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BIOTECHNOLGY - A Challenge for Europe

Agriculture and food processing, forestry, health care, pharmaceuticals and major sectors of the chemical industry are among the areas of activity which may be radically altered by the recent breakthroughs in biological science, and their technological applications. Biotechnology is of fundamental importance to every society, and to many businesses. In the United States, over 200 new companies have been created, and several billion dollars invested in biotechnology, over the past 10 years; giant multinationals are reorienting their strategies towards the applied life sciences, and spending massively on research. In Japan, the exependiture is more modest, but the coordinating role of MITI's "Bio-industry Office" brings together all the major groups in a concerted assault on the commanding heights of this, the other "microtechnology". The dynamo of change is the breathtaking pace of scientific progress, and Europe is strong in all the key areas - molecular and cellular biology, microbiology, process engineering and fermentation science. But will the Old World, with its fragmented markets and complex political machinery, manage to hold its place in the race to commercialization?

The European Community cannot be passive, faced with the massive challenge of the new opportunities, and the sharp competitive threat from the other industrialised countries. The means exist within the Community - the human skills, the financial resources, the potential scale of the home market. These need mobilisation by a concerted effort, involving decision-makers both in private industry and the public sector; in small and large firms; at national Ministries, and in the Community institutions.

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The studies and the experience are available, on which to build a Community effort. The Commission has argued since the mid-70s for a collaborative R and D programme in the key areas of genetic engineering and enzymology. The futures group FAST (Forecasting and Assessment in Science and Technology) argued for a comprehensive Community strategy for biotechnology - of what use the advanced research, if firms are being driven out of the Community because of the price of agricultural raw materials? Meanwhile, the development of biotechnology in the countries of Europe proceeds slowly and sporadically; constrained by history to gradual innovation and institutional change, condemned by future competition if it fails to move quickly enough.

Biotechnology is a "knowledge-based business", and therefore R and D capability is central. That capability has to achieve "critical mass", by developing centres in Europe with the equipment, the people (above all the broad interdisciplinary teams), the intellectual stimulus and density in "brains per square metre". The best young researchers in each area must be able to find and move to centres of world class within the Community. By all means, with transatlantic collaboration and exchange - but a two-way shuttle, not a one-way brain-drain.

To stimulate the development of these advanced technologies, at a pre-competitive level under-pinning applications capability, the Community first launched a programme oriented towards the transfer of the scientific breakthroughs into European agriculture:

a Multi-annual (1982-86), 15 million ECU, cost-sharing Research and Training Programme

This programme, started in April 1982, now includes 104 research contracts, covering periods between 24 and 40 months, and involving Commission co-finance averaging 40 000 ECU per year per laboratory. The six areas, all oriented to agriculture and the food industry, comprise:

- development of advanced bioreactors for agriculture and the food industry;
- improved production of materials for stock breeding and for agriculture and the food industry through application of biomolecular engineering techniques;
- improvement of plant products;
- development of methods for the identification and transfer of new genetic information in plants;
- improvement of the symbiotic relations between cultivated plants and soil micro-organisms;
- development of methods for cell selection and regeneration in other plants.

Wider in its scope, the training programme covers all aspects of biomolecular engineering, including methods of risk assessment in biotechnology.

The need for a wider concept of strategy is reflected in the Commission's new proposals for a five-year, Biotechnology Action Programme (1985-89), of which Research forms only the first of six points:

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1. Research and Training - prolonging the activities of the outstandingly successful first R and D programme, and enlarging its scope to a broader range of topics in basic biotechnology; ranging from such frontiers as "protein engineering", to work on the development of better health diagnostic tools, and better methods of toxicological testing for new drugs. A "Contextual Measures" sub-programme aims to strengthen the research infrastructure for biotechnology, in data banks, information services, and banks of genetic materials (cells, microorganisms, etc.)

2. Concertation Action - for monitoring, coordination, and the essential communication functions, between Commission services, between biotechnology policy makers at Community and national levels, between the various scientific disciplines and economic sectors, through informal networks spanning the internal national frontiers of the Community.

3. Access to Raw Materials - sugar, starch or some such organic and digestible energy source is fundamental to all the fermentation industries of biotechnology; but it must be available at a competitive price, if Europe's biotechnology firms are to thrive. Proposals for the necessary changes of agricultural regimes have been put to Council. The development, through biotechnology, of high-added-value and non-food uses for agricultural materials is of strategic importance for the future of Europe's agriculture.

4. Regulatory Regimes - the long-standing efforts towards the creation of a true Common Market acquire a new urgency from the needs of biotechnology, which include the need for a clear, responsible and uniform regulatory environment. In pharmaceutical products, foodstuffs, feedstuffs, chemicals and other areas, the need is the same: to derive the economies of scale and consequent benefits of a market of 300 million people.

5. Protection of Intellectual Property - the law of patents, and the conventions for the protection of plant varieties, find some of their basic concepts brought into question by the radical innovations of biotechnology. Thus the existing proliferation of different national systems, both within the Community and worldwide, is further complicated by technical uncertainties at the interface between science and jurisprudence. Industry - particularly within Europe - chafes at its impediments, and at the more advantageous conditions in the USA and Japan; while jurists at national, European and OECD level wrestle with the slow processes of legislative innovation and the modification of international conventions. The Commission's working group on patenting in biotechnology is battling to assert in this complex domain the urgent and growing need for a Community approach.

6. Demonstration Projects - and other forms of closer collaboration with industry, are seen as essential to the Community's long-term strategy.

Action and proposals on this plan have been intensifying through 1984, the new five-year Research Programme being timed to start in early 1985 to run at roughly 15 million ECU per year to 1989.

The Commission's plan attempts to address the strategic challenge, but the resources are modest, the constraints on implementation, many and complex.

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What are the competitors doing?

USA

The USA are seen by themselves, and many others, as leaders in biotechnology. Since 1974, the proliferation of venture capital firms and the heavy investment in facilities and research contracts, have created a thriving and fast-growing industry. Early leaders such as Genentech, Cetus, and Hybritech are now capitalised at a value of several hundred million dollars; and in spite of the ups and downs of market values, shareholder expectations and scientific success or failure, only a handful of the hundreds of new firms have so far failed.

The science is in many cases capitalising on the long-term heavy spending by the US federal institutes - the National Institutes of Health, the National Science Foundation, and the great departments of state (Defence, Agriculture, Energy). Public sector funding for biotechnology has been estimated at around $550 million per annum (1982-83). New products - for health care, agricultural productivity, and other applications are currently under test, some of the first products of genetic engineering already on the market. New forms of agreement between academic centres and industry are being developed, as the major chemical and pharmaceutical groups buy access to the key strategic resource - knowledge.

Japan

Althoughthe country's long history of fermented foods and drinks is usually cited as the major initial strength of the Japanese in biotechnology, a factor of no less strategic significance is the country's ability to put together coherent, long-term sectoral strategies, pursued with the necessary persistence over many years. The techniques and applications of biotechnology are now the subject of such a strategy, many firms seeking to establish their basic capabilities in the new pharmaceuticals by adopting as a target the production of one of the interferons (a class of natural molecules of significance in the body's defence system against virus disease).

In 1980 on the initiative of the MITI (Ministry of International Trade and Industry) national programmes were launched: the Biomass Programme covering a period of seven years, in which 22 firms are cooperating in five sectors (manufacture of ethanol from cellulose; manufacture of ethanol from starch by using stable enzymes; gasification of waste to produce wood-cellulose materials; the breeding of plants for the manufacture of biofuels; the cultivation of algae for fuel manufacture), and the Biotechnology Programme covering a period of 10 years, in which 14 firms in the pharmaceutical, chemical and food industries are cooperating in three sectors (bioreactors; cell culture; and recombinant DNA).

It is in the last of these that the Japanese are conscious of lagging behind Europe and the USA, and are therefore particularly concerned to close the gap.

Both for scientific needs and to exploit market opportunities, active collaboration is sought by Japanese firms with leading companies elsewhere.

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The countries of the Community have each developed initiatives and re ponses to the problems and challenges of biotechnology.

Germany was amongst the first to give official recognition to the imp rtance of the field, when in 1974 the Ministry for Research and Technology (MFT) took up the suggestions of a DECHEMA report (the German Chemical Equi ment Manufacturers' Association). This association has remained an active pro- moter of biotechnology, both in Germany and at European level: being founder association and secretariat of the European Federation of Bic ech- nology (founded in 1978, and now comprising 49 scientific societ es, from 18 European countries). The German research effort is focussed n major centres at Braunschweig and Jülich, as well as at many other pu lic or private institutions, such as the Technical University of Berlin.

Hoechst, the world leader in pharmaceutical (particularly antibiotic) production, has also pioneered production of single-cell protein for h man consumption (with BMFT co-finance). Boehringer Mannheim is a leader the new biochemicals - restriction enzymes and oligonucleotides - used ir genetic engineering. Boehringer Ingelheim produces specialty chemic s by fermentation (citric acid). Bayer, number two in pharmaceuticals wor d- wide, applies enzymology to the production of semi-synthetic penicill ns. Schering uses microbial transformations in producing steroid hormone: Degussa produces amino acids (for animal nutrition) using immobilise biocatalysts. There are some twenty other significantly active comp ies, although these are usually established firms rather than venture-cap al activities on the US model.

Of the European Community countries, the United Kingdom has the stro est research base in biotechnology, with world class centres in many of e key disciplines. The institutes of the Medical Research Council (e. molecular biology, Cambridge), and of the Agricultural and Food Rese ch Council (e.g. the John Innes Institute, Norwich) complement strong university departments; and another public institute of special impo ance to biotechnology is the Centre for Applied Microbiology and Research it Porton Down, strong in fermentation science, and home of a recently founded centre for animal cell lines.

Industrial biotechnology in the UK is represented by leading chemica firms, as in ICI's 'Pruteen' plant for single-cell protein combining major innovation in engineering (the air-lift continuous fermenter) ith a major innovation in nutrition. In fermentation for pharmaceuticals Glaxo and Beechams are well known, and G. D. Searle and Wellcome are also ted for their capability in genetic engineering. In agro-food, Unilever success in cloning cells of the oil-palm is a breakthrough in applie genetics of major practical benefit; Ranks Hovis McDougall's mycopro ein is another promising food innovation.

The UK also has many smaller, venture-capital companies, with specia skills or application areas, or providing ancillary services and sup ies to the larger firms. Celltech, launched by government co-finance wi industry, is strong in animal cell culture and in the production of no- clonal antibodies (for diagnostic or analytical applications), as is o be expected in view of its original links with the institutes of the Me cal Research Council; a similar link with the Agricultural institutes pr ides access to the knowledge base for Agricultural Genetics Co. Ltd.

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France, the country of Louis Pasteur, seemed to be falling behind in biotechnology until a strongly renewed government interest was signalled in 1979-80 with the publication of strategic analyses and reports, by Gros, Jacob and Roger ("Sciences de la Vie et Société"), de Rosnay ("Bio-Industrie"), and subsequently Pelissolo ("La Biotechnologie, Demain?"). The Pelissolo recommendations for the creation of a "Mission Biotechnologie" were accepted, leading to the launch of the national "Programme Mobilisateur" now being implemented. This focusses national efforts in biotechnology on four 'poles' in particular: Toulouse, Compiègne (long known for its enzyme engineering and bio-process technology), Pasteur Institute (a private foundation, 50% financed by government, with capabilities in genetic engineering, hybridoma technology, virology and immunology), and Paris-Grignon (the newly rebuilt centre of fermentation technology of INRA, the National Institute for Agricultural Research). A particular objective of these centres is to improve the transfer of knowledge into industry. The strong molecular biology at the University of Strasbourg should also be mentioned.

In addition to the many multi-nationals with strong bases in France, major French companies using biotechnology in fine chemicals and pharmaceuticals include Rhone-Poulenc (antibodies, and world leader in production of vitamin B12), with its subsidiaries Institut Mérieux (for vaccines) and Genetica (for genetic engineering); and Roussel-Uclaf (a subsidiary of Hoechst) for antibodies and steroids. But the largest commitment to biotechnology comes from the oil company Elf Aquitaine. In human biologicals, it has acquired Sanofi, Clin Midy, Choay and Institut Pasteur Production. Elf Bioindustries and Elf Bioresearch are developing biotechnology in the food and agricultural sectors. There are research-minded companies in the dairy industry (Bel-Industries, BSN-Gervais-Danone, Entremont), and in starch conversion, Roquette Frères are world leaders in sorbitol production. In animal feeds, amino acids are produced by Orsan, Eurolysine (associated with Ajinomoto) and Rhone-Poulenc.

Of new biotechnology companies set up, Genetica has been mentioned; and Transgène, in genetic engineering, benefits from its proximity to the University of Strasbourg.

Italy

A report on "Biotechnology in Italy" was recently prepared by the Federation of Scientific and Technical Associations (FAST - Federazione Associazioni Scientifiche e Techniche). The report lists 142 university institutes, the "Consiglio Nazionale delle Ricerche" (CNR - National Research Council) and public and private bodies and laboratories of the ENEA (Ente per l'energia nucleare e energie alternative - Association for Nuclear Energy and Alternative Energy Resources). The FAST report examines the key aspects of biotechnology, which in future will affect the pharmaceutical and chemical industries, agriculture, new construction materials and energy. In this connection, a number of application-oriented projects conducted by the CNR should be mentioned (fine chemicals, biomedical technologies, further resources for improving agricultural yields).

The FAST list mentions eight industrial undertakings: Farmitalia-Carlo Erba (Montedison Group): Assoreni (this association conducts research activities for the companies of the ENI Group). Lepetit, the Cesare Serono Institute, Sorin Biomedia (Fiat Group), Spa (a company for the manufacture of antibiotics), Recordati and Solavo. According to the FAST study, Italy has no lack either of undertakings or of research capacities that could conduct key programmes in the field of biotechnology: where applicability is concerned, however, everything would have to be better coordinated.

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In addition, mention should be made of the International Centre for Gen tic Engineering and biotechnology set up on the initiative of Italy under t e aegis of UNIDO, for which the Italian Government allocated about 40 mil ion dollars, divided between the first two scientific facilities, namely th se at New Delhi, India, and at the Trieste Research Centre, Italy, which ar intended both for training and for exchanges with developing countries.

The Netherlands is outstandingly strong in biotechnology, in industria companies, academic departments, and a light but well-organised structu for national coordination.

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

The company Gist-Brocades is Europe's major producer of penicillin, wit corresponding expertise in fermentation technology. It is also one of ie world's major producers of enzymes, and is carrying out intensive study on their production, isolation and application, on laboratory and commerci scale. Related research is under way at the universities of Delft and Wageningen. In the food industry, Dutch breweries and dairy plants are sophisticated and internationally competitive.

Academic strengths in biotechnology include the universities of Amsterd (microbial physiology), Leiden (genetics), Groningen (protein crystallo aphy, molecular dynamics), Wageningen (which along with the various research institutes there, covers a wide range of agricultural sciences) and Del (where the Technical University has a close association with industrial fermentation).

Biotechnology is also very strong in Denmark, whose economy is based on agriculture (24% of output), food processing (34%) and chemical industry (10%). Everyone has heard of the Carlsberg brewery, with its tradition skills in brewing, which have supported the creation of an internationa research centre with outstanding competence in plant genetics and cell biology. Everyone has also heard of Novo, which dominates the world ma et in industrial enzymes. Novo practised biotechnology before the word wa invented, and is now arguably the world's leading company in the field.

In 1978, the Danish Technical Research Council, under the chairmanship Prof. O. B. Jorgensen, of the Technical University, took the first init tive in the field and supported projects in genetic engineering scale-up probl ms (with particular reference to genetic stability), product recovery (wit 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 biotec - nology because the subject was of such widespread interest that it neede to be practised widely.

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 a so attracted by the high quality environment provided by the research teams in the various universities of the country.

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At the level of the regional authorities, Wallonie, Flanders and Brussels are seeking to attract foreign investment in high technology sectors such as biotechnology; Wallonie and Flanders have each created two R and D companies. Hybritech (the US leader in hybridoma technology and marketing) has established a plant at Liège; Biogen (the Swiss and US-based group owned by Monsanto, International Nickel, Schering-Plough and Grand Metropolitan Hotels) has established a subsidiary at Ghent (Biogent). At the level of the national authorities, the IRSIA - a national industrial research association - is coordinating R and D projects on biotechnology topics, and its Biotechnology Committee comprises 32 companies from various industrial sectors and university laboratories specialising in monoclonal antibodies, fermentation, immunology and genetic engineering.

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 Board for Science and Technology (NBST), "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 US companies is noted. Innovative companies include Biocon (enzymes), and several of the agricultural cooperatives (e.g. Kerry Farmers).

In 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, in the context of the 1983-88 5-year plan for economic and social development. This includes a programme for scientific and technological development, an element of which concerns "key technologies", containing three themes:

a) microelectronics and informatics
b) biotechnology
c) technologies relating to marine exploitation.

This choice reflects top-level political decisions, and ambitious plans are now being implemented to create the necessary foundations.

Biotechnology and life sciences research are being vigourously promoted at the new Institute for Molecular biology and Biotechnology in Heraklion, Crete; as well as at several other universities (Athens, Patras, Thessalonika) and at research centres such as the National Hellenic Research Foundation, the Cancer Research Centre (Salonika), and NRC Demokritos (Athens).

Professor Stavropoulos, associated with the science-based biotechnology company Vioryl (food additivies, preservatives, flavourings, plant nutrients), is working with the government planners to identify new industrial opportunities in biotechnology. There has been created a national company, "Bio-Hellas", which will work in close association with the research centres mentioned.

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The new strengths of European biotechnology are based not only in cour ries of the Community. Switzerland's great pharmaceutical companies (Roche Ciba-Geigy, Sandoz) are active in the new molecular genetics and immur logy, and Biogen (Geneva-based) is one of the leading new companies in inter eron and vaccine synthesis, and the manufacture of diagnostic reagents. Th Technical High School at Zurich is a centre for fermentation research. In Scandinavia too there are leading centres - the university of Uppsala as close links with Sweden's pharmaceutical groups (Fortia, Pharmacia, Ka i- Vitrum), while in Finland there are biotechnology strengths ranging fr m alcoholic drinks to the management of chlorinated effluents in the pap r industry.

The role of the European Community

The strength and diversity of European capabilities in biotechnology h ve been briefly indicated. These capabilities include all application ar as in industry, agriculture, health care and environmental or resource management, and all the relevant areas of fundamental science and adva ced technology. Of no single European country could this be said. Indust ial- ists need to recover the heavy R and D costs and capital investments b the economies of scale achieved only at European and world level. Stuc nts and researchers need access to world-class centres where the key resou ces and accumulated multi-disciplinary expertise are available; such acces , for collaboration, service and training, is no less necessary for thos concerned with applications.

To create in biotechnology this "espace européen", continuing Communi y initiatives are needed in several policy areas: in research, in agricu ture, in regulations, in industrial policy. These policy initiatives have t be based on a concerted approach, not only within the Commission services but between the Community institutions and national administrations, and i association with those groupings or institutionswhichcommand the key scientific, industrial and agricultural strengths. In this way, Europe can reasonably expect to win and retain a position in world biotechnology commensurate with its high potential.