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FOREWORD

The European Parliament and, more particularly, its Committee on Research, Technological Development and Energy, were quick to focus on issues concerning the international competitiveness of European industry, and the significance of biotechnology in particular.

The significance of biotechnology was highlighted above all in two crucially important Council Directives (Nos. 90/219/EEC and 90/220/EEC, OJ L 217, 8.5.1990) on genetically modified organisms. Their adoption intensified the debate in Europe on the importance of regulating the biotechnology industry and the impact of regulation on the international competitiveness of Europe's biotechnology industry.

The Commission's White Paper entitled 'Growth, competitiveness and employment - the challenges and ways forward into the 21st century' emphasized the significance of biotechnology for future technological development in Europe and the international competitiveness of European industry. Strengthening the international competitiveness of European Biotech-Industry is also the target of a specific research and demonstration programme in the field of biotechnology (part of the 4th Framework-Programme of the European Union, see: Commission document: COM(94)0068 and the Tannert-Report of the European Parliament: Doc. A4-0064/94 and the respective Resolution of 18.11.1994, OJ C 341 of 5.12.1994, p. 229).

The Directorate-General for Research commissioned an external study specifically to clarify the impact of regulation on the international competitiveness of the biotechnology industry in Europe and the USA respectively and to assess the current and future international competitiveness of this sector in Europe and the USA. Comparative in nature, the study also analyses differences and similarities in industrial and research organisation between Europe and the United States. This study, which follows on from two recent studies ((Biotechnology: Industrial Structure and Policy Development in the European Community, the United States and Japan, Energy and Research Series No. 13, December 1991 and Regulation and Competitiveness of the European Biotechnology Industry, Energy and Research Series No. W13, December 1994, both carried out by Martine Kraus) was prepared by Dr. Gérald Assouline, Qap Decision, Grenoble, France and Dr. Joanna Chataway, Segal Quince Wicksteed Ltd., Cambridge, United Kingdom.

DIRECTORATE-GENERAL FOR RESEARCH

Luxembourg, November 1995

CONTENTS

Page

EXECUTIVE SUMMARY

Summary and conclusions

This study discusses the conditions of competitiveness of European biotechnology research and innovation capacity.

An earlier study entitled 'Regulation and Competitiveness of the European Biotechnology Industry' (EP, Series Energy and Research, n°W 14), explained that new biotechnology does not constitute an industry but is a series of techniques for identifying, removing, inserting, expressing, multiplying, enhancing and modifying genetic traits.

This set of techniques is increasingly used in all 'life sciences' industries. The main participants in the development and commercialisation of biotechniques are universities, research institutes, small biotechnology research based companies, chemical, pharmaceutical and agri-food multinational companies. Each of these plays an important role in the biotechnology R&D chain.

The actions of companies are based on global technological and competitive strategies. Leading European chemical, drug and agri-food companies are investing substantially in biotechnology and have various ways of improving their R&D capacity including in-house R&D investment. Intensive relations between US and European universities, externalisation of important research programmes, contracted with highly specialised partners, acquisition or partnerships with dedicated biotechnology firms (DBFs), mainly from the US, building up decentralised networks, with various types of partners, all form part of an increasingly complex transnational web of interrelationships.

Relations between European companies and European research institutes are being strengthened. More applied research programmes are being developed. Various initiatives are being undertaken to strengthen the links between research and industry, for example:

- science parks and other types of local innovation systems, designed to concentrate research capacity, training and education, and industry, in a geographical area

- national 'Strategic Programmes ' are elaborated to fund and develop institutional and research partnership between research and industry: BioAvenir in France, Biotechnology 2000 in Germany, IOPB and PBTS in the Netherlands

- programmes initiated by the European Commission which incorporate public and private sector actors.

As well as drawing on national and European resources, European companies are investing in US biotechnology, both in universities and in DBFs. Various factors account for this, including the fact that drug and agri-chemical companies urgently need breakthrough products and processes that they cannot access in Europe. Additionally, DBFs actively seek powerful partners, because of costs of clinical trials, the public equity markets' frosty reception of some conspicuous failures at the clinical trial stage, and difficulties in direct marketing. Large European companies are therefore attractive to US DBFs.

Relative EU strength and constraints

Countries within the EU, particularly the UK, Germany and France have substantial biotechnology resources with which to compete on global markets. Although the US remains the world leader in many respects, Europe is in a relatively good position in many areas of the new technology. The science base upon which biotechnology rests is key to the development of the sector and requires support from both public and private sectors.

The EU is widely regarded as having lagged behind the United States in terms of technology transfer. Partly this is because of the strength of the science base sustained with enormous resources received from the US Federal Government and partly because of a number of cultural factors, institution and public policy mechanisms which have facilitated effective transfer.

Constraints in capitalising fully on biotechnology in the EU fall into two broad categories:

- constraints which have a general impact on the quality and quantity of innovation across a wide range of sectors and technologies. These include for instance, overall levels of funding for the science base, mechanisms to facilitate technology transfer from universities to industry, fiscal and tax policies and overall education policies

- factors which have a particular impact on biotechnology, such as: availability of finance for biotech firms; public opinion; the regulatory environment; allocation of resources to specific relevant areas of the science base; quality of information about biotechnology innovation; biotechnology-specific technology transfer mechanisms and appropriateness of skills offered by universities to industry.

Although the first category of constraints is important, this paper focuses on the second.

Recommendations

The creation of a European technological policy has to integrate two kinds of factors:

- The global nature of industries innovating in biotechnology.
  Some of the most important actors related to biotechnology may be located and compete in Europe, but this does not automatically signal the existence of a 'European Biotechnology Industry' and the associated 'virtuous cycle' dynamics between different parts of industry, academia and research institutes. To get this positive relation, industrial actors need a long term visibility of the science and technology resources which will contribute to their competitiveness.

- The competition between the national innovation systems in Europe.
  In Europe, the state members define their science and technology policy in a national perspective, trying to reinforce their science base, their innovation capacity by a better relation between research and industry and finally to strengthen the competitive advantage of their innovation system, in terms of attractiveness for global investors.

Policy needs to address constraints and to enhance the attractiveness of the EU as a site for corporate biotechnology investment and small biotechnology firm development. The following issues are of key importance.

The knowledge infrastructure

In most European countries, as in the US, the importance of bio-sciences and the future importance of biotechnology to industry is now reflected in government science funding. There is an increase of overall funding for biotechnology and a number of other measures are being taken:

- 'centres of excellence' are being created in several countries to concentrate high level research capacity and get positive scale effects

- market oriented research is considered as a major priority. EU programmes have actively contributed to accelerate co-operation in Europe, by promoting transnational networking activities

- studies designed to tackle the gap between skills offered by higher education and training systems and demand from industry in Europe

- efforts to harmonise different national educational systems and facilitate the mobility of skilled people

- assessment of the relative strengths and weaknesses of the science base is being undertaken in some countries which feeds into decision making about how best to allocate resources to R&D programmes.

These initiatives make positive contributions and should be continued and built on. The paper makes concrete suggestions with regard to future programmes and policies eg:

- harmonisation
- multi disciplinary, towards industry need.

Technology transfer

All EU member states are trying to develop technology transfer mechanisms. Dedicated biotechnology firms are widely thought of as an important instrument in the transfer process. Around 500 biotech companies exist in Europe, while there are 1300 in the USA.

To stimulate start-up and growth of small biotech firms, new vehicles for public financing such as EASDAQ and AIM are necessary. At regional national and European levels support, advice and information can improve the performance of firms. The creation of publicly supported venture capital funds could be also an option.

A range of broader technology transfer initiatives are being implemented by European member states. Evaluation of various current mechanisms would contribute to future policy making. As noted, biotechnology is not an industry, but a series of techniques which feed into several sectors. Technology

transfer policy mechanisms need to be sensitive to sectoral differences. For example, high profit margins and high R&D spend in the medical and pharmaceutical sector inspire an intensity to technology transfer activities which is not found in some other sectors.

Public opinion

Public acceptance of biotechnology and genetic engineering will be crucial to the success of products resulting from the technology. Reticence amongst influential sectors in society has to be taken into account and addressed as a factor in public technological and industrial policies. Whatever its rationality or irrationality, this social concern, on technology risk and uncertainty must be confronted sensitively by policy makers and industrial actors. A number of initiatives, including consensus conferences, publications and public debates provide opportunities for sharing of information and influencing public opinion. This in itself will inform the regulation elaboration process and the acceptance of biotechnology based products.

The regulatory process

Competition needs 'rules of the game'. The regulatory framework establishes this and provides mechanisms through which various concerns about safety (risk regulation), protection of investments (patents) and fair and free competition (labelling, monopolies and mergers regulation and trade policies) can be addressed.

This study does not provide recommendations concerning the content of regulation. However, it is clear that the construction of the regulatory framework must be improved and accelerated. The following actions are required:

- creation of channels for permanent dialogue between the main actors in the regulation process: NGOs, industry, EU political and technical institutions

- regulations governing biotechnology are currently being revised; acceleration of the harmonisation and implementation of the new rules in all the member states is necessary

- implementation of a flexible procedure designed to continually adapt regulations to reflect scientific and technical progress and knowledge about the long term effects of biotechnology related products on environment and health.

1 INTRODUCTION

This paper considers the competitiveness of Europe's biotechnology sector. The primary comparison made is with the United States. Explanations of the terms competitiveness and biotechnology are provided below.

Key issues

Countries within the EU, particularly the UK, Germany and France have substantial biotechnology resources with which to compete on global markets. Although the US remains the world leader in many respects, Europe is in a relatively good position in many areas of the new science. The science base upon which biotechnology rests is key to the development of the sector and requires support from both public and private sectors. Further investigation into the strengths and weaknesses of the science base is needed in order to inform policy and resource allocation decisions.

The EU is widely regarded as having lagged behind the United States in terms of technology transfer. Partly this is because of the strength of the science base sustained with enormous resources received from the Federal Government and partly because of a number of cultural factors, institution and public policy mechanisms which have facilitated effective transfer.

Several other constraints need to be addressed, including a lack of harmonisation in educational structures within the EU which prohibits mobility, a gap between skills offered by higher education institutions and demand from industry, negative public opinion, problems with the regulatory framework and a relative lack of dynamism within the small biotechnology firm sector.

The creation of a European technological policy is clearly complicated by the global nature of industries innovating in biotechnology. Some of the most important actors related to biotechnology may be located in Europe, but this does not automatically signal the existence of a 'European Biotechnology Industry' and the associated 'virtuous cycle' dynamics between different parts of industry, academia and research institutes.

Report contents

The second section discusses some of the industrial patterns and trends associated with biotechnology. This includes a discussion of alliances and collaborative ventures which have characterised relations in the new technology.

The third section of the report discusses some of the environmental factors which impact on biotechnology innovation and makes some comparisons with the United States.

The fourth section of the report provides an overview and commentary on EU policy, its goals, mechanisms and limitations.

The fifth section makes recommendations.

A few definitions

- Competitiveness: competitiveness can be thought of from a number of angles, for instance from the point of view of the firm or from a sectoral perspective. Competitiveness in this paper refers to the ability of an industry, or industry segments to compete. Industries in EU economies are, of course, made up primarily of private sector firms. Policy initiatives focused on individual firms are, however, limited. Broader policy mechanisms aim at facilitating and encouraging developments within firms by creating a favourable environment.

- Competitiveness in biotechnology: the discussion about competitiveness in biotechnology is complicated by the fact that biotechnology is not in itself an industry. Rather, it should be considered as a set of enabling techniques. Biotechnology feeds into a number of industries and industry segments including, among others, chemicals, pharmaceuticals, food and waste management. In this report, biotechnology companies are defined as companies whose commercial activities depend on the industrial application of recombinant DNA, cell fusion and novel bioprocessing techniques. However, large multinational companies, while they may not depend totally or primarily on biotechnology also increasingly find that their overall performance is linked to their ability to exploit this new technology.

- European competitiveness: Since the formation of the Common Market, Europe has been concerned that member states should improve their own individual economic performance in the context of a regional approach which benefits all EU member countries. There are two very basic constraints on the extent to which policy can be identified as totally 'European'; first, states within Europe compete amongst each other, which sometimes creates difficulties in constructing a European policy; second, companies have international strategies and are working with a global rather than regional focus. The internationalisation of research and production must be taken into account in the creation of viable national and European policies. Despite these constraints there clearly are policies which can be designed to build on European strengths, address weaknesses and facilitate economic growth.

2 COMPANY STRATEGIES

This section of the report aims to present some important characteristics of industrial structures pertinent to biotechnology development. The following questions are addressed:

- what are the main decision making factors, justifying the way investments in biotechnology are carried out by European industrial actors?

- what are the major trends and forms of the investment in biotechnology conducted by those firms, to assure their competitive advantage in strategic markets?

This part of the study is essential to understanding the difficulties of establishing a national and European policy trying to develop biotechnological research and industrial capacity in Europe.

European companies' investment in biotechnology

The importance of biotechnology for a wide range of industrial sectors

Biotechnology is becoming increasingly important to EU companies. According to a Senior Advisory Group on Biotechnology (SAGB) an industry lobby group report (1994):

- 7.3% is the current estimated proportion of dependent biotech sales of the industrial sectors using biotechniques, in a broad sense

- there is a total annual expenditure on biotechnology-related research and development of ECU 185 million

- in its communication to the European Parliament and the Council, the Commission predicts that for the year 2000, industrial sectors using biotechniques will create 2 million jobs (SEC(91) 629 final).

It is understandable that SAGB wishes to emphasise the widespread and increasing use of biotechnology across important industrial sectors. Biotechnologies are not defined and the figures may be over-estimated. Nevertheless, it is clear that biotechnology is having a major impact on European industrial structures.

The level of investment in biotechnology from European companies

The long term interest of big pharmaceutical and chemical companies towards biotechnology, is demonstrated by acquisitions and alliances with US and European small biotech companies. Some 1994 events and decisions (Ernst & Young, 1995) illustrate this movement:

- Rhone Poulenc Rorer (F) establishes a transatlantic gene therapy network
- Ciba Geigy (CH) pays ECU 1.8 billion for 49.9% of Chiron (US)
- Glaxo (UK) bids ECU 411 million for Affymax (US)
- Zeneca (UK) invest ECU 17 million in Sugen (US)
- Hoechst-Roussel (D/F) unveils ECU 30,8 million in a 5 year R & D alliance with Allelix Biopharmaceuticals (CAN)
- Roche (CH) acquires Syntex (US).

Biotechnology development as part of the global chemical and pharmaceutical industry competitive strategy

European domination in the chemicals industry has been built throughout this century with recognised skills and know-how in organic chemistry. For this reason, some big European companies came late to biotechnology as a major focus for R & D. In the 1980's, the development of their biotechnology

capacity has been accomplished by technology transfer from fundamental research to industry, to compensate for historical weakness in biology and genetics. An important component of transfer has involved linkages between European big companies and American universities.

During the last few years, big companies abandoned broad learning biotech strategies of the mid 1980's to adopt much more focused approaches, mainly for human and animal drugs, and agrochemicals. The externalisation of specific R & D research programmes through acquisitions and alliances with US biotech companies has been one of the main tactics (Sharp, 1994). The following table indicates comparative strength of the US, Europe and Japan.

	USA	Europe	Japan
Top 30 pharma companies	13	13	4
Top 15 pharma products	7	8	-
Top 15 biotech companies	14	1	-
Top 10 biotech products	10	-	-

(Source: British Biotechnology Group, 1993)

Intensive international competitive pressure on the chemical and pharmaceutical industry

The following factors contribute to the intensification of the competition between the main chemical and pharmaceutical companies and make biotechnology a corporate priority to renew the product catalogues and processes of those actors:

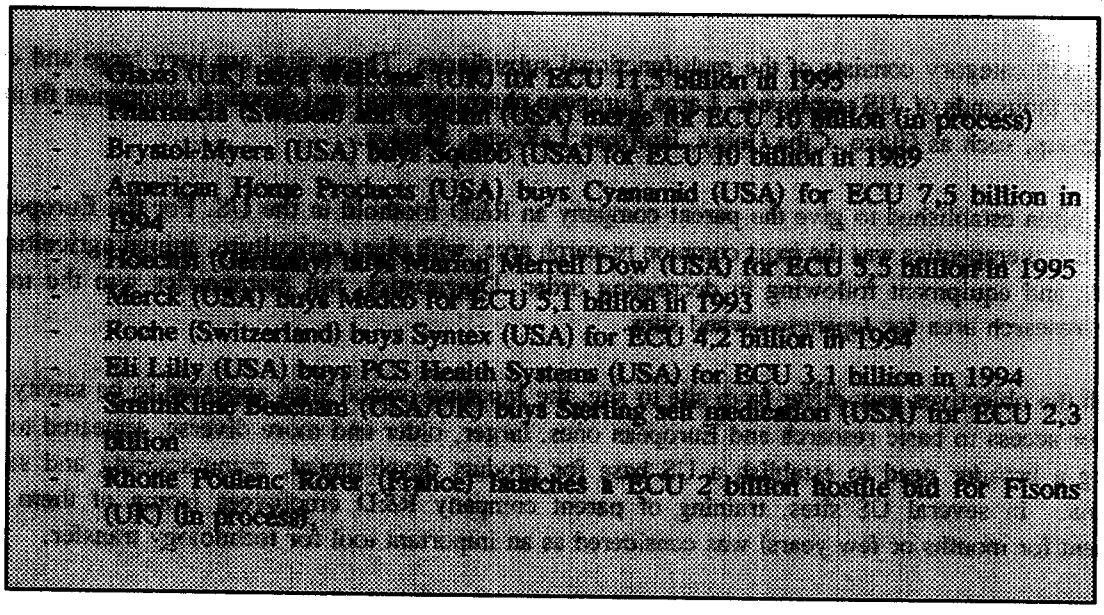
- decreasing creativity of the chemical trajectory to put new products on the market
- vigorous competition of generic products
- more selective regulation of product approval, particularly for pesticides
- stagnating health and agricultural markets due to the economic recession of the early 1990's, new constraints and public policies in developed countries limiting price increases and expenses, and generating world-wide price competition, even among branded drugs that are still patent protected.

With shorter product life cycles, and diminishing returns on me-too products, discovery programmes must accelerate and generate clinical candidates more efficiently .

The reactions of the industry have been diverse:

- consolidation and mergers within the chemical and pharmaceutical industry
- re-organising and/or splitting up corporate structure to get more flexibility in the decision making process, more decentralisation of profit, and more capital for high value activities, for example, ICI/Zeneca, Sandoz, Cyanamid, Hoescht/Roussel
- investing to control generic product producers
- building a wider health management strategy; by highly valued acquisitions of pharmacy benefit managers (PBMs), which manage the bulk purchasing of drugs for pharmacists and hospitals
- restricting their funding of in-house R&D programmes
- considering biotechnology as a decisive instrument to build a global competitive advantage, contributing to make R&D more efficient and less costly, to get new products and rationalise production processes and capacities.

Some important recent mergers and take-overs



(Source: Financial Times, 21/08/95; Le Monde, 22/08/95)

The need for breakthrough products and methods

A variety of strategies have been implemented by European companies to improve their innovative capacity, including the following:

- setting up laboratories in the US
- multiplying alliances and partnership with biotech companies, mostly US
- taking control of US biotech companies
- building networks with academic research, especially in Europe.

US research capacity

The Institute for Biotechnology Information of the North Carolina Biotechnology Centre (Dibner & al., 1992) investigated the US R&D sites of European and Japanese companies. Four categories have been defined from the observation of 76 sites (60 European and 16 Japanese):

- the first consists of sites that are involved primarily in R&D, with few other activities, such as the BASF Bioresearch Corp

- a second category consists of non-profit research institutes set up in the US, with the fruits of the research earmarked for the parent company: an example is the Roche Institute for Molecular Biology Hoffman-LaRoche Pharmaceuticals in Nutley, NJ

- a third category is made up of former US biotechnology firms purchased by European and Japanese companies

- the fourth category consists of the multifunctional subsidiaries. These sites are very large and can employ thousands of US employees. Large European pharmaceutical and chemical companies fit into this group, such as Glaxo, Ciba Geigy, Hoffman LaRoche, Sandoz.

Sites are often established to give the parent company an R&D foothold in the US. For the European-owned sites, therapeutics was the most common research area, with plant agriculture, animal agriculture, chemicals and equipment following in decreasing order. Diagnostics, not therapeutics was the most common research area for Japanese-owned sites.

Although the objectives may differ from site to site, the Japanese-owned sites appeared to be satisfying a need for access to basic research and European ones, larger, older and more diverse, appeared to be satisfying a broader need to establish a US base for product development, manufacturing and sales operations. In several US sites, training of parent company R&D employees (some of them on assignment for months or few years) was considered as an important tool for technology transfer.

Collaboration with US universities are far more frequent than collaborations with other US companies. It seems that the parent company, but not the US site, had formed strategic alliances with US biotechnology firms. This potentially has positive implications for transfer back to the European base.

Relations between companies and academic research in Europe

At the same time, companies and chemical and pharmaceutical groups are increasing their relations with university and academic research in their own country and in Europe. It remains quite difficult to establish the content of those relations with the academic world and the 'division of tasks' between European companies, European academic research and US public and private research.

In the 1980's, a focus of collaborative agreements was to give access to fundamental research, to orient programmes and to allow technology transfer to companies. In the 1990's, there is a pressure from public funding bodies to stimulate industrial innovation, and increase market oriented and applied research and joint research programmes defined between academic research and industry.

An illustration of the intensity of the relations between industry and academic research can be obtained looking at the scientific publications, especially those written in collaboration. Using the Science Citation Index (Hicks, Martin, Isard, 1993, quoted by Sharp et al, 1994), it seems that the number of collaborative scientific articles increased by 85 % between 1980 and 1989.

National collaborations are more important for some big companies than European ones, with the exception of Ciba Geigy. This is, amongst other things, an indication of the weak involvement of the big chemical and pharmaceutical groups in the European co-operative programmes.

Collaborative articles between industry and university research labs (1989)

	ICI	BASF	BAYER	HOECHST	CIBA GEIGY	TOTAL
Total number of publications	363	91	119	210	311	1094
% of collaboration	66	42	46	63	51	57
Total number with universities	203	23	40	99	120	485
% with national universities	80	71	71	68	36	65
Total European collaborations	223	34	51	112	124	544

(Source: non published data from Hicks, Isard, Martin, 1993, quoted by Sharp et al, 1994)

Consolidation of local innovation systems

In several European countries, the creation of 'science parks ' which concentrate research capacity, training and education and industry in a particular location, is used as a way to stimulate technology transfer: Compiègne and Strasbourg in France, Groningen and Leiden in the Netherlands, Heidelberg in

Germany are examples. Networking is also a goal of the 'virtual' research centres which are being created in the Netherlands and Germany and publicly funded. More spontaneously, in Cambridge (UK) for instance, important research capacity is attractive enough to facilitate biotech starts-up and intensive networking between research institutions and industry.

The organisation of national 'strategic programmes'

Several national strategic programmes involving industrial parties have been established. An example is the French BioAvenir life sciences programme. It is a five year, ECU 250 million biotechnology research programme that began in 1991. The French government supports the programme for a proportion of 38 % and Rhone Poulenc has added substantial support. This important budget illustrates how closely the interests of the French government and Rhone Poulenc are perceived to converge (Bio/Technology, July 1993) and the central role of Rhone Poulenc for the development of biotechnology in France.

The programme crystallises co-operation between Rhone Poulenc and the most important French public research institutions: Institut Pasteur, CNRS, INRA, INSERM, CEA. About half of the funds under BioAvenir are for tightly focused pharmaceutical projects, investing in basic research that might reach application through in-house development. According to Rhone Poulenc "The initial results are ...extremely positive and even better than originally expected, notably regarding the rapidity with which they have been obtained" (Bio/Technology, July 1993).

In a very different scheme, ICI and Zeneca now also play a formative role in the development of British biotechnology, giving priority to participation and management of national research programmes such as LINK and having intensive relations with the more important research centres in Britain for example at Leicester University and Cambridge University (Sharp et al, 1994). Evaluation of these programmes would be a useful contribution to further thinking about European Biotechnology Policy.

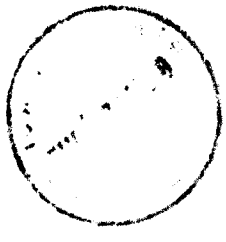
The attraction of US biotech for big European companies

A study (Dibner, Bulluk, 1992, quoted by Sharp, 1994) analysed 1303 agreements involving US biotechnology companies from 1982 to 1991. Some of the results are as follows:

- 183 implicated a Japanese partner and 346 a European partner: British (76), Swiss (71), German (45), French (36), Italian (36), Swedish (27) or Dutch (9)

- 55% of the European agreements involved a US biotech firm and a big European company and 29% involved small companies of both sides

- for more than 70% of the US-European alliances, the flow of technology (product or process) goes to Europe, with some cases of technology transfer to the United States (25%)



- the number of agreements has been growing during the 1980's from 12 per year (1980) to 30 (1985) and 60 at the end of the period.

A KPMG Peat Marwick study reported by Bio/Technology (October 1993) analyses some 215 strategic alliances formed by biotech companies and established pharmaceutical companies. The study found that money is the main driver of strategic alliances, as 31% of biotech companies cite access to capital as their primary reason for partnering:

- the purchaser contributes cash and perhaps part of its business to the consolidated company and may enter into other commercial arrangements

- the purchaser obtains a majority (but not all) of the consolidated company's stock and may purchase the remaining equity

- the purchaser does not take complete control of the consolidated company's board or management, leaving the consolidated company's corporate culture quite intact (Lyons et al, 1993) .

Other reasons for forming strategic alliances include:

- reducing their product's time to market entry as a driving force
- partner's clinical skills
- validation of technology.

The content of the alliances has also been evolving according to the evolution of European company needs: from financial and research towards growing licence and commercialisation rights agreements. Several factors have made working with big companies attractive:

- uncertainties associated with clinical trials and the consequences of those uncertainties, among them, the corporate layoffs, and the frosty reception of some failures on the public equity markets

- difficulties in direct marketing, due to the strength of drug distribution systems, more or less under control of large pharmaceutical companies.

Three examples of strategic alliances, involving European big companies and US biotech firms are provided. They illustrate the complementarity and convergence of interests between biotechnology firms and big companies, and the 'virtual' integration process being implemented (Ernst and Young, 1994), through quite different organisational forms.

Acquisition scenario: Ciba/Chiron, Glaxo/Affymax

Ciba-Geigy/Chiron

[illegible]

By this agreement, Chiron has been looking to get access to a more secure cash position, to global distribution, and a full diagnostic and vaccine product pipeline, through the acquisition of Ciba's diagnostic division, Ciba Corning Diagnostics [illegible]

For its part, Ciba received a more innovative product pipeline.

Glaxo/Affymax

In January 1995, Affymax (Palo Alto, CA), a [illegible] combinatorial chemistry company, was acquired by Glaxo for $533 million. [illegible]

Among the reasons for this strategic merger, there are the lack of its own clinical-stage products, as an obstacle to access to the public equity market, and the potential valorisation of its broad combinatorial chemistry technology for a vast number of projects.

For Glaxo, this acquisition gives access to the combinatorial-chemistry technology, as a tool for rapid synthesis and screening of compound libraries in search of potential drug leads.

Integrated network scenario: RPR/Gencell

RPR/Gencell is a 14 member consortium [illegible] by Rhône-Poulenc Rorer.

In 1993, RPR's first step came with the purchase of 37% of Applied Immune Sciences (AIS, Santa Clara, CA) for $ [illegible] million.

Then, RPR implemented "an integrated network of internal and external scientists that will share the tools and expertise necessary to build successful cell therapeutics on an accelerated timeline" said Robert Cawthorn, RPR's [illegible]

A variety of technologies are needed to develop these therapeutics, such as gene sequencing, gene identification, regulation of gene expression, gene vectors, packaging cell lines, antigen presentation.

In 1995, RPR/Gencell's operating budget is about [illegible] cancer-related research. [illegible]

One of the RPR/Gencell's roles will be to co-ordinate a [illegible] network with complementary techniques and common goals. Another will be to [illegible] for therapeutics developed by the consortium.

The members of the consortium are:

- 7 corporate members: AIS, Darwin Molecular, Genetix Pharmaceuticals (NY), Genopoietic (Paris), Introgen Therapeutics (Austin, TX), Pasteur Mérieux Connaught (Lyon, France), Transgene (Paris)
- 7 research institution members: BioAvenir (Paris), CNRS (Paris), Généthon (Paris), Institut Gustave Roussy (Paris), Institut Pasteur (Lille, France), Berkeley Laboratories' Human Genome Project (Berkeley), University Louis Pasteur (Strasbourg, France).

The development of small biotechnology companies in Europe

There are 485 biotech companies in Europe; this figure represents a 25 % increase over last year's 386 companies. Some caution is necessary in interpreting these statistics: some companies were not included in the Ernst and Young survey in the past years and new member state companies (like Finland and Sweden) have been taken into account in the new survey. 45 % of companies have been created since 1986.

Amongst this total, 140 are located in Britain, 85 in Germany, 85 in France, and around 30 in the Netherlands. 100 (20%) are therapeutic product companies, and the others are diagnostic firms, agrobiotech and equipment suppliers. The USA has a total of around 1300 biotech companies, and more than 500 (38%) of them are therapeutic product firms.

Whilst DBFs potentially have a very important role to play within the EU, a number of constraints have limited their presence. This is discussed further in the following section.

Policy implications

Several points emerge from this section to inform policy:

- biotechnology is clearly an important growth area and viewed as a key ingredient for further competitiveness in a number of sectors. European firms in the chemicals, pharmaceutical and agri-food sectors are committed to building capacity in the new techniques. Private sector commitment to biotechnology underlines the importance of public sector support; the private sector particularly requires strong public support of research and technology transfer infrastructure

- forming collaborative programmes and projects with universities is a key part of many companies' strategy. Making universities accessible and facilitating this type of collaboration is crucial

- alliances between firms are a characteristic of biotechnology innovation. They are important both for large and small firms. Policy initiatives to facilitate networking, improving information flows and providing forums for formal and informal contact between potential partners can contribute to activities here.

3 ENVIRONMENTAL FACTORS AFFECTING BIOTECHNOLOGY INNOVATION

A number of 'environmental' factors impact on EU firms' competitiveness in biotechnology, including: research, education, technology transfer infrastructure, regulatory frameworks, financial mechanisms and public opinion. These are briefly discussed in this section.

Knowledge Infrastructure: research and education

The science base is notoriously hard to quantify. It is clear, however, that while Europe's position is improving in important respects, EU member states lag behind the US in many areas.

Patents are often offered as data to indicate levels of invention, but are problematic because so much relevant research is not patented. A recent report using patent based measures of innovation found that drugs/medicines and biotechnology (together with advanced materials, polymers and chemicals) are sectors in which the EC has best kept pace with Japan and the USA over the last decade (Narin and Albert, 1994, quoted in Technology Foresight, Health and Life Sciences Report).

A report prepared as background for the UK Technology Foresight Programme, Health and Life Sciences Panel provides detailed bibliometric data on 12 OECD countries, combining measures of output and quality. The following table gives a weighted (for quality) analysis of health and life sciences publications world-wide (these figures do not include most areas of clinical research, and cover a broad but not complete cross section of relevant disciplines). The figure shows the dominance of the US, but also indicates the relative strength of the UK, Germany and France.

National percentage shares across all 18 sub-fields on simple counts (SC) and weighted counts (WC), 1991-93

Country	SC	WC		Country	SC	WC
US	42.80	49.96		JPN	9.71	9.02
UK	8.96	8.82		DE	7.28	7.01
FR	6.22	6.24		CA	5.50	5.40
IT	3.98	3.45		NL	2.88	2.79
SWE	2.48	2.30		AU	2.47	2.27
ES	2.02	1.78		CH	1.94	2.30

The UK Technology Foresight process resulted in considerable detail about strengths and weaknesses in relevant areas of the science base. This information will be used, in conjunction with other relevant data to inform policy and resource allocation decisions, particularly with regard to developing market oriented research. Similar information may be available for other European countries and would be helpful in identifying overall strengths and weaknesses and informing decision making. Efforts to compile this data should be supported.

In most European countries, as in the United States, the importance of bio sciences and the future importance of biotechnology to industry is being reflected in government science funding. In the US, biotechnology and the basic science which feeds into it, is recognised as being of strategic importance and receives very substantial support. For fiscal year 1996, the Clinton administration proposes that overall US federal R&D spending will receive a 0.2% increase. However, several research and development programmes related to biotechnology will receive increases of between 3 and 5%. The National Institutes of Health (NIH) is due to receive an overall budget increase of Ecu 365 million, or 4% to Ecu 9,2 billion for FY 1996. Some of that increase is targeted at specific diseases, but an increase of Ecu 95 million is aimed at several specific areas of biotechnology, including DNA-sequencing technology, gene therapy, structural biology and rational drug design. Several other key biotechnology research programmes are also likely to receive increases in budgets (Bio/Technology, 1995).

In the UK, the creation of a new science funding council, The Biotechnology and Biological Sciences Research Council, (BBSRC) (replaces the Agriculture and Food Research Council) indicates the importance being given to this area of science. The BBSRC 1995/1996 budget is Ecu 215 million. Allocations for 1995-1996 increased by Ecu 5,6 million in cash terms. This together with a further Ecu 10,9 million from the Council's baseline funds, will be targeted on a number of priority projects including genome analysis, bioprocessing innovation, wealth creating from plants and bioinformatics (BBSRC, 1995). Another important funder of UK biotechnology research is the Medical Research Council (MRC), which also has substantially increased its funding for relevant scientific areas and is devoting significant resources to technology transfer.

Germany is also increasing its funding for biotechnology and setting up new infrastructure designed to facilitate excellence in the science base and development of biotechnology. The principal government actor is the BMBF (Ministry for training, education science and research). Its spending represents over half of government expenditure on R&D. Within BMBF there is a department responsible for life sciences and biotechnology. This division implements the 'Biotechnology 2000' programme, which funds and promotes specific activities. In 1994, the total expenditure on biotechnology research in Germany was Ecu 1,4 billion, of which just over half was from central and regional government.

In France this year the Ministry of Education and Research has selected 7 priority areas for life sciences. These areas comprise 14 co-ordinated actions for which scientific and research technical committees are being set up. The global budget for 1995 is close to Ecu 78 million of which Ecu 40 million are being allocated to the strategic plan for R&D within the life sciences. The main national research institutes (INRA, CNRS, INSERM, Institut Pasteur) also invest in biotechnology.

One major consideration which educational authorities in Europe are currently addressing is to what extent education systems are oriented towards the needs of a growing biotech sector. A recent survey found that many biotechnology companies are not able to fill vacant posts. While the number of undergraduate courses being offered throughout Europe, and the number of students enrolled suggests that there should not be a problem, companies are finding the reality different. Contributing factors include: a need for post graduates rather than undergraduates combined with dwindling numbers of students continuing to do post graduate studies; a failure of university courses to satisfy the requirements of industry; lack of mobility in the work force, exacerbated by the lack of harmonisation of qualifications

and the training period for PhDs. The report recommends much more interaction between universities and businesses, training for existing employees and a more rounded education which would enable students and researchers to deploy their scientific skills in commercial settings with greater ease. Modular courses which incorporate business skills are favoured (Hayward and Griffin, 1995).

Technology transfer and support to industry

The EU is widely regarded as having lagged behind the United States in terms of technology transfer. Partly this is because of the strength of the science base in the United States (which attracts industry) and the enormous resources which the Federal government pours into supporting this base and partly because of a number of cultural factors, institution and public policy mechanisms which have facilitated effective transfer. Amongst the factors which have contributed to relative success in transfer in the US is the presence of dedicated biotechnology firms (DBFs), entrepreneurial academics, university infrastructure and norms which facilitate dynamic collaboration with industry and effective public/private partnerships which have facilitated the growth of biotechnology.

The emergence of DBFs in the US was in itself associated with a number of factors, including favourable tax structures, relatively easily available finance and cutbacks within some university departments. According to an Ernst and Young survey (Ernst and Young, 1994a) there are currently 1,311 dedicated biotechnology firms in the US, compared to 485 in Europe. DBFs have a longer history in the US and have been a vital part of the development of biotechnology. Many have their roots directly in universities and research institutions. As such they have performed a vital role in technology transfer. Many predicted that once large companies had gained a sufficient foothold in the new techniques, DBFs would be bought up or disappear. This is not what has happened. There have been a significant number of buy-outs and mergers amongst early DBFs, but there has been a second round of companies emerging. This can be interpreted as indicative of their importance as a technology transfer mechanism.

Investment by European companies in US biotech companies and universities combined with collaborative ventures with a few key European DBFs and European universities will hopefully result in increased competitiveness; it may be that Europe does not need more DBFs and should follow a different model of innovation. Certainly policy designed to stimulate competitiveness in biotechnology should not exclusively concentrate on supporting small firms or support firms which cannot compete. European DBFs, however, are becoming stronger as a sector and are increasingly contributing to technology transfer, growth and competitiveness in the sector. It does seem important, therefore, to construct policy which facilitates continued expansion.

Other policy mechanisms to facilitate transfer need to address a number of constraints: finance (discussed below) taxation policy, education and research policy and innovative mechanisms to promote collaboration between academia and industry (incubators, science parks, programmes which part fund industrial/academic collaborations, etc.). A wide range of institutions, mechanisms and programmes have been implemented throughout the 1980s and 1990s within the EU. These include in addition to those initiatives listed above, bioparks, information and advice services, support for network, regional initiatives, awards for promising innovations. In the UK, research funding councils are increasing their focus on market oriented research and actively pursuing technological transfer opportunities.

Interestingly, the BBSRC and the MRC have quite different technology transfer strategies, with the MRC being considerably more 'hands on'. The MRC has a commercialisation unit which promotes development of potentially commercially interesting research in various ways, including playing a role in establishing small firms. The MRC approach is partly based on internal decisions but partly is related to the sector which research feeds into; the pharmaceutical sector has a very high R&D spend which allows for projects which would not be viable in other sectors. It also seems to provide more opportunities for small technology-based firms.

Germany and France tend to pursue technology specific programmes to a greater extent than the UK. The Netherlands have been active in promoting biotechnology and in particular in trying to attract foreign companies. For some observers and analysts the decentralised style of UK support for technology transfer and the focus on removing barriers to growth rather than more proactive initiatives is indicative of uncertainty and a lack of direction in biotechnology policy. However, most European governments, the UK included, have programmes which aim to facilitate innovation in general and those which target biotechnology as a key strategic area. Evaluation studies would help to identify advantages and disadvantages associated with each of these mechanisms and approaches.

Certainly, there are experiences which could be usefully adapted from the US. One initiative which has recently attracted attention is the Massachusetts Biotechnology Research Institute (MBRI). The MBRI is a private, tax-exempt economic development organisation, which receives public money. It constitutes an integrated set of programmes aimed at the following:

- company formation and investment
- education and training
- reinvestment in basic research
- technology evaluation and transfer.

Since its inception in 1986, the MBRI has succeeded in leveraging approximately $6 million in public funding with over $55 million in new, private venture capital funds which has been utilised exclusively to start-up new companies, assisted in the creation of 18 new biotechnology companies and created over 2000 jobs. The institute is also involved in training public school teachers about biotechnology and life sciences and in industry-specific biotechnology job training programmes. The MBRI could serve, at the least, as a source of ideas for new mechanisms to facilitate transfer within the EU.

Regulation

There are three types of regulation which particularly impact on biotechnology companies. These are: risk regulation which governs the contained use and deliberate release of genetic organisms; labelling; and patent legislation. Each of these sets of regulation establishes the 'rules of the game' and are a compromise between different pressure group lobbies within industry and society.

Risk regulation

A previous report written for the European Parliament discusses in detail the impact of environmental risk regulation on firms (Kraus, 1994). The conclusion drawn in the report is that risk regulation does not constitute the main problem for the development of biotechnology in Europe. Other more structural reasons explain the attraction of the USA for large European countries and the difficulties associated with the emergence of DBFs.

This is not to underestimate the impact of safety regulation in general on sectors into which biotechnology feeds. Regulation is a primary driver of the pharmaceutical sector and fundamental to the nature of markets and industry structure. Small firms are severely limited by the burden of regulation in this sector and others, but specific regulation governing biotechnology is not considered a main problem.

This said, there are a number of key issues such as harmonisation and decreasing the bureaucracy associated with regulation in some European countries which could ease the regulatory burden. Moves are being made towards a single "door", flexibility and increased efficiency in evaluation. The establishment of the European Medicines Evaluation Agency (EMEA) based in London has been widely welcomed. Indeed it is reported that many US biopharmaceutical executives "look enviously at Europe's biologic evaluation procedures, saying that they wish that the US system was modelled on it" (Bio/Technology, July 1995). The establishment of EMEA has increased pressure for the FDA to reform.

Labelling

Labelling of food products resulting from genetic engineering is likely to be a controversial issue over the coming months. The creation of EU regulations for marketing approval of genetically engineered food has been welcomed by consumer organisations, especially in countries where there is no legal requirement for manufacturers to seek official approval (like the UK).

Debating very intensively at EU level, member states attempt to build a compromise between demands by consumer organisations for labelling of all genetically engineered foods and industry reticence to labelling. In May 1995, the European Commission Group of Ethical Advisors gave its own advice on this question. According to its conclusions (Biofutur, July 1995), labelling would be necessary to inform the consumers, mainly for two types of genetically engineered food:

- where the food contains material (genes) giving rise to ethical concerns, for example animal genes in plants, or genetically engineered animals

- where the food contains genetically manipulated organisms (GMOs) in which genetic engineering was not merely for an agricultural purpose. This would include the FLAVR SAVR tomato, which is engineered for consumption purposes. It would exclude oil produced from genetically engineered oil seed rape.

Nonetheless it seems that some European consumer organisations are not fully satisfied with the proposal because it does not contribute to comprehensive and full information about sensitive processing methods.

Industrialists are keen to establish that labelling is not a safety issue; safety will have already been established and genetically engineered products are not inherently more risky than non-genetically engineered products. In some countries such as France, opposition by industry and public authorities seems stronger than in other countries.

Patenting

Patenting is the subject of heated debates within the EU. Different points of view are expounded from sectors with a range of interests:

- scientists, with a concern for communication and collaboration are often reticent about patents

- industry, which requires a return on R&D investment and which, in order to invest, must have a way of protecting IPR (Intellectual Property Rights)

- social organisations, with ethical and social concerns about the effect of patenting living organisms.

There is an important ongoing debate about the scope of patent protection; broad approaches offer protection and are therefore thought by some to encourage innovation, but opponents argue that they inhibit others from developing innovative products and therefore discourage overall levels of innovation. The construction of patent protection which enhances innovation and at the same time justifies the huge investments which companies make in biotechnology is a critical issue facing the EU and will have major implications for competitiveness.

Public opinion

Public acceptance of biotechnology and genetic engineering will be crucial to the success of products resulting from the technology. Public perception and acceptance is a complex and highly political area. The dynamics of the debates differ significantly both within Europe and certainly between the US and Europe.

Opinion polls tend to show fairly high levels of wariness about the technology, especially in Northern Europe, but also a relative openness to the potential benefits of the technology. One very general poll showed the following: "Biotechnology is seen as more beneficial than synthetic food (82 percent, Spain 1990; 50 percent Europe 1991) and space exploration (45 percent, Europe 1991), but less so than solar energy (96.6 percent, Spain, 1990; 76 percent, Europe 1991) organ transplantation (98.7 percent, Spain 1990), or informatics (74 percent, Europe 1991) (Bio/Technology, September 1994).

These polls are useful in that they provide information about consumer attitudes, however, they say nothing about the complex dynamics and politics involved in acceptance and attitudes towards products of biotechnology. Several attempts have been made to learn more about these dynamics by in depth dialogue between key decision makers involved in producing, regulating and shaping opinion about biotechnology and consumers. Consensus conferences held in Denmark and the UK are one example of these types of exercises. As biotechnology products start to come on to the market and play a much more

central role in the creation of a wide variety of products and processes these types of event will become much more important. Efforts to facilitate the exchange of information and views should be encouraged and supported.

Finance

It is widely perceived that the United States offers better opportunities for small dedicated biotechnology companies needing finance. Undoubtedly lack of finance is one of the primary constraints on small firms within the EU. However evidence suggests that it is also increasingly problematic for US counterparts.

Public investment

Public investment has been characterised by notable peaks and troughs in the US, but has up until now been a serious option for young biotech companies seeking to raise money. Public investment, however, can no longer be relied upon. Without new additional financing, the number of dedicated biotechnology firms (DBFs) operating in the US pharma industry will be significantly reduced over the next three years. Nineteen of the 100 companies in Cowen and Company's (Boston, MA) biotechnology-tracking universe now have less than one year of cash reserves, based on their burn rate, while 33 of these firms have 1-2 years of cash, and 18 of them have 2-3 years of cash (Biotechnology, July 1995).

This 'dry' period follows an enormous boom in biotechnology financing during the early 1990s. It is possible that the public market will pick up, but unlikely that the boom will ever reach the heights of that period again. It is clear that estimates of future earnings which lay behind that boom were overestimated. A number of factors account for reduced expectations, including the following identified by McGlynn and Heidrich (Biotechnology, July 1995)

- promising science and research do not necessarily equal successful product development as recent failures at phase II and phase III clinical trial stages demonstrate

- research and product development are long and costly, often requiring more than 10 years and well over $200 million for one successful product. Many investors have calculated that they are better served by investing at a later stage of the process and reducing the risk of failures at later stages of the clinical trails.

Public funding for start ups has been a much less significant feature of the European biotechnology scene. However, access to public equity markets is widening. Relaxation in the London Stock Exchange rules now makes it easier for biotechnology companies to raise public equity on the main LSE. In 1994, biotech companies raised ECU 192 million through the LSE (Ernst and Young, 1995). Although it should be recognised that conditions are still stricter than they are in the US; Amgen and Genentech could not have developed in the US under European conditions (Ernst and Young, 1995).

A European version of the US NASDAQ, shortly to be instituted, may also further ease the situation. The European Association of Securities and Dealers Automated Quotation (EASDAQ) is being proposed by the European Venture Capital Association and others; the independently funded pan-European market

will serve both institutional and private investors and will establish its identity as a market of higher return on risk.

One key factor which will have a significant role in the success of EASDAQ will be the availability of skilled analysts to advise investors of the desirability of stock options. Ernst and Young see EASDAQ as potentially valuable but not guaranteed to work:

"EASDAQ's success may depend upon whether the NASDAQ experience can be repeated. Copying the criteria does not ensure success. NASDAQ succeeded primarily because it had dealers that were prepared to risk capital, a pool of entrepreneurial companies, investors with a desire to invest their own money in growth companies and a regulatory framework that promoted rapid improvement in price visibility and market efficiency. For EASDAQ to succeed, a market-maker structure like that for NASDAQ will be needed to create the demand and volume. At the same time, sponsorship, research, sales and trading will create necessary visibility, liquidity and order flow" (Ernst and Young, 1995).

Another potential new funding route is the Alternative Investment Market (AIM) for small and medium sized enterprises (Ernst and Young, 1995). AIM would be a market with less stringent regulations and would give access to capital markets to early stage companies which have little chance of meeting the full requirements of the LSE. AIM will also offer an earlier exit route for venture capitalists.

Venture capital

The creation of EASDAQ and AIM should also stimulate venture capital investment in biotechnology. Provision of an early exit mechanism for venture capitalists is particularly important as it is one of the main requirements for initial investment. Relaxation of the LSE rules has already had an impact on venture capital availability; in 1992, levels of venture capital earmarked for biotech in the UK, Germany and France were about equal. In 1993, with the LSE changes in the pipeline, the amount of UK venture capital invested in biotech almost doubled, whereas the rest of Europe saw a decline. It is possible, however, that the UK companies may be particularly reliant on venture capital and public investment; German banks have a very different approach to longer term financing for small companies than their UK counterparts for example and German biotech companies may find that they can access finance through the banks to a greater extent.

4 EUROPEAN COMMISSION POLICY TO IMPROVE COMPETITIVENESS

Two documents in particular provide insight into the EU Commission's conceptual framework for creating policy to enhance competitiveness and create favourable conditions for industrial activities related to biotechnology. These are:

- SEC (91) 629 final: Promoting the conditions of competitiveness of industrial activities based on biotechnology in the Community

- COM (93) 700 final: Growth, Competitiveness, Employment, the Challenges and Ways forward into the 21st century. White Paper.

The Commission's approach

The Commission recognises that policy to support biotechnology must not encroach upon individual companies' freedom and responsibility to pursue their own strategies and developmental path. The broad approach is spelt out in the following paragraphs from SEC (91) 629 final:

- "...the responsibility for competitiveness is principally of the company's duty. Amongst the different factors which determine this competitiveness, a great number are specific to each market, such as market size, public perception, and overall investment policy of the companies...EU companies will have better chances to improve their competitiveness if the Community environment allows single market achievement, contributes to R&D improvement and stimulates co-operation at the Community and international level..." (SEC (91) 629 Final: 6)

"The concerned industrial sectors do not suffer any structural weakness in terms of R&D, production capacity, investment, financial capacity or market penetration in the Community or at the world level...Nevertheless, to strengthen the competitiveness of biotechnology in Community, it's advisable to resolve some problems:

- insufficiency of patent protection

- fragmentation of the Community market" (SEC (91) 629 Final: 14).

Although these statements indicate limited policy initiatives aimed at improving the regulatory and market environment, the Commission is also concerned by the perceived 'gap' between the US, Japan and Europe.

The 'gap' argument

One of the most important arguments underpinning Commission policy is the gap which exists between Europe, the USA and Japan. On this point, there is clear agreement between the Commission and the Senior Advisory Group on Biotechnology (SAGB), an industry lobby group, representing chemical, pharmaceutical and food companies, based in Brussels.

Common propositions	Specific recommendations	
Commission/SAGB	**Commission**	**SAGB**
Vertical regulation for GMPs (product based)	Scientific Advisory body for Risk Assessment	Reduction of social costs
Support to SME	Development of R&D programmes on focused areas	
Fiscal incentives	Co-ordinate and stimulate co-operation	
Training and mobility		

(Source: Commission, 1993; SAGB, 1994a)

SAGB (SAGB, 1994:5) and the Commission (White Paper 1993) both refer to several indicators which demonstrate the gap:

- the relatively small number of European patents for new biotechnology products granted around the world
- the small proportion of biotechnology based products currently marketed in Europe
- difficulties in marketing some products produced in Europe within EU.

Factors which are currently jeopardising competitiveness in Europe include:

- the relative weakness of public R&D expenditure within the Community as compared with the US and Japan
- the current 'horizontal/process based' risk regulatory regime which deters innovation
- hostility to biotechnology which is more pronounced in Europe than in the US and Japan.

This analysis leads the Commission to advocate a broader range of policy initiatives.

Policy priorities

The Commission has identified a number of priority areas and implemented policy to overcome weaknesses in these areas.

Consolidating the knowledge infrastructure in Europe

Through its different R&D programmes, such as (BEP) (1982-1986), (BAP) (1985-1989) BRIDGE (1990-1993), 3rd Framework Programme (1990-1994), 4th Framework (1995-1998), the Commission has sought to:

- develop R&D capacity by focusing biotech R&D and co-ordinating EU and national level programmes
- stimulate scientists with training and increased mobility.

Building a favourable environment

Recommendations outlined in the White Paper are designed "to achieve a fuller realisation of the community's strength in biotechnology...overcoming existing constraints by creating appropriate channels for biotechnology policy development and co-ordination". The main priorities are:

- the modification of the regulatory framework from a horizontal (process based) to a vertical (product based) approach for genetically modified organisms
- the constitution of a single drug approval agency (EMEA)
- the protection of intellectual property rights on biotechnology inventions
- the adoption of incentive and fiscal measures to stimulate small biotech company creation and development
- the creation of a network of existing and new biotechnology science parks to develop European co-operation
- the creation of a Scientific Advisory Body for Risk Assessment.

Some comments on the Commission's biotechnology policy

Commission policies have had a number of positive results and enhanced the quantity and quality of R&D within the EU. However, a number of contradictory and confused statements weaken the Commission's approach to enhancing competitiveness.

First, the Commission's written statements do not adequately distinguish between biotechnology and the specific sectors into which biotechnology feeds. This is linked to a lack of clarity between science and technology policy and industrial policy, supporting sectoral based developments.

Second, there is a tension between a 'free market principles' approach and a more interventionist orientation. On the one hand the Commission considers that 'biotechnology industries' do not suffer from structural weaknesses and the main responsibility for competitiveness lies with companies. On the other hand, the Commission does apparently recognise several structural weaknesses and factors which jeopardise competitiveness and advocate measures to rectify this (Wheale and McNally, 1993). A question arises for policy makers about how far public policy should go in seeking to make industry competitive. Although the focus must be on facilitating competitiveness rather than direct intervention, there are still numerous grey areas at the border between creating a competitive environment, and attempting actively to direct developments. Deeper consideration of these issues might give the Commission's policy increased clarity.

Third, the Commission policy has not highlighted the role of a range of non-industry organisations such as consumer groups, environmental organisations or special interest groups. Even given the limited objective of wishing to increase biotechnology competitiveness, the process of widespread consultation and public ownership of policy is essential; in the end, the success of biotechnology will greatly depend on consumer acceptance and appreciation.

5 RECOMMENDATIONS

The following recommendations do not constitute a comprehensive policy for biotechnology in Europe. Rather, they are key elements that need to be incorporated into biotechnology policy in Europe.

The construction of the regulatory framework

A primary requisite for regulatory policy is that it is seen to be legitimate. The expression of public opinion on technological risk related to the uncertainty of long term effects of genetically modified organisms or on ethical aspects of patenting biotechnology-derived products and processes, is a key component of public technological and industrial policies. Whatever its rationality or irrationality, this social concern on technology must be acknowledged.

Policy makers need to work towards a social acceptance of programmes involving public funding and education, and impact on employment, consumption, health and environment. Regulation is one way in which societies express opinions about new technologies and legitimise their use by establishing 'rules of the game'. For this reason it is a focal point for dissenting views on patents, safety of genetically manipulated organism (GMO) release and on food labelling. Controversy about biotechnology is likely to continue and regulations need to reflect concerns from different sectors of society.

Industrialists have an interest in the creation of a framework which achieves these objectives. Public acceptance is a key to potential commercial success which biotechnology related products need to enjoy. It is likely that food and agricultural products are more sensitive than pharmaceutical products, although areas such as gene therapy are subject to controversy. Companies, by engaging in public debate can be active in influencing opinion and also make sure that they are developing and investing in products which respond to social need.

The following recommendations concern the process of elaboration and implementation, rather than the content. Policy in the area of regulation should be constructed around facilitating mechanism to inform, listen, respect public opinion.

- creating strong channels for permanent dialogue between the main actors in the regulation elaboration process: industry, Commission Directorates, designated competent authorities in each member state

- accelerating the harmonisation and implementation of the new rules within all the member states

- implementing a flexible procedure designed to modify regulation according to scientific progress and knowledge about the long term effects of biotechnology-related products on health and environment.

Knowledge infrastructure

Research capacity

The UK Technology Foresight exercise generated extremely useful data on strengths and weaknesses in the science base. A study to compile this information at the EU level (and identify gaps in available sources of information) should be undertaken. This would allow meaningful comparisons with the US and Japan and also serve as an aid for decision and policy making.

Science and education priorities and funding must to some extent reflect strategic choices, based on an understanding of social, industrial and economic needs. However, it is important to recognise that the most significant scientific breakthroughs have often been unpredictable. Even viewed from the standpoint of 'increasing competitiveness', funding for basic science and 'blue skies' research must be maintained.

'Centres of excellence' are being created in several European countries. They concentrate the research capacities to get critical mass effects: lower costs and less duplication. However, some studies suggest that competition and diversity of research teams stimulate creativity and innovation (Pavitt, 1991). Further evaluations are needed to establish the role which these centres play in enhancing competitiveness.

Market oriented research is a key component of research strategies in many countries and EU programmes and is fundamental for facilitating innovation within industry. Commission programmes have actively contributed to accelerate co-operation between European researchers in private and public sectors and mobility of labour across Europe by promoting transitional networking activities. Hopefully, this will be reinforced through the 4th Framework Programme on biotechnology. Universities, research institutes

and small biotechnology companies have been the most active in the process. Research is needed to understand whether or not it is possible or useful to increase the participation of large firms in European Commission programmes.

Communication and collaboration between scientists from academic institutions and industry is crucial for competitiveness. Many British scientists opposed patents on human genes in written submissions to the British Science and Technology Committee of the House of Commons (1995) on the grounds that patents inhibit communication. (GenEthics News, July 1995). The issue of patenting and its impact on research needs further investigation.

Education and training

It seems that there is a gap between skills offered by the higher education system and demand from industry in Europe. Steps should be taken to resolve this major problem; flexibility allowed for by appropriate skills is vital to a firm's competitiveness.

Universities are unable to offer industry enough skilled people in key areas of engineering, fermentation technology, immunology, information technology, biological processes (in the environmental sectors) (Hayward & Griffin, 1994). A lot of products are currently in the development process. This will induce important needs for marketing jobs, for people with solid scientific background. At a European level, specific weaknesses in areas of training capacity in fermentation technology, animal sciences, plant sciences and engineering are also a problem for industry personnel.

While science and industry are being internationalised, the pools of people who undertake those activities are still educated and trained nationally, according to national priorities and policies (Hayward & Griffin, 1994). This co-existence of non-harmonised education systems within Europe generates at least two problems: a lack of mobility of labour and the high cost of attracting skilled personnel.

Higher education systems in Europe must move towards a harmonised infrastructure and integrate into the curricula industry needs for specific skills and a multidisciplinary background.

Technology transfer

Almost all member states attempt to develop relations and partnership between research and industry. In the United States, one of the main instruments of this relation is the small biotechnology company. Originally, small companies had a function to perform, namely to identify and bring forward basic research with interesting commercial perspectives. Simultaneous, big companies have maintained strong direct relations with academic research and universities, whose benefits have compensated budget cuts. The European situation is quite different due to the weakness of small biotech companies.

Policy in this area should facilitate the creation of new vehicles for financing such as EASDAQ and AIM, and regulatory regimes which allow them to function effectively. This would allow mobility for venture capital, which is a key point for this financial sector. Financing, however, should be considered in

conjunction with other constraints and technology transfer support mechanisms, and not as an isolated issue.

In some countries, public regional or local development agencies are actively supporting the development of small business and high-tech activities. They finance technological park infrastructure, try to attract companies, and implement 'company nurseries' or incubators.

Evaluation needs to be carried out to establish whether or not this concentration of capacity and funds is effective, according to criteria such as job creation and investment, creative innovation, intensity of relations between research and industry. On the basis of this evaluation a judgement can be made on relevant priorities for national and European authorities.

Formal and informal relations between academic research, university and industry must be reinforced. Mobility of researchers from industry to academic research institutions, from public research to industry, via long term training sessions, or stimulation for researchers to create their own firms, with some technical, commercial and financial public support; and the EU Human Capital Programme should stimulate more public/private researchers mobility.

The goals and forms of this networking process may be diverse:

- research partnership and collaborative research programmes
- informational networks
- training and educational networks
- localised networks
- non localised networks.

EU support programmes must reinforce the diversity and multiplication of those relations, as a positive part of the dynamics of innovation. Selection and evaluation criteria for funding networks must integrate long term aims and informality as conditions for building solid and sustainable relationships.

Incentives for large companies

As pointed out previously many of the important actors of biotechnology development are international companies, whose R&D expenditures are higher than ECU 100 million per year. For them, subsidies or fiscal incentives would not be decisive factors for locating their investment in Europe. Strong knowledge infrastructure, access to market or existing industrial partners (suppliers or subcontractors) are likely to be more important factors in location of investment (Sharp et al, 1994).

APPENDIX

[illegible]

Estimated biotech dependent sales				
Sector	Total sales of sector (ECU billion)	Current		Year 2000 (ECU billion)
		(ECU billion)	(% of total sales)	
Chemicals	144	4	3	15
Human and animal health	69	15	22	35
Agri-supply	12	1	3	3
Food	289	10	3	18
Diagnostic and equipment	13	8	59	20
Total	527	38	7,2	91

(Source: SAGB, 1994)

[illegible]

Sales $ million	Name	Disease	Developer	Marketer	Approved
719	Neupogen	Neutropia	Amgen	Amgen	Feb 91/Jun 94
587	Epogen	Anaemia	Amgen	Amgen	Jun 89
572	Intron A	Immune protection	Biogen	Schering Plough	Jun 86/Jul 92
560	Humulin	Diabetes	Genentech	Eli Lilly	Oct 82
500	Procrit	Anaemia	Amgen	Ortho-Biotech	Dec 90
480	Egerix-B	Hepatitis B	Genentech	SKB	Sep 89
245	Recombivax	Hepatitis B	Chiron	Merck	Jul 86
236	Activase	Myo infarction	Genentech	Genentech	Nov 87/Jun 90
217	Protropin	Dwarfism	Genentech	Genentech	Oct 85
172	Roferon	Leukaemia/ Kaposi	Genentech	Hoffman-LaR	*Jun 86/Nov 88

(Source: Bio/Technology, July 1995)

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