With Compliments

David Leathers

9th March 1982

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FINANCIAL TIMES 8 MARCH 1982

Finance for U.S. genetic engineer

By David Fishlock

BETHESDA Research Laboratories (BRL), the troubled U.S. biotechnology company, which recently announced a major cutback in staff, has obtained the first $1m tranche of "bridge" financing, through Now York investment bankers, F. Eberstadt.

BRL was one of the first of a large crop of biotechnology companies seeking to exploit recent advances in genetic engineering. Its policy was to finance its own research out of sales of the special reagents and instruments needed by genetic engineering researchers.

But BRL's rapid expansion last summer left it with losses running at an estimated $1m a month by the end of last year. It has since reduced staff from 490 to 300 and brought it a new chairman, Mr Frederick Adler, a New York venture capitalist who has a reputation as "company doctor" for high technology companies.

Mr. Leathers

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PRESS CUTTINGS

Financial Times Thursday March 4 1982

Cuts hit U.S. biotechnology jobs

BY DAVID FISHLOCK, SCIENCE EDITOR

STAFF CUTS of more than 30 per cent are planned by Bethesda Research, of Maryland, U.S., one of the biggest and fastest growing of the rash of biotechnology companies set up in the past five years.

The company, which has small offshoots in Britain and West Germany, plans to cut its U.S. workforce to just under 300 from 450.

Bethesda's move is a further indication of the serious strains facing the biotechnology industry in its efforts to raise capital

Dr Leslie Glick, chief executive of Genex of Maryland, says part of the problem is that new equipment and techniques needed to perform genetic engineering are "coming along a lot quicker than we imagine."

The need for a high rate of recruitment of scientists and heavy expenditure on laboratories is believed to have driven a number of companies into financial difficulties.

Others, however — being newer and less cash-hungry or because they are recognised as more soundly based—are continuing to attract venture capital.

Biotechnology Investments, the Rothschilds fund devoted to investment in such companies, has just invested in Integrated Genetics of New York.

The company is only one year old and has obtained its first major financing from several venture capital funds, including $1m (£550,000) from the Rothschilds fund.

This fund recently reported that it had rejected 45 out of 61 proposals examined for biotechnology investments. It has invested in five—all U.S. companies—and is considering another.

The fund turned down Bethesda Research, even though the company was one of the longer-established, dating from 1976, with an income of more than $10m in 1981 from the sale of research tools and reagents for genetic engineering.

City estimates put the number of new biotechnology companies established in the last five years at about 150, mostly in North America. At least 70 are practising genetic engineering.

The Geneva-based Biogen company, formed in the late-1970s with strong corporate backing, estimates that by the end of this year it will be spending £10m a year in research laboratories in Geneva and the U.S. Biogen raised only £10m compared with a hoped-for £25m in a placement in the City last autumn.

Mr Robert Cawthorn, its president, said last week that of perhaps 150 companies, about four were well-established today, and eventually perhaps a dozen "will probably make it."

Mr Leathers

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PRESS CUTTINGS

Financial Times Friday February 12 1982

Biotechnology investment funds remain unused

BY DAVID FISHLOCK, SCIENCE EDITOR

N. M. Rothschild is having difficulty finding sound biotechnology investments for the £25m venture capital fund the bank opened last year.

Of a total of $47.8m (£25.8m) subscribed to Biotechnology Investments, a Guernsey-registered fund, only $11.6m has been invested so far.

An interim report from the fund says it is likely that the assets will not be fully invested "for some time."

The fund, of which Lord Rothschild, the biologist and former head of the Whitehall "think tank," is chairman, has exacting scientific and financial standard for its investments.

It has made four investments in unquoted biotechnology companies, all in the U.S. In the case of the biggest Agrigenetics —a plant science company whose chairman is also a director of Biotechnology Investments— it has made two investments of $625,000 and $547,000.

Other unquoted investments are Applied Biosystems of San Francisco, Applied Molecular Genetics of Los Angeles, and Repligen of Cambridge, Massachussetts.

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TECHNOLOGY

BIOTECHNOLOGY INVESTMENTS' LATEST REPORT HIGHLIGHTS AN IMPRESSIVE PORTFOLIO

Blue chip genes promise high returns

BY DAVID FISHLOCK, SCIENCE EDITOR

"OUR INTENTION is to seek a much higher than average return on the unquoted part of your portfolio within a three to seven-year time-scale," Lord Rothschild says in the second annual report of Biotechnology Investments. His report suggests that it is making good progress—indeed, it reads like a catalogue of the "blue chip" end of the spectrum of new biotechnology companies which have blossomed in the past few years.

Left: Lord Rothschild—gathering together a wide range of biotechnology investments

BIOTECHNOLOGY INVESTMENTS: UNQUOTED STOCKS

Company	Equity interest %	Country	Business
Advanced Mineral Technologies	25	U.S.	Mining/pollution
Agrigenetics	1.2	U.S.	Seeds, etc.
Amgen†	1.6	U.S.	Health care, etc.
Applied Biosystems†	7.4	U.S.	Instruments
Catalytica	10.4	U.S.	Catalysis
Celltech	11.4	UK	Health care, etc.
CW Ventures	3.1	U.S.	Bio-funds
DNA Plant Technology	3.8	U.S.	Plant science
Genetic Systems	2.5	U.S.	Health care
Genzyme	5.6	U.S./UK	Diagnostics
Immunex†	6.7	U.S.	Health care
Integrated Genetics†	4.5	U.S.	Health care
Plant Genetics	9.1	U.S.	Vegetable crops
Queue Systems	6.0	U.S.	Laboratory equipment
Repligen	9.5*	U.S.	Health care and agri-science

* Shortly to be increased. † Now public.

Increase

With two-thirds of the $61m fund now invested, almost equally in quoted and unquoted biotechnology companies, it is showing a 25 per cent increase in net asset value per share on the year, and 35 per cent over two years.

Biotechnology Investments, set up on the initiative of Lord Rothschild, as an offshoot of N. M. Rothschild Asset Management, now has a portfolio of 31 investments, both big and very small. All unquoted companies must still meet the strict criteria laid down by the directors. Lord Rothschild summarises the five rules as follows:

- It must employ not only scientists of high calibre but also first-rate business managers, so that the team is "ready and able to establish a successful venture."
- Its business plan should clearly define its research and product areas, and contain both a market analysis and a realistic assessment of the competition.
- Its potential rate of return must be in line with the risk being taken.
- It must have a sponsor to act as lead investor and to accept responsibility for the venture. (Although the fund itself has been known to act in this role.)
- The company must have plans for releasing the investment, normally through a public share issue.

In the year ending May 31, the fund received 82 investment proposals, of which 57 came from the U.S., compared with 16 from Britain, three from Israel and one apiece from Belgium, Canada, Finland, France, West Germany and Ireland.

Of these, it chose three U.S. companies in which to invest: Catalytica, where the $1m invested will go mainly to support the use of enzymes in petrochemical processes; CW Ventures, a fund which invests in health care; and Immunex, a company with close links to Hoffman-La Roche and high hopes of leading the field with a treatment for AIDS (autoimmune deficiency syndrome).

Change

By this summer the scene had changed dramatically. No fewer than four of the fund's investments have gone public, in each case advantageously: Amgen, Applied Biosystems, Integrated Genetics and Immunex (see table). Mr David Leathers, investment manager, says that the fund has no intention of selling companies which go public, but will still continue to apply the five rules by which they judged the original investment. Even so, he admits that the fund it did not expect so many of its unquoted investments to go public so soon.

Another dramatic change is the view the fund takes of British biotechnology investments. In the past Lord Rothschild has been forthright in expressing disappointment with the calibre of companies coming forward with investment proposals. Other London finance houses have suggested that they see the need for a more creative approach in Britain, to produce packages appropriate to a situation, rather than passively judge a proposal as Biotechnology Investments has tended to do in the UK.

During the year the fund made its first-ever investment in an unquoted British company. It is also its biggest investment in this sector. The fund has £3.1m in Celltech, the company with an inside track to the

Criteria

Celltech, to quote brokers Scrimgeour, Kemp-Gee and Co. last month: "fulfills the main criteria necesary for mounting a successful operation in this fast-developing, highly-technical, field. The management team comprises both eminent scientists and sound commercial/financial managers and the company is able not just to make scientific discoveries but to scale-up, extract, purify, and market its products, as evidenced by its first product, the anti-interferon monclonal antibody."

The current position, according to David Leathers, is that the fund is evaluating half-a-dozen British potential investments but has no new ones "on the front burner" from the U.S. It is, however, considering the investment of another $1m in Repligen, one of its first investments, which now needs more cash to help build a pilot fermentation plant.

Coy

Of the British prospects, the fund is coy for the moment. One that interests them is the Agricultural Genetics Company, set up this summer as a "country cousin" of Celltech, to try to exploit the plant genetics research of the Agricultural Research Council.

As Biotechnology Investments see it, the new company has been very modestly funded by its three partners — British Technology Group, Advent and Ultramar—at the outset, until the investors see the first business plan. Then the partners and other investors will be invited to plunge more heavily.

Two of the funds older U.S. investments, Genetic Systems and Applied Biosystems, have just announced a joint venture in imunodiagnostics, to develop two new diagnostic systems, one simple and inexpensive for doctors' surgeries; the other automated for clinics and hospitals.

These systems are aimed at the diagnosis of bacterial and viral infections, chronic illness, and cancer, cardio-vascular and genetic disease. Round at Rothschilds, they see the move as an important one for both companies.

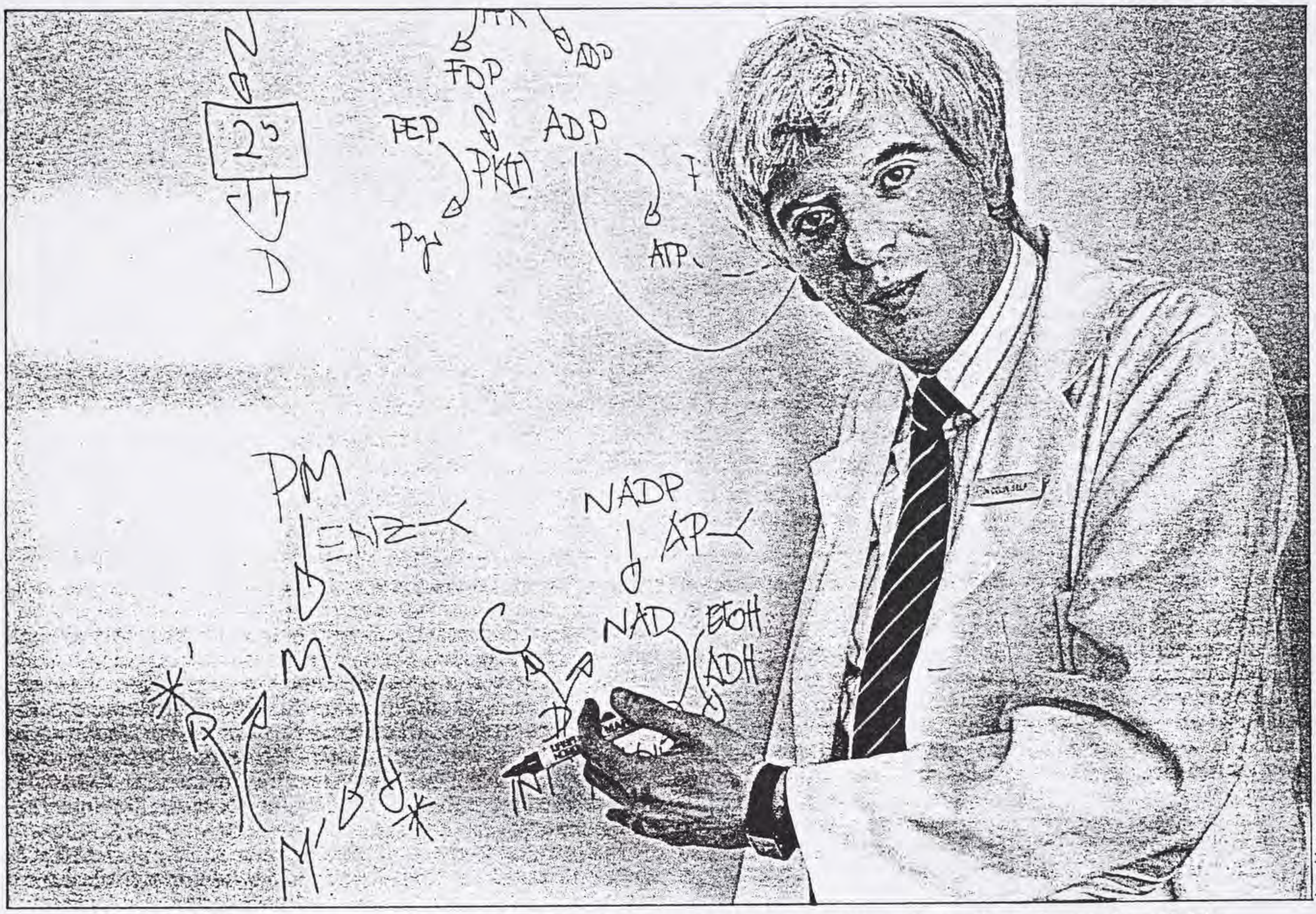
One further recent investment which excites the fund managers is the $1m they have plunged on Genzyme, a U.S. company set up to acquire Whatman Biochemicals in Britain. This company makes diagnostic enzymes. It has since bought Koch-Light Laboratories, another British company, making fine chemicals.

Genzyme plans to use these two UK companies as a base for developing biotechnology interests. Biotechnology Investments see the company as virtually British but driven by American entrpreneurial initiative.

A licence on life

The business of making money out of genes is having a difficult birth. The biotechnology industry would like to make things easier by having patents on both genes and living organisms

Steve Connor



Colin Self: His private research led to an invention that proved to be worth millions of pounds, and more than 60 jobs

ON A SUNDAY morning in 1979, a young medical student went into his laboratory to do some extra-curricular research. He wanted to test a hunch he had that heat might be a simple way of isolating a certain enzyme from a bacterial soup. The university had turned the gas off, so he had to warm his broth of bacteria on a camping stove. The hunch proved right. Having isolated the enzyme, the young student went on to develop a technique that he later patented. The patent became the property of a new company, established to develop a suite of products based on the invention. In June of this year, a Danish firm, Novo Industri, bought that company for £8 million.

Colin Self, who is now a doctor at the Hammersmith Hospital in London, had little idea on that Sunday morning that he was on the road to success. Industrialists are now designing a plethora of diagnostic kits, such as pregnancy tests, based on his invention. The success of his patent is measured by the amount of money Novo paid for IQ Bio, the company that Self helped to establish seven years ago. As a result of those Sundays spent bent over a camping stove, more than 60 jobs now exist because Self patented his invention without mishap. Novo says that it will now create even more jobs at IQ Bio's laboratory in Cambridge.

Self's patent is the key to this success. Britain, however, does not have a happy record of patenting inventions in the field of biotechnology. Cambridge, in fact, was the location for what has become the most celebrated example of a missed opportunity for patenting a remarkable invention. Two scientists from the Medical Research Council's Laboratory of Molecular Biology, Georges Koehler and Cesar Milstein, developed a technique that, if properly patented, might have been worth millions of pounds in royalties. By fusing two types of cell, they cloned a group of cells that would produce identical antibodies, proteins that identify and attach to a given type of antigen—in this case the blood cells of sheep.

The blame for failing to patent "monoclonal antibodies" lies somewhere between Cambridge and the National Research Development Corporation in London. The NRDC then had the right of first refusal on inventions from public research centres in Britain. Self was fortunate because, as a medical student doing research in his spare time, he had the rights to his own work and could therefore patent the invention himself. He did this with the help of Hans Kornberg, the head of the biochemistry department at Cambridge, and Donald Braben, the head of the BP's Venture Research Unit. Kornberg introduced Self to Braben, who has, he says, money to give away, and the match proved perfect. The Venture Research Unit undertook to pay the cost of

Tony Sleep

In the US, companies can lay claim to patents on higher forms of life, something that Jeremy Rifkin and others find morally repugnant

patenting Self's invention internationally. "BP provided the fuel to keep the thing going," Self says. He had tried and failed to find funding from more conventional sources.

Like the work of Koehler and Milstein in the mid-1970s, Self's invention in 1979 came about with the help of work on antibodies. Self wanted to detect extremely minute quantities of a substance, a hormone for instance that indicates pregnancy. And he wanted to do this quickly, without having to use expensive equipment. It was possible to develop antibodies that could identify a substance, but how do you know that the antibody and antigen have bound together, so showing that the antigen is present?

One technique at that time was to coat a surface, the side of a glass slide for instance, with an antibody that would recognise the substance in question. This antigen would stick to the antibody, and stay on the surface, after washing. Scientists then add a second antibody that also recognises the antigen in question and so stick to the combination of first antibody and antigen. If this second antibody is labelled in some way, with a fluorescent marker say, then the sandwich of antibody-antigen-antibody still sticks to the fixed surface after washing, and the labelled antibody can be detected.

This simple technique is now the subject of a patent dispute between several biotechnology companies in the US. Hybritech, in San Diego, which is a subsidiary company of Eli Lilley, has sued two other companies, Abbott Laboratories and Monoclonal Antibodies, over Hybritech's rights to a patent on sandwich antibodies. Hybritech filed its patent in 1980. Other companies argue that the technique was an old one and all that Hybritech did was to apply it to monoclonal antibodies. The Patent and Trademark Office and the appeals courts in the US have so far ruled in favour of Hybritech, although this dispute is not yet over. Hybritech wants a permanent ban on the sale of products made by other companies that are designed on the process. At issue is a market worth several million dollars.

A variation on the process that Hybritech claims it owns is to attach an enzyme to the second antibody. This enzyme makes certain chemicals change colour, another way of visually recognising that the sandwich is sticking to the solid surface. There is a problem, however, with using a second antibody that is labelled in some way. If the substance that the scientist wants to detect exists in tiny amounts, then it can be a long time before the solution changes colour, too long perhaps to be of any use in a busy clinic or surgery. A test also becomes less accurate if it takes time because, for instance, the chemicals can degrade.

Self wanted to speed up the chemical reactions in order to detect minute quantities of antigen. His idea was to choose an enzyme for the second antibody that would turn an otherwise inactive chemical into one that then acted as an enzyme for a secondary chemical reaction. Self describes it as "a catalyst making a catalyst". The important step in Self's invention is that the secondary reaction does not consume the second "catalyst". All it takes is for a tiny amount of antigen to cause a tiny amount of the first catalyst to make a tiny amount of the second catalyst: this second catalyst then causes further chemical reactions, which changes the colour of the solution. The system is "exquisitely sensitive", Self says.

Biochemists now call the technique "enzyme amplification". When Self first described it to a young entrepreneur from the computer industry, Chris Curry, who then ran Acorn Computers, Curry remarked on the similarity with amplification in electronics. "My God," Curry told Self, "you've invented the transistor." Curry and his business partner, Hermann Hauser, had established IQ Bio just before meeting Self, and now their company had a *raison d'être*.

IQ Bio and its range of diagnostic products owe their existence to the patent of Self's technique of enzyme amplification. Larger companies are developing similar products for the biotechnology industry; they know the importance of proper patenting in this new market. William Duffey, the patent lawyer for Monsanto, an American chemicals company, describes just how important patents are to bio--technology: "Those companies in the private sector which are investing hundreds of millions of dollars in this new

science do not accept the theory that patents are unimportant. Such a concept is particularly repugnant to patent-conscious, research-intensive pharmaceuticals firms dealing in global markets with drugs which require staggering investments of time and money before ultimately yielding a commercial return. To them the patent shelter is paramount. It is quite literally their sole incentive for risk taking."

Duffey says that the average cost of developing a new drug, including failures, is about £100 million. "Without the crucial period of patent protection there would be little chance for the pioneer to break even because the generic producers and the imitators would have marched in much earlier to capture the market share at his expense through price cutting."

There seems to be an overwhelming case for patents in biotechnology, as in any other innovative field. But what exactly is a patent? Andrew Sheard, a patent lawyer specialising in biotechnology with Kilburn and Strode, a firm of patent attorneys in London, describes patents as a "bargain between an inventor, or those backing the invention, and the state. The deal is effectively this: if the innovator discloses his invention to the public in so clear and comprehensive a way that anyone can repeat his invention so as to get the benefit of it, then the state will, providing that the invention fulfils certain criteria, allow him a monopoly in the invention for a certain number of years—20 in most countries of the world."

The inventor must conform to certain criteria in order to patent an invention. The "invention" must be new, it must be truly inventive, and not just an obvious development of what is known already. The invention must be useful and the patent laws must not specifically exclude the invention in question. In the new science of molecular biology and genetic engineering, which did not exist 20 years ago, the same rules of patenting apply. Over the past 10 years, however, a number of disputes between inventors, and the patenting authorities have raised questions concerning the interpretation of the patenting rules.

The latest case occurred in July at the High Court of Justice in London. A British pharmaceuticals company, the Wellcome Foundation, questioned the patent on a genetically engineered protein awarded to Genentech, a biotechnology company in California. The protein, tissue plasminogen activator (t-PA), appears to be twice as effective as existing remedies for dissolving blood clots and so could become a very useful drug for people at risk of heart attack. The market for such a drug could run into $1 billion a year by the early 1990s. Genentech's patent gave the company the rights over all t-PA manufactured by splicing a t-PA gene into cells that could then be cultured to produce the protein in bulk. Wellcome also wanted to produce t-PA by a similar method and felt that Genentech's patent did not cover a technique that was truly novel and inventive. Wellcome therefore sued Genentech on the day the Patent Office in London granted Genentech the patent, 26 February 1986, and so the case went to the High Court.

Patent lawyers around the world watched the case of Wellcome versus Genentech carefully. They wanted to see whether the judge, Mr Justice Whitford, would treat the new techniques of biotechnology as inventive and novel purely because they are so new. In the event, Mr Justice Whitford took the view that Genentech's patent must be revoked. In his judgment, extending to 90 pages, he said: "As a claim to a product, t-PA produced by any known or hereafter discovered route in the field of recombinant-DNA technology, is too wide and is bad . . . It is a claim to an obviously desirable and potentially possible end reached by routes on which only limited guidance is given." The patent, he said, is too "broad".

This case dose not end here. Genentech said immediately after the judgment that it intends to pursue "vigorously" an appeal against Mr Justice Whitford's decision: "This patent decision relates solely to the UK," the company said, "We will continue to press our patent claims in the United States and in other jurisdictions" (*New Scientist*, 16 July 1987, p 25).

It is not unusual for patent cases such as this to drag on and on. The first patent on recombinant gene technology, based on a discovery of Stanley Cohen of Stanford University and Herbert Boyer of the University of California, San Francisco, was still the subject of dispute 10 years after Stanford first filed the patent in 1974. Cohen and Boyer developed the

What is a patent?

A PATENT must first of all be new. No other inventor must have filed a patent on the same invention, and nobody must have published the discovery before filing for a patent, although in the US there is a "grace period" of up to a year between publishing and filing a patent.

The next criterion for patenting is that an invention must involve a truly inventive step. Routine, trivial or unexpected modifications of an existing technology therefore do not count as fulfilling what patent attorneys call the "inventive step".

This is often the criterion that lawyers end up arguing about in the courts. The court then has to decide whether the invention is obvious "to someone skilled in the art". Biotechnology is such a new industry that patent lawyers often try to convince a court that something is inventive merely because the technology is so new and "unobvious". The recent court case in Britain between Genentech and Wellcome indicated that the court was not prepared to treat biotechnology any differently than to other technologies.

For a patent office to grant a patent, the invention must be industrially applicable. □

Companies line up to claim rights over the genetic map

MAPPING the position of genes in the human genome will be as arduous a task as untangling the legal rights to the knowledge that will result. In the US lawyers and scientists are now trying to decide how patent and copyright laws might apply to the products of gene mapping.

Two organisations in particular have brought the issue to a head. Collaborative Research, a biotechnology company near Boston, Massachusetts, wants to patent valuable genetic markers called restriction fragment length polymorphisms (RFLPs). Everyone posseses his or her own unique complement of RFLPs. Some are always associated with a defective or missing gene and doctors can use them to diagnose a carrier of inherited disease. Collaborative Research has found about 400 RFLPs, including a marker for cystic fibrosis.

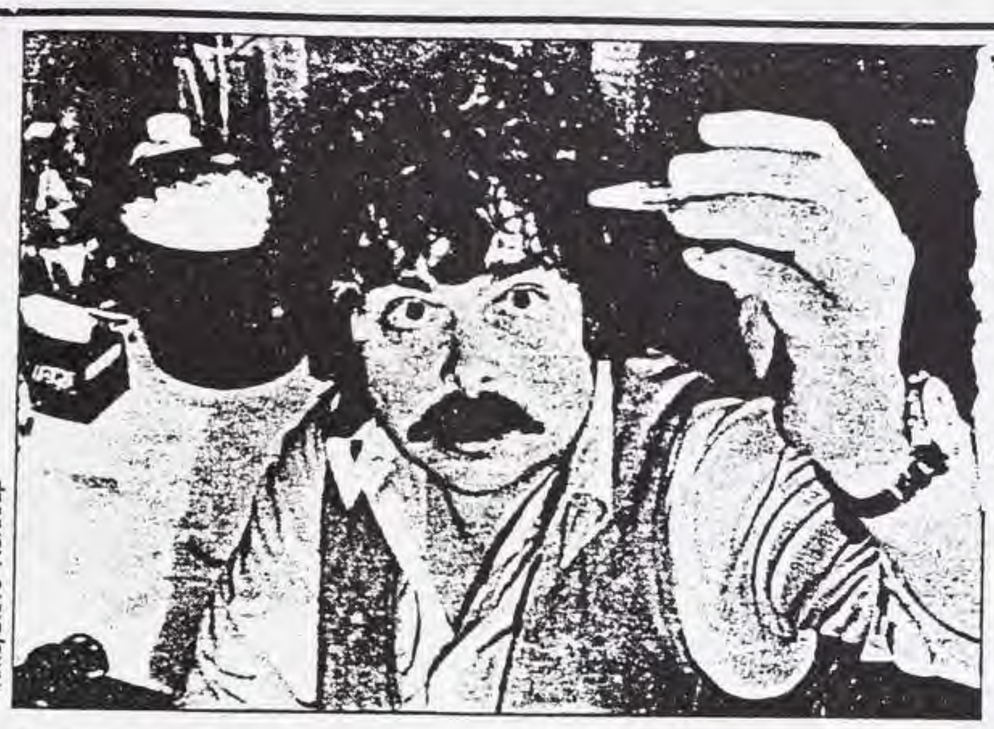
Researchers have complained that the company refuses to share its data except with a few academics who are sworn to secrecy. At a recent meeting in Washington DC, held by the US Congress's Office of Technology Assessment (OTA), Collabrative's lawyer defended the patenting of genetic sequences. "How can we communicate while trying to protect our proprietary rights?" said Bernadette Alford.

The other source of concern is Walter Gilbert, a Nobel prizewinner and founder of a new company, Genome Corporation. Gilbert says he will copyright genetic sequences just as publishers copyright words in a book. Scientists would pay to have access to his sequence data.

The US Patent and Trademark Office says that sequencing data from the human genome are patentable. Several patent applications are now pending, including one filed seven years ago by scientists associated with Collaborative Research. Advocates of patenting say that tradition allows experimental use of a patented invention as long as no commercial gain is implicit.

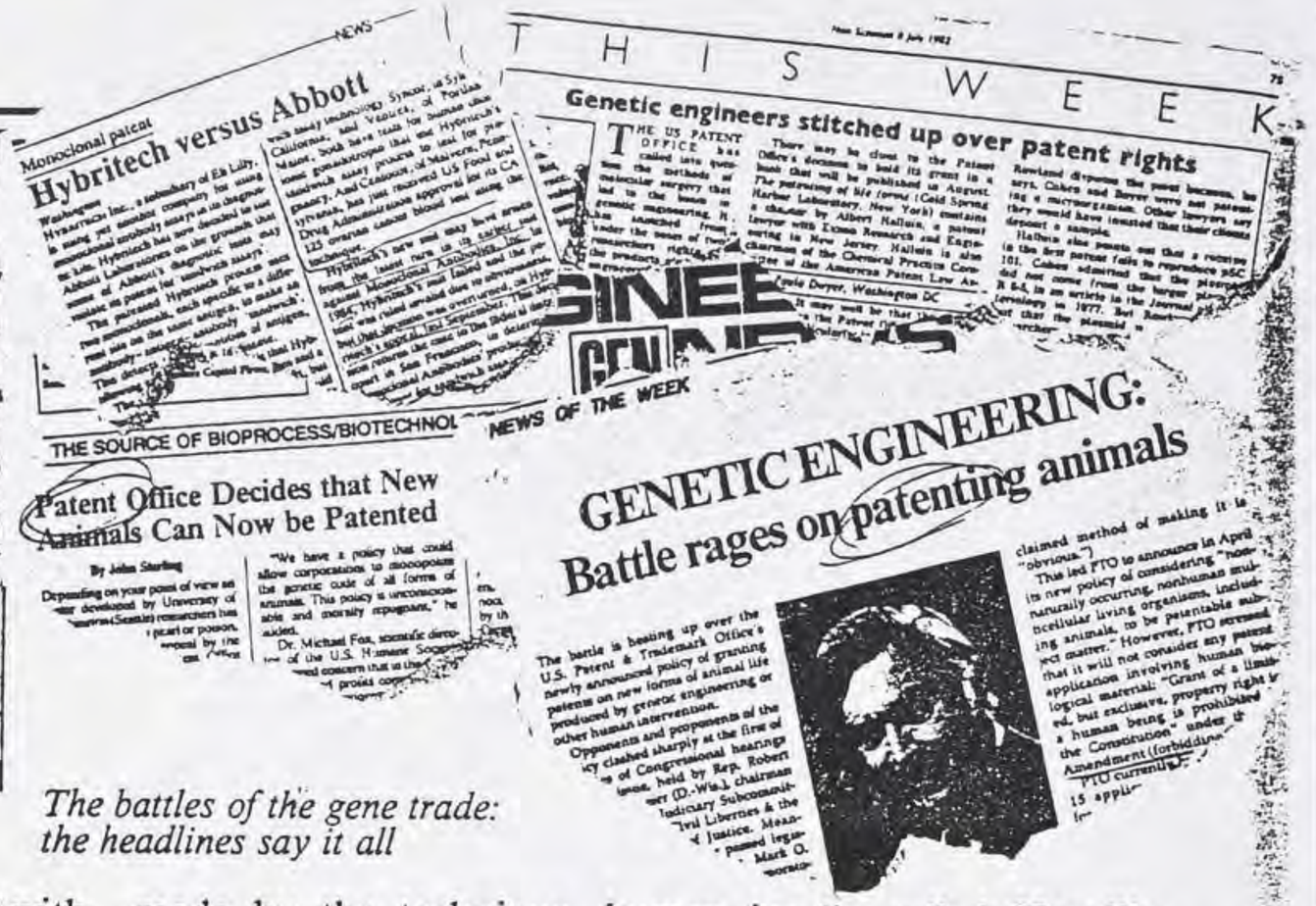
Susan Rosenfeld, a lawyer with the Association of the Bar of the City of New York, is studying copyright and genetic information: "The concept behind it is that DNA is like a computer program," which can be copyrighted, she says. Unlike patent law, however, US copyright law does not bar the commercial use of the same product if someone else creates it independently.

Christopher Joyce



Time/Steve Northrup

Herbert Boyer, one of the architects of plasmid technology



The battles of the gene trade: the headlines say it all

technique for inserting foreign DNA into a bacterial cell with the help of bacterial plasmids—circular pieces of DNA that behave like "Trojan Horses"—taking the foreign DNA into the cell under guise of it being bacterial DNA.

Stanford University, acting on behalf of both universities, filed two patents on the technique, one for the process itself and one on the products arising from the technique. Bacterial plasmids have become so commonplace in the laboratories of biotechnology companies that if the US Patent and Trademark Office approved both patents, the royalties would be worth millions of dollars. Everything seemed to run smoothly, with the patent office granting the first patent without fuss. But a couple of weeks before the patent office was due to issue the second patent, the office froze the application: it wanted Stanford to present a more convincing case for rights over the technique.

New life forms

An important part of filing a patent that involves living things is to deposit a new life form with a recognised authority. This is part of the process of describing the invention so that others can repeat it. Cohen and Boyer did not place their bacterial plasmid in a public depository, in this case the American Type Culture Collection in Maryland, which stores collections of microorganisms, until six months after they applied for a patent. In the US, as in Europe, the law says that an inventor must deposit a new organism with a recognised authority at the same time as the inventor applies for a patent. Stanford argued that the plasmid was not an organism and that other researchers did not need the plasmid to repeat the invention, so deposition was irrelevant.

Another issue that the US Patent and Trademark Office wanted to clear up was whether Cohen and Boyer's invention was published or discussed publicly more than a year before the date they filed the patent. If it was, then the patent would be invalid. This marks an important difference between American patent law and European patent law. In Europe, an inventor must not publish anything about an invention before applying for a patent. In the US, inventors are allowed a year's "grace". Unfortunately for Cohen and Boyer, a scientist, Edward Ziff, described in *New Scientist* a speech made by Boyer at a "closed" scientific conference. The article appeared on 25 October 1973, a year and 10 days before Stanford University filed for a patent. Did this article constitute a disclosure?

Stanford defended its patent successfully and, in 1984, the US Patent and Trademark Office granted the second patent to the university, which then sent letters to 100 biotechnology companies asking them to pay a licence fee in order to use the technique developed by Cohen and Boyer (*New Scientist*, 6 September 1984, p 7). At that time, the company had recouped about $3 million in royalties from licences to 66 companies. Eli Lilley was the only company selling a product made by the technique, human insulin called Humilin. Today, the university has 80 licences on the patent, each bringing in at least $10 000 a year, and 22 products are now sold that have been developed with the technique. Stanford says that it earned $1·2 million on the patent in the year 1985-86, and expects to earn about $10 million a year by 1992. Meanwhile, Cohen and Boyer have not received a penny because, in a magnanimous gesture, they waived their rights to a share in the royalties on the patent.

Stanford's patent does not apply in Europe because Cohen and Boyer published their work before filing for a patent. The year's grace in the US protected them only in the US. The lack of a similar period of grace in Europe angers many patent specialists because it appears to put European scientists at a disadvantage. The American Intellectual Property Law Association agrees that there should be a grace period in Europe: "Instead of applauding [the inventor] for making the earliest possible dissemination of information by prompt publication in a scientific journal, all to the benefit of mankind by increasing the knowledge in a particular field, we punish him by refusing to give him a patent," the association told a meeting in 1985 of the World Intellectual Property Organisation, the United Nations body concerned with international patent law.

An added frustration for European scientists is that although the US adopts a "first-to-invent principle" in the US, whereas it is the "first-to-file principle" in Europe, inventions outside the US do not count. In other words European scientists still have to file for a patent in the US, or Europe, before anyone else in order to have the patent granted in the US. There are signs, however, that this may soon change. In March of this year, Donald Quigg, the Assistant Secretary and Commissioner of Patents in the US, said: "The United States has offered the possibility of dropping its 150-year practice of granting a patent to the first inventor of an invention instead of granting it to the first person filing an application for patent protection. Moving to a first-person-to-file practice would put foreign inventors on the same footing as US inventors with respect to obtaining patent protection in the United States."

One of the most famous patent disputes in recent history involved just such a contest between scientists in Europe and America. Luc Montagnier of the Pasteur Institute in Paris filed an application for a patent for a blood test for antibodies to the human immunodeficiency virus, the virus that causes AIDS. Montagnier based his application on his discovery of the virus, before his counterpart in the US, Robert Gallo of the National Cancer Institute in Maryland. Even so, the US Patent and Trademark Office gave Gallo the rights to the patent. After the Pasteur Institute appealed to the US Claims Court, the patent office made Montagnier the "senior party" and put the onus on Gallo to prove that he invented the test first. In the end, they settled the dispute out of court.

Further disputes over patents are brewing now that the US

Peter Gardiner

Montagnier (left) and Gallo: once the centre of a patent row

has decided that it is possible to patent "multicellular animals". On 3 April 1987, the US Board of Patent Appeals ruled that scientists from the University of Washington, Seattle, who genetically engineered oysters to give them more than one set of chromosomes, called polyploidy, can patent the animals. These oysters grow larger and tastier than normal oysters; and, being sterile, do not go through the normal sexual cycle, during which time they are inedible.

Already, the environmental activist Jeremy Rifkin says that he is looking for ways of fighting the patenting of higher animals on the grounds that it is morally repugnant for companies to have rights to the genetic code of animals, Rifkin has formed a loose coalition with farmers' organisations and religious groups in the US to fight the decision. He has enlisted the support of Arie Brouer, the general secretary of the National Council of Churches in the US, who said: "The gift of life from God, in all its forms and species, should not be regarded solely as if it were a chemical product, subject to genetic alteration and patentable for economic benefits." Patenting life is now a moral issue.

The US's decision to patent multicellular animals stems from a ruling in 1980 which made it possible for the first time for scientists in the US to patent microorganisms. This case concerned a Pseudomonas bacterium that had been genetically altered to include two plasmids that enabled the bacterium to "eat" oil slicks. This set a precedent: biotechnololgy could now patent not only the altered genes, but the organisms that possess these altered genes. Going from microorganism, to plant, to multicellular animal is a logical extension of the process.

In Europe, the European Patent Convention states that governments cannot grant patents on "plant or animal varieties" (except for microorganisms). Nevertheless, lawyers in Europe, who are always keen to argue over words, now think that the convention may apply to "animal varieties", but not to "animals". Biotechnology companies will want to test this in the courts now that the US has granted a patent on a higher animal. Meanwhile, in the US, people such as Rifkin argue that patenting oysters is a short step to somebody trying to patent the highest animal of all, *Homo sapiens*. What is to stop biotechnology companies from trying such a thing now that *in vitro* fertilisation is so common and profitable?

According to Donald Quigg, the US Constitution prohibits patenting of humans: "A claim directed to or including within its scope a human being will not be considered to be patentable subject matter... The grant of a limited, but exclusive property right in a human being is prohibited by the Constitution." The part of the US Constitution that Quigg says will prevent biotechnology companies from patenting human beings is Article 13, passed in 1865 to abolish slavery. The question is whether the article, which applies to humans, also applies to their embryos. Could the next patent row erupt over the right to own a new type of test-tube baby? □