Gazing Into Future in Biotechnology

Availability of venture capital impacts development; large companies seem to be taking leadership

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Biotechnology broadly divides into two main areas. There are the older types of industry based on the biological sciences such as fermentation, which have been progressing steadily without dramatic changes in recent years. The newer type of biotechnology based largely on recombinant DNA technology and monoclonal antibodies has been making dramatic strides in the last five or ten years. Much of what can be said today could not have been said five years ago and may be of no interest in five years' time.

Undoubtedly the initial major contributor to commercial activity in this area has been the United States. A brief review of significant developments in other countries shows that in Japan it was not until 1981 that MITI entered the biotechnology field when biotechnology was included in its System for Promotion of Research on Next-Generation Industrial Technologies.

In Great Britain a Government Committee published the Spinks Report[1] in 1980 identifying weaknesses in the development of biotechnology and in 1982 a new three year plan to spend 16 million pound sterling in support for biotechnology in industry was launched by the Government. In Germany, The Federal Ministry for Research and Technology (BMFT Bundesministerium Fur Forschung and Technologie) presented its first official policy specifically for biotechnology in 1982.

It might be said that the American reaction to this very quick rise in foreign competition was to produce an exhaustive and useful report in 1984, commissioned by the Congress of the United States and entitled Commercial Biotechnology an International Analysis.[2] In a rapidly-moving field it is difficult to draw balanced conclusions as there can be large changes in the course of two or three years. To provide an overview, it is necessary to rely on newspaper reports, private communications and generally unsubstantiated sources of information of a type that a lawyer dislikes.

Much of the analysis will be on a country-by-country basis as I am attempting to identify the European contribution and compare it with developments in Japan and the United States, but the terms used will have a familiar ring for those with experience in analyzing technology transfer in other subjects as we have to think of the contribution of university workers, new-venture financing, small and large companies, and licensing in and out. These are all the usual subjects discussed in many ways at meetings on technology transfer.

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INTERNATIONAL COMPETITIVE POSITION

In the opening address to the Annual Meeting of the Licensing Executives Society of the United States in October 1984, the Chairman of Control Data Corporation said:

"The most significant problem is that access by the United States to Japanese technology is pitifully small compared to the technology access that the U.S. provides to Japan. Research results from Japan are less accessible by other countries than from any other noncommunist country. Most research in the U.S. is performed in universities and is accessible by other countries through the movement of graduate students, the widespread licensing of research results, and the practice of open publication of research results. In contrast, much of Japan's research is carried out in government laboratories and private companies whose laboratories are closed to American corporations. Thus, transfers of technology between the U.S. and Japan are heavily imbalanced in Japan's favor.

"Furthermore, Japanese companies frequently obtain licenses for advanced technology developed in this country at low costs which inadequately reflect the cost of the technology, the risks assumed in its pursuit, or the time it takes to perfect it. This is particularly true of licenses obtained from universities and small companies. In contrast to the open flow of low-priced technology from the U.S. to Japan, all advanced technology licenses flowing from Japan require approval by the Ministry of International Trade and Industry (MITI) which allows no bargains.

"Having outlined the essence of the regional approach and the reasons for selecting Japan as one of the initial partners, let me now review the two main reasons for selecting Great Britain as the other initial partner. One is that past studies have shown that Great Britain is second only to the U.S. in the number of technological possibilities that are generated from its research and development effort. In contrast to its great creativity in generating technology, however, Great Britain has consistently lacked the ability to exploit it through the complete process of innovation. On the other hand, the U.S. has a much better innovation record. Hence, the stage is set for a highly productive technological cooperation between the U.S. and Britain."

This was a generalistic observation, and of more direct interest is the recent report of the Office of Technology Assessment of the Congress of the United States which included the following:

"The U.S. Competitive position.

"A well-developed life science base, the availability of financing for high-risk ventures, and an entrepreneurial spirit have led the United States to the forefront in the commercialization of biotechnology. . .The flexibility of the U.S. industrial system and the plurality of approaches taken by entrepreneurial NBFs and established companies in the development of products have facilitated the rapid development of biotechnology in the United States.

"Japan is likely to be the leading competitor of the United States for two reasons. First, Japanese companies in a broad range of industrial sectors have extensive experience in bioprocess technology. Japan does not have superior bioprocess technology, but it does have relatively more industrial experience using old biotechnology, more established bioprocessing plants, and more bioprocess engineers than the United States. Second, the Japanese Government has targeted biotechnology as a key technology of the future, is funding its commercial development, and is coordinating interactions among representatives from industry, universities, and government . . .

"The Federal Republic of Germany, the United Kingdom, Switzerland, and France lag behind the United States and Japan in the commercialization of biotechnology. The European countries generally do not promote risk-taking, either industrially or in their government policies. Additionally, they have many fewer companies commercializing biotechnology.

"The European countries are not moving as rapidly toward commercialization of biotechnology as either the United States or Japan, in part because the large established pharmaceutical and chemical companies in Europe have hesitated to invest in biotechnology and in part because of cultural and legal traditions that tend not to promote venture capital formation and, consequently, risk-taking ventures."

There has been an explosive growth in biotechnology in the last five years. Admittedly the structure of DNA was discovered in 1956, but the basic recombinant DNA technology was not developed until 1973, and a second line of innovation was started by the British Medical Research Council in 1975 with the development of Hybridomas. Most of the initial commercialization was in the United States and therefore any comparative study conveniently starts with a study of the American scene where the emphasis in early development came from new firms using new venture capital.

NEW VENTURE CAPITAL AND ITS IMPORTANCE

Does the growth of commercial biotechnology depend on new venture capital? It is accepted common ground that the early predominance of the United States has been due to the ready availability of venture capital.

Small companies—new biological firms (NBFs)—started forming in the mid-1970s, first slowly and then rapidly. There are now more than 200 companies in the United States that have been set up in the last 10 years. The relationship between university researchers and these companies and the relationships between these companies and large companies are significant. They have features that were not found in the past.

What is also significant is the technology transfer that has taken place between some of these small companies and large companies in other countries, by way of contract research and also financial investments by the foreign companies.

Many large U.S. companies have started to take a position in biotechnology aided either by in-house research and development or by investing directly in a new biotechnology firm. Thus, whatever happens in the future there has not been a repetition of the commercial development of penicillin that was undertaken by large U.S. companies who built on the basis of research carried out at London and Oxford Universities.

It is completely outside the scope of this paper to discuss the relative contribution of Alexander Fleming. Howard Florey and Ernest Chain as it has been described in many books. However, in 1984 a new biography on Alexander Fleming was written. Its author is Gwyn MacFarlane[3] Emeritus Professor of Clinical Pathology at Oxford University. It is well worthy of study by any serious student of the problem of technology transfer in biotechnology.

On the other hand there may be a parallel with the early developments of the tetracyclines where at least one large U.S. company bought a small company that had done some pioneering work with tetracycline.

By definition these small firms are high-risk investments. How many of them will be financial successes and how many of them will be commercial failures? Can the small firms compete in an area where large companies become interested? Outside the United States the availability of finance for new-venture capital is very different, but is this going to affect the commercial development of biotechnology in other countries?

Do we simply have another situation where the age-old argument of the advantages and disadvantages of large companies versus small companies have to be considered financial muscle as against the ability to react quickly to a new situation.

Japan

I am advised that in Japan, the small entrepreneurial firm has little place in developments in this area. The developments broadly come from big industry.

It would generally be inappropriate for me to talk in Tokyo on the Japanese contribution, but Westerners must admire the dynamism of Japanese developments. Thus, in April 1983, the Japanese Association of Industrial Fermentation established the Bio-Industry Development Centre (BIDEC) and within months, BIDEC news began publishing in Japanese and by February 1984, an English version of this monthly newsletter appeared!

Germany

In Germany, the venture capital industry, as it is known in the U.S.A., has no real counterpart, but some attempts are being made to encourage small, new companies of this nature. Thus, the *London Financial Times* reported on April 9, 1985, that changes were under way.

"The big banks were reluctant to put up loans for exotic-looking schemes in advanced-technology fields, and there were almost no venture capital outfits available either.

That has changed. There are now about 30 venture capital organizations in West Germany (and Berlin), with some DM 700 mm (£190 m) available for investment. The attitude of the banks is changing too, with Deutsches Bank Berlin playing a pilot role."

In April 1985, it was reported that the government hoped to introduce a bill into the Bundestag to encourage the formation of companies that will invest funds in technologically innovative concerns. However, this is very much for the future and any biotechnology commercial developments are expected to come from large industrial companies with a large base in the chemical/pharmaceutical field.

Great Britain

In Great Britian, new companies have been started to commercialize biotechnology as new-venture capital is a recognized part of the industrial scene, although it lacks the size and dynamism of its counterpart in the U.S.A.

Mentioning individual names can be misleading but Celltech was established in 1981 with funds from the government and private investors and began marketing products in 1983. The initial government investment through the state-owned British Technology Group was just under 50%, but this has now been reduced to about 10% as private institutional investors have taken a larger share. It is interesting to note that Biotechnology Investments with an initial capital fund of $55 million made most of its early investments in the U.S.A.

According to *Financial Times* of April 21, 1985, since the beginning of the year, four different companies funding new ventures raised respectively, 36 million, 20 million, 23 million and 20 million pounds. Interestingly, the last to announce its fund-raising exercise (Fleming Ventures Ltd.), stated that 2 million of the 20 million came from Japanese sources. Thus, there is an active venture-capital market in Great Britain.

Switzerland

In Switzerland there is little new venture capital in this area and most of the work is sponsored by the large Swiss pharmaceutical companies.

One of the most recent authoritative comments on new-venture capital in Europe is in the London weekly journal, *The Economist:*[4]

"*Thanks mostly to rightish governments keen on entrepreneurs, Europe's venture capitalists are putting on speed. But more needs to be done if they are to catch up with America's pace-setters. Britain is on course to raise £100m ($120m) in the first four months of this year to invest in new or growing, and mostly innovative firms. France's small firms are thriving around Lyons, the buckle of its high-tech sunbelt. More than 30 firms in West Germany now have upwards of DM 700m ($220m) in venture capital to invest. Snag: too much European venture capital goes abroad.*

"*Only 10-20% of the West German venture capital pile has actually found a home, some of it in America. The French have been better hoarders than investors, though they are starting to take risks. The British, with Europe's most active market, do better, investing 70% of the venture capital they raise at home. But despite a strong dollar, Silicon Valley, North Carolina's Research Triangle and Boston's Route 128 continue to fascinate Europeans more than European high-tech centres do. Almost a fifth of the $3.2 billion raised by America's venture-capital limited partnerships last year came from foreigners, mostly Europeans.*"

The short conclusion to be drawn from these few examples is that the importance of small, new companies in the commercial development of biotechnology is very different in Europe and Japan as compared with the U.S.A. If the conclusion in the Report of the Office of Technology Assessment, quoted at the beginning of this paper is to be believed, however, this does not reflect their importance as competitors. Japan, Germany and Switzerland, are all possible major competitors, but do not have well-developed new-venture capital markets!

THE EUROPEAN CONTRIBUTION

Substantially all discussion of activities in Europe refer to contributions from individual European countries. We talk of work being done in Germany, Great Britain, France, Sweden and Switzerland. Is there any such thing as a European contribution or a contribution from the Common Market (European Economic Community)? Indeed, since Switzerland, which is not a member of the Common Market, is the headquarters of several important pharmaceutical companies who are active in this area, any activity from Switzerland could hardly be activity by the Common Market.

Three separate matters should be mentioned in considering the activities of the Common Market as such.

1. In March 1985,[5] the government of the Common Market, The Council of Ministers, adopted seven European research programs to assist in Europe's economic growth and its future competitiveness as follows:

The adopted programs are:

- Promotion of scientific and technological cooperation and exchanges (85-89) — 60 million ECU
- Basic technological research and application of new technologies (BRITE) (85-89) — 125 million ECU
- Biotechnologies (85-89) — 55 million ECU
- Controlled thermo-nuclear fusion (85-89) — 640 million ECU
- Non-nuclear energies (85-89) — 175 million ECU
- Management and storage of radioactive waste (85-89) — 62 million ECU
- Radioprotection (85-89) — 58 million ECU

1 ECU is approximately 1.5 U.S. Dollars

In explaining the purpose of the research program for Biotechnology, they stated as follows:

"The community's financial participation borders on 50% in the case of shared-cost contracts, but covers all the expenses of training researchers (training contracts and 'pre-doctoral' grants).

"Particular attention will be paid to research proposals which involve integrated participation of public laboratories (universities and national institutes) and of the industrial sector as well as to joint proposals coming from two or more laboratories situated in different Member States.

"Moreover, the program includes a complementary program of discussions designed to achieve increased harmonization of national and community policies.

"In view of the above, the program as a whole should contribute greatly to the transfer of technology to industry and facilitate transnational collaboration."

This shows some attempts to promote activity in Europe by the Common Market as such, but this is a very recent development.

2. In December 1984, Commission Regulation No. 418/85 was adopted setting forth criteria under which joint research and development with subsequent commercialization is automatically exempted from the requirements for notification and exemption or negative clearance. Two companies are only exempt from the requirement to notify:

> 1. Where the parties are not competing manufacturers of products capable of being improved or replaced by the contract products, the exemption provided for in Article 1 shall apply for the duration of the research and development program and, where the results are jointly exploited, for five years from the time the contract products are first put on the market within the common market.
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> 2. Where two or more of the parties are competing manufacturers within the meaning of paragraph 1, the exemption provided for in Article 1 shall apply for the period specified in paragraph 1 only if, at the time the agreement is entered into, the parties' combined production of the products capable of be-

ing improved or replaced by the contract products does not exceed 20% of the market for such products in the common market or a substantial part thereof.

3. After the end of the period referred to in paragraph 1, the exemption provided for in Article 1 shall continue to apply as long as the production of the contract products together with the parties' combined production of other products which are considered by users to be equivalent in view of their characteristics, price and intended use does not exceed 20% of the total market for such products in the common market or a substanital part thereof. Where contract products are components used by the parties of the manufacture of other products, reference shall be made to the markets for such of those latter products for which the components represent a significant part.

4. The exemption provided for in Article 1 shall continue to apply where the market share referred to in paragraph 3 is exceeded during any period of two consecutive financial years by not more than one-tenth.

5. Where market shares referred to in paragraphs 3 and 4 are exceeded, the exemption provided for in Article 1 shall continue to apply for a period of six months following the end of the financial year during which it was exceeded.

In view of the intense competition from Japanese and United States companies, it is arguable whether this regulation is or is not really helpful in this area. How one could ever advise a client that a joint venture falls within or without the regulation is difficult to see. In a fast-moving technical field, it is an impossible task.

3. The third matter is not really any example of activity by the Common Market at all. The European Patent Office is probably the best example of joint work in Europe in this and many other technical fields and is the reason why patent law in many European countries is being harmonized. However, as some member states in the Common Market do not belong to the European Patent Office while some non-EEC countries do belong to the EPO, we do not have an example here of activity by the Common Market as such.

Limited Progress

Regretfully, the conclusion must be reached that in terms of united activity in this area, the Common Market has made little progress at the present time. Any similarity between the common activity of the separate states of the United States of America and the Member States of the Common Market is misleading. If one adds together the activities of the individual countries in Europe, and compares them with Japanese activity and the activity in the U.S.A., the relative competitive position of all three is very different, but this appears to be of little real economic significance at present.

The views of the leaders of big industry on the European contribution vary.[6] In April 1985 at a conference in Munich on "Multinationals: Innovators in High Technology," the Chairman of Phillips, the Dutch electrical multinational, is quoted as saying: "If Europe does not unite, industrial innovation will pass Europe by: multinational companies will then be forced to adjust their geographic priorities."

The chief of research technology of Siemens was more optimistic in that he stated that the European community was starting to take up the technological challenge. He noted that the EEC's strategic program in information technology, called Esprit, was getting off the ground, although its financing was modest compared with that of U.S. and Japanese programs.

A similar optimistic note was struck by the Chairman of ASEA, the Swedish-based electricals group, who pointed out that ASEA had decided to put its head "into the robot lion's den" of Japan in 1982 and was now busy expanding production there.

PATENTS

This is not a paper on patent law, but any international comparison would be incomplete without a discussion of some of the problems. Some statistics on the number of patents applied for and granted are useful for a different reason and these are considered in a separate section.

Experience with the patenting of inventions in the biotechnology field is limited and relatively recent in origin. Many patent offices must be suffering from a lack of skilled examiners in the field and the allowable types of claim are uncertain. Even less clear is the value of patents, in the sense that they can be used to enforce rights in the inventions and doubts have been expressed whether the nature of the inventions are such that any valuable enforceable rights are possible.[7] There may be some truth in these doubts and the patents may be of limited value without the know-how that is necessary to practice the invention, but this situation is not unique to biotechnology and there are many fields of technology where the patents themselves are of little intrinsic value.

Many of the companies most interested in biotechnology have a background in the pharmaceutical industry where the possession of patents can be of decisive importance. Are they therefore stressing too much the value of patents? In any event I will make two observations:

The patenting of new drugs made a quantum leap in the 1950s with the synthesis of chloramphenicol and some of the tetracyclines. Doubts were then expressed as to whether patents would be of value and whether they could not be easily avoided. Claims were restricted to the production of a new antibiotic using specifically named strains, and it was said that such claims could easily be avoided. Likewise, claims to newly-synthesized antibiotics were restricted to compounds where the formula set out the substituents very precisely and it was argued that a third party could easily avoid these patents by changing the substituents. How true have these worries been in practice and are not some of the worries with patents in the biotechnology field very similar?

The second observation is that there is much transfer of technology in this area as discussed in another part of this paper and without doubt this will involve patent licenses and an increasing number of patents will be taken out. There is no real alternative, and technology transfer will be hindered unless there are patents.

The requirements for patentability in the major industrial countries are similar, but as the field is new, we can expect very inconsistent legal decisions because of the absence of precedents. There is a very significant difference between United States law and European or Japanese law as regards the availability of deposited microorganisms. In the United States these have to be available on grant or issue of the patent, while generally in Europe, they must be available on publication of the patent application. This is sometimes said to be an advantage of United States law, but this is only true in the unlikely event that the American inventor only wishes to obtain protection in the United States. There are some cases where American applicants at the European Patent Office have lost their European patent applications because this has not been realized in advance.

Within Europe itself, the law is generally the same as that of the European Patent Convention and the laws of the individual states in Europe generally correspond with the EPC. Indeed, as already stated, the contribution from Europe as such may best be shown from looking at the EPC. There is a possible conflict between German National Law and the EPC in that the Federal Republic requires that the patent application should describe how a microorganism can be reproduced before a patent can be granted for a microorganism and simple deposition is not enough.[8]

Litigation concerning biotechnology patents is only just starting, but we already see the beginning of the problems facing any small company. Litigation can be very expensive and taking or granting a license can be a very attractive alternative.

In talking about litigation, the difficulty of explaining a subject that is developing rapidly is particularly apparent. On August 15, 1984, the Swiss firm Biogen was granted European Patent No. 0032134 for the production of alpha interferon. By May 1985, at least one opposition had been filed and others are expected. Biogen is referred to elsewhere but one can say it is a small Swiss company and has solved the problems of the cost of litigation by assigning the patent to Schering-Plough of the United States. Hoffman la Roche have been awarded a U.S. Patent for a similar invention.

There are two important patents (inventors Stanley Cohen and Herbert Boyer) where the licensors are Stanford University and the University of Californai, one being granted in 1980 and the other in 1984. The policy[9] followed in licensing these patents has been to ask for reasonable royalties so as to avoid litigation, and this policy has so far worked very well. But Cetus Corporation has recently announced [10] (April 1985) that it does not propose to continue paying royalties for a license under these patents, and there is the prospect of expensive litigation.

All of these law suits or potential law suits are current events and no definitive judgment of the value of biotechnology patents is possible. However, to quote[11] the chief counsel of DuPont's Division, "Litigation is going to play a very important role in this area over the next few years."

A reasonable assumption is that substantially all of the inventions in this area, from whichever country the inventors originate, have been the subject of patent applications in the United States. Thus, a study of the statistics of patents issued in the United States should reveal useful information. A year-by-year analysis of biotechnology-related patents is set out as follows:

1970	92	1982	372
1980	234	1983	734*
1981	313	1984	826*

*first nine months only

Thus, the number of patents issued yearly continues to increase, which is not surprising. What is unexpected is the distribution of those patents in that almost half of those issued in 1984 were to foreign corporations. Japanese companies acquired almost half of the foreign-owned patents. European countries were much less active. Germany and France being poor second and third in that order. What does this mean? Is the early predominance of the United States in biotechnology disappearing, or are non-U.S. inventors deciding to patent inventions while U.S. inventors, for whatever reason, are deciding not to?

Of equal significance is the distribution of those patents. In spite of the fact that smaller companies have received more public attention than large corporations, it is the latter who obtained more patents in the periods concerned as will be seen from the following Table.

	1984[b]	1983[b]
Agrigenetics	5	1
Ajinomoto	3	13
Baxter-Travenol Laboratories	6	3
Bethesda Research Laboratories	0	0
Biogen	0	0
Boehringer Mannheim	2	8
Cetus	3	0
Collaborative Research	0	0
Corning Glass Works	1	2
Damon Biotech	0	1
Du Pont	10	2
Enzo Biochem	0	0
Genentech	5	0
Genex	1	1
Green Cross	2	2
Hoffman-LaRoche	10	14
Hybritech	0	1
Kyowa Hakko Kogyo	4	4
Lever Brothers	4	2
Eli Lilly	11	10
Merck	21	25
Miles Laboratories	17	14
Molecular Genetics	1	0
Monoclonal Antibodies	0	0
Nabisco	8	5
Novo Industri	2	3
Ortho Diagnostics	5	1
Pfizer	7	5
Phillips Petroleum	5	4
Sanraku-Ocean	4	1
SmithKline Beckman	2	2
Stauffer Chemical	3	2
Takeda Chemical Industries	7	4
Upjohn	10	6
Other	423	425
TOTAL	582	581

b Data are for first nine months of each year
Source: OMEC International

For example, in the 18-month period covered, Ajinomoto (Japanese) obtained 16 patents, Merck (U.S.) 46 patents and Hoffman la Roche (Swiss) 24 patents. In contrast, well-known small companies such as Cetus (U.S.) obtained 3, Genetech (U.S.) were awarded 5 and Biogen (Swiss) no patents at all.

The figures quoted in this section are taken from an article in *Chemical and Engineering News,* December 10, 1984, p. 19, and refer to the first nine months of each year. It may be that it is not correct to make any detailed deductions from these statistics. Possibly, statistics based on the residence of the inventors would be more meaningful as work may have been done under contract in one country and assigned to a company in another country. Thus, inspection of the official statistics published by the European Patent Office gives the following figures for published European Patent Applications:

	1981	1982	1983
Cetus	4	5	8
Genentech	3	5 (+1 with HLR)	13 (+1 with HLR)
Monoclonal Antibodies	-	-	-
Celltech Limited	-	1	2

Are the smaller companies doing more contract research for large companies or are the large companies simply doing more research because of their greater resources? In the section on technology transfer some other problems raised by these figures will be discussed.

SOURCES OF INNOVATION OR TECHNOLOGY TRANSFER

The crucial question for the future must surely be the sources of innovation and these may determine technology transfer or the desire for technology transfer may determine the sources of innovation! Enough publicity has now been given to the importance of biotechnology to see that inventions that may be worthwhile are considered. Let us look at some crucial dates:

1932	— Penicillin "discovered" by Fleming at London University England.
1940/42	— Crucial work by Florey and Chain on penicillin carried out at Oxford University, England.
1944	— Penicillin mass-produced in the United States.
1953	— Structure of DNA elucidated by Watson and Crick at Cambridge University, England.
1973	— Recombinant DNA technology conceived by Cohen at Stanford University and Boyer of the University of California.
1975	— Monoclonal antibodies-hybridoma technology suggested by Kohler and Milstein during work for Medical Research Council in Cambridge, England.
1982	— First commercial DNA/pharmaceutical product (human insulin) introduced by Eli Lilly.

Objectively, it is true to say that the majority of this work was done in English universities, but the inventors were of many nationalities.

As shown earlier, it was not until 1980 or later that many governments began to appreciate the importance of biotechnology and the present state of affairs is that new products having commercial potential are fully assessed. What are the sources of new inventions, and are Europe, Japan and the United States proceeding independently? Are the universities the main sources of innovation or will the research departments of large and small companies provide us with the new products? Used in broadest sense, will technology transfer from one country to another be a critical factor? The picture is a confused one because of the speed of development, and in many instances only general impressions are possible and questions suggested for someone else to answer.

Switzerland is the headquarters of three important international pharmaceutical companies, (Ciba-Geigy, Hoffman la Roche and Sandoz). All of them spend a large part of their R&D expenditure abroad and this is true of their expenditure on biotechnology. Contract research for Japanese companies, among others, is carried out by Biogen S.A. which is a Swiss Company set up in 1978 with venture capital provided by large companies from the United States. Thus, we have American money being used to fund a Swiss company which conducts research for Japanese companies!

GREAT BRITAIN

There is probably a much bigger and more sophisticated new venture capital market in Great Britain than in any other European country, but some of the capital is not invested in Great Britain. However, as one would expect in Great Britian in a country with a relatively wide industrial base, innovation in biotechnology is taking place in many different ways.

In 1980, Celltech Ltd. was set up jointly with money provided by the state-owned British Technology Group and private institutional investors. This is a typical British approach! Initially, the company was intended to build on results of research carried out under the auspices of the Medical Research Council (state-owned) on monoclonal antibodies. Other new companies have been developed in Britain in a similar way. The innovations started with a Research Council, which is a state-funded institution, and the initial commercial developments were also partly dependent on government funds.

However, large British companies are spending substantial sums on biotechnology research and in the European environment, may be better equipped to commercialize new products.

In Germany innovation appears primarily to be coming from the large chemical companies and from state-funded bodies such as some of the Max Planck Institutes, and there is little sign of new companies using venture capital. However, one very interesting development was that in 1982 Farbewerke Hoechst signed a $70 million contract with Massachusetts General Hospital to support work in molecular biology.

This type of innovation/technology transfer leads to the last subject for discussion. To what extent does technology transfer cross national frontiers?

CROSSING NATIONAL FRONTIERS

There have already been a number of references to this in different parts of this paper. Thus, Biogen is a Swiss-based company using American capital to carry out research for Japanese companies. Biotechnology Investments Ltd., was started in England to invest in this area and made its initial investments in the United States. The collaboration between Bayer of West Germany and Massachusetts General Hospital has just been noted. Another recent example [12] is that Wellcome, a large British pharmaceutical company, is to build an £18-million research center in collaboration with the Terry Fox Medical Research Foundation at Vancouver, Canada, in a new hospital on the campus of the University of British Colombia. Wellcome are negotiating similar ventures in Britain, Japan and the United States.

According to the 1982 Annual Report of Genentech, Corning Glass (of the United States) and a group of four Swedish organizations each invested $20 million in the company in 1982.

These examples could be multiplied, but no accurate survey is possible in this rapidly moving field. However, it is clear that the interplay between universities, small companies and large companies both in one country and in different countries will be very significant.

Similarities with the commercialization of penicillin and the development of the tetracylines are only slight as will be apparent from what has been said earlier.

CONCLUSION

The office of Technology Investment in its recent report stated that the United States was still the leader in the commercialization of biotechnology, with Japan a very good second. If we accept that the number of issued U.S.

Patents is a guide to inventive activity, and this could be a wrong assumption in this technology, this conclusion is supported. If we put together the European contribution from the European Economic Community, the number of its patents is almost equal to the number of Japanese patents, but does this have any real meaning in the commercial world?

The nonavailability of new-venture capital for start-ups has had no significance at all on Japanese development. Do we therefore need to expect that new, exciting technological developments need new-venture capital? Small high-risk companies may have provided the initial thrust in this area, but it seems that the large companies may be taking over. This is supported by the patent statistics, and one can think of many reasons why this is true. Development costs are high in relation to the risk of failure, large companies are much better equipped to stand any financial strain, and the large company can either pay for contract research by the small company or buy that company.

How important are patents for the future of commercial biotechnology? The modern synthetic drug industry is heavily dependent upon a strong patent system, but will the same be true for commercial biotechnology? There will obviously be significant litigation in the next few years and this may answer this question, but it may be that the know-how is equally important or more important than the patents.

What is the importance of the European contribution? Individually no European country is as significant as the United States or Japan, but collectively, the picture is different. However, this may simply be a politician's way of looking at the facts, and in the commercial world they may act substantially independently.

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