XII-37/83/EN

P L A N   B Y   O B J E C T I V E :

B I O T E C H N O L O G Y

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Forecasting and assessment in science and technology
Directorate General Science, Research and Development
Commission of the European Communities
Brussels - Belgium

January 1983

The plans by objective are the result of studies which were entrusted by the Commission to eminent outside personalities or to experts of its services. They provide an analysis of the circumstances and prospects for R, D&D in the field considered, as well as suggestions bearing upon the priority objectives which it is in the Community's interests to pursue, taking account of the activities which have been built up or which are envisaged at national and international level.

It was partly on the basis of these documents that the First Framework Programme for community scientific and technical activities 1984-1987 was prepared by Commission staff.

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PREFACE

This "theme plan" is one of a series of parallel documents prepared for Directorate-General XII (Science, Research and Development) of the Commission of the European Communities, to support and inform the debate leading to the definition of the Framework Programme for the Community's Science and Technology activities, 1984-1987.

Most of the parallel documents have been externally commissioned. For biotechnology, however, a substantial amount of relevant work in assembling information, commissioning studies, and considering R&D policy options had already been undertaken within the context of the FAST programme in D.G. XII.(1)

This is a 5-year pilot programme, established by decision of the Council of Ministers in 1978, with a mandate requiring FAST to contribute to the definition of long-term R&D policy in the Community. Although the perspective of the FAST sub-programme "Bio-Society" is long-term, the purpose of considering possible developments over some decades ahead is still to contribute to the improvement of current decisions and plans. It seemed therefore wholly appropriate to draw upon the resources of FAST in the current report ; and inevitably the opinions and judgements reflect the author's personal views as developed in the context of FAST.

The views expressed should in no way be seen as an expression of the official policy of the Community.

The author, while accepting full responsibility for the errors, inaccuracies and opinions expressed, must acknowledge with gratitude the extensive help received from colleagues within DG XII and other services of the Commission. Thanks are also due to those outside the Commission, in Member State administrations and elsewhere, who have similarly contributed advice and information.

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(1) Forecasting and Assessment in Science and Technology.

SUMMARY

This report is in six sections, progressively moving from presentation of basic factual material towards interpretation, judgements, and consequent recommendations.

Chapter I introduces biotechnology, showing why it is of major long-term strategic significance to all countries. Difficulties of definition - particularly of the boundary, or overlap, with other major sectors of applied life science such as agriculture, health care and environmental management - lead to major problems of statistical comparability between countries or between different data sources ; but however approximate some of the figures may be, these uncertainties should not be allowed to divert one from recognition of the essential unity and significant development of biotechnology.

Chapter 2 reinforces this message by describing the responses to biotechnology, in both public and private sector R&D activities, by the United States and Japan.

Chapter 3 similarly presents briefly the activities of the Member States of the European Community, drawing mainly on published sources (i.e. not fully checked with staff of national administrations in the detail that would be desirable).

Chapter 4 describes R&D programmes of the European Community, current or planned, in which biotechnology features significantly.
Again, much depends on definition : the Community has several major programmes which contain "some" biotechnology but only one small, recent programme - the Biomolecular Engineering Programme - to which biotechnology is central.

Chapter 5 argues the case for giving greater coherence and visibility to the subject, by explicitly considering not only Community R&D strategy, but "Community Strategy for European Biotechnology".

This would be based on recognition of the predominant role of Member State and private sector activity, but would seek to enhance through Community action and policies (including R&D policies) the effectiveness of the total European effort. Such effectiveness can be enhanced by :

1) communication channels to co-ordinate national policies and strategic choices ;

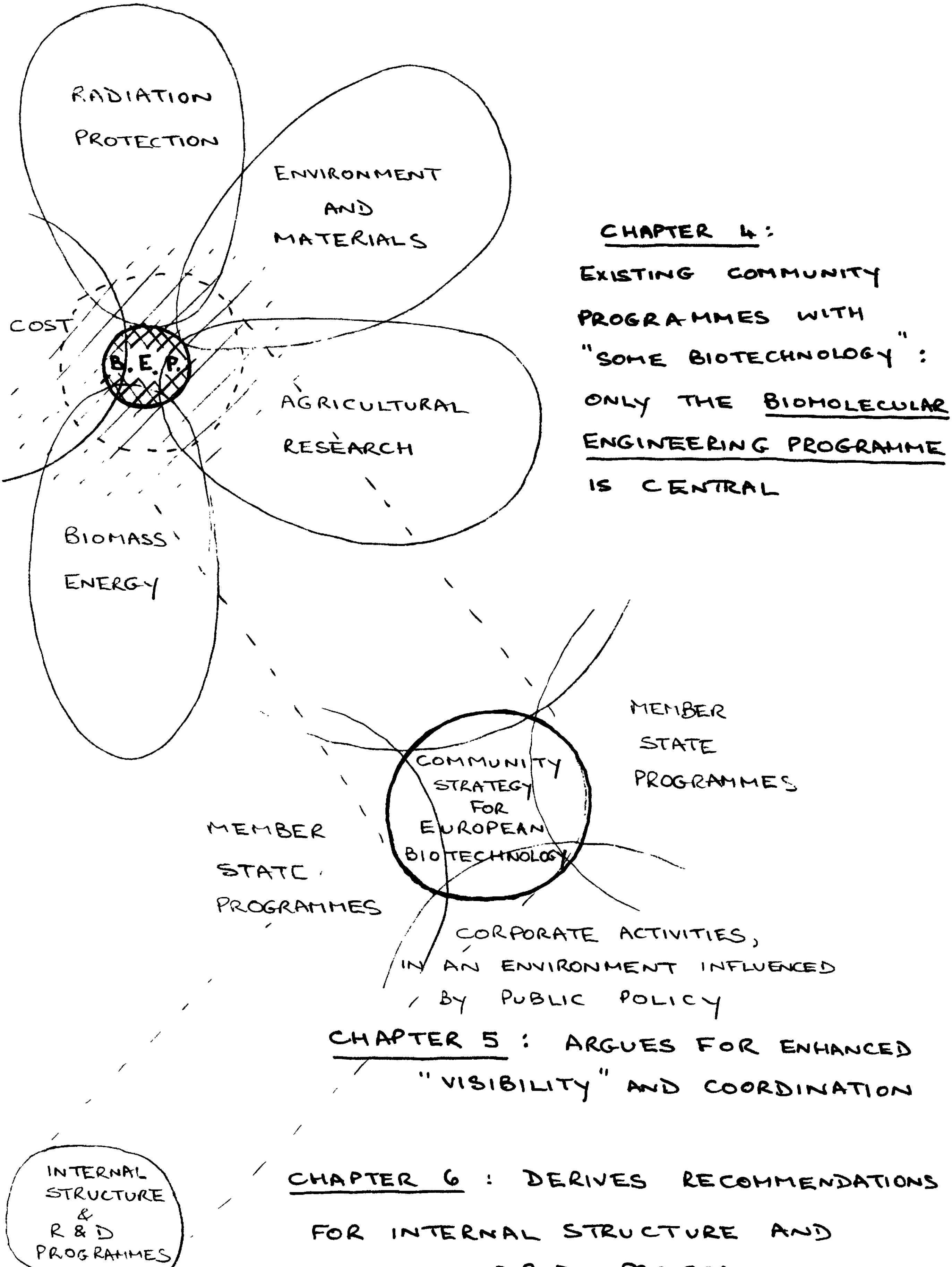
2) Community cost-sharing R&D programmes such as those under way or planned, plus further programmes aimed at 3) and 4) :

3) actions designed to reinforce foundation capabilities for European biotechnology : stimulating institutions (education and research), networks and mobility to enhance human resources, and improving logistic support services, e.g. including developments of culture collections and data banks in support of life sciences and technologies ;

4) actions designed to enhance the operating context for biotechnology companies in Europe : including such non-R&D topics as agricultural feedstock prices and the regulatory environments.

Chapter 6 draws together the resulting recommendations for both the management of "biotechnology strategy" within the Commission , and the specific R&D recommendations resulting from the preceding strategic analyses.

The logic of chapters 4, 5 and 6 is summarised by the accompanying diagram.


RADIATION PROTECTION
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BIOTECHNOLOGY

1. THE SIGNIFICANCE OF BIOTECHNOLOGY

1.1. Biotechnology : old and new technologies, broad and narrow definitions

Man has always depended upon the cycling of materials, information and energy through the complex, self-reproducing systems of the biosphere ; even in a modern industrial state, over 40% of manufacturing output is of biological nature or origin. The standard of civilisation, the very size of the sustainable population, depend critically upon knowledge of the applied life sciences ; in a broad sense upon biotechnology.

In these terms, one can trace the history of biotechnology in man's progress from hunting and gathering, to herding and pastoral farming, to agriculture of ever-increasing intensity, culminating in our own time in the use of micro-organisms in the controlled environment of fermenters to produce high value pharmaceuticals (penicillin), foodstuffs or additives (vitamin C, citric acid) or bulk foodstuffs (single-cell protein): a continuous increase in productivity, for the support of human population and purposes. The need for mastery of the life sciences and related technologies is greater than ever, as our population (expanded by the past successes of biotechnology - Jenner, Pasteur, Koch) presses upon or exceeds the sustainable limits of the planet.

In a broad **sense**, biotechnology is about the sustainable management of systems using living elements or their derivatives - a definition which would include much of agriculture and food production, waste recycling, health care, the production of chemicals, pharmaceuticals, textiles, organic commodities such as wood and rubber, and biomass energy ; and extending into more exotic applications such as enhanced oil recovery and mineral leaching.

The European Federation of Biotechnology, a federation of over 40 learned societies founded in 1978, has adopted a narrower definition, based on three disciplines :

"The integrated use of biochemistry, microbiology and engineering science in order to achieve the technological application of the capabilities of micro-organisms, cultured tissue cells, and parts thereof".

The OECD expert report (Bull, A.T., Holt, G. and Lilly, M.D. : "International Trends and Perspectives in Biotechnology : A. State of the Art Report", OECD, September 1982) has adopted a broader view :

"The application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services... In our definition we include not only the actual process in which the biological agent is used but also those processes concerned with its preparation and with the processing of biological materials resulting from its action".

These differences of definition are typical of an inter-disciplinary field in rapid evolution, but they give rise to two specific problems in this "Theme Plan".

- it is impossible to produce reliable internationally comparable figures, because of the absence of standardised definition, or of uniform interpretation of definitions such as those quoted ;

- much of the "biotechnology" research work taking place at both national and Community levels is occurring under other labels, rather than under research budgets explicitly labelled "biotechnology" ;
  to this problem we return in the later chapters.

There is nonetheless good reason for using the single term "biotechnology" to refer to what will be a key sector of future industrial development. For there is a fundamental unity in the bases of the applied life sciences, rooted in the common evolutionary origins of living materials, and elucidated by the biological discoveries of recent decades. Because of this common basis, advances in one sector are likely to have implications for others : witness, for example, the moves by pharmaceutical groups, masters of the new molecular genetics, to acquire companies with skills in the classical genetics of plant breeding, and familiarity with the agricultural markets.

Scientific Breakthroughs which justify the term "new biotechnology"

- fundamental discoveries in the life sciences, particularly of the role of DNA as the molecular carrier of the stored information in all genetic material ;
- techniques for the manipulation, alteration, and synthesis of genetic material (either directly or via cell fusion) to create new life forms ;
- techniques based on microbiology for cultivation, screening and selection of useful cells or microorganisms, and manipulation of their behaviour under controlled conditions ;
- techniques for plant cell and tissue culture for accelerated propagation of useful plants ;
- downstream processing techniques for extraction, treatment, purification and conversion of useful materials following the biomass production stage.

These advances in biotechnology, the speed with which they have occurred and the intensity with which further research is being pursued, are strong reasons for supposing that they will lead to key sectors of science-based industries in the 21st. century.

The significance arises also from the number and size of the sectors already being affected : a selection are briefly described below.

1.2. Application Areas

Health : important new products of greater precision and specificity, such as monoclonal antibodies ; enzyme diagnostics ; the use of genetically engineered bacteria to produce by fermentation and separation processes hitherto unobtainable quantities of human proteins or synthetic analogues ; these and other products and processes offer some immediate benefits for therapy and research and the prospects of major innovation in the pharmaceutical market ($ 76.3 bn. world-wide).

Food and feed : large quantities of animal feedstuffs are currently imported by Europe. The cereal deficit in the Third World is currently some 85m. tonnes, and likely to increase as world population grows by 50% between now and the year 2000. Biotechnology could be used to reduce imports and to make Europe's food supplies less vulnerable in the face of increasing world demand. Single-cell protein for animal feed is currently being produced by a fermentation process based on methanol ; other sources of fixed carbon (e.g. starch, cellulose) could be similarly used, for a wide range of energy and protein feeds and foodstuffs.

Energy : classical and molecular genetics may help to produce crops more efficient as carbon or energy sources. In the longer term it may prove possible to develop biofuel cells able to convert solar to chemical energy by splitting water into hydrogen and oxygen.

Other industrial applications : the provision of renewable feedstocks for the production of chemicals by fermentation may extend further into larger quantities of lower value materials (it being already economic for certain fine chemicals and pharmaceuticals). The ability of micro-organisms to concentrate materials can be used in decontamination - e.g. sulphur removal ; microbial "leaching" is already widely used in mining of metals from low-grade ores.

Land use and related policies : the development of biotechnological opportunities in the increasingly interacting fields of food processing, forestry, agriculture, chemicals, energy and waste management will demand a reappraisal of the use of land. Clearly some traditional agricultural products risk being made superfluous, which will make it both highly expensive and ultimately wasteful to continue subsidising or encouraging their production. On the other hand there is an equally significant opportunity for attention to be switched to other products which biotechnology can either make more feasible in European conditions or can convert into economically or strategically important materials.

At the same time, biotechnology offers more effective means of environmental control, particularly in the efficient treatment or upgrading of wastes, and the recycling of useful materials.

1.3. Third World Impacts

It is clear that biotechnology will bring both threats and opportunities to the existing system of agro-food and commodities trade between Europe and the Third world. Europe's biotechnology can offer know-how, hardware and genetic material, which can improve "bio-system management" : a term covering food and cash crop production in a sustainable manner, as well as post harvest storage and conversion. Biomass energy production can also be developed, where appropriate. Europe's biomedical science also has much to contribute to the fight against parasitic infections of man, his livestock and his crops and food-stores.

1.4. The Challenge to Europe, and the Role of the Community

In all the sectors described in the foregoing, and in the key scientific disciplines on which biotechnology rests, Western Europe currently holds a key position. It has some industrial strengths and major, occasionally outstanding, skills in vaccines, antibiotics, brewing, genetics, animal and plant production. It has physical, geographical and cultural diversity giving it a range of terrain and vegetation which is as wide as the reservoir of its creative potential is deep.

However, one has only to study the example of micro-electronics to appreciate how quickly Europe could lose the competitive benefits currently conferred by its advantages.

In these circumstances, governments throughout the world and throughout the European Community are demonstrating their awareness of the special importance of this multidisciplinary activity, and are seeking the most effective ways to stimulate, direct and support it : witness the series of reports listed in Table 1.

The Community has specific responsibilities and capabilities which must shape its response to the challenges and opportunities of biotechnology. It has to perceive and define the nature of these challenges, and show where joint action by the Community as a whole is necessary. Some of the challenges presented by biotechnology are :

. the need for new policies and regulations : e.g. on feedstock prices (starch, glucose) or on the production of substitutes (single-cell protein, isoglucose), with implications for agricultural policy ; foodstuff and pharmaceutical regulations ; patent law ;

. the avoidance of wasteful duplication of effort within the Community : e.g. the coordination of national policies on culture collections of micro-organisms and cells ; data banks and related information services ; fundamental research programmes ;

. the fostering of co-operation between national industries, universities and research centres ;

. the creation of a climate encouraging innovation.

The need for some coordination of strategies for biotechnology within the Community arises both from the internal logic of efficiency <u>within</u> the Community, and from the strong challenges presented by our major <u>external</u> competitors ; some description of which is given in the following chapter.

TABLE 1

KEY REPORTS IN BIOTECHNOLOGY

DATE	COUNTRY	REPORT
1974	W. Germany	DECHEMA, for BMFT : Biotechnologie
1976	Japan	MITSUI : Present and Future of Enzyme Technology
1976	U.K.	A.N. Emery, for Science Research Council : Biochemical Engineering
1977	Commission of the E.C.	D.G. XII : Possible Action of the European Communities for the optimal exploitation of the fundamentals of the new biology in applied research
1978	Europe	DECHEMA organise first European Congress of Biotechnology, Interlaken, Switzerland; European Federation of Biotechnology founded.
1979	France	F. Gros, F. Jacob, P. Royer : Sciences de la vie et société, pour le Président de la République
1979	France	J. de Rosnay : Biotechnologies et Bio-Industrie
Jan 1980	W. Germany	BMFT Leistungsplan 04 : Biotechnologie
Mar 1980	U.K.	"Spinks report" : Biotechnology : report of a joint Working Party (ACARD, ABRC, Royal Society)
May 1980	Belgium	SPPS : Développements en matière de biotechnologies
Sep 1980	Canada	Miller et al : Biotechnology in Canada
Feb 1981	Canada	Report to Minister for Science and Technology : Biotechnology : a development plan for Canada
Feb 1981	France	J.C. Pelissolo : La biotechnologie, demain ?
Mar 1981	U.K.	Govt. White Paper : Biotechnology (response to Spinks)
Apr 1981	U.S.A.	O. Zaborsky : Biotechnology at the National Science Foundation
Apr 1981	U.S.A.	Office of Technology Assessment : Impacts of Applied Genetics : Micro-Organisms, Plants, and Animals
May 1981	Netherlands	STT : Biotechnology : a Dutch perspective
May 1981	Ireland	NBST : Biotechnology Trends
Sep 1981	U.S.A.	Office of Technology Assessment : Project Proposal for a Comparative Assessment of the Commercial Development of Biotechnology
Sep 1981	Spain	La ingeniería genética en la biotechnología (Centro para el Desarrollo Tecnológico Industrial, Ministerio de Industria y Energia)
Oct 1981	Japan	Report : Heading toward new Research and Development, by the Study Association for the Foundation of a Long-Term Plan for the Development of Industrial Technology
Nov 1981	UNIDO	The Establishment of an International Centre for Genetic Engineering and Biotechnology (ICGEB) : report of a group of experts
Nov 1981	Australia	Biotechnology R&D : the application of DNA techniques in research and opportunities for biotechnology in Australia (Commonwealth Scientific and Industrial Research Organization)
Dec 1981	U.S.S.R.	Speech by Academician Ovchinnikov at the Annual General Meeting of the Soviet Academy of Sciences
Apr 1982	Netherlands	Programmacommissie Biotechnologie : Innovatieprogramma Biotechnologie (Chairman : Prof. R.A. Schilperoort)
Sep 1982	OECD	International Trends and Perspectives in Biotechnology : A State of the Art Report by A.T. Bull, G. Holt and M.D.Lilly

2. R & D RESPONSES OF INDUSTRIAL COMPETITORS

2.1. Introduction

The object of this chapter is to illustrate the basic strategies in this field of competing nations outside the Community (to the extent that such policies have been formulated), their underlying strengths and trends in activity. However, in appraising the relative strengths of different countries in this field the question of defining biotechnology has to be borne in mind. Since different countries include different activities in their understanding of the term, objective comparisons are difficult.

2.2 The United States of America

2.2.1. Federal support

The main federal support for activities related to biotechnology is channelled through two sources : the National Science Foundation (NSF), which is the principal federal agency for the support of basic research across all fields of science, and the National Institutes of Health (NIH), which are responsible for basic research in medicine and health care, and are also responsible for the registration of federally funded research work on recombinant DNA. The U.S. Department of Agriculture is also funding basic research related to agriculture, some of which involves projects and techniques which may be described as biotechnology; similarly the Department of Energy's studies of biomass-based energy sources involve basic biology and biotechnology.

In fiscal year 1980, the NIH supported 717 basic research projects involving recombinant DNA at a cost of $ 91.5 million; it is not indicated what further proportion of the NIH budget ($ 3 - 4 billion) might also be classified as "biotechnology".

Zaborsky described the support of the National Science Foundation for "biotechnology-relevant" research at the 2nd European Congress of Biotechnology, Eastbourne, April 1981, giving the figures shown in Table 2, i.e. a total of $ 66.1 million.

TABLE 2 : U.S. NATIONAL SCIENCE FOUNDATION

MAJOR PROGRAMS SUPPORTING BIOTECHNOLOGY

RESEARCH – FISCAL YEAR 1980

Program	Total		Biotechnology Relevant	
	Awards (Number)	Amount Dollars in thousands	Awards (Number)	Amount Dollars in thousands
– Biophysics	202	10,007	188	9,697
– Biochemistry	222	9,087	216	9,061
– Metabolic Biol.	208	9,081	194	8,911
– Genetic Biol.	177	9,276	154	8,689
– Cell Biol.	170	9,337	150	8,632
– Devel. Biol.	171	8,580	137	7,653
– Alt. Biol. Sources	26	2,906	15	2,191
– Biol. Oceanog.	101	5,841	37	2,137
– Applied Biol.	43	3,194	17	1,377
– Chem./Biochem. Proc.	57	2,513	18	815
T O T A L	1,557	78,095	1,266	66,095

Source : Zaborsky

The Office of Technology Assessment study "Impacts of Applied Genetics : Micro-organisms, Plants and Animals" (1981) gives details of federal support for projects on plant molecular genetics and other biological topics of agricultural significance. Their figures include some NSF programmes in plant research; the other main channel is the U.S. Department of Agriculture (USDA). USDA's Competitive Grants Program (1980 : $ 15 m.) supports new research directions in plant biology.

Combining the figures mentioned suggests U.S. federal expenditure around $ 200 m. p.a. in areas relevant to biotechnology; the figure is sensitive to the definition used, particularly with respect to the various technologies used within the vast NIH budget. A recent and significant example of the latter is the $ 3.2 m. 5-year contract awarded in June 1982 to Bolt, Beranek and Newman, Inc. for the development of a nucleic sequence data bank : "upstream" from practical biotechnology, but of fundamental future importance for the life sciences. Of similar importance is the software development at NIH laboratories (Bethesda, Maryland) for systems of computer graphics representation of molecules of biological interest.

The U.S. Government is examining its strategy in the field of biotechnology. The Office of Technology Assessment is responsible and by means of a 2 year (1981-83) study will cover the issues of Government policy, funding and regulatory requirements in this field, university/industry relationships and relevant features of the educational system, industry characteristics and patent law. The study will be comparative and extend therefore to Japan, West Germany, Great Britain, Canada, France, Switzerland and the USSR.

2.2.2. The role of industry

It is clear that biotechnology research and development is being substantially funded in the U.S. As examples in the following section will suggest, industrial funding is probably at least 10 times that of federal expenditure, which is concentrated at the fundamental end of the research spectrum. Venture capital activity on the other hand is aiming for payback in the short and medium term, particularly in the bio-medical and pharmaceutical fields, whilst larger companies are also investing in longer term potential with the expectation that research breakthroughs during the next ten years will lead to commercial products in the years beyond. It is the venture capital activity which has attracted the greatest attention, due to the suddenness and the extent of support for equity offerings. It has been calculated for example that by April 1981 well over 100 companies had been launched and the overall value of public offerings had reached $ 1.1 billion. Two of the best known specifically "biotechnology" companies are Cetus (market capitalization $ 400 m. in mid 1981) and Genentech (market capitalization $ 280 m. in mid 1980). Current or recent projects of Cetus (which claims to spend $ 55 m. p.a. on R & D) include high purity fructose, a new veterinary vaccine, and human interferon; work is under way on other products in the fields of health care, chemicals, food, agriculture and energy. Genentech's main current products are genetically engineered human insulin, human and animal growth hormones, immune leukocyte and fibroblast interferons and veterinary vaccines. Forthcoming products may include hormones for bone disease treatment and human serum albumin to replace blood loss.

In general the venture capital activity in the U.S. shows signs of volatility and a significant level of bankruptcies is expected. However, it does illustrate one fundamental strength of the U.S. economy, which is the existence of entrepreneurial scientists, of a market receptive to innovative products and services, and of a financial community willing to provide risk capital. Examples of the levels of investment now taking place and of the variety of means used by companies to gain an involvement in biotechnology are :

- construction of an $ 85 m. life sciences complex by Dupont at Wilmington, Delaware for completion in 1983
- 10 year inflation-indexed contract worth $ 67 m. given by Hoechst to Massachussetts General Hospital in order to undertake molecular biology research (and train Hoechst scientists)

- an agreement worth $ 6 m. between Dupont and the Harvard Medical School to conduct research on molecular genetics
- $ 5 m. funding by Shell of Cetus' work on human interferons, with a $ 40 m. R & D agreement also reported
- investment of $ 70 m. by International Nickel, Schering-Plough, Grand Metropolitan and Monsanto in a new private company : Biogen (based in Geneva; promoters say that European capital was difficult to raise)
- participation of $ 5 m. by Dow in Collaborative Genetics
- allocation by Dupont of 21% of its research budget to the life sciences in 1982 (i.e. $ 120 m.). This proportion is intended to increase.

2.2.3. Forecasts

The enthusiasm of U.S. investors has been stimulated by a series of forecasts of the long-term market for biotechnology, for example, that by T.A. Sheets consultancy (reported in the Financial Times of 25.2.82) :

Market Value by Year 2000	($ billion)
Alternative energy products	16.3
New foodstuffs	12.6
Health care products	9.1
Industrial chemicals made by biotechnology	10.5
Agricultural chemicals	8.5
Copper and nickel leaching	4.5
Unspecified	3.3
Total	64.8

The proliferation of such projections reflect widely different assumptions, and definitions of biotechnology :

Source	Estimates of current market	(in $) 1990	2000
T.A. Sheets	25 m		64.8 bn
Business Communications Ci Inc.	60 m	13 bn	
IMSWORLD		27 bn (US only)	
Information Services (London)	10 m	500 m	
OTA report : products based on DNA technology :			
- food and pharmaceutical			7.4 bn
- chemicals			7.2 bn
Policy research Corp. :			
cumulative 1980 - 2000, products made by genetic engineering techniques :			
- agricultural			50/100 bn
- medical			50/100 bn

These estimates seem to reflect narrow definitions : the current pharmaceutical market alone, for example, is worth $ 76.3 bn p.a. worldwide; the much greater markets for food-stuffs, chemicals and organic commodities may all be influenced by biotechnology, and their combined scale is much greater than the above figures.

2.2.4. Emphasis of future activity : Agriculture

A notable feature of activity in the U.S. has been the strong emphasis, in some widely publicised studies, on agricultural potential for the new developments in biology and biotechnology, although this has not been matched by the patterns of investment.

The Chicago Group's report "An Assessment of the Global Potential of Genetic Engineering in the Agri-business Sector" points out that the market for agricultural products is "currently close to ten ti mes the size of the market for all pharmaceutical health care products in the U.S. alone" and suggests that the market for new agricultural products could outstrip the medical market by tens of billions of dollars.

The report contrasts this with the absence of significant investments, a pattern matched also in U.S. federal grants for genetic engineering research. A study completed in January 1982 by Futures Group, Connecticut, "The Impending Revolution in World Agriculture" similarly emphasises the new technological dimension in plant and animal genetics.

2.3 Japan

2.3.1. National Strategy

Government support for biotechnology dates from the beginning of the '70's. The Science and Technology Agency initiated the new government biotechnology programmes by establishing a Committee for the Promotion of Life Science in 1973. Rogers* states that "Since then, the scale of Government support for biotechnology R & D has steadily increased. Support in 1981 for Life Science in general is estimated at a minimum of Yen 50,000 million ($ 195 m.) and if one considers only the more restricted areas which are currently referred to as biotechnology the support was of the order of Yen 5,600 million in 1981 (i.e. approximately $ 22 million). Government financial support has received fresh impetus in the last year with the announcement of the Ministry of International Trade and Industry's (MITI) biotechnology national projects. These new projects are the Biomass Development Project concerned with alcohol production (7 years from 1980 - total budget Yen 12,300 million : $ 48 m.) and the Next Generation Industries national project which has three biotechnology themes (10 years from 1981 - total budget in the biotechnology sector is in excess of Yen 30,000 million : $ 116 m.)."

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* Rogers, M.D. "The Role of the Japanese Government in Biotechnology Research and Development", Chemistry and Industry, 7 Aug. 1982.

MITI is promoting its strategy through a "biotechnology forum" in collaboration with 14 industrial companies, including the major chemical groups. Other Western reports* speak of a 10 year biotechnology programme offering the industry grants and subsidies worth $ 405 m.

Apart from such action MITI is encouraging external collaboration through cross-licensing contracts with advanced groups. The aim is that such international cooperation should prevent friction whilst helping the establishment of international technology and filling gaps in existing strength. One such gap is in the field of molecular genetics. Here there is collaboration with U.S. and European research centres, exemplified by an agreement with the British Royal Society, the British Council and the Science Research Council. The agreement provides initially for exchange visits of 4 or 5 post-doctoral fellows a year and may lead to more ambitious plans, perhaps including collaborative research. As part of a plan to increase Japan's attractiveness as a location for outside firms the safety guidelines on genetic engineering have been somewhat relaxed. Other steps are designed to stimulate the competitiveness of the Japanese pharmaceutical industry through rationalisation and improvement. It has been suggested+ that the Government is prepared to contemplate the bankruptcy of up to fourfifths of Japan's 2,300 drug firms, leaving those with a strong commitment to research (like Takeda, Yamanouchi and Shionogi). It should be mentioned finally that the Japanese market has until recently been effectively protected against foreign penetration by a range of non-tariff barriers, including the repetition of animal tests and clinical trials within Japan, and "gentlemen's agreements" between the drug firms and the distribution network.

2.3.2. Industrial activity

Japan appears to be particularly strong in the field of fermentation technology and the industrialised use of immobilised enzymes. This is illustrated by Japanese dominance of world production of amino acids (which may be used as food additives

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* The Economist, 29 Aug. 1981

+ The Economist, 29 Aug. 1981

for flavouring, or in order to improve the amino-acid profile of protein foods or feedstuffs). This is a $ 1.4 billion market worldwide. Ajinomoto, one of the major food companies, has developed (and is patenting) genetic engineering methods for amino acid production, which it claims will double existing yields. A major dairy firm, Showa Brand Milk Products is building a $ 20 m. biotechnology laboratory for completion in March 1983 and later expansion; it started work on biotechnology research only in January 1981, concentrating on food, enzymes and fermentation. Future plans include pharmaceuticals. Japanese firms (Kanegafuchi, Dianippon) originated the development work on hydrocarbon-based single-cell protein production, although consumer acceptance problems subsequently delayed development. The technology was subsequently licensed to European producers such as Liquichima (Italy) and Roniprot (Rumania).

2.3.3. Licensing and Joint Ventures

As part of the strategy of establishing independent technology Japanese pharmaceutical firms are seeking to buy their way into interferon production and the genetic engineering technology which provides one route into it. Green Cross has an agreement with Collaborative Genetics for research on a yeast based process for interferon, and another with Genex for research on albumin production. In october 1981 it concluded an agreement with Biogen for marketing the latter's hepatitis B vaccine. Takeda, Japan's largest drug company has signed a contract with Hoffman-La Roche for joint research and production of interferon in Japan, using the latter's genetic engineering technology. Other companies mentioned as buying foreign genetic engineering technology are Kyowa Hakko (for interferon) and Mitsubishi. The most significant joint venture involving licensing agreements is Takeda's alliance with the American firm Abbott. Takeda-Abbott Products have manufacture and marketing rights for all new American drug patents obtained by Takeda, who also have joint ventures involving Bayer (West Germany) and Roussel Uclaf (France).

2.3.4. Overall conclusion

A recent study (1) summarised Japan's strengths and weaknesses in biotechnology as follows

Strengths :

- a traditional fermentation industry
- an established microbial fermentation business
- interchange of University and industrial personnel
- leadership in South East Asia's bioscience community
- strong financial support
- large numbers of trained biotechnologists

Weaknesses :

- rigid compartmentalisation in universities
- a slow start in genetic engineering and separation plants
- language and cultural isolation.

Japan is building upon its recognised strengths and in a variety of ways it is aiming to overcome the identified weaknesses. By the late 1980's, having pursued the strategy of rationalisation and improvement mentioned in § 2.3.1., using the approach of licensing agreements, joint ventures and wholly owned subsidiaries, the bigger companies will be in a good position to attack firstly the European and ultimately the American pharmaceutical markets.

2.4. Other countries

The Soviet Union's biotechnology is not yet seen as a competitive threat in fine chemicals or pharmaceuticals. The emphasis is rather on the improvement of domestic agriculture and the use of biomass wastes to produce animal feedstuffs and thereby diminish external dependence. Current production of single cell protein is estimated by Carter * at over 1 million tonnes p.a., with talk of expanding to 10 times this.

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(1) Rosevear A. : Koshikojima - Reflections in a Japanese Mirror - Biotech Quarterly 1, 1 March 1982.

* "Is biotechnology feeding the Russians?" - G B Carter, New Scientist, 23 April 1981, 216-218

An institution of national and claimed international significance is the Institute of Plant Industry, which acts as a centre not only for plant collection and diffusion but for fundamental research in plant genetics.

Canada's Institute for Public Policy has actively stimulated awareness in that country of the potential of biotechnology*, and a study group was established by the Federal Ministry for Science and Technology in June 1980, reporting in February 1981. The resulting proposal for a 10-year, C $ 483 m. national plan ** was officially accepted by the government in April 1981.

Principal emphasis of the plan is on stimulating industrial and provincial government investment; and strengthening government research institutes, training in multi-disciplinary biotechnology project work and university and post-doctoral training. Areas of application include nitrogen fixation in the context of forest resources; cellulose utilization and waste treatment; pest management for biomass preservation; plant genetics and mineral leaching. Recommendations on regulations for pharmaceutical patents, new plant protection and registration of DNA experiments seek also to encourage innovation. International collaboration is emphasized, and a national committee on R & D in biotechnology is recommended, with strong industrial representation, to coordinate and evaluate the implementation of the recommendations.

Australia's Central Scientific and Industrial Research Organization (CSIRO) is actively recruiting staff for its Industrial Microbiology Unit, to undertake research on microbial genetics, gene technology and industrial fermentation, and the utilization of renewable raw materials and waste treatment. CSIRO's Division of Cellulose Research is investigating options for the utilization of all forms of ligno-cellulose resources and their derivatives, in applications such as

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* "Les micro-esclaves: vers une bio-industrie Canadienne", Pierre Sormany, Institut de recherches politiques, Montréal, document hors série no. 11, septembre 1979.

** Biotechnology: A Development Plan for Canada, report of the working group on biotechnology, Canadian Ministry of Supplies and Services, Ottawa, February 1981.

- Constructional materials, of enhanced mechanical properties and durability;

- paper and similar materials;

- conversion to chemicals and fuels.

The Government of India announced in January 1982 the setting up of a National Biotechnology Board, through which it will give about UK £ 15 million for research in biotechnology over the next 3 years. The expressed preference is to work through existing research institutes, and to concentrate on specific objectives.

China is actively seeking to develop and exploit its considerable scientific potential in biotechnology. A symposium on nucleic acids and proteins was organized in Shanghai in 1981, a cooperative effort between the Chinese Academy of Sciences and the Max-Planck Institute. Reported research includes work on genetic engineering, nitrogen-fixing genes, cancer biochemistry, and the biochemical basis of folk medicine.

The Scandinavian countries have strong interests and capabilities in biotechnology, based on strong internationally competitive industries in fermentation (beer, spirits) and in timber and forest products. Sweden and Finland have strong research activities focussed on the exploitation of ligno-cellulose and the waste products of the timber and pulp industries.

An interesting indication of the geographical spread of interest in biotechnology, in Europe and elsewhere, is given by the analysis shown in Table 3 of the participation at the Eastbourne Congress, April 1981; as biassed, of course, by the cost or convenience of travel to the U.K.

TABLE 3

Analysis by country of origin of the participants in the Second European Congress of Biotechnology Eastbourne, April 1981

	No. of participants	%
- United Kingdom	338	34.6
- West Germany	129	13.2
- Netherlands	68	7.0
- Switzerland	57	5.8
- Sweden	56	5.7
- France	55	5.6
- Italy	35	3.6
- U.S.A.	34	3.5
- Finland	29	3.0
- Belgium	24	2.5
- Denmark	22	2.3
- Japan	22	2.3
- Austria	20	2.0
- Canada	19	1.9
- Ireland	11	1.1
- Spain	7	0.7
- Yugoslavia	7	0.7
- Hungary	6	0.6
- Norway	6	0.6
- Portugal	6	0.6
- Israel	5	0.5
5: Argentina, Australia, Bulgaria, China, Czechoslovakia, E. Germany, Egypt, India, Kuwait, Mexico, Poland, South Africa	20	2.0
TOTAL	976	100.0

3. R & D RESPONSES : MEMBER STATES OF THE EUROPEAN COMMUNITY

The following sections give fuller details of activities and R & D policies relating to biotechnology, in various member states of the Community. Although inevitably brief and uneven, being summarised from heterogenous source materials, these descriptions indicate the common perceptions and needs, and hence provide a background for the discussion of European Community activities and policy for R & D in biotechnology in the following sections, 4 to 6.

3.1. Comparative National Expenditure Statistics on R & D

Reference has been made to the inter-disciplinary character of biotechnology and to its diverse fields of application. These make it particularly difficult as yet to obtain a clear and comparable quantitative picture of biotechnology R & D activity in the member states of the Community. In particular, the subject cuts across four of the "NABS" categories (Nomenclature for the analysis and comparison of science programmes and Budgets) customarily used in European Community R & D expenditure statistics:

3. Protection and improvement of human health.
5. Agricultural productivity and technology.
6. Industrial productivity and technology.
10. General promotion of knowledge.

However, in order to give a context against which to appraise the figures quoted below, Tables 4 and 5 indicate, in national currencies and ECU, the level of national expenditure on these NABS chapters for the years 1979 - 1981. Of the 23.2 billion units of account (bua) budgeted for all areas of civilian R & D for 1981, the Federal Republic of Germany accounted for 7.1 bua, France 6.1 bua, United Kingdom 6.0 bua, Italy 1.7 bua, Netherlands 1.1 bua and Belgium 0.5. The 1980 total was 19.7 bua. A more detailed analysis of the 1980 figures is available, and Table 6 shows expenditure by country on 12 areas more closely related to biotechnology; the expenditure on biosciences is most likely to be correlated with strength in at least the foundation disciplines of biotechnology, but there are problems of comparability caused by the mapping of different national systems into the NABS categories. The U.K. figures appear

TABLE 4

PUBLIC R&D FUNDING OF SELECTED NABS CHAPTERS, 1979-1981 (National currencies)

← NABS CHAPTERS →

IN NATIONAL CURRENCIES, IN CURRENT PRICES		③ PROTECTION AND IMPROVEMENT OF HUMAN HEALTH			⑤ AGRICULTURAL PRODUCTIVITY AND TECHNOLOGY			⑥ INDUSTRIAL PRODUCTIVITY AND TECHNOLOGY			⑩ GENERAL PROMOTION OF KNOWLEDGE			TOTAL ALL NABS CHAPTERS			③+⑤+⑥+⑩ AS % OF TOTAL		
		'79	'80	'81	'79	'80	'81	'79	'80	'81	'79	'80	'81	'79	'80	'81	'79	'80	'81
F.R. GERMANY	DM m.	986	1031	1082	305	318	348	1443	1701	1825	6792	7344	7821	15838	17046	17930	60,1	61,0	61,8
FRANCE	FF m.	1459	1719	2223	1047	1214	1573	2710	2902	3758	6246	6917	8242	26477	31100	36555	43,3	41,0	43,2
ITALY	LIT b.	71,0	86,1	115,3	50,1	64,3	70,4	96,9	270,0	234,2	370	553	887	1051	1550	2129	55,9	62,7	61,4
NETHERLANDS	FL m.	206	143	198	218	262	264	154	194	264	1615	1732	1762	2884	3106	3301	76,0	76,7	75,4
BELGIUM	FB m.	2381	3356	3480	1039	1007	993	2960	3147	3164	5612	6700	7002	18834	21099	21652	64,1	67,3	67,6
UNITED KINGDOM	£ m.	57,2	61,0	71,1	88,3	102,5	131,7	82,4	154,5	249,4	449	507	703	2026	2477	3226	33,4	33,3	35,8
IRELAND	I£ m.	2,6	4,3	5,6	11,9	10,6	15,0	3,9	2,5	5,4	11,1	15,4	18,4	38,0	41,2	56,4	77,6	79,6	78,7
DENMARK	DKR m.	205	229	223	147	149	188	244	230	325	643	664	710	1684	1698	1988	73,6	74,9	72,7
EUR 9	EUA m.	961	1062	1211	625	712	863	1421	1834	2213	5031	6301	7376	16716	19417	22869	51,7	51,0	51,0
EUR. COMM.	EUA m.	38,0	30,2	39,3	2,9	2,4	4,2	26,3	25,1	33,2	[illegible]	0,5	0	237,7	2843	346,4	28,5	23,6	22,1
EUR. 9 + EUR. COMM.	EUA m.	999	1101	1251	628	715	867	1448	1859	2247	5632	6302	7376	16954	19701	23215	51,4	50,6	50,6

Source : Statistical Office of the European Communities,

CREST / 1235 / 81

TABLE 5

PUBLIC R&D FUNDING OF SELECTED NABS CHAPTERS, 1979-1981 (M. EUA)

NABS CHAPTERS

IN M..EUROPEAN UNITS OF ACCOUNT (E. U. A. (m.))	(3) PROTECTION AND IMPROVEMENT OF HUMAN HEALTH			(5) AGRICULTURAL PRODUCTIVITY AND TECHNOLOGY			(6) INDUSTRIAL PRODUCTIVITY AND TECHNOLOGY			(10) GENERAL PROMOTION OF KNOWLEDGE			TOTAL ALL NABS CHAPTERS			(3)+(5)+(6)+(10) AS % OF TOTAL		
	'79	'80	'81	'79	'80	'81	'79	'80	'81	'79	'80	'81	'79	'80	'81	'79	'80	'81
F.R. GERMANY	393	409	427	121	126	137	575	674	719	6308	2909	3083	6303	6753	7070	60,1	61,0	61,8
FRANCE	250	293	371	180	207	263	465	494	628	1071	1179	1317	4542	5299	6109	43,3	41,0	43,2
ITALY	62,3	70,8	91,0	44,0	54,0	55,6	85,1	226,9	184,9	325	465	700	923	1303	1681	55,9	62,7	61,4
NETHERLANDS	75,1	65,8	70,4	79,3	96,9	93,8	56,1	70,1	93,9	588	628	627	1049	1125	1174	76,0	76,7	75,4
BELGIUM	59,3	82,7	83,7	25,9	24,8	23,9	73,7	77,5	76,1	142	165	168	469	520	521	64,1	67,3	67,6
UNITED KINGDOM	88,5	102	132	137	171	244	128	258	463	695	848	1305	3135	4139	5985	33,4	33,3	35,8
IRELAND	3,9	6,0	8,1	17,8	15,7	21,6	5,8	3,7	7,8	16,5	22,8	26,4	56,8	61,0	81,1	77,6	79,6	78,7
DENMARK	28,5	29,2	27,9	20,4	19,0	23,5	33,8	29,4	40,7	89,2	84,8	88,8	237	217	249	73,6	74,9	72,7
EUR 9	961	1062	1211	625	712	863	1421	1834	2213	5631	6301	7376	16716	19417	22251	51,7	51,0	51,0
EUR. COMM.	38,0	39,2	2,9	2,4	4,2	26,3	29,1	33,2	0,5	0,5	0	0,5	2377	2248	3464	28,5	23,6	22,1
EUR. 9 + EUR. COMM.	999	1101	1251	626	715	867	1448	1853	2247	5632	6302	7376	16954	19701	23215	51,4	50,6	50,6

Source : Statistical Office of the European Communities,

CREST / 1235 / 81

TABLE 6

PUBLIC R&D FUNDING OF SELECTED NABS SECTIONS 1980 ('000 EUR)

Within NABS chapter :	SECTION	FED. REP.. GERMANY	FRANCE	ITALY	NETHERLANDS	BELGIUM	UNITED KINGDOM	IRELAND	EUR 9 *
(3) : protection & improvement of human health	31 : Medical research (incl. biomedical & engineering)	96,513	217,074	34,876	7,958	31,435	50,766	712	439,335
	32 : Food hygiene & nutrition	17,664	17,550	2,670	-	4,482	7,193	1,879	51,437
	33 : Pollution	133,651	58,273	12,399	32,680	14,901	35,479	365	287,750
(5) : Agricultural productivity & technology	50 : Research of general nature	50,280	25,217	9,391	7,779	3,905	28,986	808	126,367
	51 : Domestic med. animal products	5,961	64,918	8,176	10,363	9,578	60,688	8,586	168,270
	52 : Crops (incl. forestry) + wine	60,525	97,973	34,527	35,633	10,074	60,855	3,652	303,260
	53 : Fisching and fishery products	9,067	18,743	1,950	2,364	1,200	13,594	2,627	49,546
(6) : Industrial productivity & technology	632 : Pharmaceutical products	-	-	11,435	-	1,736	-	-	13,170
	681 : Food, drink & tobacco	16,875	24,877	4,997	-	3,766	2,508	222	53,245
	686 : Utilisation of industrial agricultural & domestic wastes	-	-	1,560	-	1,563	979	12	4,114
(10) : general Promotion of Knowledge	1013 : Biosciences	126,811	196,798	30,934	-	26,005	3,619	1,092	385,258
	103 : Research in medical Sciences	632,238	121,657	68,076	-	-	98,025	71	920,067

Source : Statistical Office of the European Communities,

CREST / 1235 / 81

* no comparable Danish figures

to under-represent the country's degree of activity as compared with France and Germany. The total under biosciences, 385.3 mua, may perhaps be set against the figure quoted by Rogers for Japanese government expenditure for life sciences in general : 50 bn Yen, i.e. 195 mua : it is probable that this is of the right order in indicating by how much the spending of the European Community countries in total exceeds that of the Japanese.

Adding together chapters 31 (Medical research = 439.3 mua) and 103 (Medical Sciences = 920.1) gives a figure for the EC approaching $1\frac{1}{2}$ bn eua; approximately half the budget of the U.S. National Institutes of Health.

A general omission from the public sector R & D statistics is the public provision of staff and facilities in the university or polytechnic institutions of the higher education sector. Although generally provided under the Ministry of Education budgets, the extent and quality of these are of primary importance for R & D capabilities. A Commission sponsored report on the training facilities for biotechnology in various countries of Western Europe has been assembled by the Education Working Group of the European Federation of Biotechnology.

3.2. Federal Republic of Germany

Germany has for many years had outstanding industrial strength in all major areas of biotechnology. Initiatives by DECHEMA (Deutsche Gesellschaft für Chemisches Apparatewesen) led to a major report in 1974 on the significance of biotechnology, and a revised version was subsequently commissioned by the Bundes Ministerium für Forschung und Technologie (BMFT)*.

BMFT has summarised in "Leistungsplan 04" a clear picture of federal expenditure on R & D in biotechnology : Figure 1 is based on the plan as at January 1980, showing the breakdown of the planned expenditure of DM 53 m. on project expenditures. To this should be added some DM 17 m. for support of the institutions listed. More recently announced plans speak of increasing expenditure from the current DM 55 m. to DM 70 m. p.a. (from 22 to 28 mua).

The major single public commitment to biotechnology is the Gesellschaft für Biotechnologische Forschung (GBF), at Braunschweig-Stockheim, where a wide range of research is undertaken; ranging from genetic manipulation to fermenter operation and the exploration, with pilot-scale plant, of downstream processing operations. 1982 total budget DM 31.6 m., of which DM 5.4 for investment in expanded facilities.

The BMFT also makes extensive use of collaborative agreements in research with many other countries, including Japan, Sweden, and Canada as well as with EC partners.

The major strengths of German biotechnology lie in its large chemical and pharmaceutical companies : Hoechst, Bayer, Boehringer Mannheim and Boehringer Ingelheim. There is close collaboration with educational institutions, and with the industrially-orientated activities of the GBF and DECHEMA (the chemical equipment manufacturers' association). Full-time degree courses in biotechnology are

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* Biotechnologie : Studie über Forschung und Entwicklung : Möglichkeiten, Aufgaben und Schwerpunkte der Forderung, DECHEMA, 1976.

Figure 1 : Breakdown by objectives and activities of FRG Biotechnology R & D

OBJECTIVES

- Security and quality of food supply
- Reduction of burden on environment
- Improvement of medical diagnostics and therapy
- Security of raw material feedstocks
- Development of management and diffusion of knowledge

PROGRAMME

- Bio-technology 04

PROGRAMME SECTION	ACTIVITIES	PROJECT EXPENDITURE (m.DM, 1982, planned)
Biotechnology in protection of food supply 0401	Biotechnical sources of unconventional food-and feedstuffs and natural additives 040101	6.0
	Nutritional physiology and medical value of unconventional food-and feedstuffs 040102	
Reduction of burden on environment 0402	Natural materials for pest control 040201	12.0
	Specific insect viruses for pest control 040202	
	Special biological methods for air and water purification 040203	
Pharmaceutical bases and natural substances 0403	Pharmacologically active substances from plant cell culture 040301	12.0
	Extraction of medicines and vaccines from animal cell culture 040302	
	Improvement of useful plants with the help of cell culture techniques 040303	
Extraction and recycling of raw materials 0404	Biological methods for obtaining useful materials from plant by-products 040401	8.0
	Anaerobic fermentation techniques for the preparation of basic chemicals 040402	
	Microbiological methods for extracting metals 040403	
Development of bio-technological methods 0405	Development and testing of bio-reactors for cellular systems 040501	12.0
	Development and testing of bio-reactors for cell-free systems 040502	
	Measurement and control techniques, sterilisation and further processing 040503	
Foundations for bio-technological methods 0419	Research on development & evaluation of new biological techniques 041901	3.0
	Collection of biotechnologically important cultures.	
		53.0

provided only at the Institute for Fermentation and Biotechnology in Berlin; but many universities and technical high schools include courses supplementary to basic courses in microbiology and biochemistry. There are links also with the Technical High School, Zurich.

Hoechst is the largest of the chemical/pharmaceutical companies, and attracted considerable comment when in 1981 it signed a 10-year $ 67 m. research agreement with Massachusetts General Hospital for work on molecular biology and genetics. This should be seen in the context of the company's total pharmaceuticals R & D budget of some $ 270 m. p.a. With BMFT support, Hoechst has developed a single-cell protein now being tested for human nutrition (production scale 2000 t.p.a.).

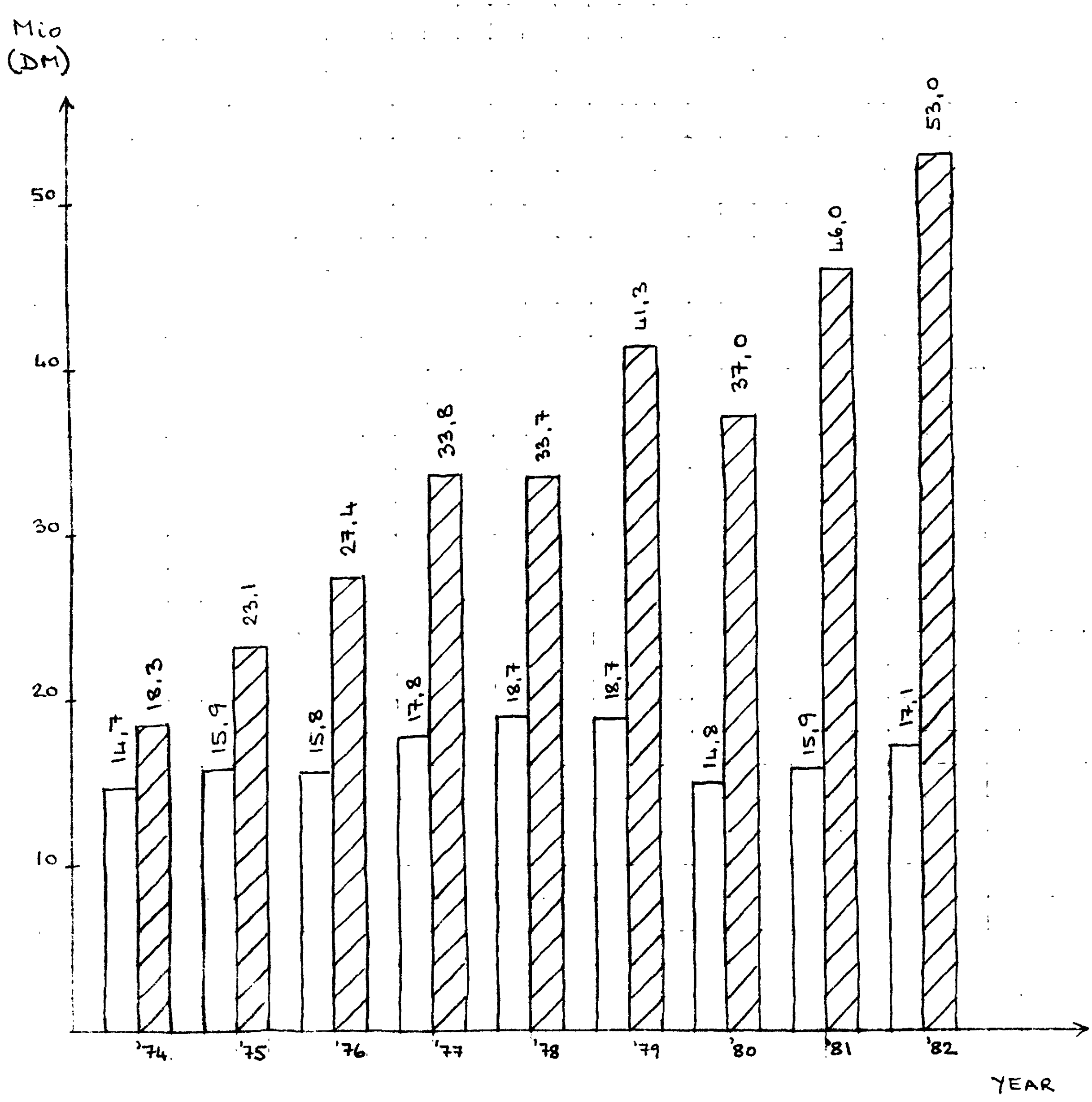

Figure 2 : growth of expenditure on biotechnology R&D in FRG, 1974 - 1982.

Project expenditures

Institutional support :
Gesellschaft für Biotechnologische Forschung
Gesellschaft für Strahlen und Umweltforschung
Kernforschungsanlage, Jülich

3.3. France

The President of the republic commissioned from Professors Gros, Jacob and Royer a major study, "Sciences de la Vie et Société", whose publication in October 1979 is a convenient starting point for the consideration of public policy towards biotechnology.* This report was very "European", emphasizing that the diversity and complexity of advanced teaching and biological research have become such that a sufficiently large and competent group can be organized only on a european rather than a national basis. Concerning the basic tools of biological research - measuring devices, biological materials, buildings, databanks and stocks of living materials, France is seen as excessively dependent on foreign sources; but with adequate investment, the authors believe that French industry should be able to correct the situation within 10 years.

Food production is seen as an essential issue - perhaps by the end of the century, as great a problem as energy; a strategic challenge of particular significance to a country with France's vast agricultural potential. French industry is seen as strong in foods (though other sources see it as fragmented in comparison with major U.S. or even U.K. firms), as comfortably placed in pharmaceuticals, but as weak in biological and medical technology. The research proposals made by Gros, Jacob and Royer include:

- Fixation of nitrogen - interdisciplinary collaboration involving botanists, biochemists, geneticists and agronomists.

- Bioconversion of cellulosic resources and wastes - including an inventory of cellulose resources.

- Fuel alcohol programme - based on existing fermentation alcohol capability, cellulose wastes and skill in yeast biochemistry.

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* An English summary of the Gros, Jacob and Royer report, the de Rosnay report and the Pelissolo report, together with comments, has been made by K. Sargeant. Available from FAST, DG XII, Commission of the European Communities.

- Mass culture of animal and plant cells, for biological derivatives, pharmaceutical products, monoclonal antibodies; importance of cell banks and gene banks is again emphasized.

- Biological equipment and reactor engineering : a major development effort needed to produce modern, well-instrumented equipment.

Parallel to the Gros, Jacob and Royer report, Joël de Rosnay produced an informative document* giving details of French and foreign capabilities in each area of biotechnology.

A briefer and more succinct, policy-oriented report was requested by the Prime Minister, and J.-C. Pelissolo was charged with this responsibility. His report** considers in turn public sector research, industry and the controlling administrations. It aims to identify strengths and weaknesses, and identify the principal problems to be solved to ensure industrial success.

Public sector research is seen as of good quality, but its transfer to, and exploitation by, industry is restricted by inflexibilities. Pelissolo sees French industry as backward in biotechnology, behind not only the U.S. and Japan, but also Germany, the Netherlands and Britain. There is insufficient knowledge in the leading industrial teams. He considers several specific fields in detail :

- Health : strong in pharmaceuticals (Rhone-Poulenc, Roussel Uclaf), but a major deficit in antibiotics; strong in immunology.

- Agriculture : risks of external dominance of the seed industry; need to exploit INRA genetics research and in vitro plant propagation know-how.

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* "Biotechnologies et Bio-industrie", Joël de Rosnay, Documentation Française, 1979.

** "La Biotechnologie, Demain?", Jean-Claude Pelissolo, rapport à M. le Premier Ministre, Documentation Française, December 1980

- Agro-food : traditional brewing and cheese-making lacks research and innovative strength; more active are the food- and feed-additive industries, with 10-50% (depending on product) of world amino acid production (70-80% exported), and a major converter of maize (1.3 m. tonnes of maize processed into 300 different products). The EEC iso-glucose regulations are seen as damaging, benefitting only the Japanese and still more the American producers in the long term.

- Chemicals : biotechnological applications currently modest, but expected to increase : French industrial interest lagging behind American and German activity.

Pelissolo sets as first objective the increase of France's research potential, and of its utilization by industry. High quality fundamental research must continue to be financed by the state. France must make good from foreign sources what she cannot find at home, buying foreign firms, and promoting academic and industrial exchanges of research fellows with the best foreign laboratories. Amongst his many specific recommendations, Pelissolo includes the creation of an international mission for biotechnology, to orchestrate and stimulate national competence in the field.

The subsequent change of administration in France has reinforced the strong public commitment to biotechnological development, coordination now being focussed by the creation of the new "Mission Biotechnologie", under Professor Pierre Douzou.

This has a budget of some FF 70 m. (10 mua) to spend on research, but as its Director has pointed out, funds from other national agencies (such as the Agence Nationale de Valorisation de Recherches) could double or treble this amount. The research Ministry's new strategy involves the creation of four technology transfer centres for biotechnology : Compiègne, Toulouse and two in Paris : Institut Pasteur and an expanded INRA fermentation centre. At these scientists will be encouraged to work in collaborative "cells" with engineers and technologists from local companies. Also planned are some 60-80 fellowships to encourage scientists in universities and in industry to do applied research and/or update their knowledge.

Altogether it is estimated that the French Government will spend some FF 200 m. (29 mua) on education and research in biotechnology in 1982. Strategic planning of industrial biotechnology is centering particularly on the capabilities of Rhône-Paulenc and Elf-Aquitaine.

A study by SEDES*, for the Ministry of Industry's Delegation for Innovation and Technology, illustrates the emphasis placed on the potential role of small and medium-sized enterprises in biotechnology. This emphasis tends to be linked with the exploitation of agricultural products, by products and wastes.

3.4. Italy

The Italian government's support for life sciences and biotechnology research is channelled mainly through the Council for National Research (CNR). The CNR has announced a Task Programme on Genetic Engineering, to run 1983-1987, with a financial commitment of the order of 15 m. ecu over the 5 years (i.e. same 3 m. p.a.).

There has also been reported (scrip, 26 July 1982) a plan to spend $ 91 M. on biotechnology over the next 5 years, over half of this from government and the rest from private industry. The intention is to draw extensively upon the experience gained in CNR's biomedical technology research programme (say 10 m. p.a. ; 10 + 3 = 13 m. ecus p.a.)

O her public sector initiatives include support for biomass energy projects, and generous financial support for the installation of anaerobic digesters to cope with the effluent problems of intensive animal units.

Of special interest is the recent agreement between FIAT (Soria), ENI (Sclavo) and MONTEDISON (Carlo Erbe - Fasmitalia) for common precompetitive research in the field of monoclonal antibodies for diagnostic methods and developments. Financing of this project (1983-1986) has been approved by the government amounting to 5 m. ecu, through an IMI contract (via Tecnobiomedica).

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* "Les Bio-Industries ... des Opportunités pour les PMI", Ministère de L'Industrie, Programme National d'Innovation, no 5.

CNR also supports research centres in universities such as the Institutes of Genetic Biochemistry at Pavia and Naples. There are several other strong centres in the life sciences (Milan, Genoa, Bari...) and others in agricultural research.

Turning to industrial research, mention should be made of the advanced work in immobilised enzymes for detoxification, particularly within FIAT (Soria) and ENI* (SNAM progetti).

Italy**has developed a substantial fermentation industry for pharmaceuticals, citric acid and single cell protein.

Pharmaceutical producers include the following companies :

Ankerfarm (Milan) : Glaxo subsidiary : tetracyclines and semi-synthetic penicillin

Archifar (Milan) : owned by Montedison and ENI : erythromycin and semi-synthetic penicillin

Ciba-Geigy (Fervel) (Naples) : steroids, eifamycin, cephalosporins

Cynamid (US) : tetracyclines

Farmitalia : (Montedison) (Milan) : semi-synthetic penicillins under license from Beechams : tetracyclines, doxorubicin, alkaloids, cephalosporins C

Icar (ESF) (Milan) : semi-synthetic penicillins and cephalosporin

Istituto Biochemica Italiano (Milan) : penicillins and cephalosporin

Lepetit (Milan) : Dow subsidiary : sifamucin, anti-tuberculosis antibiotic, tetracyclines

Peirrel (Milan and Capra) : erythromycine and tetracyclines

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* ASSORENI, the research association of the ENI group, have recently conducted, with partial Community support, a wide-ranging review : "Blood detoxification : Problems and Perspectives", published (1982) by Frances Pinter, London.

** This section draws inter alia upon information provided in J. de Rosnay's "Biotechnologies et Bio-industrie", Documentation Française, 1979.

Squibb (US) (Milan) : penicillin G

Proter (Milan) : tetracyclines, cephalosporins

Lark (Milan) (Montedison subsidiary) : cephalosporin.

de Rosnay comments that the rapid growth of pharmaceutical production over the last 30 years was attributable to the absence of patent protection for these products, a situation which has given rise to international friction in the past.

In the other fields of fermentation, single-cell protein from hydrocarbons was previously seen as of major importance.

ANIC of Milan, the petrochemical branch of ENI, was in partnership with BP for the production of single-cell protein (SCP) in Italy. A factory based on n-alkanes as feedstock, using yeasts to convert this into protein, was constructed in Sardinia, with a capacity of 100,000 tonnes p.a. Restrictions on the sale of SCP caused the termination of the project, without the plant being commissioned. The experience of Liquichemica, who licensed the Japanese process from Kanegafuchi was similar; delays in clearance for the marketing of the product forced the group into liquidation.

3.5. The Netherlands

An extensive review of both biotechnology and of Dutch national capability was published in April 1981* by STT, and some key points from this are summarized below. A government-sponsored committee was set up in May 1981, under the chairmanship of Professor Schilperoort of the University of Leiden, with the aim of coordinating research on the Netherlands and increasing its emphasis on commercial applications. The committee includes experts from industry, universities, and the governmental applied research organization TNO. Four million florins a year has been made available for the biotechnology committee to allocate to selected projects.

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* "Biotechnology : a Dutch perspective", ed. J.H.F. van Apeldoorn; Stichting Toekomstbeeld der Techniek (Netherlands Study Centre for Technology Trends)

The committee reported in April 1982, and has emphasized not the creation of new centres for biotechnology, but the strengthening of cooperation between government institutes, universities and industry. It urges the government to provide extra support to stimulate innovation in biotechnology - at least an extra 75 m. florins (28 mua) over the period 1982-1988 - drawing on the government's fund for industrial innovation, and in addition to a separate (and much larger) planned budget for biotechnology. (Other reports speak of a $ 1 billion 5-year plan for government expenditure to encourage R & D by industry into biotechnology and micro-electronics.)

The committee emphasizes applied research in areas of existing strengths of Dutch companies - agriculture, dairy industries, fermentation and antibiotics; and for future research, the development of host-vector systems, somatic cell hybridisation, second generation enzyme reactors, and downstream processing technology.

The committee, echoing widespread earlier calls from industry, universities, and the STT report, recommends bringing the Dutch regulations on DNA experiments into line with the less strict criteria adopted elsewhere, and harmonized on a single national, rather than municipal, basis. The construction of a laboratory for work at P3 containment level at TNO has been delayed pending advice from the Committee on the Ethical Implications of Genetic Engineering.

Professor Schilperoort sees the need to improve internal communication structures : Dutch industry and universities often have extensive contacts abroad at the expense of national collaboration. The country has a large fermentation industry, in many respects of international standard. Research facilities outside industry are very limited, reducing the potential for international competitiveness. In the food industry, Dutch breweries and dairy plants are sophisticated and internationally competitive.

The Netherlands has an excellent tradition of microbiology, biochemistry and process engineering, and has a leading international position in effluent treatment, developed in response to the needs of the food industries.

The company Gist-Brocades is Europe's major producer of penicillin, with corresponding expertise in fermentation technology. It is also one of the world's major producers of enzymes, and is carrying out intensive study on their production, isolation and application, on laboratory and commercial scale. Related research is under way at the universities of Delft and Wageningen; details of these and other university research centres are given in the STT report. Gist-Brocades has acquired other enzyme producers such as Wallerstein (in the U.S.A.) and Rapidase (in France).

Akzo has also a range of pharmaceuticals based on fermentation technology. Its subsidiary, Organon, produces steroids (including contraceptives), and has been one of the first companies to market a product based on monoclonal antibodies (a pregnancy test). Another subsidiary, Glucono, is one of Europes principal producers of gluconic acid.

The Netherlands has a major sugar industry, Centraal Suiker, and its subsidiary Chemie Combinatie produces lactic acid by fermentation of sucrose.

3.6. Denmark

Biotechnology is critical for Denmark. The agricultural (24%), food (34%) and chemical (10%) industries together dominate the "manufacturing" economy. Everyone has heard of the Carlsberg brewery, with its traditional skills in brewing, which have supported the creation of an international research centre with outstanding competence in plant genetics and cell biology. Everyone has also heard of Novo, which dominates the world market in industrial enzymes. Novo practised biotechnology before the word was invented, and is now arguably the world's leading company in the field.

Denmark spends about 700 m. Kroner annually (86 m. e.u.a., private and public sector) on biotechnology research, somewhat less than 1% of product value, but heavily biased towards the chemical sector (Novo contributes 200 m. of this). It is now being argued by some that research investment in agriculture and food should be increased.

In 1978 the Danish Technical Research Council, under the chairmanship of Prof. O.B. Jorgensen, took the first initiative in the field and supported projects in genetic engineering scale-up problems (with particular reference to genetic stability), product recovery (with special reference to selective recovery of intracellular products) and on protein synthesis. More recently a Ministry of Industry "initiative group" recommended against creating a new institute specially for biotechnology because the subject was of such widespread interest that it needed to be practised widely.

In April 1981 another Ministry of Industry "initiative group" was formed under the chairmanship of Prof. Ulrik V. Lassen, research manager of Novo, to consider applied genetic engineering in Denmark. It reported in November 1981 and recommended that individual research proposals should be supported and that appropriate guidelines or rules to govern applied research and industrial use of genetically manipulated microorganisms should be developed. Its principal recommendation was that a Working Group to study the genetic manipulation of microorganisms should be set up at the Technical University, with a view to the appointment of a Professor at a later date. This working Group was started in October 1982 and now comprises 4 scientists and 3 technicians. It will aim to provide a microbial genetics service to industry.

Denmark is developing a unique biotechnology, based on a unique biotechnology company, with cooperation from government and university.

3.7. The United Kingdom

3.7.1. Government policy and Research Council activity

A major report on biotechnology was published in April 1980 by a Joint Working Party drawn from the Cabinet's Advisory Council for Applied Research and Development, the Advisory Board for the Research Council and the Royal Society. This report is usually known as the Spinks Report after the Chairman of the Working Party Sir Alfred Spinks, formerly Director of research at ICI.

Seeing large potential growth in the field, both for existing industries and new ones, the report recommended a policy of "technology push" reflected in a firm commitment to strategic applied research, and funded by Government intervention. Detailed recommendations were that Research Councils should spend at least £ 3 m. (5 mua) annually on biotechnology research, and that the Government should spend about £ 2.5 m. a year (including existing projects) in a coherent programme of industrial R & D to involve industry, Government research establishments, universities and research associations. A further specific recommendation was for the establishment of a research-oriented biotechnology company (suggested cost £ 2 m.).

The initial response of the Government, in a White Paper on the subject, was strongly to emphasise the role of market forces and the private sector, to exploit British scientific and technical discovery and build up its competitive position by importing good developments through licences or otherwise as well as from its own research and development.

Initally at least this attitude, and the lack of specific policy on the vital area of education for biotechnology, were seen as clearly differentiating the Government's attitude from that of France, West Germany and Japan.

Subsequently however, many aspects of the Spinks report have been implemented, illustrated by the following developments :

- the Research Councils now spend more than £ 7 m. between them on narrowly defined biotechnology, and a coordinating committee has been set up; indeed their evidence to the Parliamentary Committee currently investigating biotechnology gave the figures shown in Table 7, suggesting a possible total exceeding £ 25 m. (43 mua), mainly attributable to the medical "underpinning" research.

TABLE 7 : U.K. Research Councils annual expenditure on biotechnology (£m)

- Agricultural Research Council (total 1982/83 budget about £92 m. p.a.)=	
• genetic manipulation (primarily of plants) =	1.5
• other areas of biotechnology including veterinary, vaccines and monoclonal antibodies etc for veterinary diagnostics	2.5
• related "under-pinning" research =	"of the same order"
total	"about £5 m."
- Medical Research Council (total budget about £107 m. p.a.)	
• on a rigorous definition (research directed specifically to the development of something with a foreseeable commercial end such as a vaccine or diagnostic reagent) = of the order of	1.7
• conceptual underpinning = molecular biology, molecular genetics = "approximately 10" (verbal answer); underpinning research (e.g. in the chemistry, organisation and function of genes) = "the Council spent £17 million in 1980-81" (written submission)	17
total	18.7
- Science and Engineering Research Council	
• current annual expenditure on biotechnology research (divided roughly into two-thirds for basic biological research and one-third for engineering research) = £1 million; including DNA, aspects of microbiology and molecular genetics, immobilised enzyme and cell systems, fermentation including downstream processing, waste treatment and the leaching of metals from ores. Planned to increase to £2.5 million by 1985/86	1
total	1
- Natural Environment Research Council present role relatively minor (£0.6 million p.a.), but many interactions and areas of research activity of relevance :	
• management of biomass production (seaweed, organic wastes, woodlands, algae, fish)	
• selection, sterile culture and propagation of tree clones	
total	0.6

- pest control
- ecology, physiology, biochemistry and genetics of micro-organisms (soil and aquatic)
- taxonomy, culture technology and collections

For the 4 councils :	25.3

Source: Minutes of Evidence of the House of Commons Education, Science and Arts Committee, Session 1981-82, "Biotechnology" : 21 April and 10 May 1982.

- a special Biotechnology Directorate has been established within the Science and Engineering Research Council to coordinate SERC grants for research in the field and encourage British scientists to take up research in related areas.

- a coordinating committee between Government departments has been set up.

- Department of Industry support for R & D is now at least at the level recommended in the Spinks report (£2.5 m.) and support for industrial investment in the area is around £15 m., a further £ 16 m. industrial support programme was announced in December 1982.

- the University Grants Committee has been given increased funds of £1 m. per annum to finance 20 extra teaching posts and research (a recent report estimated that over the next 10 years, Britain would require 1000 extra graduates and 4000 technicians trained in biotechnology);

- a research-oriented company, Celltech, has been launched, its £12 m. capital being 44% public (via the British Technology Group), 56% private (Prudential Assurance, Midland Bank, British Commonwealth Shipping, Technical Development Capital). Celltech has a special responsibility for commercialising useful discoveries from Medical Research Council supported laboratories; plans are also well-advanced for the launch of a corresponding company to exploit the results of work financed by the Agricultural Research Council.

3.7.2. Industrial activity

Whilst the United Kingdom's academic strength in the field of biotechnology rests on the large number of University departments in the life sciences, many associated with research units dependent on the Research Councils, its commercial strength is based on large and successful companies in chemicals, pharmaceuticals and food processing, whose research and production facilities, like those of some important subsidiaries of non UK firms (e.g. G.D. Searle), are based in the UK. Imperial Chemical Industries Ltd. has played a major role in the development of biotechnology in Britain, in fields as diverse as plant protection chemicals (esp. pyrethroids) sewage treatment (e.g. the deepshaft process for recycling, on limited land space, water contaminated by organic effluents) and single cell protein. The last has been widely publicised, with the bringing on stream early in 1981 of the "Pruteen" plant producing 60.000 tons of single cell protein rich in the essential amino acid lysine. Based on a feedstock of methanol, produced from North Sea gas, this product competes with soya and other protein sources. It has also had to overcome the regulatory hurdles faced by any novel feedstuff. The project itself is of great significance as a prototype for large-scale biotechnology and the development of the related process engineering. Attempts to improve the energy efficiency of the micro-organism have included the use of genetic engineering to produce a manipulated variant. Others strong in the field of biotechnology include innovative pharmaceutical firms such as Glaxo and Beechams. Groups such as ICI, Shell and BP have significant research and production capabilities in pharmaceuticals and agricultural chemicals. Major food firms and brewing groups in the UK are also showing active interest in biotechnology, eg. Rank Hovis McDougalls fungal single cell protein and Grand Metropolitan Hotels investment in Biogen (the only European shareholder).

Unilever's expertise at all stages of vegetable oil production (palm tree cloning) and manipulation (inter-esterification, e.g. to convert palm-oil mid-fraction to the equivalent of cocoa butter fat) is another strong point of Anglo-Dutch biotechnology : the examples cited indicate also the Third World implications.

3.8. Belgium

Belgium has a strong chemical industry, and outstanding strengths in its universities and research institutes in the biomedical sector (e.g. the Institute for Cellular and Molecular Pathology) and in plant genetics (University of Ghent), as well as in other areas (e.g. bacteriology in various institutions). The international pharmaceutical companies are also attracted by the high quality environment provided by the research teams in the various universities of the country. The rather open economy and the presence of numerous multinational companies (chemicals, pharmaceuticals, foods) create the problem for the public authorities of balancing the advantages of attracting foreign investment against the drawbacks of a potential internal "braindrain" into these companies, with insufficient spin-off benefits to the local economy.

At the level of the regional authorities, Wallonie, Flanders and Brussels are seeking to attract foreign investment in high technology sectors such as biotechnology. At the level of the national authorities, the IRSIA - a national industrial research association - is coordinating R & D projects on biotechnology topics (e.g. on vectors, yeasts, plant tissue culture) at Belgian research centres, and funded by 14 Belgian companies (2 year budget, some BF 200 m).

The SPPS (National Science Policy Department) is supporting centres of excellence in molecular biology, through "Concerted Research Actions" in the last 10 years (yearly budget 200 MFB).

In addition, the organization of a coordinated collection of micro-organisms has been started, with fungi at Louvain-la-Neuve, and bacteria ät Ghent.

3.9. Ireland

Ireland, like Belgium, is vigorously seeking to attract foreign investment, to take advantage from its developed educational system, and to stimulate greater exploitation of the country's under-utilised agricultural potential.

The 1981 report by the National Branch for Science and Technology, "Biotechnology Trends", emphasised chemicals, pharmaceuticals, health-care and food processing as sectors within which there are processes and products of special potential significance. The possibility of gaining technology transfer from innovative U.S. companies is noted.
A comprehensive major policy document is planned to appear by mid-1983, outlining a development plan for Irish biotechnology. Focussing on pure and applied biological research and on industrial needs, it is the product of close liaison between the NBST and the Irish Development Authority.

3.10. Greece

The Ministry of Coordination, in consultation with the Ministries of Science and Technology, Education and Agriculture, is currently developing plans to stimulate awareness, education and application of biotechnology. This will be developed on the country's existing university groups in biology, chemistry and agriculture - particularly using dairy industry and viticulture expertise - and the national research institute N.R.C. Demokritos.

3.11. European Associations and Federations

In describing the response of the member states of the European Community to the challenges of biotechnology, it is relevant to consider the private sector commercial activities, and the public policy initiatives including education and publicly-funded research ; but no less relevant to the co-ordination of responses is the individual and voluntary effort which finds expression through professional societies and federations (see box).

Most relevant to biotechnology in Europe is the European Federation of Biotechnology, founded in 1978. It includes both the basic disciplines - biologists, biochemists, microbiologists, chemical engineers, and application areas such as fermentation and public health engineering. Through specialized working groups, it brings together multi-national, multidisciplinary groups on such topics as the following :

- Education for biotechnology.
- Standard methods for the evaluation of bio-reactors, and bio-reactor standards.
- Immobilized biocatalysts.
- Cell culture technology.
- Environmental biotechnology.
- Safety in biotechnology.

The EFB Newsletter, the activities of the working groups (several of which are preparing reports), and the support of the EFB for major conferences such as the European Congresses of Biotechnology (Interlaken, 1978 ; Eastbourne, 1981) can contribute significantly to the strength and self-awareness of European biotechnology, based on the broad networks of its member societies.

Responses of the European scientists, via voluntary and professional associations, to the challenges of the life sciences and biotechnology.

Long-established federations in the three basic disciplines :

- the Federation of European Microbiology Societies (FEMS)
- the Federation of European Biochemical Societies (FEBS)
- the European Federation of Chemical Engineering (EFCE)

Collaboration through the

European Molecular Biology Organisation (EMBO) has led to the creation of the

European Molecular Biology Laboratory, Heidelberg - a successful example of European collaboration. Similar to EMBO in concept is ECBO :the

European Cell Biology Organisation (1st Congress in Paris, July 1982, a major success).

For collaboration on school and university teaching of biology, and wider social questions, ECBA :

European Communities Biologists Association.

For special support needs, particularly on culture collections : the

European Federation of Cell and Virus Collections, and the

European Culture Collection Curators' Organisation

have recently been formed (1981, 1982)

In the application areas, there are active and effective groups : e.g. EUCARPIA, the European association of plant breeders, with its 16 specialist working groups and sub-groups; and the European Association for Animal Production,

whose 9 study groups have just produced a long-range assessment of "Livestock Production in Europe" (Elsevier). Useful communication centres for European industry are CEFIC (European Association of Federations of the Chemical Industries), CIAA (Council of the Agro-food Industries), EFPIA (European Federation of Pharmaceutical Industry Associations), as well as more specialist groups (e.g. AMFEP : Association of Microbial Food Enzyme Producers).

Major focus for biotechnology in Europe is the

EUROPEAN FEDERATION OF BIOTECHNOLOGY,

founded 1978, linking over 40 learned societies, supported by ca. 10 specialist working groups, and organised by the 3 secretariats :

DECHEMA (Frankfurt)
Society of Chemical Industry (London)
Société de Chimie Industrielle (Paris)

4. EXISTING AND PROPOSED COMMUNITY PROGRAMMES

4.1. The Range of Community Activity

4.1.1. The manner in which the Community has acquired research programmes containing aspects of life-science and biotechnology may be described as gradual. 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. Nevertheless there has been some cross-support between them and they provide a significant point of departure in considering future developments.

4.1.2. Succeeding sections of this chapter describe some of these programmes or sub programmes in more detail, but the following listing gives an indication of the range of Commission scientific activities which are involved :

- Energy research - solar energy research programme, project E : biomass as an energy source, project D : photobiological mechanisms to split water to produce hydrogen
- Radiation Biology programme
- Medical Research Programme
- Environment & Raw Materials programmes have included potential of fermentation hydrolysis of organic wastes ; wood as a raw material.
- Cost programmes, exchange of information on eg. Sewage sludge treatment & disposal methods ; studies of single cell protein, early weaning of piglets, plant tissue culture, derivation of animal feedstuffs from ligno-cellulose.

- Agricultural research programmes, including 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.

- Science & Technology for Development ; including tropical agriculture, medicine, health and nutrition.

- Databanks such as EURONET-DIANE arising from Community programmes on information and documentation in science and technology are helping many areas of life science and related industrial products and environmental concerns to develop their information bases.

4.1.3. Many other areas are touched by biotechnology ; for example the Commission's industrial or economic responsibilities for harmonisation of standards and regulations require the consideration of products, processes and terminology in industries such as animal rearing, food processing and pharmaceuticals.

4.2. The Biomolecular Engineering Programme.

4.2.1. Objectives.

Of a different nature to the foregoing, having a longer term strategic intention, is the Biomolecular Engineering Programme, which was the outcome of several years of reports and consultations with industrial, academic and government interests.
The general objectives of the programme 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,

to be achieved through the removal of the bottlenecks which prevent application to industry of modern biochemical and genetic methods.

4.2.2. Phase I.

The programme is to have two distinct phases, the first consisting of both training and research actions and having a budget of 8 MioECU. The training will cover all areas involving enzymatic and genetic engineering, and the improvement of risk assessment methods so far as agricultural and industrial applications of biomolecular enginnering are concerned. The research, using shared cost contracts, concerns the application of modern biochemical and genetic methods to agriculture and to agro-food production and will include

- development of 2nd generation bio-reactors (multi-enzyme, multiphase, etc...) for agro-food industries
- improving production, via biomolecular engineering methods, of safer substances for animal husbandry and the agro-food industry (there is a link with the Agricultural Research programme : see section 4.3)
- Upgrading of plant products, particularly ligno-cellulose, by means of biomolecular engineering methods.(link with Raw materials sub programme on wood, see 4.5)
- Methods for identification, transfer, expression and transmission of new genetic information in cultivated plant species (Link with sub programme on wood, and with Energy and Agriculture research programmes)
- Improvement, by means of genetic engineering, of symbiotic relations between cultivated plant species and micro organisms in the soil
- Development of methods making possible the selective screening of cells and protoplasts, and their regeneration into fertile and differentiated plants
- Improvement of methods for assessing the risks which may result from the experimental, industrial or agricultural use of genetically manipulated micro organisms.

4.2.3. Phase 2.

The second phase will retain training and mission oriented research designed to allow the exploitation by agriculture and industry of the materials, methods and konw-how developed in the field of molecular biology. In view of the very high demand for funding which was registered during the first phase and of the need to consolidate the actions now in progress, only few modifications have been made, for the second phase, to the programme of the first phase. Research actions in genetic engineering will continue to be restricted to plant-breeding, animal husbandry, agro-food and the transformation of agricultural products They will include, however, the use of biomolecular engineering methods for the early detection of genetic changes in cultivated plants. Research actions in enzyme engineering will be extended to detoxification and to the complete range of industrial applications. Work on safety shall be focussed upon the development of methods for detecting contamination and for the assessment of possible risks associated with applications of biomolecular engineering in agriculture and industry.

Training will cover, as in the first phase, all areas involving enzymatic and genetic engineering.

4.3. Agricultural research.

The objectives of the Common Agricultural Policy have been supported by the related research programmes of which the second is nearing completion. This is a 5-year programme, 1979-83, 18,6 m.u.a., with the following objectives :

A. SOCIO-STRUCTURAL OBJECTIVES

1. Land use and rural development
2. Mediterranean agriculture
3. Wastes from agricultural industry and effluents from intensive animal-rearing.

B. REMOVAL OF OBSTACLES TO INTRA-COMMUNITY AGRICULTURAL MARKETS

4. Animal pathology.

C. PRODUCTIVE EFFICIENCY

5. Improvement of productivity of the Community beef herd
6. Biological and integrated pest control
7. Methods and means to be developed to improve the resistance of plants to disease and environmental stress
8. Agro-food (new outlets for surplus products, good quality)
9. Dutch elm disease (pilot coordination project on tree diseases).

D. ALTERNATIVE PRODUCTS (EXPLOITATION OF FORAGE CROPS)

10. Improved production of vegetable proteins.

Following the success of these projects, a third five-year programme (1984-88), with a proposed budget of 54 m.u.a., is now under discussion ; the outline programme shown in Table 8 has been approved by the Standing Committee on Agricultural Research.

Table 8 : PROPOSED AGRICULTURAL RESEARCH FRAMEWORK PROGRAMME 1984-1988

	I	II	III
POLICY THEMES	Utilization and Conservation of Agricultural Resources	Socio-Structural Aspects	Improvement of Plant and Animal Productivity
RESEARCH PRO-GRAMMES	1. Energy in Agriculture 2. Land and Water Management and Utilization	3. Regional Problems 4. Agro-Food	5. Cropping Practices 6. Animal husbandry
PRIORITY SUBJECTS	Economy 1.1. Integrated plant protection including all useful combinations of biological, genetic, agronomic and chemical methods for the control of diseases pests and weeds, aimed at systems with low energy input 1.2. Alternative sources of energy, including solar energy in protected crops and in other farm uses Production and Application 1.3. Biomass production including . Industrial uses of existing crops for energy purposes . Specialized crops including aquatic crops . Improved photosynthesis . Improved use of by-products of existing crops 1.4. Biological nitrogen fixation ------ 2.1. Land resource evaluation including crop mapping, and identification of areas of high suitability for production of specific crops in different areas 2.2. Prevention of soil erosion, soil degradation, orfanic matter content and maintenance of soil fertility 2.3. Water management and utilization, including drainage reclamations, water control,water pollution avoidance etc...	3.1. Mediterranean Agriculture * . Systems and methods of production - Sylvo-pastoral aspects of extensive Livestock production - Irrigation . Selected alternative products of regional interest, e.g. - Tobacco (incl.oriental tobacco) - Fast growing forest verieties in mountainous zones, etc.. 3.2. Other regions 3.3. Integrated rural development (e.g. Multidisciplinary resource studies) ----- 4.1. Food quality . Intensive versus extensive production (crops and animals) . Protected versus unprotected crops 4.2. Selected marketing aspects	5.1. More efficient agronomic practices (e.g. optimization of fertilizer use, bio-engineering and plant breeding practices) 5.2. Protein and oil seed crops 5.3. Other deficit crops ----- 6.1. Factors affecting herd profitability . Reproduction (including physiology and neurobiology) . Genetics . Nutrition 6.2. Animal pathology . Strategic research on emerging diseases . Immune mechanisms and disease protection . Disease occurence and cost-benefit analyses 6.3. Animal welfare . Social space requirements . Disturbed behaviour and stress

* In addition to subjects of exclusive Mediterranean interest, to be dealt with under this heading, research programmes 1,2,5 and 6 will include specific references to other subjects of Mediterranean interest which can be more effectively treated in a wider context

Source : Doc. CPRA 45/VI/1981 (Rev. 2)

4.4. Bioproductivity of biomass for energy (Energy Research Programme projects D & E).

4.4.1. Objectives.

The aim of the extension of project D is to contribute studies of how to improve bioproductivity in order to optimise net energy output per hectare, involving basic photobiology and physiology as related to productivity in species chosen for their biomass energy productivity.
There are three areas of work

- understanding factors which limit the potential of the photosynthetic system for energy production
- understanding the various forms of stress which prevent the expression of this potential in the field
- development of field oriented tests for easier recognition of productive plants based on their photosynthetic capacity under a variety of conditions.

4.4.2. Key areas of work.

Fundamental work needs to be carried out on systems chosen on the basis of their suitability for solving the particular problem under study. In general the choice is related to the form of the plant, absence of inhibitors, availability of mutants, reproducibility of growth, etc.. Key areas for future work include :

- Limitations to photosynthetic efficiency : product partitioning, photoinhibition, protective mechanisms and other wasteful processes
- genetic and hormonal control of photobiological reactions
- membrane composition and structural changes brought about by temperature, water and nutritional stress
- tissue culture, alternative methods of propagation and speeding up development and stabilisation of the genetic characteristics of potential biomass plants
- the basic components of nutrient cycling, including

- the effects of increased removal of organic matter and depletion of soil nutrients which could result from larger scale biomass plantations
- modelling biomass energy sustems and the influence of external factors upon net energy yields.

4.5. Raw Materials sub programme : Wood.

4.5.1. At its meeting of 17 May 82, the Council of Ministers agreed a new raw materials programme worth 54 MioECUS, including 12 for forestry studies.

The European Community depends on external sources to provide more than half of its needs in wood and wood products and the objectives of the new programme "Wood as a renewable raw material" are :

- to increase the physical and economic availability of wood and wood products,
- to reduce the cost of growing, harvesting and processing wood,
- to upgrade the quality and value of products,
- to promote a more complete utilisation of wood and wood residue.

4.5.2. These objectives have been translated into 6 broad research areas of which two are of particular interest in the field of Biotechnology :

1) Wood production.

(including selection and improvement of forest reproductive material, improvement of growth (silviculture), prevention of losses and forest inventory). Contracts under this heading may amount to 1 MioECUS.

6) Wood as a source of chemicals.

(including development processes to separate chemically the main components of materials containing ligno-cellulose substances, the utilisation of lignin, hemicelluloses and cellulose, and the recovery of by-products from fibre processing). The cost may again be of the order of 1 MioECUS.

4.6. Science and technology for development.

4.6.1. Objectives.

European Community policies in the field of Development have in the past concentrated primarily upon infrastructure and agriculture. However, there has in recent years been growing emphasis upon the scientific component in the economic and social development process. An R & D programme proposal has therefore been developed which seeks to complement existing Community policies on co-operation with developing countries and to reinforce the activities of Member States in their scientific and technical potential for research of likely benefit to the economic, social and health development problems of the Third World.

4.6.2. There are two subprogrammes. The first (A) relates to tropical agriculture, and includes areas where biotechnology and related disciplines have great potential, particularly in the light of recent developments in areas such as plant cell biology or in the fermentation techniques by which the protein content of carbohydrate foodstuffs can be enhanced. The sub-programme includes these activities:

A.1. Improvement of agricultural production.

Food crops (esp. rice, maize, sorghum)
industrial crops (esp. cotton, ground nuts, soya, coconut palm, oil palm)
protein products of animal origin.

A.2. General areas of research and utilisation of the environment.

Water resources and use

soil protection, stabilisation and regeneration

crop protection.

A.3. Post harvest techniques.

Product conservation

processing of products.

A.4. Training.

4.6.3. The second sub programme (B) concerns tropical medicine, health and nutrition.

B.1. Medicine and Health Care.

Transmissible diseases (involving parasitology, bacteriology, virology)

Mother and child care (esp. gastroenteritis)

Genetics (host factors affecting susceptibility, parasite and vector genetics, control of genetic disorders with high prevalence)

Environmental hygiene.

B.2. Nutrition (esp. overall protein, energy and iron deficiencies).

B.3. Training (two way mobility).

4.7. Health and Medical Research.

4.7.1. Two concerted action programmes have been agreed, and a recently proposed third one is under consideration *.

* see COM (81) 517 final

The first two dealt with the following issues

1st programme
(1.1.1978-31.12.1981)

1. Registration of congenital abnormalities
2. Cellular ageing
3. Extra-corporeal oxygenation

2nd programme
(1.6.1980-31.05.1984)

4. Detection of tendency to thrombosis
5. Hearing impairment
6. Perinatal monitoring
7. Quantitative electrocardiography.

4.7.2. The proposed third programme continues and integrates the actions of the first two programmes as appropriate, and develops new themes within three sub programmes :

. Health problems

Area 1 : Pre, peri and post-natal care (to include chromosome analysis)

Area 2 : Ageing, disabled and handicapped (including cellular and sub cellular studies)

Area 3 : Breakdown in adaptation

. Health Resources

. Personal Environment.

Summarising these diverse programmes from the point of view of biotechnology, one can make three points :

- the programmes generally have specific, practical objectives and can be classified as "biotechnology" only under a broad definition ;

- many of them nonetheless depend upon, or will be greatly assisted by, progress in the core areas of biotechnology and genetic and enzyme engineering ;
- the one programme which directly addresses these basic needs, the Biomolecular Engineering Programme, at 4 m.u.a. for its first two years is on a very modest scale in relation to the needs.

5. MEDIUM-TERM OPTIONS AT COMMUNITY LEVEL : THE NEED FOR STRATEGY

5.1. Community Strategy for European Biotechnology

The European Community can and should have a major influence upon the development of biotechnology in Europe. In the following section are summarized the aspects which indicate this need for coordination and a European policy role. If this "positive" option is not exercised, then it may reflect a judgement by at least the larger countries of the Community that they are big enough, are doing enough, and their major firms can collaborate as necessary with centres of expertise or strong firms elsewhere - particularly in the U.S. and Japan. In the public sector, policy-makers in each Member State, operating on similar evidence, under similar pressures and in similar positions, will make similar decisions. Therefore when the available opportunities are ranked in order of attractiveness, the same top choices will be selected, the same secondary topics will be neglected. With only slight exaggeration, one can envisage a scenario in which :

- everybody will attempt Nitrogen fixation
- everybody will (relatively) neglect culture collections
- everybody will pursue monoclonal antibodies and immunology
- nobody will look after cryopreservation and plant cells
- every farm and Ministry of Agriculture will pursue maximum short-term yield

- genetic diversity, disease resistance and soil science will be neglected
- industrial research laboratories will follow the well-beaten track to E.coli
- few will embark on fundamental studies of microbial physiology in lesser known organisms.

An integrated view, or even some modest co-ordination between existing national strategies, would produce different answers. But the confidence to abandon a potentially promising sector, or to spend on another sector greater effort than would be merited on purely national criteria, can only be justified if there is political confidence in a Community approach, and some de facto sharing of costs, risks, and benefits at European scale.

The influence of the Community will be exercised both through R & D policy, and through its other policies : for maximum effectiveness, they should be mutually reinforcing, and therefore require coordination by the Commission of the European Communities. At the same time, Community policies should be related to the actions being taken at national scale by member states, and at international scale through such bodies as the OECD or the United Nations and its agencies. Reference is therefore made as appropriate to these international activities.

5.2. National and Community Strategy : Coordination and Key Centres

All the national studies cited give independent confirmation of the strategic significance of biotechnology, a significance which will persist in spite of the current journalistic "over-selling". It is widely recognized that the quality of a nation's biotechnological capacities will be of importance for its long-term industrial competitive strength in several major sectors.

The external challenge to the Community, from its major trading partners, will be a strong one. In the area of public sector support, it is clear that the U.S. will outspend the European Community in total, particularly in all areas related to medical applications. Table 9 brings together the figures presented in the earlier chapters. The Japanese, through the Science and Technology Agency as well as through the Ministries (MITI, Agriculture and Health), although spending less than the EC in total, appear (on past form) to be likely to achieve more effective coordination of industrial strategy. The pharmaceutical industry is the subject of intense current developments, but is only one sector in which capability in the life sciences will be reflected.

Table 9 : A ROUGH SUMMARY COMPARISON OF PUBLIC SECTOR R & D EXPENDITURE RELATED TO BIOTECHNOLOGY

U.S.A. ($ M = m.u.a.)

National Institutes of Health	90	(out of $ 3 - 4 bn on health
National Science Foundation	60	and related ; cf 1,8 bn for
U.S. Dept of Agriculture, Office of Technology Assessment		EC - see Table 6)
Dept of Energy, etc...	?	
	200	

Japan

Life sciences total expenditure	195	(cf EC 385 : i.e. twice as great - see Table 6).
including biotechnology	22	
add. MITI special programmes	10	
	32 + industrial grants	

European Community

Biotechnology expenditures :

F.R. Germany : 22 (project) + 7 (institutional) =	29
France	29
U.K.	43
Italy	13
+ other EC countries	?
	? 130 + industrial grants

EC Biomolecular Engineering Programme : 4 p.a.

(Figures for current or recent years, with many potential pitfalls of comparability, definition, coverage, etc..).

For Europe to respond effectively to this challenge, there must be developed a "holistic" view of the nature of capability in biotechnology, overcoming the several dimensions of potential fragmentation :

- National efforts require co-ordination within the Community ;
- different disciplines have to work together ;
- "pure" and "applied" scientists and technologists have to collaborate ;
- academic knowledge has to be transferred to industrial application ;
- public and private sector efforts have to be complementary.

The need for coordinated efforts is illustrated by the behaviour of the major companies, where even the largest - several of them spending more on biotechnology R & D than national research budgets in the field - see the need for collaborative and consortial activity, to spread the risks and costs. This is all the more true for the longer term fundamental research financed by governments.

At national and Community level, the need is perceived for research and development work variously described as "strategic applied", "pre-commercial" and "long-lead-time". Normal commercial incentives will drive short-term innovation, but strategic strength rests on a relatively large number of fundamental disciplines or capabilities. These will not generally or necessarily arise if their development depends on short-term economic criteria. The key capabilities include genetics (molecular and classical), physiology, biochemistry, fermentation and culture technology (from laboratory industrial scale), and all aspects of process technology ; all of the disciplines being understood as including microbial, plant, animal and hybrid materials.

World-class capability in all of these fields is not a realistic objective for any one member state of the European Community ; it must be an objective for the Community as a whole. Europe must reinforce or develop a limited number of strong centres, in existing universities and research institutes.

Each such centre (or polycentric consortium) should aim to be of unsurpassed quality within its field, based on experienced staff and the best physical equipment and facilities. Its activities will typically include teaching, research, advisory consultancy, contract work, and possibly pilot plant and production activity. It will represent, not only within its country but throughout Europe and further afield, a natural point of reference for academic, industrial or other enquiries.

Complementary to the individual disciplines represented in the centres, and no less essential to their effectiveness, is the ability to form and manage inter-disciplinary teams : focussed on the determined pursuit of a clear and significant joint objective. The major successes of biotechnology have depended on this type of project management : penicillin production is a classic example. The definition of appropriate strategic priorities could be a matter for joint discussion involving member state policy-makers, industry and academic experts, and Community staff : several possible foci for such activity are offered in 5.5 and 5.6 below.

5.3. Influencing Company Strategies

The commanding heights of biotechnology are likely to be dominated by a limited number of multi-national companies ; technologically sophisticated, with strong current positions enabling them to invest on a large scale in areas of long-term future potential. These companies will have R & D centres in several countries, manufacturing (or service) locations in more, and marketing activities almost everywhere. They will have effective freedom to shift the centres of gravity of their R & D and other operations from country to country and continent to continent, in response *inter alia* to the conditions, the resources and needs, opportunities and constraints, in each location.

Biotechnology activities will be influenced by the following factors :

- Feedstock availability and cost ;
- human resources ;
- supporting services and facilities ;
- regulatory environment.

All of these can be influenced by public policy, at national and/or Community level.

5.4. Feedstocks

Locally available feedstocks are likely at present to be channelled through existing and traditional activities, institutions and structures, such as the agriculture and agro-food system. These are encouraged to defend themselves, by productivity improvements, rationalization, adding more value to the materials. They may either develop biotechnology themselves, or their ability to supply to biotechnology. Since the prices of agricultural commodities are controlled by the Common Agricultural Policy, this is one point of influence for Community policy.

5.5. Human Resources and Education

Human resources are developed primarily through national education systems, at least in their foundations. At more advanced level, public research policies can influence the availability of research posts in universities and public institutes. Finally, the experience in both productive industry and industrial research laboratories adds greatly to the value and potential of the individuals concerned. In a multi-disciplinary field such as biotechnology, the experience of working within multi-disciplinary project teams is also a vital aspect of education. In many national environments, including even the largest countries of the European Community, there will not be full opportunities for specialists to develop experience in all respects of biotechnology ; there is consequently a need for international exchange of individuals, particularly to the "key centres" referred to.

The economics of mounting advanced level study courses also demand their organization and promotion on a larger than national scale, again based on the "key centres".

5.6. Supporting Services and Facilities : Culture Collections

Amongst the supporting services crucial for biotechnology, the most important is the human resource, already mentioned. One might add also the availability of process plant and instrumentation, and the accompanying expertise. But a specifically biological resource is the genetic material itself - micro-organisms, plant and animal cells. This subject is not only important in itself, but in its diversity, complexity and "information intensity", illustrates some of the general characteristics of support services in an "information society".

The importance of culture collections of micro-organisms and of other biotic material (e.g. plant cell lines and germplasm, animal cell lines, viruses, plasmids, enzymes ...) is being increasingly perceived as an essential foundation for both academic and industrial research and exploitation. The accumulation of research results and understanding of these complex entities is generating vast quantities of potentially useful information, which demands the organized storage and retrieval facilities of computer databanks. The technologies of storage demand considerable expertise, and for many organisms are not yet fully understood, so that industrialists and researchers still frequently lose their stored cultures (through death or denaturation). The relevant know-how is not prestigious, and even in those countries well endowed with collections, continuing budgetary and technical support is in many cases problematic and uncertain.

Perceiving this problem, the British and Germans are seeking to develop a collaborative policy for their collections. The Pelissolo report has emphasized the French needs, and other countries of the Community also share the perception of this need. Danish scientists have participated in work organized by the Nordic Council on a register of culture collections. At world level, UNESCO finances a "World Data Center" in Brisbane, Australia, which has just published the second edition (1st was in 1972) of a World Directory of Collections of Cultures of Micro-organisms (with some financial support from the European Commission).

Within Europe, policy for culture collections is being helped by the formation (first meeting May 1982) of the European Culture Collection Curators' Organization (ECCCO), and the European Federation of Cell and Virus Collections (EFCVC). Specialists in plant cells and plant tissue culture techniques have also been approached by the initiators of EFCVC (whose primary interests are human and animal cell lines and viruses). Plant tissue conservation interests are also supported by the International Board for Plant Genetic Resources of the UN Food and Agriculture Organization.

These activities can be helped by coordination and support as necessary, at Community level, particularly through the Task Force for Biotechnology Information, which reports via the Biomedical Working Group to the Commission on Information and Documentation in Science and Technology. Within the draft Work Programme of this group, mention should particularly be made of the coordination of European development work on nucleic acid (DNA or RNA) sequence data banks : a perfect example of a topic of fundamental importance for future work in the life sciences. The European work at several centres (EMBL Heidelberg, Lyon, Bari, Cambridge) is significant, but there must be effective coordination to develop capabilities which can co-operate on a basis at least of parity with the U.S. work, now being strongly pursued by the NIH (reference was made in 2.2.1 to the $ 3.2 m. contract, June 1982).

5.7. Regulatory Environment and patents

Industry operates simultaneously in many regulatory environments, which the Community is seeking to harmonize at least within the member states : product standards, pharmaceutical testing, feedstuff additives, and food additives are examples of areas where regulation impinges upon industrial biotechnology.

In the research context, the long debate on the conjectural hazards of re-combinant DNA work now appears to be stabilizing, with the relaxation of guidelines in the U.S., the U.K. and elsewhere following recognition that no new special risks have appeared, beyond those normally encountered where the organisms used are known pathogens. The Commission draft directive on the subject has been left at advisory status.

In the regulation of the pharmaceutical industry, the best interests of the public require an intelligent balance to be struck between rigorous pre-release testing, which increases costs and delays, and post-release monitoring. While seeking harmonization within the Community, the Commission has to seek also a wider acceptance externally of European standards. Reference has been made (2.2) to the coming liberalization of Japanese standards. Other countries should also be encouraged to see the European standards as no less acceptable than the sometimes very conservative standards of the U.S. Food and Drug Administration.

Forthcoming studies by the OECD are likely to focus upon a number of public policy implications of the development of biotechnology : particularly

- patent legislation (an enquiry has been launched) ;
- regulations ;
- university - industry links.

The OECD studies will undoubtedly produce useful comparative surveys. In parallel with these, the Community has a role to play in coordinating the European response on questions such as patent legislation, in ensuring that any international conventions established strike an equitable balance between the interests involved. The difficulties are illustrated by a fundamental point of contention which has arisen between biologists/biotechnologists and traditional patent lawyers. The former may screen many thousands of different micro-organisms to select and propagate a useful mutant ; if the lawyers still call this "discovery", it may not be patentable, since the ancient principle is that only "invention" is patentable. Given such difficulties, and the problems of characterizing an organism in ways which will define whether one is "identical" to another, commercial firms are likely to protect their intellectual property by secrecy rather than patenting. Such a tendency inhibits the diffusion of knowledge which is one of the fundamental objectives of the patent systems.

Also inhibiting innovation is the use of patents as blocking mechanisms : defending intellectual property, but perhaps preventing the exploitation of the process in certain countries. To overcome such abuse, conditional on "permanent diligence" in the exploitation of the patent.

A more recent role of the patent system has been to provide statistical information on patent registrations ; subject to various caveats a useful indicator of the innovative strength of the various companies or countries in each sector.

For these several reasons, patents are a subject meriting significant attention at Community level in the context of strategy for European biotechnology.

5.8. Small Companies

Reference has been made (Section 3.3) to the SEDES study of the opportunities for small and medium-sized enterprises in biotechnology. Several studies of biotechnology* have emphasized its dual nature : "big" biotechnology, characterized by concentration, capital intensity, high technology and economy of scale, as typified by the ICI single-cell protein plant ; and "small" biotechnology, based on local resources or wastes, as typified by biogas digesters at farm or Third World village level.

Most studies emphasize that there is potential,,indeed need, for both to exist. The presence of strong centres of activity of large companies will create opportunities for smaller companies as suppliers; the existence of a network of efficient suppliers creates a more favourable environment for the large companies. Community policy for encouragement of innovation and venture capital activity can help such developments.

5.9. The Policy Interfaces

In developing policy for biotechnology, the Community has to ensure that the objectives of the common R & D policy are compatible with and supportive of other community policies. The development of biotechnology in Europe has interactions with each of the areas summarized below.

Economic growth - stimulus of new growth sectors of industry.

Industry - sectoral policies : agrofood, feedstuffs, chemicals, forestry & wood products, leather, textiles, regulatory & patent policies

Education - technical and scientific.

Health - fundamental support for pharmaceutical development, information exchange to support societal learning.

Agriculture - genetics of plants and animals, fertilizers, growth promoters, crop protection, feedstuffs, post-harvest protection.

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* For example, "Impacts prévisibles et stratégies de développement de la biotechnologie dans les filières agro-alimentaires européennes : cas des filières protéiques", study by Promotech, in the FAST programme of the CEC.

Development - science and technology for development, impact of biotechnology on Third World and commodity trade patterns.

Environment - waste treatment, control of toxic effluents, emission and quality standards.

Scientific Information - databanks, culture collections.

Fisheries - processing, alternative protein sources.

Energy - biomass.

This "horizontal" character of biotechnology typically creates a need for corresponding structures to coordinate the interactions with existing "vertical" government bodies and institutions : a number of the Member States of the EC have created inter-departmental, inter-sectoral, inter-disciplinary "Biotechnology Committees" or "Missions" to respond to this need. Similar measures are being taken within the services of the Commission of the EC, to ensure the necessary co-ordination of different policies - including the research policy, discussed in the final chapter.

6. RECOMMENDATIONS

6.1. Major Goals of Community Science and Technology Policy

The five previous chapters have attempted to illustrate the challenge which the development of biotechnology and its related disciplines poses to Europe, and to compare the responses of the individual Member States and the Community with that of Europe's competitors. Some idea has also been given of the options open to Europe in the medium term. It might also be useful, before setting out some specific recommendations in the field of biotechnology, to recap the overall objectives which influence Community Science and Technology policy. These are summed up in the seven major goals defined in the Framework Programme :

- Promoting agricultural competitiveness
- Promoting industrial competitiveness
- Improving the management of raw materials
- Improving the management of energy resources
- Strengthening aid to developing countries
- Improving living and working conditions (Health, safety, the environment)
- Stimulating the efficacy of the Community's R & D potential.

Biotechnology is relevant to every one of these goals, as is demonstrated by both the preceding discussion and the recommendations below.

6.2. Contextual Recommendations (non R&D)

The recommendations which have arisen in the context of strategy for European biotechnology repeatedly lie outside the specific boundaries of R & D policy. The following recommendations have therefore to be addressed to the other services of the Commission, to Member States, and other authorities as appropriate. The recommendations have as their common objective the creation of a context within which European biotechnology can be successfully developed and exploited :

a. Raw material resources : should be available to the fermentation or other biotechnology industries, at prices (excluding transport) not greater than those of the open world market. This measure should form part of a financial strategy in relation to improved land use.

b. Human resources : Member States are urged to consider the quality and scale of their educational provision in the fundamental disciplines of the life sciences in schools and universities ; and the specific provision for training in biotechnology at technician and at post-graduate level. Member States and the Commission are urged to consider also specific provision to facilitate scientific mobility and international exchange in biotechnology, between universities, and between universities and industry (e.g. part-time industrial professors).

c. Support services : Member States and the Commission are urged to encourage the development of the support services and facilities shown to be desirable for the encouragement of biotechnological industrial development. These could include, in addition to the educational services mentioned, the following :

- research and consultancy services ;
- support for vocational training in biotechnology - e.g. for the production of audio-visual materials, including general public education.
- bibliographic and information services ;
- culture collections of cells and micro-organisms ;
- small and medium-sized firms, for supply of specialist materials and services ;
- patent advisory service.

d. Regulations : the creation of clear and consistent regulatory frameworks, applicable throughout the Community, on all aspects of laboratory development, factory manufacture, testing, and marketing of products and services ; with particular reference to the novel products and services likely to arise in the fuel, food, chemical and pharmaceutical industries.

In view of the strategic significance of biotechnology, in both the products it offers and the new industrial technologies it develops, the regulatory stance should (while maintaining normal standards of public security) be neutral or favourable ; and avoid being pressured by arguments of doubtful scientific validity towards de facto defence of existing established interests against competitive innovation.

6.3. Scientific and Technological Objectives for Community R&D in biotechnology and related areas.

The preceding chapters have emphasised the significance and pervasiveness of the applied life sciences, and the energetic responses by companies and national authorities to the opportunities presented by the recent and continuing advances. All national authorities in developed industrial countries acknowledge the need for public research programmes, particularly in fundamental science, and in the areas variously described as "long-lead-time", "strategic applied" or "pre-commercial" research.

Table 9 suggests the intuitively reasonable picture that Community total spending on biotechnology R&D appears to be at a rate somewhat greater than Japan's, less than the U.S.A.'s ; in both cases, the effort is likely to be better co-ordinated than within the still fragmented environment of the European Community.

In presenting below a collection of recommendations for Community R&D in biotechnology, these have been organised into three groups, in all of which emphasis has to be placed upon enhancing the coherence of the European efforts :

1. as a stimulus and support to national programmes

2. in support of other research and action programmes : the "interaction" areas

3. for pioneering in biotechnology.

6. 3. 1. Community R&D as a stimulus and support to national programmes and centres

The case for joint Community R&D action is a familiar one - the avoidance of duplication, the pooling of major expenses or of scarce resources, etc., but points of particular importance in the context of biotechnology are the following :

a) the enhancement of the value of national programmes through the opportunity to compete for and to participate in Community programmes (such as the Biomolecular Engineering Programme). Such opportunities will stimulate standards and reinforce the strong centres around which national policies are generally based, enabling them to become in some senses "European" resource centres.

b) the enhancement of specialised training facilities by providing opportunities and support for mobility and training; these form part of the Biomolecular Engineering Programme, and are a feature of the "stimulation" activity.

These stimuli to foundation capabilities in the Member States could also be seen as part of the "contextual" effort, whose "non R&D" aspects were introduced above. R&D actions to enhance the context for European biotechnology should include actions :

a) in support of culture collections - see for example references below to cryopreservation of plant cells and tissues,

b) in support of the nucleic acid sequence databank at the European Molecular Biology Laboratory,

c) research into taxonomic aspects and information requirements of information systems associated with collections of biotic material (culture collections, cell and tissue banks, seed banks, ...)

6. 3. 2. Community R&D through, or in support of, other research and action programmes : the "interaction" areas

The cross-cutting nature of biotechnology is illustrated by considering the following current or proposed research or action programmes, to which the Biomolecular Engineering or other specifically "biotechnology" programmes can contribute significantly ; we term these the interaction areas. Details have been given in Chapter 4 :

- agricultural research
- raw materials - starch, sugar, wood etc.., fermentation hydrolysis of organic wastes
- biomass energy
- environment programmes
- medical research
- radiation biology
- science and technology for development (tropical agriculture, health and nutrition)
- several of the COST programmes : particularly those on single-cell protein; plant tissue culture; feedstuffs from ligno-cellulosic wastes; and sewage sludge treatment (now incorporated in the environment programme).

Of particular importance is the interaction with agriculture, the sector in which the Community policy role has for long been of major significance. Community R&D can play a positive role in developing cost-effective ways of exploiting agricultural resources. While this can include research into new uses for products currently in surplus, the full exploitation of the potential of the new biotechnology implies :

- efforts to reduce production, storage and distribution costs, and thus to increase the competitiveness of European agriculture.

- upgrading the quality of agricultural products

- rather than increasing production of products in surplus, extending the potential for economic production of materials currently in deficit.

In short, expanding the range of economically viable and technically feasible uses for land. This interacts strongly with the Agricultural Research Programme (see section 4. 3, Table 8); but requires also industrial R&D (e.g. in food processing or agricultural machinery); and will benefit from the opportunities created by progress in the fundamental sciences (see following section, 6. 3. 3.).

What is needed is an integrated approach to :

plant genetics, rapid replication techniques, plant nutrient uptake systems, whole crop harvesting and integrated land management systems.

The relevant research activities range from the plant genetics of the Biomolecular Engineering Programme to the integrated land use studies of the Agricultural Research Programme.

Research planning has to integrate, or at least coordinate, the targets for crop breeding, machinery development and other on-farm downstream processing techniques (see below). Such a "total systems approach" will lead to widely varying solutions in the different land and climate conditions of different regions of the Community, but will provide a basis of understanding in depth and organised knowledge, which will in all those regions provide greater adaptive capability, both tactical and strategic.

6. 3. 3. Community R&D for pioneering in biotechnology

The Community R&D policy can provide support for national programmes, can improve the context for European biotechnology, and can support related policy objectives such as the "interaction" areas described above. Reference has been made in particular to what may be termed a "vertical" role, support for the specific sector of agriculture : the general objective being the creation of a less costly Common Agricultural Policy, without reducing farm incomes.

There are other sectors in which such vertical, sectoral support is equally appropriate. For example, the pharmaceutical industry,

a) because of the particular relevance of biotechnology;

b) because of the prospect of strategic competitive challenge (see section 2.3. above);

c) because of the high and growing costs of illness, its prevention and cure; in both the developed countries and the Third World. There are widespread needs - e.g. for an influenza vaccine - where the current structure of incentives is not necessarily leading to the lowest total costs, and where a Community initiative could be appropriate.

Pioneering in biotechnology has to embrace both the specific requirements of sectoral policies (agriculture and food, pharmaceuticals, chemicals, environment, ...) and the more general, horizontal (i.e.non-sector-specific) needs for strategic applied research. In this context, the current modest Biomolecular Engineering Programme should be seen as only a beginning. The number and quality of proposals submitted in 1982 have demonstrated the interest and capability of the European research centres, and the resources and terms of reference of B.E.P. are far from covering the total needs. The topics below - not an exhaustive list - illustrate areas of strategic need, and are loosely grouped into three categories :

1. removal of significant current obstacles to biotechnological development;

2. methodological advances in fundamental techniques;

3. research in support of long-term strategic goals.

1. Removal of significant current obstacles to biotechnological development.

Microbial physiology (recommended by FAST and by the OECD study).
The maintenance of the performance and stability of microorganisms (wild or cultivated, manipulated or not) in fermentation conditions, particularly in long-term continuous culture, is a significant problem in industrial biotechnology. Unpredictable problems, unforeseeable from bench-scale tests, reflect basic lack of understanding of some aspects of microbial metabolism and physiology.

But this is only the negative aspect of the subject - the other side of the coin is the enormous, and as yet largely unexplored, potential for optimising the behaviour and performance of microorganisms, through manipulation of the nutrient and environmental conditions, with respect to any chosen objective. For example, pursuing lipids as a goal, Ratledge has persuaded organisms to reach 85% lipids (dry weight basis); ICI pursuing polyhydroxybutyrates have obtained 80 % (dwb) of this, in a 2-stage continuous process. These are illustrative examples, but a great deal of scientific work remains to be done, to underpin the general goal of using fermentation to add value to simple or readily available materials.

Such a project could offer widespread benefit and stimulus to European industrial biotechnology : a preliminary reconnaissance study should be commissioned.

Downstream processing. A wide range of technologies may be relevant to the separation, purification and other processes which follow the fermentation step; and the costs of these downstream processes are a critical obstacle to the extension of biotechnology from high value low volume products to larger scale possibilities (see reports prepared by UMIST for FAST). Each industrialist works out an ad hoc, inadequate solution for his own problem; fundamental work on filtration, flocculation, separation etc.. is neglected.

Cryopreservation of plant cells and tissues. The storage of plant materials has been relatively neglected as compared with that of mammalian cells (looked after by medical research interests) and microorganisms (bacteria, algae, yeasts, fungi - simpler to store, and supported by industrial interest). Plant cell and tissue culture is of major long-term potential for propagation and for the production of complex natural chemicals, and the long-term cold storage of the materials is not well understood. The technology would also be of major importance as a support to genetic conservation programmes in Europe and the developing world.

As the "Economist" expressed it (9th October 1982) :

"Chemists studying cell membranes believe that, with a modest push in the right direction they could lick most of the outstanding problems associated with preserving living organisms. The results would provide an enormous benefit to industry.
Some, however, fear that it would also lead to (possibly unpatentable) laboratory techniques which would then benefit their competitors. Few biotechnology firms are therefore enthusiastic about splashing out on much research. This is precisely the sort of work that needs to attract industry wide (or even international) support".(our emphasis).

2. Methodological advances in fundamental techniques

Of importance are developments in sensitive techniques, increasingly "information-intensive" : embracing processes for analysis, detection, separation, various spectrometries, and systems of molecular representation.

Molecular Graphics

The use of computer modelling and visual display of molecules of biological interest is rapidly becoming one of the most important tools for both pure research and the development of pharmaceutical products ; it represents a move towards "computer-aided design" in biology. Many other applications will develop from it, enlarging our understanding of mechanisms and our ability to predict - e.g. the action of new drugs or chemicals on DNA. Current leadership in hardware and software development is with the U.S., through work at NIH (Maryland), and elsewhere (Stanford, San Francisco, Washington). An immediate "reconnaissance" study should lead to an assessment of the need for Community action.

2-dimensional gel electrophoresis

This technique provides a simple graphical analysis of the thousands of proteins in a small sample of cells or body fluids (blood, urine, spinal,..) When further developed, a richly informative and non-intrusive diagnostic tool may result. Again, U.S. effort is leading ; but European centres of activity exist (Aarhus, Pasteur, ...).

Associated work should be undertaken on computerised data-capture from gel-reading. Reconnaissance study should lead to an assessment of the need for Community action.

Laser flow cytometry Another field in which the interface of modern physics and information technology (high frequency lasers, various spectrometries, high speed computers) can interface with biological progress (e.g. in mammalian cell culture and selective staining) to produce bulk quantities of sorted cells, chromosomes and DNA fragments ; for medical and genetic research, and an unpredictable range of further potential applications.

In vitro culture and test techniques The cost,time and animal sacrifice involved in meeting current regulatory requirements for the development of pharmaceutical, chemical and cosmetic products may be significantly reduced by further progress in in vitro cell and tissue culture techniques. Such progress could be of major significance, not restricted to the industries mentioned.

3. Research in support of long-term strategic goals

Fundamental research on chemo-autotrophs and methanotrophs

In the longer term, the chemical industry will have to switch its raw material basis from the convenient hydrocarbon chains of crude oil, and will have to develop the chemistry of small molecules, e.g. from coal (via synthesis gas, giving hydrogen and carbon oxides) or from methane and methanol of renewable biological origin.
The chemo-autotrophs and methanotrophs are micro-organisms capable of using these basic materials to synthesise complex and potentially useful molecules, e.g. storage polymers such as polyhydroxybutyrate (a biological plastic). Fundamental research on these is necessary to underpin the long-term future of the European chemical industry, and to shorten the reaction times when the need for change becomes urgent.

Biomolecular pathology The FAST programme has recommended, in the light of trends in biomedicine and advances in biotechnology, that the proposed programme in biomolecular pathology should be revised, updated and re-considered (see Commission Publication EUR 6348, "Cellular and molecular biology of the pathological state : a proposal for a Community programme in biopathology", by C. de Duve, 1979).
Such a programme would be of particular value in reinforcing the much-needed bridges between molecular and cellular biology, on the one hand, and clinical medical research on the other.

6. 4. In Conclusion

It has been emphasised that the above list is not exhaustive. It cannot be : for one of the most striking characteristics of the life sciences in current times is their dramatic rate of progress. Significant scientific breakthroughs have been occurring almost monthly during the preparation of this report. Long-term R&D policy must therefore be robust, dynamic and flexible.

It must therefore be the subject of extended debate, at both expert and popular levels, in a process of mutual and continuing education. If the present report contributes to this process of debate and learning, it will have served its purpose.