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BIOTECHNOLOGY IN THE COMMUNITY

(Communication from the Commission to the Council)

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1. THE SCOPE AND SIGNIFICANCE OF BIOTECHNOLOGY

1.1. THE SCOPE OF BIOTECHNOLOGY

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

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

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

These breakthroughs are numerous and include the following :

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

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

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

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

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

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

1.2. SIGNIFICANCE OF THE NEW BIOTECHNOLOGY

1.2.1. The applications in sight

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

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

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

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

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

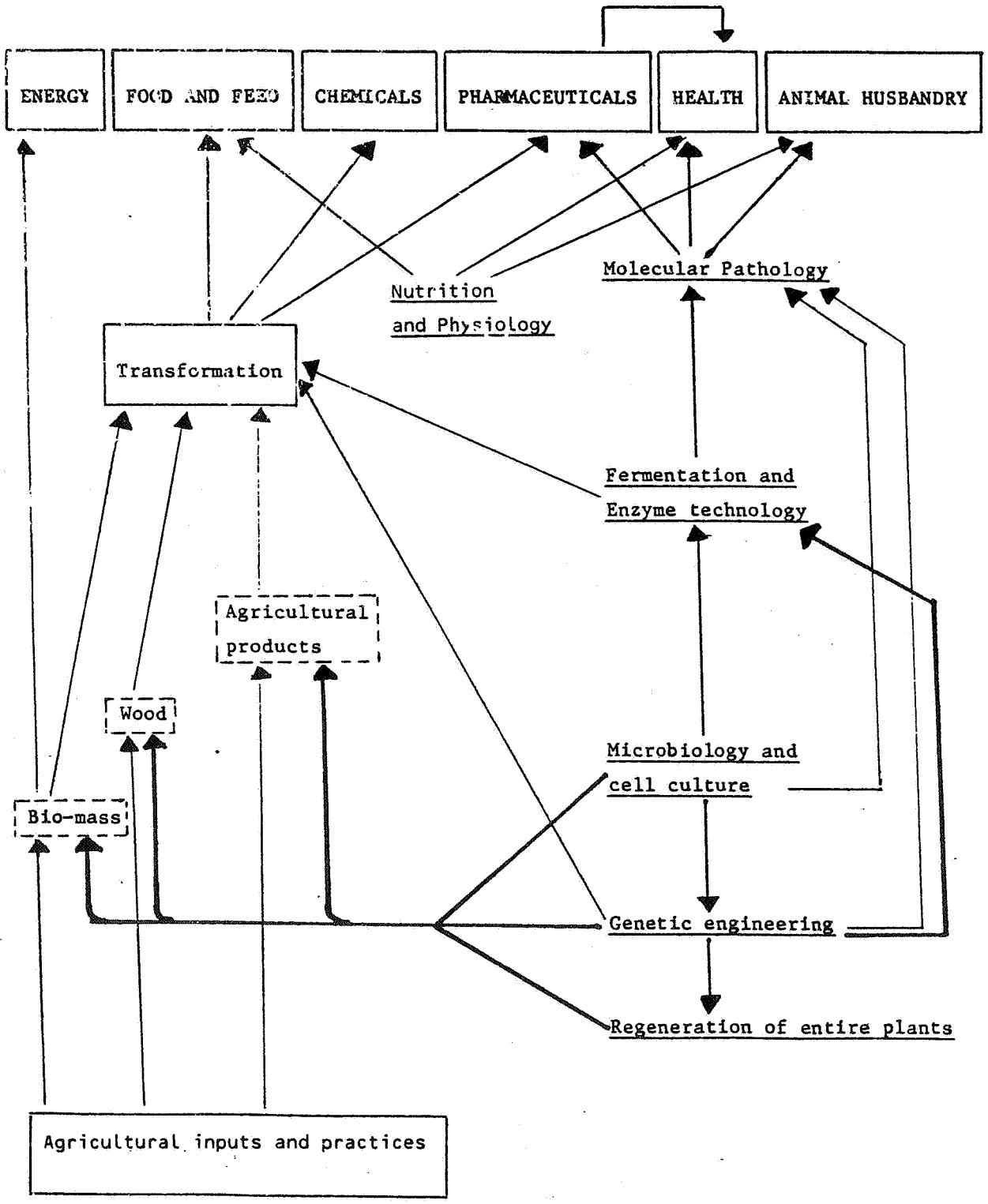

Figure 1 : Biotechnology : a multidisciplinary approach to the domestication of biological organisms. Research in molecular pathology, fermentation and enzyme technology, microbiology and cell culture, genetic engineering and plant cell differentiation contributes to the development of new approaches,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

1.2.2. Market potential

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

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

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

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

1.2.3. Company responses

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

Some examples of biotechnology related R&D expenditures and investments

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

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

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

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

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

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

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

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

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

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

1.2.4. Strategic significance

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

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

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

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

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

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

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

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

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

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2.1. BIOTECHNOLOGY IN THE COMMUNITY

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

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

2.1.2. The slow emergence of modern biotechnology in European countries

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

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

2.1.3. A substantial but incomplete effort in the Member States

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

2.2. EUROPEAN EFFORTS : IMPORTANT BUT FRAGMENTED

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

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

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

On Western Europe's biotechnology :

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

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

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

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

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