Scientists debate safety of research on *E coli* strain

A STRONG bid is being made to exempt a large body of recombinant DNA experiments using a disabled strain of the bacterium *Escherichia coli* from the research guidelines laid down by the National Institutes of Health.

Exemption has been proposed to the NIH's Recombinant DNA Advisory Committee (RAC) by Dr Wallace Rowe, head of the Laboratory of Viral Diseases at the National Institute of Allergy and Infectious Diseases, and Dr Allan Campbell, Professor of Biology at Stanford University.

The two scientists base their recommendation on new information which has recently emerged on the potential risks of recombinant DNA research. This evidence, they claim, makes it unreasonable to apply restrictions on most experiments involving the cloning of plasmids inside the 'disabled' *E. coli* K-12 strain, over and above what would normally be considered as safe laboratory practice.

Other members of the committee meeting in Washington last week, however, expressed concern at the implications of such a move. They suggested that, given the many uncertainties still involved, a total exemption from current controls would be premature. However, the committee agreed to set up a working party to study the available data on the safety of experiments using the K-12 strain and suggested that it should consider a proposal that all such experiments are carried out under the minimal P1 physical containment conditions.

In a statement to the committee, Dr Rowe said that information pointing to the safety of K-12 host vector systems included extensive analysis of the biology of the organism and molecular segments cloned inside it, the negative results of monitoring laboratory personnel for acquisition of the bacterium and its plasmids and the results of risk experiments involving the cloning of polyoma virus DNA which he and other research workers had carried out at Fort Detrick last year.

"The basic message from every one of these experiments is that there is no cause for concern about recombinant DNA research with K-12. I do not know of a single piece of new data that has indicated that K-12 recombinant DNA research could generate a biohazard", Dr Rowe said.

For a recombinant organism to become a health hazard, it had to escape from a laboratory, survive outside the laboratory environment, establish itself in some ecological niche, and finally have some detrimental effect on a higher organism. "Since the original guidelines, data and information have accumulated that indicate that each of these steps is so highly improbable with the K-12 cloning system that each step alone gives sufficient assurance of safety, much less the combination of all four."

Dr Rowe's interpretation of the safety of the K-12 system, however, is not shared by all scientists. In a letter to the RAC commenting on the proposal to exempt most of the experiments using this strain from the guidelines, Dr Roy Curtiss, Professor of Microbiology at the University of Alabama in Birmingham, who has done much work on the development of enfeebled organisms, said he felt such a move would be premature.

In particular, said Dr Curtiss, although it was generally agreed at the Falmouth conference of 1977 that one could not convert K-12 into an epidemic pathogen, a number of studies had since indicated that "the overall probability for transmission of recombinant DNA from *E. coli* K-12 hosts and vectors are higher than I or others believed."

Some of these observations included the excretion of EK1 hosts by human subjects several weeks after receiving a dose, the survival of the disabled λ1776 strain in the human gut for up to four days, and the selective survival of EK1 hosts in individual mice and rats.

"I surmise that if the participants at the Falmouth conference had been aware of these data, more consideration would have been given to possible consequences of transmission of recombinant DNA to indigenous microorganisms of various natural environments," he said.

In addition to the scientific arguments about the safety of such experiments—other scientists, in particular Dr Jonathan King of MIT and Dr Jon Beckwith of Harward Medical School have raised the possibility of biologically active recombinant organisms inducing an auto-immune response from the human body—the committee's discussions also brought in wider considerations.

Dr Rowe has made no secret of his feelings about the guidelines, calling them "wastful, expensive, inefficient, inflexible and inhibitory". The perception or risk need not be zero before restrictions were lifted, he said. "We have to do a cost-benefit analysis. If the guidelines are harming research, which I believe they are, then this has to be entered into the equation". Dr Campbell expressed similar sentiments in support of the proposed exemption. "In my judgement the NIH guidelines as presently written and administered do more harm than good. We should now be examining the guidelines section by section for the hazards that exist."

However, other members of the committee expressed the view that total exemption for a large group of experiments was inadvisable, since risk assessment experiments had not gone far enough to demonstrate that dangers did not exist, while laboratories could not be relied upon to adopt safe procedures (such as a ban on mouth pipetting). "Society is facing a mounting load of hazards, and the RAC is in the vanguard of responsible research in general. You cannot legislate morality, but you can provide a framework for responsibility", said Dr Richard Novick, chairman of plasmid biology at the Public Health Research Institute in New York.

After considerable debate, it was decided to set up a working group to synthesise the data both supporting and not supporting the proposal made by Dr Rowe and Dr Campbell. It was also agreed that the proposal should be modified so that, rather than considering a total exemption for this class of experiments, the committee should consider reducing them to requiring P1 containment levels, as well as registration with local institutional biohazard committees. □

DNA advisers recommend the same controls for industry as universities

RECOMBINANT DNA research carried out by private industry should be legally required to observe the same guidelines as those in force for federally-funded research in university laboratories, the US National Institutes of Health's Recombinant DNA Advisory Committee (RAC) recommended last week.

Members of the committee, which is responsible for advising the director of NIH on recombinant DNA issues, expressed concern that private companies can register their experiments voluntarily with NIH. (Although many companies are now engaged in such research, only one institution—the Roche Institute of Molecular Biology—has yet asked to be registered.)

"I do not see any justification for maintaining that a system of voluntary compliance that was not deemed

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adequate for the scientific community should be adequate for the private sector. Why should you treat the private sector differently?" Dr Sheldon Krimsky, acting director of the programme in Urban, Social and Environmental Policy at Tufts Medical School and a member of the RAC, asked the committee last week.

The committee voted nine to six to support mandatory compliance by non-NIH institutions with the NIH guidelines covering recombinant DNA research. Six members of the committee abstained—NIH Director Dr Donald Frederickson, when appointing individuals to the committee, had made it clear that he expected them to abstain from votes where they might have a conflict of interest (for example, where a scientist was a consultant or a stockholder in a company that might be affected by a RAC decision).

The committee also decided to set up a working party to study containment requirements and related issues for large-scale experiments which would involve both committee members and outside consultants, possibly including trade union representatives. Mr Peter Libassi, General Counsel at the Department of Health, Education and Welfare, met public interest and industry representatives last week to discuss new proposals which the NIH has put forward on how the RAC could guarantee the confidentiality of information which companies would be required to provide in seeking approval for certain types of experiment.

Mr Libassi told both groups that the DHEW will shortly publish in the *Federal Register* the details of the ways in which NIH will register companies on the basis of voluntary compliance with the guidelines. Industry is keen to support such a procedure as an alternative to the regulation of research by the Food and Drug Administration.

However, the public interest groups

"I'm trying to evolve some guidelines that are as weak as we hope our bacteria are!"

at the meeting made it clear that, given the experience of voluntary requirements in other fields such as toxic waste disposal, they felt it unlikely that voluntary compliance would work adequately. Mr Libassi was told that these groups supported legally-backed requirements as recommended by the RAC.

Meanwhile in California, where a number of small companies are now moving rapidly towards large-scale experiments of possible industrial applications of recombinant DNA research, various state legislators, environmentalists and labour representatives have expressed concern over the possible health hazards to workers. The Chairman of the San Mateo Central Labour Council has written to members of the RAC claiming that current federal efforts that rely on voluntary compliance by industry "are no longer adequate to protect the health and safety of recombinant DNA laboratory workers and other Bay Area cities."

Similarly state senator Barry Keene has urged the RAC to deal directly with the "major policy issues posed by increasing industrial development of this new technology". He wants the state to set up a panel of scientists and lay people to study the issue in California. **David Dickson**

Industry spends more on research

Private companies in the US are expecting the total amount of money spent on research and development to be about 13% higher in 1979 than in 1978, according to a survey published last week in New York by McGraw-Hill Publications. Replies from over 500 companies indicated that the total expenditure on R and D would reach $40,000 million, $4,600 million more than 1978. Allowing for inflation, this means a real increase of 4.6%.

However the amount of money spent on R and D has declined as a proportion of manufacturing sales, from a peak of 3% in the early 1960s to just over 2%. Over a fifth of research was directly involved with energy and pollution.

Meanwhile, the National Science Foundation has issued figures showing that the proportion of R and D funding financed by the federal government has fallen below 50% of the total national R and D budget for the first time since full statistics were collected in 1953. The survey suggests this is partly because of cuts in research spending on space and defence and an increased emphasis on civilian R and D programmes. The survey also says that job prospects for scientists and engineers are expected to expand in 1980, particularly in industry. □

Northern hemisphere observatory agreement signed in Canary Islands

LAST weekend, Sweden, Denmark and the UK finally signed an intergovernmental agreement with Spain to cooperate over the building of a major observatory at La Palma in the Canary Islands. When it is fully operational (in 1984 at the earliest), the observatory will provide British astronomers with facilities for observing the northern sky equivalent to those at the Anglo-Australian telescope in the southern hemisphere. According to Professor F. Graham Smith, director of the Royal Greenwich Observatory, telescopes at the new observatory could compete in terms of image quality with larger telescopes in the US and Soviet Union, because of the particularly fine seeing conditions at the site.

The UK has been planning to build a 'northern hemisphere observatory' for some years. The Canary Island site was decided on, but progress has been slow because of the long time taken by the Spanish Council of Ministers to put its signature to the intergovernmental agreement. The agreement allows for cooperation in astrophysics and states that Spain will provide the site and facilities in return for some of the telescopes' time and training for Spanish astronomers.

Of the four participating countries, the UK is making the biggest contribution. It is building a new 1m diameter telescope and is planning to move the 2.5m Isaac Newton telescope (INT) from the RGO to the Canaries site. The latter has already been dismantled so that it can be refurbished before shipment next year. The UK Science Research Council, the body involved in the setting up and funding of the observatory, hopes to place a contract for building the domes to house the telescopes this summer.

The UK also has plans for a 4.2m diameter telescope, the largest likely to be built on the site. Although this is only in the design phase and has not yet received the official go-ahead, an order for its mirror blank has already been placed in the US. Even if approval and funds for the whole telescope were given now, however, it would be at least 1984 before it could come into operation. The total cost of the new observatory to the UK, according to Professor Smith, could be about £2.5 million for the 1m telescope, £8 million for moving and refurbishing the INT and in excess of £10 million for the 4.2m telescope.

Sweden's and Denmark's contributions will not be so great. Sweden is planning on transferring, almost immediately, a 16m-high solar tower and a 60cm diameter stellar Cassegrain telescope

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