties, for any given scientific or technical problem, in providing the national industry with the wide range of potentially relevant solutions which need to be tested within short periods of time for rapid innovation and conquest of the market. Similarly, with the exception of a few major European firms, hardly any industry in the Member States is sufficiently diversified to explore the application of new discoveries by testing them simultaneously against a wide range of different problems. Lack of concertation of national research policies in basic biotechnology and the isolated manner through which they are implemented accounts, in addition to duplication which can be useful in effect, for gaps in research capacities. Several areas of industrial microbiology, agricultural genetics and enzyme technology, suffer from the absence in each Member State considered separately of sufficient high-level expertise and know-how for undertaking on a systematic basis the analysis and control of the most complex molecular mechanisms and biological functions upon which the biotechnology of tomorrow will establish its foundations. The fact that several European biologists of

outstanding ability have hired their services to US firms is, moreover, a clear indication of a lack of mobilization within the Member States and of the incapacity of a single country, even as large as the United States, to depend entirely upon its own scientific resources.

Significant weaknesses can also be found in the developmental capacity of European industries where innovation, except for a few large-sized commercial enterprises, is usually insufficient. The inertia of industrial R&D activities is greatest in areas where the short term commercial incentives are insufficient. This is particularly the case in the health industry where the strong trend for replacement of the private customer by the state customer has revealed the need for a reorientation of R&D leading to the production of new drugs for the prevention and/or rapid treatment of widespread "expensive" diseases and for cheaper, more reliable, in vivo non-invasive tests and for in vitro methods for pharmacological and toxicological testing. Similarly, the ever-increasing problems faced by the Common Agricultural Policy and their effects on the prices of industrial feedstocks have underlined the necessity for large scale developmental efforts conciliating the needs and interests of both agriculture and industry.

2.2.2. Structural factors : the absence of a favourable context.

Because the decisive importance of applied biology was neither recognized immediately by the Member States nor considered by them as a justification for collaboration and concertation at Community level, biotechnology in Europe lacks the supportive context which is necessary for its expansion. The absence of an appropriate environment can be strongly perceived in those areas where basic biotechnology needs to be promoted and industrial competitiveness established.

Research in basic biotechnology cannot be properly implemented in the absence of an appropriate logistic support (data banks, biotic collections, patent counselling, multidisciplinary training ...) for laboratories. The efficiency of such support depends directly upon the scale of market they serve and the total resources and abilities contributing to the support facilities. Within the Community, these resources and skills

are generally dispersed or grouped on a national basis on too small a scale in proportion to the importance of the research problem and to the supportive context from which laboratories in the USA or Japan are able to benefit. With the exception of a few recent and still restricted initiatives from the Commission services, no attempt has yet been made to provide basic biotechnology research with the supportive context which EMBO has so successfully established for fundamental research in molecular biology.

The promotion of industrial and agricultural competitiveness in a very rapidly evolving area like modern biotechnology depends to a large extent upon clear and well adapted regulatory regimes at all stages from laboratory development and testing through marketing to post-marketing monitoring. There is, in the Community, an obvious conflict between these regimes, national in concept and in scope, and the Community market, continental in its dimensions and structures. Examples of the unsuitability of the general frame within which European biotechnology is presently compelled to develop are numerous. They range from the prohibitive prices of certain raw material resources needed by European transformation industries, to the adoption of regimes which are contrary to the development of a European strength in biotechnology. The production of single cell protein (SCP) constitutes, in this connexion, an interesting example of a biotechnological venture which was halted by regulatory and acceptability problems in one country.

## 2.3. THE NEED FOR A COMMUNITY APPROACH : THREE STRATEGIC AREAS

As emphasized above, in section 2.1, the weaknesses of the Member States in modern biotechnology can be ascribed, ultimately, to :

- the failure to achieve "critical mass" in research capacity, which European companies often attempt to reach through mergers or joint agreements with U.S. and Japanese firms.

- lack of action in certain key areas where urgent Community needs have been identified : addition of greater value to agricultural products, adequate supply to industry of raw materials of agricultural origin, reorientation of the R&D of

health industries, adaptation of industrial, commercial and intellectual property systems,

- lack of a supportive context for research, development and industrial exploitation related to the dimensions of the European market. The current rules and regulations established at national level considerably hamper, and sometimes prevent, the possibility of market unification at Community scale.

In addition, one must also underline the state of neglect which is presently characterizing biotechnology in Third World countries. The applications of modern biology do offer solutions to nutrition, health and agricultural development problems in several parts of Africa, Asia and South-America. As yet, however, no great attention has been given to this potential in the promotion of agricultural and medical research conducted in the developing countries.

The Community Development Policy, as outlined in the September 1982 memorandum from the Commission to Parliament and Council (*), envisages a significant role for biotechnology-related activities : as reflected both in the current programme of Science and Technology for Development (**), and in the proposals currently being debated for a science and technology programme within the developing countries (***).

It is obvious, as stressed in section 2.2., that these deficiencies essentially result from the fragmentation of biotechnology R&D in the Community and that they will not be overcome without :

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(*) COM(82) 640
(**) COM(81) 212
(***) COM(83) 354

2.3.1. The establishment of strong Community foundations in basic biotechnology

It is from such foundations that European industry and European agriculture, now very closely related and interdependent, will be provided with the wide range of different solutions against which a wide range of different problems may be tested simultaneously with the maximum rapidity and minimum of expense. Specific skills and competences, industrial know-how and appropriate research facilities do exist at several sites within the Community but the present efforts, carried out at national level, are dispersed and lack the coherence and efficiency which can result only from the mobilization of potentialities within the Community.The Member States need a strong Community nucleus of expertise to serve as a driving force for a systematic and coordinated implementation of mission-oriented research in basic biotechnology. The action to be undertaken is considerable and involves, through multidisciplinary training and research, the transfer of academic knowledge to industry and agriculture and the removal by multiple solution-problem testing approaches of technical bottlenecks to large scale applications.

2.3.2. The stimulation of specific industrial R&D

Although the relatively large investments now agreed by European industries in biotechnology and the confidential nature of these activities render unnecessary and even inopportune a direct stimulation through massive Community funding of industrial R&D, there are still two domains where specific Community incentives appear to be urgently required.

2.3.2.1. A need for European feedstocks of agricultural origin.

In the first of these domains, half-way between industry and agriculture, there is, as stressed in the FAST report and in the "Plan by objective : biotechnology", an obvious necessity to provide the industries of the Member States with

European-grown feedstocks of agricultural origin which harmoniously combine the industrial requirements for quality and price with the maintenance of agricultural productivity. Such a goal, a prerequisite to the competitiveness of European industries and to the stability of the Common Agricultural Policy, will not be reached without specific research for extending the properties of the plant species presently exploited in Europe and for designing new crops adapted to the modern needs of transformation industries. The research in plant physiology, genetic engineering, technological design of new crops and land assessment which needs to be executed in this area has up to now been largely restricted to the national scale ; the European dimensions of the problem clearly call for an initiative at Community level.

Such developments will also respond to the longer-term global challenges of possible shifts in the patterns of land-use. If, for example, the strategic objective of greater food self-sufficiency is approached in many developing countries, this would accentuate the tendency in Western Europe and North America to withdraw land from food production, and increase the need to re-direct it towards other useful outputs.

2.3.2.2. New drugs and new testing methods.

The second domain is that of the health industry where, as underlined in section 2.2., the increasing costs of medical care and the replacement of the "private customer" by the "state-customer" render necessary a new orientation of R&D strategies. There is now a pressing need for the prevention or rapid treatment of "common and expensive diseases" and for efficient "structure-function" approaches to the routine screening of compounds for pharmacological or toxicological activities. These actions are particularly important for the public interest. The discovery of new preventive or more rapid therapeutic approaches to illness could possibly reduce the financial burden of social security in the Member States. The development of new in vitro, testing methods, although it

will never replace completely the present in vivo procedures, could nevertheless provide (together with new non-invasive in vivo testing methods) a very attractive solution for the rapid and accurate detection of the activities of new compounds. The establishment of such methods and their standardization throughout Europe could facilitate the setting of unified norms and regulations within the Community (see 4.2. below) which would meet the criterion of simplicity requested by health industries; conversely, the existence of a harmonised Community market will provide greater incentive for the development of such methods.

While the development and standardisation of tests are of great interest to the pharmaceutical industry, it is difficult under normal commercial criteria for firms to invest in the long-term and expensive work required, uncertain as to whether or not the outcome will be generally and officially accepted. Such development should therefore be undertaken by the Community as a whole since the benefits will be felt by the whole Community.

2.3.3. A supportive context for biotechnology

The reasoning in favour of creating a supportive context for biotechnology research at Community level has been presented above in paragraph 2.1. It is essentially based upon considerations of mass-efficiency relationships which show that the pooling of logistic facilities, such as data banks, biotic collections and training resources, will be beneficial to the Member States because biotechnology is multidisciplinary in its approach, complex (and therefore expensive) in its requirements and rapid in its evolution. The requirements of modern biotechnology in skills, materials and information (even in the case of published data) are so large that new approaches have to be devised and implemented at Community scale. The list of contextual measures to be taken in support of biotechnology research is provided in section 4.1.

The reasoning in favour of developing a supportive context for the industrial and commercial expansion of biotechnology at Community level has been presented above in section 2.2. It has

stressed the need to facilitate access by bio-industries to raw materials of agricultural origin and to harmonize the regimes which regulate innovation, intellectual property, production and commercialization of bio-products and bio-processes : only in this way can be created the true Common Market which is the primary economic necessity.

The actions to be taken in each of these areas are multidisciplinary, multiple in their applications and complex in their requirements from both the private and the public sector. As outlined by the Commission at the European Council of Stuttgart and stressed in section 2.3., they require a pooling of skills, a harmonization of legislation and procedures and common decisions on prices and policies which cannot be achieved without strong and coherent initiatives from the Community. The effort considered necessary is presented in section 4.

3.

## ACTIONS CURRENTLY CARRIED OUT AT COMMUNITY LEVEL : NECESSITY FOR THEIR EXPANSION

## 3. ACTIONS CURRENTLY CARRIED OUT AT COMMUNITY LEVEL : NECESSITY FOR THEIR EXPANSION

The arguments of section 2. underlined the necessity for Community actions in several areas of biotechnology. The present section lists the few activities at present implemented by the Commission which display relationships with biotechnology R&D. This inventory is followed by considerations on the insufficiency of these activities.

### 3.1. THE RANGE OF COMMUNITY ACTIVITIES

The Community has acquired research programmes containing aspects of life-science and biotechnology in a gradual manner. This reflects the range and pervasiveness of biotechnology across the various areas of responsibility of the Commission, and the fact that the various programmes have been individually approved, each for specific reasons, rather than having been conceived as elements of any more embracing plan for biotechnology research. The biotechnological component in these programmes is often small and incidental or, when directly supportive of biotechnology (Biomolecular Engineering Programme), limited in scope and budget.

These activities cover :

#### 3.1.1. Research programmes with a component in biotechnology or in applied life sciences

. Research Action Programme (RAP) "Materials" : includes wood as raw material in the sub-programme "Renewable raw materials".

. RAP "Environment" : one of its sub-programmes provides for fermentation and hydrolysis of organic wastes.

. RAP "Health and safety" : the sub-programme "Radiation Protection" contributes much more abundantly than is

generally known to the basic research in enzymology and in cell culture work upon which the foundations of modern methods in genetic engineering were built.

. RAP "Non-nuclear energies" : two projects of the sub-programme "solar energy research" concentrate, respectively, on bio-mass as a source of energy and on photobiology.

. Agricultural Research Programme : projects implemented in the 1979-83 programme cover land use and rural development, mediterranean agriculture, treatment of wastes from intensive agriculture, animal pathology, livestock productivity, biological pesticides, plant improvement, outlets for products in surplus, tree diseases, enhanced production of vegetable proteins; the third (1984-88) programme is now being launched.

. COST (*) actions : where information is shared with non-member countries on specific research activities, including : sewage sludge treatment and disposal methods, studies of single cell protein, early weaning of piglets, plant tissue culture, derivation of animal feedstuffs from ligno-cellulose, food processing, amongst other subjects

. Databanks and communication networks : such as EURONET-DIANE and its hosts, arising from Community programmes on information and documentation in science and technology which help many areas of life sciences and applied biology to develop their information bases.

(*) COST : European co-operation in the field of scientific and technical research. COST constitutes a framework for co-operation, through concerted actions, between the European Community and European non-Member States in the field of research and development.

### 3.1.2. Activities related to the harmonisation of standards and regulations and for the assessment and prevention of bio-hazards.

Several actions of the CEC in this connection, are related to biotechnology. The Commission's responsibilities for harmonization of standards and regulations require, for instance, the consideration of products, processes and terminology in industries such as animal rearing, food processing and pharmaceuticals. It is in the framework of such activities that the study of K. SARGEANT and C.G.T. EVANS on the "Hazards involved in the industrial use of microorganisms" was issued in 1979 and that the services of the Commission prepared a recommendation on the registration of recombinant DNA which Council adopted in June 1982.
The Community's regulatory role in relation to the development of biotechnology is discussed in further detail in 4.2.4 below.

## 3.2. THE BIOMOLECULAR ENGINEERING PROGRAMME (1982-1986)

The only Commission programme really central to biotechnology is, as mentioned above, the Biomolecular Engineering Programme, adopted by Council in December 1981 after several years of discussions in the various committees which advise the Commission and Council.
The general goals of this programme, elaborated after extensive consultation with more than 200 national experts in the Member States and discussion with leading representatives of European industries, are to promote and stimulate the development of new technologies leading to :

- the manufacture of improved agricultural and bio-industrial products
- the determination of more efficient and safer production methods.

Such objectives are to be achieved, in this programme, through the removal of the bottlenecks which prevent applications to industry and agriculture of modern biochemistry and molecular genetics.

The programme consists of two distinct phases. The first phase, now in implementation with a budget of 8 MioECU, includes training and research components. Training covers all areas of biomolecular engineering as well as the improvement of risk assessment methods in biotechnology. To date 20 training contracts have been concluded with well qualified scientists who have now started specific research activities in host-institutions selected among the best laboratories in Europe. In contrast with training, the research actions, implemented by means of cost-shared contracts, are restricted to safety and to the applications of biomolecular engineering to agriculture and to agro-food production. The call for tenders issued by the Commission stimulated a very large response from national laboratories in the Member States and 180 high quality applications were received by the services of the Commission. The resources available restricted to 50 the number of research contracts finally concluded with the applicants. Research activities at present executed in the framework of these contracts include :

. Development of 2nd generation bio-reactors (multienzymatic, multiphasic or co-factor requiring) for agro-food industries.

. Improved and safer production, by means of biomolecular engineering methods, substances important for animal husbandry (vaccines, ...) and for agro-food industries.

. Upgrading of plant products, particularly ligno-cellulose, by means of biomolecular engineering methods.

. Development of methods (and, in particular, of host-vector systems) for the identification, transfer, expression and transmission of new genetic information in cultivated plant species.

. Improvement, by means of genetic engineering, of symbiotic relationships between cultivated plant species and microorganisms in the soil.

. Development of methods which render possible the selective screening of cells and protoplasts and their regeneration into fertile and differentiated plants.

A proposal for the second phase (7 MioEcu) has been presented to Council in June 1983, to consolidate the above work.

## 3.3. THE NEED FOR AN EXPANSION OF COMMUNITY ACTIVITIES

The Community activities relating to biotechnology reviewed above have not the resources to cover in depth the three strategic areas identified for Community action in section 2.3. In some instances, as with the development of basic biotechnologies through training and research, small nuclei of European skills have been created in the framework of current Community Programmes. These nuclei (second-generation bio-reactors, animal vaccines, upgrading of ligno-cellulose, host-vector systems for plant cells, plant cell regeneration, improvement of symbiosis) are however too small in size(*) and number.

While some international organisations exist which provide support for basic research (European Science Foundation, European Molecular Biology Organisation), there is no equivalent support for basic technological development in the life sciences. A similar concern in the U.S. inspires current debate on the creation of a "National Technology Foundation", to complement the work of the National Science Foundation.

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(*) : The group on "vaccines" for instance, which at the moment includes only four contracting laboratories, concentrates upon one major disease and is therefore unable to ensure a comprehensive coverage of the sector. The same holds true for the other groups where the number of contractants are 5 (symbiosis), 9 (ligno-cellulose), 11 (bioreactors) and 16 (host vector systems).

Significant action could easily have been implemented in this area of basic biotechnology if more substantial means had been provided to the ongoing programme in Biomolecular Engineering. From a consideration of the number of high quality of research proposals received, the number selected and the ratio of support granted to each laboratory in relation to that requested it can be shown that the Commission funded in the Biomolecular Engineering Programme less than 10 % of the needs expressed by the laboratories; even within the areas carefully selected for support, there was concern at the risk that in these areas the effort was only just achieving the necessary minimum. It can therefore be concluded that the scientific capacities for a significant Community action in biomolecular engineering do exist and that the primary limitations, from a quantitative (size of research nuclei) and a qualitative (number of research nuclei) point of view, were of budgetary nature.

With regard to the other areas defined for Community biotechnology in section 2.3 (establishment of the factors necessary for the development of Community biotechnology ; support for Community policies in the agricultural and health industries by specific R&D projects ; the promotion of biotechnology in Third World countries) very few specific actions have been or are being conducted at Community level. However, worthwhile initiatives have been started recently in relation to the development of European databanks and information systems, for biotic materials, biologically active macromolecules, and other information support for biotechnology, within the framework of the 3rd Action Plan (1981-83) for Information and Documentation. These activities are all quite specific, having been chosen not only for their relevance for biotechnology, but also for their suitability for joint development at Community level. Their scope is still quite small in relation to the total effort needed in Europe for the promotion of competitiveness in modern biotechnology, and they will have to be expanded and supplemented progressively, as new needs are identified.

## 4. PRIORITIES FOR COMMUNITY ACTIONS IN BIOTECHNOLOGY

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### 4.1. RESEARCH AND TRAINING

The programme, detailed below, for research and training in biotechnology follows the recommendations of FAST and takes into account the experience acquired during the implementation of the first phase of the Biomolecular Engineering Programme. It was established after intensive consultation of national experts and representatives of European industries.

Its content is in agreement with the specific objectives for R & D in the field of biotechnology as defined in the Framework Programme for Community S/T Activities 1984-1987(*). These objectives have been recently approved by Council (**).

It is subdivided, on the basis of the Community needs identified in section 2, into horizontal and specific actions.

Horizontal actions are always precompetitive and bear on all branches of modern biotechnology. Their objective is the establishment of a supportive background for biotechnology research in Europe and the promotion of basic biotechnology, thus contributing to the elimination of barriers (technical bottlenecks, obstacles to the transfer of information, materials and know-how) which prevent the exploitation by industry and agriculture of the fundamental advances made by modern biology.

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(*) COM(83) 260 final

(**) Council Resolution of 25 July 1983 (O.J. C 208/1)

Specific actions are designed for stimulating in depth certain specific developments in well-defined sectors of biotechnology which relate directly to important sectoral policies of the Community. Their objectives are focused upon :

- the development of new industries utilising European feedstock of agricultural origin,
- the containment of costs for health care and the stimulation of health industries through the development of new products.

All research activities, horizontal or specific, foreseen in the programme are to be implemented by means of cost-shared research contracts concluded between the Commission and laboratories located within the Community.
In addition, two COST activities (Aquatic primary biomass : marine macroalgae and Plant in vitro culture) which relate to the objectives of the programme are to be developed as in association with the general actions described below.
Other activities of cooperation with non-Member States are also envisaged in the framework of the programme (in preparation) of the working group on Technology, Growth and Employment which was established by the heads of States and Governments at the Versailles summit of June 1982.

Horizontal activities

### 4.1.1. Contextual (infrastructure) measures for R & D

The measures presented below are restricted to the requirements for the development of a strong research base for biotechnology within the Community.
Other measures aiming at the establishment of a suitable context for the expansion of European industry and the increase of its competitiveness are proposed in section 4.2. Reference is to be made for training and safety to the sub-programme Basic Biotechnology (section 4.1.2). The contextual measures proposed to develop supportive infrastructure for biotechnology R & D can be grouped in two categories : bio-informatics and collection of biotic materials.

4.1.1.1 Bio-informatics

As has been pointed out by Manfred Eigen (*), the limiting factor in life sciences research and application is neither energy (as with particle physics), nor distance, nor materials : but complexity, or the organised information which describes it.

The rate of development and exploitation of biotechnology will become increasingly dependent upon advances in technologies of data capture, information processing, storage and retrieval, and upon the arrangements by which the
data are made available to potential users. Among a number of important areas there is scope and need for :

- development work in applying recent developments in physics and biochemistry (e.g. the various spectrometries, sequencing techniques, 2-dimensional gel electrophoresis, enzyme electrodes) to the data capture needs of biotechnology ;
- the organization of data banks for scanning and retrieving details of all levels of biotic material and its biological properties (especially nucleic acid and protein sequences, crystallographic co-ordinates, functional characteristics, structural information e.g. of active sites or receptors ; and the information held in cell and culture collections) ;
- the development and pooling of experience with mathematical models of structure, function and dynamics at all levels : from macro-molecular (bio-physics) and cellular sub-systems (metabolic cycles, membrane function), to reactor contents (as basis for automatic control systems) ;
- and the development of sophisticated interactive software (particularly molecular graphics and "expert systems", as steps towards "computer-aided design" in biology - e.g. protein engineering - and more incisive planning and interpretation of experiments, e.g. in genetic engineering ; and the more efficient extraction and processing of results produced by biological experiments, through professionally developed image analysis software.

(*) Speech at European Molecular Biology Laboratory, Heidelberg, 19 March 1982.

These are all specialist areas, of fundamental importance and high cost, in which the case for coordination and/or support at European scale is powerful. The European lag behind U.S. federally-financed activities is particularly significant in computer graphics and the use of "artificial intelligence" in life sciences research.

4.1.1.2 Culture collections and gene banks

This applies also to the collections of biotic materials themselves : microorganisms, plant and animal cell lines and tissues, their viruses and plasmids. There are related research needs on cell culture and tissue storage (e.g. cryopreservation) and propagation techniques. There is no public depository in Europe for animal and plant cell lines ; the case for international collaboration has to be explored in depth, possibly on the lines of the extensive arrangements already in place for gene banks of plant genetic resources (seeds and other propagules), or starting to develop for culture collections of microorganisms.

Needs have been assessed through specific studies, through the Commission's experience of collaboration with European and international bodies (EUCARPIA, the European Association of Plant Breeders ; the International Board for Plant Genetic Resources ; the Food and Agriculture Organisation), and through the Task Force for Biotechnology Information, an advisory group of Member State representatives.

4.1.2 Basic biotechnology

4.1.2.1 Programme objective

This part of the programme represents the continuation of the present Biomolecular Engineering Programme. The main objectives are not to be modified and continue to be focused upon what is certainly the basic priority in modern biotechnology, namely, the removal of bottlenecks which prevent the applications of modern genetic and biochemical methods to industry and agriculture. The research efforts will thus be concentrated, as in the present Biomolecular Engineering Programme, upon the development of the second generation of enzyme reactors, that

is to say the exploitation of complex enzymatic reactions for the synthesis of elaborated new industrial products, and upon the improvement of technical knowledge which aims at the directed transfer and expression of foreign genes and the modification of the genetic properties of commercially important organisms.

However, developing and supporting this advanced front of research is not sufficient if one recognizes that the central problem is to domesticate and exploit as efficiently as possible, for the benefit of agriculture and industry, the basic properties of microorganisms, cultured cells, animals and higher plants. In that case, basic long term research efforts must be organized, concentrating on the detailed analysis of the molecular genetics, enzymology, biochemistry and physiology of those metabolic functions which man needs to control in order to increase the performance and stability of bio-systems.

The Commission proposes to include, as in the present Biomolecular Engineering Programme, two projects for the training of European scientists and for the promotion of safety. The training action, in view of the fact that biomolecular engineering conditions the evolution of biotechnology, represents an essential element of the programme. It will cover key areas in basic biotechnology which are still insufficiently explored and should provide European scientists with adequate possibilities for mobility and the improvement of skills and knowledge. The Commission will also study manpower needs in the Community for skilled technicians in biotechnology applications and will consider the need for further proposals in this area.

With regard to safety the proposed programme is to concentrate on the improvement of methods for the assessment of risks possibly associated with the development of modern biotechnology. The establishment of such methods is the prerequisite to any further action which the Commission may consider necessary for ensuring the continuance of high standards of safety for workers in biotechnology and for the general population.

4.1.2.2 Proposed projects

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The projects to be implemented are the following :

- Development and evaluation of bio-reactors (and particularly those which are multienzymatic, multiphasic or co-factor requiring) for industrial applications, depollution and detoxification.

- Modifications of enzyme properties, protein design, synthesis of artificial enzymes and development of new methods for large scale and highly selective separation of proteins and other substances with industrial or agricultural value.

- Development of genetic engineering, enzymes and all process engineering methods for the production of substances (food, intermediates for chemical syntheses, vaccines, hormones...) with industrial or agricultural value and for the upgrading of plant products (particularly ligno-cellulose).

- Improvement of organisms by means of genetic engineering of the basic properties, including symbiosis, of microorganisms, cultured cells, animals and plants which play an important role in agriculture and industry. The actions to be stimulated include the characterization of the structure and expression of microbial, animal and plant genomes, the study of the molecular mechanisms of interactions between plants and microorganisms, the development of methods for the identification, transfer and expression of new genetic information and the control of plant cell regeneration into mature organisms.

- Biochemical genetics, enzymology and physiology of the basic functions and properties of species which are essential to the promotion of modern biotechnology. The list of organisms to be studied will include the microorganisms which are most promising for future industrial use, chemo-autotrophs, methanotrophs, mycorrhiza, and representative species of families important to agriculture and feedstock production.

- Research on continuous cultures containing more than one organism in order to gain an understanding of their efficiency and stability as a basis for the industrial use of mixed populations.

- Research on factors affecting the stability of organisms under long-term continuous cultivation and of immobilized systems, particularly in relation to the expression of genes contained on plasmids.

- Developing micro-analytical methods for the identification and quantitation of biologically important macromolecules.

- Development of new methods for detecting contamination and for the assessment of possible risks associated with applications in industry (particularly during downstream processing) and agriculture of biomolecular engineering.

- Training of scientists in all fields of the above-listed projects.

Specific activities

4.1.3. Agro-food and chemical industries

The relatively independent planning and evolution of agriculture and of the food, animal feed and chemical industries could be tolerated in Europe before the rise of modern biotechnology, at a time when the speed and scale of technological change allowed gradual mutual adjustment where necessary. Now, with the acceleration of scientific progress and the suddenly increased potential for interacting changes, there is a greater need to establish in the Community, between agriculture and these industries, adequate channels for continuous concertation to promote a growing interdependence, which should result from the increasing opportunities for cross-fertilisation of research between them. To improve competitiveness within this whole sector, several research actions must be implemented.

European agriculture has improved its efficiency so much since the CAP was instituted that some products (milk, cereals, sugar, grapes...) are now in substantial surplus, though others that are more difficult to produce in Europe (wood, vegetable proteins and oils...) are still in major deficit. The Commission's proposals in document COM(83) 500 indicate how the market situation could be improved. Further actions to be

supported under this section seek to develop new crops (e.g. fast-growing trees, better oilseeds) and new markets (e.g. supply of feedstock for chemicals) through building a closer relationship between agriculture on the one hand and the animal feed, food and chemical industries on the other.

The links between agriculture and these industries have been growing rapidly in recent years. Thus sucrose production from European beet is becoming ever more efficient because of integrated developments linking improved seed, cultivation, harvesting and processing : yet sucrose faces challenges in various markets from sugars derived from starch and from non-carbohydrate sweeteners. Again soya bean meal, the most important protein-rich animal feed supplement, now faces some competition from colza meal derived from newly developed strains of European grown colza and from newly developed single cell protein produced by European chemical industry. These developing links are what make it unwise to treat agriculture and the animal feed, food and chemical industries in isolation. In recognition of this the Commission has already decided to adjust the system in force for supplying agricultural raw materials for non-food use in the chemical industry so as to ensure that the Community industry benefits from the same conditions of competition as its outside rivals (*).

The European chemical industry was developed rapidly after World War II with the benefit of secure and inexpensive supplies of petroleum from the Middle East. Today, though it is somewhat less dependent on external supplies of petroleum that it was, these external supplies are both less secure and more costly than they were. At the same time, the industry faces challenge, particularly from bulk chemicals made in new plants built near to abundant petroleum sources. What are the prospects for basing European chemistry on agricultural feedstocks ? A FAST study by Gibbs and Greenhalgh, "Biotechnology in the Production of Chemical Feedstocks and

(*) COM(83) 328 final.

Derived Products" concluded that while proposals to supply heavy chemical feedstock from European agricultural raw materials are not credible, the prospects for producing some materials of higher value are already good and likely to improve. Thus they foresee growing opportunities for the production of oxygenated hydrocarbons, carboxylic acids, lipids, sterols, polymeric materials, amino acids etc, opportunities that will be enhanced now that agricultural raw materials are to be available in Europe at world prices.

A move towards reliance on agricultural feedstocks by the chemical industry could be compatible with the growing interest of that industry in specialty chemicals and "effect" chemicals of higher specific value because agriculture feedstocks can offer desirable structural features exploitable in the manufacture of some of these products, for example plasticisers, surfactants and lubricants.

Areas where biotechnological research is particularly needed in Europe are reviewed in Table 1. Many of these actions are to be executed in the framework of the other sub-programmes of the Biotechnology Action Programme and through special efforts at Community level to deal with the agricultural surplus problem. The activities anticipated for this purpose are outlined in sub-programmes 1 (Contextual Measures), 2 (Basic Biotechnology) and through initiatives taken to deal with with the problem of agricultural surpluses within the Community.

In parallel to the implementation of these sub-programmes and initiatives, it is suggested to carry out, in the framework of the Biotechnology Action Programme, projects specifically designed as contributions to the establishment of efficient agro-industrial developments within the Community.

The objectives are to encourage the development of :

- crop systems for supplying high quality agricultural feedstocks of European origin to the food, animal feed and chemical industries. (cf. L. Munck and F. Rexen "Cereal crops for industrial use in Europe", study contract CEC-1001-B 7210-83 DK, report in preparation),
- bioindustrial processes (both traditional and novel) for the production of manufactured foods and chemicals derived from agricultural feedstocks.

Improvement of fermentation processes :

- new fermentation systems for oils and fats
- development of continuous fermentation for production of alcohol, beer, wine, or food additives
- development of control systems for fermentation reactors with newly designed sensors enabling errors to be recognized and rectified at early stages.
- production of chemicals (special polymers, xanthian gums, etc.)

Use of enzymes (immobilized or otherwise) or of immobilized cells for :

- production of oils and fats
- production of amino acids, peptides or proteins
- immobilization of lactic acid bacteria producing flavours and other products
- liquefication and processing of raw material during manufacture of alcohol, beer, wine, fruit juices
- elimination of undesirable components (diacetyl, esters, sulphurous compounds, anthocyanins, flavonoids ...) in manufacture of beer, wine, fruit juice, dairy and other products
- production of vitamins and antioxidants in combination with purely chemical syntheses
- production of food additives (colours, flavours, aromas, stabilizers, thickeners, antimicrobial substances)

Genetic improvement, through mutagenesis or genetic engineering, of :

- bacteria for transforming dairy products
- yeast for producing alcohol
- yeast for fermenting wine and beer
- microorganisms for producing oils and fat
- microorganisms for producing amino acids, peptides and proteins
- microorganisms for producing food additives
- plant cells in culture for production of lactone flavours, food additives, and pharmaceuticals.

Table 1 : possible contributions of biochemistry, genetics and biomolecular engineering to the quality, production and secondary transformation of agro-food (modified from "Biotechnology : a Dutch perspective", STT, May 1981)

The projects to be executed in priority order are as follows :

- Technological and economic assessment of the use of soil microorganisms, agricultural crops, new marine and land species, and of new plant parts in order to provide chemical industries (particularly for fine chemicals and some specialized oxygenated hydrocarbon products required in greater bulk) with agricultural feedstocks of European origin. The ability must increasingly be developed to "tune" the choice of plants flexibly to the downstream needs.
- Analysis of the microbial, biochemical, physical and chemical processes which regulate the production, storage-life, organoleptic properties and nutritive value of agro-foods produced through conventional methods in Europe. To ensure exploitation of results by industries of the Member States, all contractual research activities for this project should be carried out by units associating universities and industrial laboratories. Specific proposals for research contracts will be formulated by such units and implemented by them.

4.1.4. Health industry

An analysis of the causes of foreseeable difficulties for the European health industries, in particular the pharmaceutical industries, leads to the conclusion that Community R&D can play a role in maintaining or improving the competitiveness of these industries. In this respect, changing market patterns and financial consequences of regulatory systems are two of the major parameters which must be taken into account.

4.1.4.1 Pharmaceutical screening and tests

European pharmaceutical and biomedically oriented industries represent a major sector of European economy and employment. They contribute to export and are still competitive world-wide. They are however facing several obstacles which could become very detrimental in the near future. Estimates of the cost of developing and obtaining approval for a new drug at present range from 40 to over 100 million ECU. Part of this cost is due to :

- the long and expensive assessment of pharmacological activity,
- the examination process to which a drug is submitted before being registered and marketable.

Therefore, action should be taken along the following lines:

- development of new methods for the screening of pharmacological activity of new molecules.
- development of new methods for toxicological screening in order to accelerate the present lengthy testing processes.

In this respect, emphasis should be placed on the development of in vitro methods which should reduce the cost of screening and, as they would be developed in common, would help in providing the basis for common acceptability.

In fact, in vitro activity tests would improve the chance of detecting new pharmacological effects, as they allow for testing separately for specific functional properties instead of having to rely on the globally integrated results which are obtained by using whole animals. This approach, although it cannot be expected to replace current in vivo procedures for the final evaluation of effects, may also be seen as contributing to the design of new drugs (see 4.1.4.2 below), as it can be extended to the concept of relationship between body or organ function and structure of the molecule being tested. At the same time, special efforts must also be made to develop new non-invasive in vivo tests which remain the ultimate objective for clinical diagnosis.

Finally, it is worth mentioning that problems of confidentiality and intellectual property, normally a constraint on the scope for Community action in health industry projects, are less serious in the case of developing new tests for activity or toxicity : for the general interest in their common acceptability requires details of the tests to be published.

### 4.1.4.2 Health expenditures, and new technologies

Health expenditures, and most particularly hospitalization costs, are continuously increasing in Europe. The burden of these costs - which falls predominantly on the state customer has such consequences on the public purse that there is now an absolute necessity to contain, without hampering the quality or efficiency of health care, the costs of treatment and hospitalization in the Member States. An essential solution to this problem may in the long term be found through the promotion, at Community level, of techniques, devices or drugs which could contribute to the prevention of diseases and thus to the reduction of the associated costs. National efforts should be integrated and stimulated particularly in areas where there is need for long term research and venture investment, for example in improving the present methods of detecting, preventing and treating costly diseases. The new technologies offer an arsenal of approaches for the production of vaccines and hormones through genetic engineering, the development of new diagnostic tools (monoclonal antibodies, protein separation methods...), treatment (antibodies against generally inactive epitopes, hormones, analogues of newly discovered neuropeptides, intracellular signal molecules...) and the preparation of new drugs by computer aided molecular design. These technologies, which are not sufficiently developed by industry in the present fragmented state of the market, should be harnessed for the benefit and interest of the Community of Member States and of developing countries.

## 4.2. CREATING A FAVOURABLE CONTEXT FOR BIOTECHNOLOGY IN EUROPE

### 4.2.1 The administrative challenge : the need for concertation

The development of biotechnology in Europe depends upon the separate decisions of many independent actors - scientific researchers, financial investors, corporate managements, final consumers - whose individual decisions can be indirectly, but often decisively, influenced by the actions of the public authorities. To create a context favourable and encouraging for the development of biotechnology in Europe demands some coherence in these actions. This presents the challenge not only of coherence between the Community and the Member States, but between separate Ministries and agencies within each State, and across the services of the Community institutions. For as Nature's new publication, "Bio/Technology" has expressed it, "One of the central challenges of biotechnology is organizational : it is a boundary-crossing, multidisciplinary, statistician's nightmare... It challenges the organization of our universities, our government departments, our economic statistics and our minds." (*)

To this challenge, industry has responded by forming alliances and consortial activities (e.g. Biogen, a medium-sized specialist biotechnology company, owned by a few major multinational groups), inter-sectoral and international). Within the scientific community, the European Federation of Biotechnology (founded in 1978) has brought together over 40 learned societies, and industrial participants are prominent in the specialised, but international, working groups which meet under its umbrella. In government, many countries have created ad hoc co-ordinating committees, inter-departmental groups, or special "missions" to integrate and mobilise national efforts.

(*) August 1983, p. 526

A similar need is felt within the Commission services, for what is termed concertation of the various activities relevant to biotechnology : linking horizontally across services within the Commission, and relating also to the national coordinating bodies for biotechnology, to facilitate concertation of Community and Member State actions. Similarly Community actions have to relate coherently to world developments, be it in scientific networks, patent conventions or trade agreements.

The need for concerted measures aimed at improving the context for European biotechnology has been analysed by the FAST programme (*), which emphasised three "contextual" policy areas as being of special importance :

- the provision to European industries of raw materials of agricultural origin at competitive prices ;

- the effective protection of commercial and intellectual property rights, on a basis consistent within the Community and equitable in relation to conditions elsewhere in the world ;

- the creation of a common regulatory environment (and hence more truly a common market) within the Community.

These needs, and the corresponding actions, are presented below (Sections 4.2.2 to 4.2.4).

In order to identify the necessary actions, to promote timely initiatives, and to assist concertation between Community and Member States in matters affecting the development of biotechnology, it is essential over the next few years to have a significant capability within the Commission services to monitor developments and to promote the necessary concertation.

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(*) CEC, FAST Programme : Results and Recommendations. Vols. I & II. December 1982.

An essential tool to be used in the improved monitoring function will be an expanded series of networks, established in cooperation with the Member States to provide an ad-hoc system of collaboration between individuals, specialized groups and institutions. This will be coupled with an information base, regularly updated by scanning, selecting, interpreting and storing in an organized way the incoming flow of information.

In particular these activities will relate to the 4 domains identified by FAST studies as of basic importance for the future of European biotechnology :

- Foundation capabilities (human, institutional and other resources) - strategic strength in biotechnology rests on a relatively large number of fundamental disciplines and practical capabilities.

  World class capability in all these fields is a realistic objective for the European Community as a whole, but is beyond the resources of even the largest Member State. It is one of the objectives of the basic biotechnology R & D programme to encourage the competitive emergence of world class capabilities in all key areas ; it will be one of the objectives of monitoring and assessment to identify where weaknesses or new needs are emerging, and to initiate debate on action required.

  Land use - as noted in the Comission's recent communication to Council (*), biotechnology will offer a growing number of new opportunities for the improvement of agricultural production, and for increasing the quantity and range of non-food products (timber, animal feeds, chemicals, fuel...).

  There will be increasing interactions between agriculture, forestry, and the food, chemical, energy and waste management industries. There is a need for an integrated view of their strategic development, and an integrated approach to Community policies affecting them ; such integration will be facilitated by the commitment to concertation.

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(*) COM (83) 500

Third World relations - biotechnology threatens commodity producers by new possibilities of substitution (e.g. isoglucose or aspartame replacing sugar), but can also contribute significantly to such basic needs as food production, storage and improvement, and the fight against diseases which plague man, crops and animals. Whether through the programme of science and technology for development, or trade agreements under the Lomé Convention, or in the self-sufficiency-oriented food strategies now being promoted, biotechnology has many interactions with the Community Development Policy (*). The monitoring of these problems and opportunities, the perception of the cross-links with the other Community policy areas, will enhance the prospects for effective anticipatory action.

- Health care and pharmaceuticals - the pharmaceutical industry is of importance to all biotechnology for the scale and significance of its research effort : it represents the technological leading edge, particularly in the all-important translation of scientific breakthroughs into pure, tested, economically produced, marketable products. Medical research represents another type of leading edge, and recent advances give hope that acceptable solutions will be found to many hitherto intractable problems including inborn genetic errors, malignant diseases and neurological disorders such as those of old age. Beyond the benefits to health, these are matters of basic importance for the competitiveness of Europe's industry, for employment, and for the quality of Europe's science : touching many issues of public and Community policy.

  In particular, the Commission has to aim, in conjunction with Member States, at the achievement of a rational regulatory stance, balancing a conservative concern for safety against demands for the speedy introduction of new and more effective treatments, with their putative benefits, possible risks (See 4.2.4 below), and implications for innovation and competitiveness in one of Europe's key industries.

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(*) Memorandum on the Community's development policy : Sept. 1982 (from the Commission to Parliament and Council).

Each of these strategic domains is of course the predominant concern of a particular ministry (in Member States) or service (within the Commission) ; but the rich and proliferating interactions arising from biotechnology demand a horizontal view, if opportunities are to be seized (cf. the fertilisation of life sciences by information technology : bio-informatics), problems avoided (e.g. uncompetitive pricing of raw materials for the fermentation industry), and coherent policies adopted (e.g. between promotion of innovation and protection of established producers or consumers).

Action : the Commission therefore proposes a reinforcement of its resources for effective assessment (or monitoring) and concertation of the new and existing activities which bear upon the 5-year biotechnology action plan. The general objectives will be to improve standards and capabilities in the life sciences and biotechnology in the European Community, and to enhance the strategic effectiveness with which these are applied to the social and economic objectives of the Community and its Member States. To achieve these, the following specific tasks have to be executed, in each case in conjunction with the relevant services :

1. Consideration of how the real value safely and sustainably derivable from the renewable natural resource systems in Europe may be maximised ;
2. promoting in co-operation with developing countries and relevant institutions the pursuit of the same task within their respective regions ;
3. consideration of the implications of developments elsewhere in the world for biotechnology-based industry in Europe. (For example development of maize-based sweeteners, chemicals and fuels production in the US has led to greatly increased offerings of maize gluten feed for animals with implications for European agriculture, chemicals, SCP production and Third World trade that require careful consideration) ;

4. identifying opportunities for enhancing through concertation and co-operation the effectiveness of biotechnology-related programmes in the Member States (e.g. planning the development of culture collection information services) ;
5. working with the services of the Community, Member States and other interested parties to identify ways in which the contextual conditions of operation for biotechnology in the Community may be further improved to promote its development in all useful applications and the supporting scientific capabilities ;
6. disseminating knowledge and increasing public awareness of the nature and potential of biotechnology and the life sciences, to raise the quality of public debate (of fundamental long-term importance) ;
7. establishing, in cooperation with Member States, an ad hoc system of collaboration between groups and individuals with interest and capability in the life sciences and biotechnology ; so creating a series of networks, as informal and flexible as possible, adapted to the particular problems under study.

   The networks to have the triple function of providing an active input into the programme, encouraging coordination through the exchange of information between the centres, and assisting the broader diffusion of information envisaged in task 6.

### 4.2.2 Provision of raw materials of agricultural origin for industry

#### 4.2.2.1 Background : raw material needs, evolution and problems of the current Community regime

Raw materials for biotechnological production originate from living or fossilized plant life. The principal fossil resources are coal, natural gas and oil whose price is determined by energy policy. In order to be used in fermentation processes fossil hydrocarbons must be converted into a usable substrate, a typical example of a current process being methane to methanol which is then fermented into single cell protein. It is ironic, and instructive to recall, that the seminal Japanese development work on SCP from paraffin (another option) was developed in order to

enable their fermentation industry to switch from "expensive" agricultural substrates to "cheap" imported oil. The point is that the basic need for a source of carbon inevitably links these alternative raw materials for biotechnology, requiring an integrated approach if public policy decisions in each area are to be coherent with desired objectives.

The long-term trend of real agricultural prices has been downwards, over the past 20 years ; while that for hydrocarbons has been rising. Consequently the interest of the fermentation industry has swung predictably back to agriculture.

The raw materials derived from agriculture are principally carbohydrates, that is starch derived from cereals, potatoes and sugar, either in the pure form or as molasses. For some processes these raw materials are interchangeable but for others the degree of purity or the specific nature of the raw material is essential to the biotechnological process.

These agricultural raw materials are subject to the market regimes of the C.A.P.

For products which find their final outlet in processed foods this has not led to a loss of competitiveness by the Community industry since the Community preference established by the system of import levies and export refunds is applied equally to raw materials and processed foodstuffs.

Only a very few non-food products enjoy the protection of variable components and the system lacks a continuous thread of basic industrial policy logic.

A few products, such as sorbitol and mannitol, enjoy the same system as foodstuffs, with both import levies and export refunds. Other products, such as citric acid, attract an export refund based on the raw material content but no variable component is levied on import. This means that for exports Community industry is on a comparable basis with

third countries but is fully open on the internal market to competition from imported products made from raw materials at world prices. Where this competition comes from EFTA countries there is no fixed component of duty protection and for non-EFTA countries the reductions resulting from the Tokyo round are eroding the already low fixed duties.

Where variable components do exist for non-food products they are not always given for all possible raw materials on which the process can be based, resulting in further distortions of the competitive position.

In 1967 (modified in 1975) a special regime was introduced for starch production which gave a refund for food and non food starch. The regime attempts to create an equilibrium between producers using maize, wheat and potato as a source material and compensates approximately for the difference in the price of starch made from raw materials within the Community and that made from raw materials at world prices.

The level of production refund is decided by the Council and although adjustments have been made they have not always kept pace with the gap between Community and world cereal prices.
A similar system exists for sugar used in producing certain chemical products.
This refund is directly related in value to the starch refund but limited to the products listed in the annex to the regulation EEC 1400/78. Again the refund in recent years gives only a partial compensation for the difference between world and EC prices.

The cost of producing both existing and new biotechnological products derived from starch or sugar is influenced by these regimes. It is frequently argued that raw material prices are not a significant proportion of production costs ; however, it is marginal costing that will determine the site of production, and for new investments such as biotechnology the investment decisions as to the location of new plant will be influenced by cost factors such as raw materials.

It would not be possible to set up for non-food products a system similar to that existing for food, since this would involve an increase in protection with a consequent renegotiation within the framework of GATT, which would be neither desirable nor feasible.

As a policy objective it is necessary to ensure the provision of raw materials at world prices for biotechnological industry making products which are unprotected. Such a step will be neutral from a budgetary point of view, for the following reasons :

- Where the production of a product from indigenous raw materials ceases in the Community and is replaced by imports there is a loss of economic activity and employment, and the raw material that would have been used in its manufacture (wheat or sugar) goes into intervention or is exported with a consequent charge on the budget.
- Where a product is produced from imported raw materials, such as maize for starch, stopping of Community production and replacing it by imports of the finished product will result in a loss of revenue for the Community budget in the form of import levies on the imported raw material.

Continuing research and development in biotechnology is giving industry the possibility to manipulate raw materials and to produce existing products by new methods as well as new products. It is therefore essential that the regimes for raw materials for biotechnology offer a free choice at competitive price level so that industry can establish a long term investment policy.

4.2.2.2 Community action : new regimes on starch and sugar for industrial use

In its Communication on the Common Agricultural Policy (*) the Commission has underlined the necessity "to provide Community raw materials for biotechnology on the same conditions of competition as for external competitors".

(*) COM(83) 500 Final (2.10)

The Commission intends to propose to the Council new regimes for starch and sugar for industrial use which will attain this objective.

### 4.2.3 A European approach to intellectual property rights in biotechnology

#### 4.2.3.1 The intellectual property problem in biotechnology

The role of intellectual property is to secure the commercial exploitation of proprietary R & D results in highly competitive markets and simultaneously to permit the beneficial dissemination and exchange of knowledge in the field of activity concerned. Biotechnological R & D and bio-industry are rapidly evolving and expanding at the international level, and it is therefore indispensable that the industrial property laws and instruments available in the Common Market match the need of science and industry and of the Community's goals.

The option, long used particularly by the fermentation industry, of protection via commercial secrecy, faces major difficulties in the context of modern biotechnology. The involvement of multi-disciplinary teams is likely to include researchers who need to publish or lecture openly to maintain their reputations : witness some of the current university-industry conflicts, particularly in the U.S.A. A greater recourse to commercial secrecy by industry will also inhibit precisely the pattern of collaborative working which is needed in this interdisciplinary field if maximum benefit is to be obtained from individual breakthroughs.

Again, when a micro-organism is involved, an imitator may be able to achieve industrial replication of the "invention" within hours, and given only a miniscule quantity of material ; unlike other industrial situations where months or years of effort and investment might be required.

Considerable legislatory work and professional thought has been devoted, at the international and national level, to enable

intellectual property law, mainly patent law, to cope with the many specific problems resulting from biotechnological R & D and industrial microbiology. But the legal situation still suffers from deficiencies or discrepancies in statute law, and a general shortage of case law. The problem is worldwide, but particularly harmful and dangerous to an entity like the European Community, where the existence of a harmonized and adequate body of law, rules and practices is of major importance to the proper functioning of its internal market and the competitive power of its industries.

The principal issues at stake concern the protection of intellectual property rights relating to genetically engineered micro-organisms per se, and corresponding problems arising from the application of such techniques to plant breeding, and potentially even to animals. The answers to these questions are of considerable importance not only to certain fundamental concepts of industrial property, but also to science, industry and society.

The present legal situation in terms of legal protection is embarrassing and far from satisfactory. Technology-related problems that affect everybody are compounded by non-explicit legislation and poor jurisprudence in and between States and sharp differences of opinion on future policy within national administrations, for example between Ministries of Justice and of Research.

Furthermore Europe has some disadvantages with respect to the protection of intellectual property rights compared with its main competitors, the United States and Japan. For example it is possible to obtain patent protection in the United States up to one year after publication of the information on which the patent is based, but in Europe publication, even orally, precludes subsequent patenting. Again it is possible to patent new microorganisms as such in both the United States and Japan but not in Europe.

Both these competitors are taking steps to protect their national interests concerning biotechnology patents and inventions. For example concerning the patentability of genetic

inventions involving recombinant DNA, the Japan Economic Journal published the following on 8 April 1980 :
"The Agency has decided that simple methods to chisel and refill the ring of any DNA, such as cutting off part of the ring and replacing the cut-off chip with that separated from the ring of a different kind of DNA, will not be patentable since they are to be considered "well-known" technology.

Also unpatentable will be any "comprehensive" kind of idea covering the whole ambit of the modern gene engineering processes."

This appears to prejudge, for Japan at least, the outcome of the Cohen-Boyer US patent application, which covers basic processes in genetic engineering.
Despite the lead the US enjoys over Europe with respect to biotechnology patents, the US Office of Science and Technology Policy report (cited in 2.2 above) believes that some problems remain. It states :

"The laws and regulations governing patent protection for biotechnology products and processes are still evolving and as is the case with emerging technologies, have not kept up with the rapid pace of development. There are a number of unresolved issues and questions which could slow the commercial development of biotechnology, such as the adequacy of international patent protection and the effectiveness of the Plant Variety Protection Act."
and goes on to make recommendations for extensive review of current procedures and their impact on innovation, and for active steps by the U.S. administration to accomplish patent term restoration (*) and other relevant measures.

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* Particularly in the field of drugs the average effective life of a new product has been greatly reduced by the long period needed for development and for securing regulatory approval. The purpose here is to extend the terms of patents by the length of time that regulatory review delayed their marketing.

4.2.3.2 Specific actions at Community level

The Commission's analysis of the need had anticipated such recommendations, and an in-house inter-service group has been studying the situation of the Community in relation to intellectual property rights in biotechnology. The aim is to identify action priorities and prepare a Community position on the current and forthcoming challenges, scientific, technical, economic and political.

A significant factor in the timing is the OECD study, launched in February 1982 : "Biotechnology and government policies : Patent protection in biotechnology". The results of this enquiry, covering practically all of the 24 member countries (which include all EEC Member States and the major industrial competitors), should be available by the end of 1983 or early '84. They will provide a valuable factual compendium, and will highlight the substantive issues on which international negotiation will have to follow.

Major unresolved issues include :

- the patentability of biotechnological inventions as such ;
- the implications and conditions associated with the rules of practical protection requirements and procedures (e.g. for the release of deposited micro-organisms to third parties) ;
- the addition to the existing problems concerning plant variety protection, of complex new relations with patent law (arising, for example, from the new ability to transfer genetic material between species, or between plant cells and micro-organisms).

In order to
- enhance the competitiveness of our industries and the functioning of the internal market of the EC
- control certain problems specific to biological materials
- assist in preparing a coherent community position in international negotiations,

The following actions should be undertaken as matters of urgency :

a) the Member States should be invited to share with the Commission information about the aims and content of ongoing and planned work, national and international, regarding the protection of biotechnological inventions or achievements (e.g. as recently provided in response to the current OECD enquiry) ;
b) the Commission should work out proposals to Council for the resolution of the issues referred to above ;
c) the Member States and the Commission should seek common principles and guidelines for the management and dissemination of biotechnological information and knowledge arising from publicly financed R & D in biotechnology.

Furthermore, the industrial property issues in biotechnology re-emphasise the desirability of all Member States' ratifying both the European and the Community Patent Conventions, as a first but necessary step towards a basis for commonly accepted regulations.

The problem at Community level is that the debate about the aforementioned issues and their implications takes place mainly outside the institutional bodies of the Commumnity, e.g. at the OECD, WIPO, UPOV (*) and in national industrial property circles ; hence the reason for the actions proposed under a), b), c) above. These will have to be implemented by joint mechanisms of consultation, cooperative studies and concerted measures, building on the existing practices of Community coordination and participation in international bodies such as those mentioned. Only in this way will it be possible to render industrial property law in the Community fully effective in the near future and thus support biotechnology research, development and exploitation in the EEC.

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(*) WIPO : World Intellectual Property Organisation
UPOV : Union pour la Protection des Obtentions Végétales.

Concrete actions would be :

i) extension of the Commission inter-service group to an EEC-national expert group in industrial property matters in biotechnology for the implementation of actions a) to c) above (say 4 meetings per year, about 20 experts) ;

ii) establishment and execution of a programme of studies on problems concerning the unresolved issues described above (about 5 to 10 studies in 1984).

A significant obstacle to progress in the rationalisation or modernisation of patent law in biotechnology is the apparently acute shortage of patent attorneys with relevant knowledge. Consequently a further concrete action proposal is :

iii) provision of financial aids to European candidates wishing to enter the patent attorneys' profession in the field of biotechnology (since in the training phase, of up to 3 years, the candidates are poorly paid). (On average say 5 candidates per year per member state).

These actions will complement the actions already proposed by the Commission in transnational infrastructure [1], utilisation of R & D [2] and financing of s.m.e. innovation [3], which apply equally to biotechnology.

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(1) COM(83) 277
(2) COM(83) 18
(3) COM(83) 241

### 4.2.4 A European approach to regulations affecting biotechnology

#### 4.2.4.1 Biological safety

Public and parliamentary opinion is divided between admiration of the new discoveries in biotechnology, and concern about some of the possible implications or conjectural risks of their use. This concern is reflected in the extensive debates, studies and reports on the need for regulation and control of various aspects of the life sciences ; a debate vigorously pursued throughout the developed industrial world. The story of the initial concern about the conjectural risks of recombinant DNA ("genetic engineering") research, the voluntary moratorium on such research by scientists following the February 1975 Asilomar conference, the institution of regulatory committees, and the gradual relaxation of controls as earlier concerns were reassessed in the light of further information and experiment (use of disabled strains, physical containment at appropriate standards) - this story is by now familiar to the general public, because of the widespread interest and corresponding newspaper coverage which the topic generated.

Although the perceptions of risk have shifted towards relaxation, public concern remains real ; fuelled in part by the continued rapid progress of the scientific capabilities and their application (or applicability) to human germ cells or the human genome. Current debate also focusses on the field release of plants modified by molecular genetics, and the possible risks of large-scale industrial fermentation.

The Parliamentary Assembly of the Council of Europe adopted on 1 January 1982 recommendations on genetic engineering (Recommendation 934 (1982)). The Committee of Ministers is currently considering a feasibility study report relating to the control of work on the human genome (genetic material) : e.g. genetic screening and gene therapy.

The OECD, through its Committee on Science and Technology Policy, has instituted a major study of government policy on the control of biotechnology in its member states, and has recently distributed a draft report for comment.

The World Health Organisation has a professional interest both in the conjectural hazards of biotechnology (possible risks of epidemics from the release of pathogenic microorganisms, old or new), and in its potential as a production tool : a general report is under discussion for publication in 1983(*). Similar interest has been expressed by the Veterinary section of the International Office of Animal Diseases.

Specialist administrative bodies and rules have been set up in the USA (National Institutes of Health : Recombinant DNA Advisory Committee : RAC), in the U.K. (Genetic Manipulation Advisory Group : GMAG), and in many other countries, often adopting the approach (registration, containment standards for various categories of experiment) of NIH or GMAG. The policy debate in the U.S. continues to be vigorous. The NIH/RAC is currently considering authorizing the release into the field of manipulated plants. Various Congressmen (Gore, Kennedy) are preparing legislative proposals. As with the Council of Europe study cited above, attention is focussing increasingly on issues of human genetic screening and (more remotely) possible interference with the human genome.

Industrialists - particularly in the pharmaceutical industry in the first instance - are concerned about the prospect of excessive restriction limiting their scope in research and hence their competitiveness : Sweden, the Netherlands and Japan were countries felt by some of their industrialists to have adopted an excessively conservative position on rDNA work, to the detriment of their biotechnology, and to have been slow in following the consensus for relaxation. In the Safety in Biotechnology Working Group of the European Federation of Biotechnology, industrialists and academic researchers have joined to draft recommended guiding principles.

There has been corresponding activity and interest in the Community institutions : numerous questions have been asked in the European Parliament, and in May 1981 the Economic and Social Committee held a colloquium in Brussels on safety in the field of recombinant DNA.

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(*) WHO regional office for Europe : ICP/RCE 602(1)(S)
Summary Report of the Working Group on the consequences of biotechnology on health, 6.1.83.

The Council adopted on 30 June 1982 a recommendation on the problems arising in safety related to recombinant DNA work. There are three main areas of risk :

- in the research laboratory
- in industrial production
- at the stage of marketing (free circulation of goods).

These are discussed in terms of technical and regulatory aspects in the sections 4.2. 4.3 to 4.2.4.5 below.

Given the continued level of widespread public and political concern, reflected in the many fora mentioned, and in the similarly persistent concern with issues such as animal welfare and their use in tests, which also impinge on biotechnology, it is clearly necessary for the Commission to maintain an awareness of the social dimensions of biotechnology and the interfaces with the various policy areas on which these dimensions impinge.

In terms of concrete action, the Commission's FAST programme launched a "Social Dimensions of Biotechnology" multi-disciplinary working group, drawing on industrialists, risk analysts, a philosopher of science and academics. This group, which met sporadically over 1980-82, produced a short report (incomplete, through shortage of staff and resources), offering 5 general "principles" which should guide public (and Community) policy in the "management of our bio-society" :

1. There can be no policy of zero risk.
2. There are limits to the competence of experts.
3. Even within these limits, their credibility/acceptability is questioned.
4. There is a need for adaptive strategic management, taking account of long-term, "total system" effects so far as currently perceivable, and accepting that perceptions will be modified by experience.
5. There is a need for continuing education at many levels, including decision-makers, the general public and the scientists themselves.

Action : in order to maintain awareness of evolving pressures for new policies or regulations, a monitoring function is needed, at least to collate at Community level the evolving views of national regulatory bodies. Of the 5 "principles" cited above, items 4 and 5 could in part be combined with this monitoring role, i.e. assessing developments, and where appropriate assisting in the production and diffusion of objective, factual information (cf. the Commission's two earlier reports in this area *). This function can be appropriately combined with the concertation role described in 4.2.1 above, and provision for it is included in the budget estimates (section 5.3).

4.2.4.2 Food innovation : industry, consumer and regulator

Of the "social dimensions" of biotechnology, its impact on feed and food has also given rise to significant debate : witness the acceptance problems in some countries of single-cell protein (SCP).

The supply, processing and storage of food and drink has for millennia been almost synonymous with biotechnology in the traditional sense of the term. The recent scientific and technological advances offer the prospect for continuing innovation and improvement :
in production efficiency, in tastes and flavours, and in functional aspects such as storage, convenience, consistency, nutritional standards and safety. Continued progress in all these respects is essential for the competitiveness of Europe's agro-food industry, and must be directed towards the benefit and satisfaction of the consumer.

That the consumer is willing to accept innovation is readily illustrated : in deep frozen foods, in the explosive growth of yogurt sales, or in the all-too-ready displacement of native cereals by imported wheat in many Third World cities.

(*) Sargeant, K. and Evans, C.G.T. : Hazards involved in the industrial use of micro-organisms. EUR 6349 EN.
Evans, C.G.T., Preece, T.F. and Sargeant, K. Microbial plant pathogens : natural spread, and possible risks in their industrial use.

On the other hand, textured vegetable protein, scientifically logical from the standpoint of cheap nutrition or global land use, has achieved only limited success as a meat replacer or extender : illustrating not only a need for further technical development by the food biotechnologist, but deeper aspects of consumer psychology in attitudes towards, and perceptions of, their food. The strength of such feelings is evidenced by the many religious restrictions on food and its processing - restrictions possibly originating in well-founded pragmatism related to health risks ; or historical social relationships. Debate on food innovation is therefore typically a complex mixture of food science and human psychology ; of concern about real risks to health, jostling with concern about real risks to market share. Examples are legion : the battles between margarine and butter ; between single-cell protein and soya ; between "natural", "nature-identical" and "synthetic".

The roles of the public authorities, at both Community and Member State level, impinge at several points upon the agro-food industry and the consumer : encouraging innovation, harmonizing regulatory regimes to create a genuine common market, and ensuring that regulations are based on rational assessment and well-informed debate ; while seeking always to maintain high standards of nutrition and safety. It is essential to maintain public confidence in the independence and integrity of the Commission and Member States as regulatory bodies. The challenge of new biotechnology cannot be met by suppressing innovation ; but the maintenance of a balanced regulatory stance, and the management of the long-term societal learning process which determines this stance, demand reinforcement or extension of public policy in three areas :

- the maintenance of high scientific capabilities in public sector agencies, research institutes or universities, of clear independence from commercial interests
- public information (or education, in the widest sense) to ensure informed debate
- the reinforcement of administrative capacities at the relevant levels (number and quality of staff) so that inadequacies or shortages do not constitute a bottleneck or a distorting factor in the control of innovation.

Action : as with the previous section on rDNA and the human genome, the need is to maintain in the Commission the staff and skills to monitor and anticipate developments in the situation, and concert necessary policy discussions and initiatives across the services, with Member States, and with other relevant groups (e.g. consumer associations).

4.2.4.3 Laboratory Research

Excluding defence research, pathogenic micro-organisms have long been used in certain specialized research laboratories and accidents are rare (e.g. smallpox Birmingham 1981). The risks are limited above all by the competent methods of work and precautions taken by the research workers, rather than by detailed regulation.

In the field of genetic engineering the Council Recommendation of 30 June 1982 envisages :

- the registration by the competent authority in each Member State of every laboratory using recombinant DNA ;
- the notification of protective measures and controls ;
- a description of the programme of research which enables the risk to be evaluated.

4.2.4.4 Industrial Processes

The risks represented by fermentation volumes from one thousand to one million litres are considerably larger than those encountered in research. These affect workers, the immediate surroundings of the plant and also the whole of the population. In contrast to chemical or radioactive pollution which can be normally limited, micro-organisms can propagate over large areas. The problem has already been encountered in the manufacture of live vaccines and other traditional fermentations. The approach is to use "invalid" micro-organisms which are not capable of developing freely outside their enclosed environment. Successive levels of biological and physical containment are laid down in some countries.

As a first approach the Directive 80/1107/EEC of 27.11.1980 on the protection of workers against the risks from exposure to chemical, physical and biological agents should be examined to see if it gives adequate cover.

The ad hoc group of the OECD fixed in December 1982 has a priority task in view of international harmonisation to identify a small number of DNA groups, particularly those coming from plasmids which are already widely used in research, and which would not cause added risks if they were subjected to auto-cloning. This work could lead to the establishment of a list of concrete examples of DNA groups for which recombination could be authorized in industrial production.

4.2.4.5 The Regulation of Products and their free Circulation

The bio-industries, given the high entry costs and long time scales (for both R & D work, and regulatory approval), have great need of the full dimensions of the European, and indeed the world, market for their products or innovative processes ; which require these dimensions and long periods of time in order to achieve profitability and justify their investments. They will be unable to develop satisfactorily in Europe if their activities or access to markets are blocked by divergent national standards, particularly in the health regulations of the Member States ; e.g. obligations to repeat identical or similar tests in each country. Regulations, while they have to be drafted leaving some flexibility for interpretation as new situations arise, need also to be clear enough to provide a basis of confidence for industrial commitments.

In order to avoid new problems in the functioning of the Community's internal market, the Commission has undertaken consultation with committees of government experts and with its own expert scientific committees in various sectors touched by biotechnology such as pharmaceuticals, chemicals, human nutrition, animal feedstuffs etc.

From a first review of the situation, it would appear that the application of current Community regulations (*) in the various fields will meet current regulatory needs, provided that there is close cooperation between the competent authorities in the Member States and the Commission. Such cooperation can be achieved by greater recourse to the existing institutional or scientific committees and, as necessary, use of the new information procedure for technical standards and regulations adopted by Council in its directive 83/189/EEC of 28th March 1983.

On the basis of its experience deriving from the use of these various instruments, the Commission will put forward general or specific proposals appropriate to create a regulatory framework suitable for the development of the activities of the bioindustries and for the free circulation of goods produced by biotechnology. In its proposals, the Commission will be careful to introduce at Community level measures meeting urgent needs, and pursuing the common interest in line with Article 36 of the EEC Treaty.

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(*) See in particular :
- pharmaceuticals : directives 65/65/EEC, 75/318/EEC, 75/319/EEC, 78/25/EEC
- veterinary medicines : directives 81/85/EEC and 81/852/EEC
- dangerous chemical substances : directive 79/831/EEC
- food additives : recommendation 80/1089/EEC
- bioproteins for animals : directive 82/471/EEC

## 4.3. RETURNS TO BE EXPECTED FROM THE PROPOSED ACTIONS

### 4.3.1 From training and research

#### 4.3.1.1 Benefits from "horizontal" actions : training and mobility of scientists

Although returns cannot be expressed in financial terms, it is obvious that considerable benefits to biotechnological R&D in Europe may result from the portion of the programme which provides for training action specifically adapted to the requirements of research in basic biotechnology. Basic biotechnology is a multidisciplinary branch, not normally taught in universities. The best experts who are able to teach specific aspects of biotechnology are scattered throughout the Community in laboratories of high scientific level. In addition, there is an urgent need to increase the mobility of European scientists who are often reluctant to speak any other language than their own or to remain outside their home countries for extended periods. Finally, one must also break the barriers which in many cases isolate industries from universities and prevent the flow of information between basic and applied research. The training actions foreseen in the sub-programme are focussed upon the improvement of scientific capabilities through the transfer of information and skills :

- between disciplines
- between public and private laboratories
- between Member States.

#### 4.3.1.2 Benefits from "horizontal" actions : basic biotechnology and contextual R & D

It is practically impossible to predict the outcome of an action, half-way between fundamental and applied research, of the type foreseen in the framework of this programme. Indeed it is the unpredictability of research which creates a problem of scale and choice, since it is difficult even for large organisations or countries to pursue all the potentially promising lines of enquiry. As C. de Duve puts it, "... research is an essentially open-ended adventure,

where the unusual or unexpected may quite possibly be of greater interest than what was planned, ..."

The pathways through which fundamental discoveries lead to social or economic returns are so complex, even with the benefit of historical hindsight, that an accurate cost-benefit assessment is hardly possible ; still less so for future prediction. But the European scale gives the opportunity to pursue a wider range of options, more effectively than if each country sought to spread its resources over all possibilities. Through participation in joint Community programmes, the emergence of strong teams and centres of specialist expertise will be encouraged, and the benefits of these strong centres will be available to the whole Community.

Notwithstanding the problem of prediction in these "horizontal" actions, it is to be expected that the "specific" actions should contribute significantly to the Community at several different levels : the following sections assess these.

4.3.1.3 Benefits from "specific" research actions : Increased added value of agricultural production

The advances anticipated in the programme through genetic engineering can be expected to lead to the production of plants with novel value as industrial feedstocks or with increased qualities such as high protein content, resistance to important diseases, improved symbiotic relationships with microorganisms in the soil. It is not possible, in view of the diversity of possible applications, to make any precise estimate of expected returns which, in some cases, could be considerable. For instance, the improvement of Rhizobium strains by conventional selection methods in the USA has been estimated to allow a net return in savings and productivity corresponding to $ 2 billions. Genetic methods are now being developed by Japanese scientists, which can apparently increase by a factor of 3.5 the nitrogen fixing efficiency of bacteria which grow symbiotically with rice. Research of this kind on certain stocks of wheat which are claimed to grow symbiotically with nitrogen fixing bacteria

could lead, if successful, to substantial economies in fertilizer requirements. Many examples of this type exist and illustrate the importance of possible benefits to be derived for European agriculture and for European transformation industries from long term research in genetic engineering and on the molecular biology of cultivated plants.

The scale of potential benefits is indicated by estimates of the size of the world market for agro-food products, and the growing proportion of these produced by biotechnological conversions.

The sales of the 25 largest European agro-food industries are of the order of 70.000 MUC. Products manufactured by biotechnological means account for 15% of overall sales. According to Bioconsult (Biofutur, 1982, 8, 40-43) from 1980 to 1990, the world market for biotechnological products will increase by 3.000 MUC for agro-food and by 10.000 MUC for chemicals.

Other market estimates for "biotechnology" (undefined) were quoted in section 1.2.2. (Market potential) : e.g. the T.A. Sheets estimates for year 2000 of $ 12.6 bn for new foodstuffs, $ 10.5 bn for industrial chemicals. But these are relatively small numbers, and subject to great uncertainty. The important point is that to maintain the competitiveness of the whole of European agro-food production, the entire sector must have available to it the best available technology. A farmer's expenditure on seeds may be a small proportion of his total costs ; but if he did not buy them, or bought inadequate ones, all his other efforts and expenditure would be wasted.

4.3.1.4 Benefits from "specific" research actions : development of new methods for the production of pharmaceuticals, new medical technologies, screening and tests

Here also, the long term consequences of research in basic biotechnology appear to be attractive in all areas dealing with the production of pharmaceutical and medical compounds. For instance, and to state only some specific examples of successful achievements among many others, the world market

for some of the reagents currently used for blood grouping is presently estimated at about $ 17-18 millions. These reagents contain small amounts of unwanted antibodies which cannot be removed during processing. Newly introduced monoclonal antibodies can now be used, in replacement of the conventional reagents, which completely eliminate these impurities. There is little doubt that many other markets will open their doors to monoclonals, particularly for diagnosing diseases, if proper mission oriented research is conducted in this area. The possibilities for production of certain high added value compounds (human vaccines, insulin, interferon, growth hormones ...) are so well known and so enormous that there is no need to consider them in the present framework. Their potential market value is such that the research requirements are adequately covered by industries in the Western world. Such a conclusion does not entirely apply to processes and substances (dyes, food additives, vaccines for farm animals) of smaller importance and for which industrial involvement is less pronounced. Market values can nevertheless be considerable and a recent estimate indicates, for instance, that the vaccine just developed against "blue tongue", a disease in sheep and cattle, may save $ 30 million per year to the US livestock industry. Similar returns are to be expected elsewhere in animal disease control.

The development, as foreseen in the present programme, of new medical technologies for the prevention or rapid treatment of common and costly diseases could lead to substantial reductions in the cost of medical care (particularly hospitalization), at least for those specific diseases (cf. polio, smallpox, tuberculosis). At present, major (social) costs result from influenza ; major hospitalisation and social costs are associated with heart disease, cancer, and diseases with significant auto-immune components (e.g. arthritis) ; major hospital/institutional costs are associated with geriatric care (senile dementia, incontinence, Alzheimer's disease, arthritis). On almost all the diseases mentioned, there are significant possibilities for progress based on the molecular approaches (e.g. monoclonal antibodies) of the "second pharmaceutical

revolution". The annual savings which could result from a decrease of only 1 % of health expenses in the Member States amount to 800 MUC.

In the medium term, production costs of drugs and new compounds should benefit from the partial replacement of present in vivo testing methods by in vitro screening techniques, which are also likely to be more informative.

### 4.3.2 Creation of conditions favourable for biotechnology

#### 4.3.2.1 Benefits from providing competitively-priced raw materials from Community agriculture to industry

The above measures will stimulate increased consumption of, and addition of value to, Community grown raw materials : particularly in the food, timber, paper, chemicals and pharmaceuticals industries. At the same time, new opportunities will be created for investment, increased employment, and improvement in the balance of trade.

The first benefit will be a better use of land in the Community through more efficient production of existing crops and through the development of new crops that better meet Community needs for food, feed, industrial feedstocks and, to some extent, energy. By encouraging the industries involved to work together in a more coherent manner the overall value added by their efforts will be increased. Agricultural surpluses will be reduced and employment in these industries will grow.

In the chemical industry increased use of Community agricultural products will tend to enhance the control the industry has over its feedstocks (as compared with current dependence on Middle East hydrocarbons), and encourage the development of special effect chemicals of high specific value by exploiting the structural diversity of agricultural products. The ability to exploit this diversity will be reinforced by the plant genetic and bio-processing projects already cited.

#### 4.3.2.2 Benefits from a coordinated Community approach on intellectual property rights and regulatory harmonisation

The contextual measures to be taken in respect of intellectual property rights and regulations will encourage the industries mentioned to build their futures on the larger and more secure base offered by the Community market rather than on individual national bases, thereby also offering a more substantial base from which to address the world market.

In international trade negotiations and in standard and familiar economics, the market of 350 million relatively well-to-do consumers is a basis for both wealth through internal free trade, and political strength. The argument is sufficiently well known to require little repetition in a community document : in the context of a technology touching such sensitive issues as agriculture, food, medicine, health care and education, it is no less relevant.

#### 4.3.2.3 Benefits from assessment, concertation and networks

Emphasis has been placed (4.2.1) on assessment, concertation, networks and administrative reinforcement as necessary to enhance the strategic effectiveness with which the Community and the Member States respond to the challenge of biotechnology. This emphasis is based on extensive and disappointing experience of the difficulty of mobilising and concerting the movement of a large number of public agencies or departments, typically heavily occupied with day-to-day responsibilities, to respond to a cross-cutting and long-term challenge.

Perception of emerging strategic needs or problems originates with knowledgeable or far-sighted individuals. Their claims and predictions have to be filtered from competing, alternative claims : evidence has to be gathered, hypotheses formulated and tested ; if significant resources are required, those who command the resources have to be persuaded - first of all to listen, then to be willing to act ; finally plans for how to act have to be formulated. Thus the essence of a strategic

policy analysis function is a combination of perception, listening, testing, analysis, persuasion and communication.

Failures of policy analysis result in technological backwardness, wasted resources, loss of market share, and economic dependence and weakness. It would be easy - with the benefit of hindsight - to quote examples of neglect or misjudgement, from microbiology to monoclonal antibodies ; science policy advisers in every country can identify their own. In companies, the response may be livelier, the penalties for failure sharper - but company action may be limited by factors outside their control, including factors within the control of government or Community institutions ; and company lobbying of government may be viewed as pleading a sectional interest.

In conclusion, the apparently unproductive activities of listening and learning, thinking and checking, talking and persuading may yield at least as high a strategic return as any scientific breakthrough in itself. Such is the logic used in Japan, first for the creation of the Committee for the Promotion of the Life Sciences (1973), and more recently in the creation of MITI's 'Bio-Industry Office' (June 1982). In the more complex structure of the Community and its Member States and their respective service units and agencies, the need for timely assessment, concertation and communication in policy for the life sciences and biotechnology is at least as great.

## 5. RESOURCE REQUIREMENTS

The mobilisation programme outlined in this communication requires a combination of measures and actions, differing widely in their nature, resource requirements and timing. In spite of this diversity, they must be seen as elements of a coherent overall approach, although for administrative and legal reasons the elements may have to be presented and considered separately for decision.

In relation to the major strategic objectives of the programme, some may consider the scale of resources discussed below derisory : less than a tenth of the scale of a typical pharmaceutical company's R & D budget, and far from closing the one-hundred-million-dollar-p.a. gap between Community and U.S. public sector R & D effort in biotechnology (documented in COM(83)328/2, the background note presented at Stuttgart).

Again, it may be asked why biotechnology, of more pervasive and fundamental significance even than information technology, calls for resources only on the scale proposed.

But such comparisons would not be apt : for the essential feature of this programme is to catalyse greater effectiveness in the resources already being deployed, by Europe's companies, and by the Community Member States in their national programmes for biotechnology.

This approach recognises Europe's existing and potential strengths in biotechnology; and by focussing selectively on points where that potential is not being realised, aims to achieve multiplier effects far beyond the scale of expenditure proposed.

The Commission proposes in order to reach the objectives outlined in chapter 4, the reinforcement of existing structures and programmes and the launching of new actions : presented below under the following headings :

5.1 Research and training

5.2 Demonstration projects

5.3 Creating the context : concertation and administrative action

## 5.1 RESEARCH AND TRAINING

Most of the projects outlined in the present proposal cover R & D activities which need to be launched or stimulated within the Community. It is thus by indirect action, implemented through cost-shared contracts with laboratories (private or public) in the Member States, that the greatest part of the programme must be executed. The only exceptions are certain elements of sub-programme 1 (contextual measures for R & D) which are to be implemented through studies, workshops and participation in activities with non-member countries. Such participation will take place

- in the framework of the COST programme
- in supporting activities for the international networks relating to the theme "Technology, Employment and Growth", which resulted from the Versailles Summit in 1982
- in other international contexts relating to global infrastructure developments (e.g. information, gene collections) wherever it is advantageous to adapt European initiatives to worldwide systems.

The methods used for evaluating budgetary needs and requirements in staff will be presented in detail in the programme proposal for Community R & D in Biotechnology which the Commission is now preparing. Essentially, the scale of effort required in each area has been based on the need to create multi-disciplinary teams of operationally effective but manageable scale, drawing on the advice of experienced academic and industrial researchers.
(See, for example, the analysis and calculations by C. de Duve*).

(*) C. de Duve, "Cellular and molecular biology of the pathological state", a proposal for a Community Programme in Biopathology, Doc. EUR 6348, 1979.

Requirements in Commission staff have been assessed by taking into consideration the diversity and breadth of the fields covered by the proposal, which will demand expertise from scientists of correspondingly diverse background, and a number of distinct administrative bodies and systems of procedure.

Table 5.1 : Tentative Cost Breakdown for the R & D Elements of the Biotechnology Action Plan

| | Staff | Management | Contracts[3] | Total |
|---|---|---|---|---|
| Contextual measures (R & D) | 1.32 | 1.87 | 9.24 | 12.43 |
| Basic Biotechnology[1] | 1.21 | 0.97 | 35.00 | 37.18 |
| Agro-food | 0.65 | 0.87 | 20.00 | 21.52 |
| Health Industry | 1.41 | 1.51 | 30.00 | 32.92 |
| Coordination with non-Member States[2] | - | 1.50 | - | 1.50 |
| Administrative support | 0.45 | - | - | 0.45 |
| | 5.04 | 6.72 | 94.24 | 106.00 |

Notes : (1) to start on 1.4.1986, immediately after completion of the present Biomolecular Engineering Programme.

(2) includes two COST actions and participation in the networks resulting from "Technology, Growth and Employment" created at the Versailles Summit of 1982.

(3) includes cost-shared research contracts, training contracts and study contracts.

At some 21 Mio ECU per year, the above action would add approximately 6% to the 355 Mio ECU currently being spent through Member States(*).
Nevertheless, the budgets proposed for each of the R & D activities outlined in chapter 4 are of a size sufficient for the execution of significant research, because they will be focussed on the selected areas.

The selection has been targetted, as explained in chapter 4, where :

- the structures and context needed at European level for a successful development of bio-industry are obviously lacking;

- there are significant gaps or weaknesses in the programmes for biotechnological R & D presently executed in the Member States.

An intangible but real benefit is the additional, "catalytic" dimension which derives from a well-executed and administered Community R & D programme, of which there are already several well-known examples.

## 5.2 DEMONSTRATION PROJECTS

In addition it is the intention of the Commission to complement as necessary the R & D activities in biotechnology, by demonstration projects, designed to facilitate the transition between research developments and full scale exploitation on a commercial basis. The budget needed for demonstration projects will be framed to relate also to the other Community actions bearing on the implementation of biotechnology - e.g. from other research programmes such as Energy, Environment, Raw Materials, Basic Technological, or Agricultural. The scale, status and timing will be specified at the appropriate stage.

(*) Doc. COM(83)328/2

Evidently it is impossible to anticipate the outcome of research with a precision sufficient for costing demonstration projects; but a realistic order of magnitude would be between 10 and 20 Mio ECU p.a. - say 80 Mio ECU over the 5-year period.

## 5.3 CREATING THE CONTEXT : CONCERTATION AND ADMINISTRATIVE ACTION

As described in section 4.2 the actions proposed by the Commission for the establishment of a proper background for biotechnology in the Community include :

(a) reinforced assessment and concertation for biotechnology, as outlined in 4.2.1 : within the Commission services, between Community and Member State level, and with the wider international context;

(b) provision of raw materials of agricultural origin for industry (4.2.2.);

(c) reinforcement of preparatory work to negotiate improvements in intellectual property rights (4.2.3);

(d) reinforcement of European approaches to regulations affecting biotechnology (4.2.4) .

The assessment of budgetary needs (including staff requirements) is difficult to make because existing structures will in every case be used to the maximum to contribute to the programme's objectives. But it would be illusory to suppose that current staff are sufficient to undertake the additional role demanded if the Community is to respond effectively to the challenges of biotechnology.

Detailed budgets have been prepared for two of the key elements of the programme outlined in chapter 4 :

(a) the reinforcement of assessment and concertation, the operation of the networks, and the related context-oriented (non-R&D) tasks outlined in 4.2.1 : 6.6 Mio ECU (see Table 5.2);

Table 5.2 : Tentative Cost Breakdown for the Monitoring, Concertation and Contextual (non-R & D) Elements of the Biotechnology Action Plan

| Budget Headings | Mio ECU |
|---|---|
| Staff (8) | 2,7 |
| Missions | 0.6 |
| Meetings | 0.2 |
| Studies | 1.2 |
| Diffusion and Communications (*) | 1.9 |
| Total | 6.6 |

(*) including particularly network communications, computer conferencing, and support for the production of publications, audio-visual materials and other means as appropriate

(b) the special studies and working group activities relating to commercial and intellectual property, as outlined in 4.2.3 : expert group (0.1 Mio ECU, 1984 only); studies programme (0.5 Mio ECU, 1984 only); training of patent attorneys (1.8 Mio ECU, 3 years) : total 2.4 Mio ECU.

In drawing together in Table 5.3 below the diverse estimates presented above, the intention is to give an indicative overall figure for the scale of resources which will be requested by the Commission in the individual proposals for decision which will follow this communication.

Table 5.3 : Estimate of the total budget needed by the Commission for implementation of its biotechnology action plan during the period July '84 - June '89

| | Mio ECU |
|---|---|
| Research and training | 106 |
| Demonstration projects | 80 |
| Contextual actions (concertation, intellectual property, ...) | 9 |
| Other administrative reinforcement, e.g. studies and investigations related to reinforcement of regulatory coordination; modification of agricultural price or market regimes; reinforcement of biotechnology in Community Development Policy : say 1 Mio ECU p.a. for 5 years ..... | 5 |
| Provisional order-of-magnitude total | 200 |
| | (40 Mio ECU p.a.) |