Biotechnology

Looking ahead

Bethesda Research Laboratories (BRL), the Maryland company that shook the US biotechnology industry by announcing that cash-flow problems had made it necessary to make redundant more than a third of its 450 staff, seems — at least temporarily — to be out of the woods.

Company officials are confidently predicting that, despite the setback to its expansion plans, BRL will double this year the $10 million sales which it achieved in 1981, thus maintaining the pattern of geometrical growth that the company has managed since its foundation in 1976. Comparable sales increases are being talked about for 1983 and 1984. Private investors in BRL have endorsed the line being pushed by Mr Stephen Turner, BRL's founder and president, that "leaner is fitter" — the argument, ironically, that is being used by President Reagan's science adviser, Dr Jay Keyworth, to justify cuts in federal support for research and development.

The company has just announced that it has been able to raise an extra $5 million from its original investors, many of whom are based in Europe. According to Mr Turner, this should be enough to provide a stable base for a steady expansion of its product range, originally focused on restriction enzymes but subsequently expanded to include other biological products such as monoclonal antibodies as well as diagnostic screening kits and a nucleic acid analyser.

Mr Turner blames the company's recent difficulties on the rapid drying up of venture capital in the United States in the past six months. Last year, anticipating that it would have little difficulty in raising an anticipated $40 million through a public stock offering, the company laid the groundwork for an ambitious expansion programme, dividing its research products division into separate molecular biology and biological chemistry sections, and significantly increasing its research staff.

In recent months, however, a declining inflation rate and new tax incentives have taken some of the glamour out of venture capital dealings as an alternative to other, more traditional forms of investment. In addition, much of the available venture capital is said to have been soaked up by some of the early public offerings — such as that launched by Cetus a year ago, which managed to raise over $100 million in the largest new issue ever experienced by Wall Street.

As a result, many of the small biotechnology companies launched in the past two or three years are experiencing severe difficulties in raising the capital they need to keep going, a situation that Mr Turner believes could last for at least another year. Several industry analysts expect that up to one half of the companies could disappear within the next few years, some being absorbed into larger corporations, others filing for bankruptcy or actively seeking mergers. BRL claims to be in a stronger situation than some of the other companies since it is already selling products on the market.

"The days of over-expectation and pure speculation are behind us and the time has come to fine-tune operations and get down to the business of running a business," says Mr Turner. "That's what we have done at BRL."

Similar sentiments are expressed by Frederick R. Adler, a New York lawyer who has helped to set up a number of high technology companies in the computer field, and who has recently been appointed to BRL's board of directors. "The computer industry taught us that business can successfully serve science. We're now translating that lesson to biotechnology", he says.

David Dickson

Rorvik versus Bromhall

Washington

Hailed in 1978 on the book jacket as "the scientific breakthrough of the century", David Rorvik's book *In His Image: The cloning of a Human* was declared by a Philadelphia judge the same year to be "a hoax and a fraud". Rorvik returns to a Philadelphia court next week when Dr Derek Bromhall from the University of Oxford, who claims that his research was misused, will sue for damages against Rorvik and his publisher Lippincott and Co. (now owned by Harper and Row).

Mr Allan Friedman, Bromhall's lawyer and an associate of the firm Raynes, McCarty, Binder and Mundy, claims that Lippincott showed "reckless disregard for publishing ethics". He says that his client's case turns on two issues. The first is the claim that Rorvik invaded Dr Bromhall's privacy by quoting his cloning techniques in the text and by mentioning his name in the book's footnotes as a "personal communication" without approval. The second claim is that Mr Rorvik fraudulently acquired an abstract of Dr Bromhall's doctoral thesis by representing himself as a scientific researcher preparing a project on mammalian cloning.

Mr Rorvik's attorney, Samuel Klein of Kohn, Savett, Marian and Graf, claims that Bromhall's information did not include "novel and unique" concepts, that the thesis was already on microfilm and that a summary had already appeared in the scientific literature (*Nature* **258**, 719; 1975). Furthermore, he adds, there has never been disagreement over the fact that all references to Bromhall's work were fully accurate.

Mr Klein also plans to argue that in the single letter written by Mr Rorvik to Dr Bromhall, his client identified himself as a freelance journalist and that Dr Bromhall's presentation of his nine-page abstract was unsolicited. There was no oral communication between Rorvik and Bromhall at the time of this correspondence.

The trial promises to become heated, for neither party plans to settle out of court. Mr Klein also says he will question Dr Bromhall's wish to keep his distance from the book in light of the fact that Dr Bromhall "voluntarily associated himself" with the film *Boys of Brazil*, which portrayed the cloning of multiple Hitlers. But Friedman says that Bromhall's voluntary association with a film presented as fiction is very different from an involuntary association with a book whose author claimed it to be non-fiction.

The trial is expected to last several weeks and many scientists will make appearances for both sides.

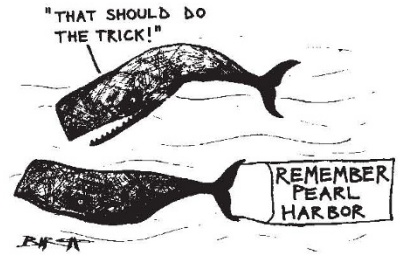
Michael D. Stein

Sperm whale catch limits

No decision

A head-on clash between conservationist countries and Japan, the main whaling nation, was averted on Thursday when a special meeting in the United Kingdom of the International Whaling Commission (IWC) agreed to defer a decision on sperm whale catch limits until the annual general meeting in July. The conservationist countries abandoned their attempt to impose a total ban on sperm whaling after the scientific committee failed to produce a conclusive report.

Catch limits are usually set at the annual meeting of IWC. Last week's special meeting was convened because the scientific committee had not been able to offer unequivocal advice to the July 1981 meeting. Earlier this year, 32 scientists from 12 countries met in Cambridge to analyse sperm whale stocks. Computer tests were run using two rival models, one backed by the Japanese, the other developed by the International Institute of Environment and Development (IIED).



All except the Japanese scientists at last week's meeting supported the IIED model. However, the committee failed to offer any definite advice on catch limits. According to IWC criteria that stocks should be protected when they fall below ten per cent of maximum sustained yield (the maximum number of whales that can be harvested on an infinite basis without a decline in population), the IIED analysis indicated

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that males should be totally protected, but a catch of 831 females could be permitted. But the analysis also indicated that even with a zero catch the stocks would continue to decline for several years. The biological reason for this is that sperm whales are polygynous so that the past removal of breeding males, favoured by the whalers because of their large size, has resulted in a decline in the pregnancy rate of the stock.

Therefore, the Japanese argue that their current quota of 890 would make little difference to the sperm whale population, particularly since the number of exploitable whales was estimated by the IIED team to be around 200,000. But conservationist countries are keen to see a zero quota, pointing to the predicted decline in population with no fishing at all.

The inability of the special meeting to come up with catch limits was not so much the result of scientific equivocation as a political move to produce a compromise. The conservationist countries feared that had they enforced a quota unacceptable to the whaling nations, Japan would have exercised its right to object and both the procedure for cooperation and the whole credibility of IWC would have been seriously damaged.

The annual meeting of IWC in July may be faced with pressure for a ban from the conservationist countries, which will be in the majority. If Japan refuses to compromise and registers an objection, the conservationists would then have to try to apply the ultimate sanction — a US ban on Japanese fishing in its waters.

Jane Wynn

Environmental law

Count the risks

Washington

A subcommittee of the House of Representatives has taken a first step towards building scientific risk analysis into the federal government's regulations on environmental and safety hazards. A bill passed by a subcommittee of the Science and Technology Committee would establish a new programme under the White House's Office of Science and Technology Policy (OSTP) "to improve and facilitate" the use of risk analysis in regulatory decisions. The bill will now go to the full committee, whose chairman, Mr Don Fuqua of Florida, supports it.

The Reagan Administration is less welcoming, feeling that the goals of the proposed law could more simply be attained by rationalizing new and existing regulations. But according to OSTP, the Administration will probably find the bill "acceptable" as long as certain amendments are made.

Various members of the Administration argued in their testimony to the subcommittee that they have already taken steps to introduce a more "rational" approach to regulation. Last February, for example, President Reagan put out an executive order requiring all proposed new regulations to be accompanied by a cost–benefit analysis demonstrating that they represented the most cost-effective way of reaching their declared goals. The White House has also announced that the Inter-agency Regulatory Liaison Group, established under President Carter to coordinate actions by different agencies, would be reconstituted as a new committee under the chairmanship of the President's Science Advisor, Dr Jay Keyworth, with the task of improving the scientific basis of regulatory decision-making.

Such changes have not satisfied the members of the House committee. Thus the new bill would assign to OSTP the specific role of establishing a mechanism for coordinating the risk analysis programmes among the participating federal agencies, primarily the Consumer Product Safety Commission, the Food and Drug Administration, the Environmental Protection Agency and the Department of Labor's Occupational Safety and Health Administration. And the National Science Foundation would be required to draw up a programme of research to make the use of risk analysis more effective. In addition, the various federal agencies would each be required to undertake a "prototypical risk analysis study".

Various powerful lobby groups, representing for example the agricultural or the nuclear power industry, have long been pushing for revisions to regulatory decision-making along these lines. The bill is therefore unlikely to lack supporters if it is sent by the full committee to the floor of the House of Representatives. But it is also likely to generate substantial opposition. Many Democrats, particularly those with close links with the labour unions, see attempts to "rationalize" regulation as a smokescreen to legitimize less stringent health and safety controls.

The Administration is likely to stand aside from any such debates. Although it claims to have made significant progress behind the scenes in eliminating unnecessary or redundant regulations, it is becoming wary of taking highly-publicized actions that might be interpreted as "anti-regulatory" given the apparent continued public support for strict environmental and health and safety controls — and the importance of the congressional elections later this year.

In a related effort to reduce the impact of federal regulations, the US Senate last week approved a proposed new bill which would give Congress the power to overturn regulations being proposed by any federal agency. The bill is being resisted by the Reagan Administration, which sees it as an attempt by Congress to place limits on the flexibility of the executive branch. It has also received strong opposition from environmental and labour groups, who argue that it would provide vast scope for individual companies and industries to lobby Congress to prevent certain regulations from coming into effect. Supporters of the new ruling, however, argue that regulatory agencies frequently exceed their congressional mandates, and that checks are now needed to limit their autonomy.

David Dickson

Join the queue for monoclonals

St Louis

The Monsanto Corporation of St Louis, Missouri, has made a multi-million dollar agreement with nearby Washington University to produce monoclonal antibodies, the second such agreement the university has made with the chemical industry in the past six months.

Monsanto says it has agreed to put $1.8 million into research projects at the university during the next three years. No contract has so far been signed between the university and Monsanto but the deal is expected to be similar to that made with Mallinckrodt Inc., also of St Louis. Last September, Mallinckrodt committed $3.9 million to monoclonal antibody research at Washington University, the largest industry agreement ever made with an American university for this type of research.

Mallinckrodt's three-year commitment is a major one for the company, which is economizing in other areas. But despite uncertainties about patents, monoclonal antibodies hold out enormous commercial promise. Dr Thomas O. Oesterling, Mallinckrodt's vice-president for research and development, says his company's primary interest is in *in vitro* diagnosis, where monoclonal antibodies allow much improved standardization in diagnostic kits, but it is looking at other uses. "A monoclonal antibody could carry an isotope for imaging to a target cell for *in vivo* diagnosis", and from there it is "a logical extension to therapy".

The contract between Mallinckrodt and Washington University provides for the university to hold the patents for useful products of the joint venture, but for Mallinckrodt to have the right to license them. The university's share of royalties is dependent on the success of the product on the market.

One aspect that is covered by the arrangement with Mallinckrodt is the right of publication. Individual investigators do not profit personally from an invention, although some of the royalties will be ploughed back into research in the individual's laboratory, but the individual does retain the right to publication, with the proviso that the company can screen for patentable material.

Karen Freeman

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