Cyclamates ban

Carcinogenicity claim questioned

Washington

THE safety of cyclamates, the artificial sweeteners, is again to be reassessed, this time by the US National Research Council. This turn of events has been prompted by a new study by the Cancer Assessment Committee of the Food and Drug Administration (FDA) which has found "very little credible data" to implicate cyclamates as carcinogens. The study report is also critical of the decision, in 1980, by former FDA Commissioner Dr Gere Goyan refusing an application to allow cyclamates back on the US market.

Since cyclamates were banned in 1969 on the suspicion that they might cause bladder cancer, FDA has been asked repeatedly by Abbott Laboratories Inc., the manufacturers, to lift the ban. In 1980, Goyan refused such an application on the grounds that studies with experimental animals had shown increased numbers of lung, liver, bladder and lymph tumours after the administration of cyclamates. Goyan also cited six cytogenetic studies showing increased numbers of chromosome aberrations.

FDA now questions not only the quality of the data cited in Goyan's judgement but also his interpretation of it. The cancer assessment committee complains that Goyan lumped together tumours at different sites so as to yield the appearance of statistical significance. The report also describes as "extremely misleading" his argument that if statistical analysis should suggest that the probability of a set of data representing the effects of an experimental treatment may have arisen by chance should be calculated as, say, 0.2, it would be fair to infer an 80 per cent probability that treatment and effects were causally related.

The committee also complains about Goyan's "uncritical" use of historical control data. FDA now says that data from different laboratories were used to control experimental data without allowing for differences between the spontaneous occurrence of tumours and differences in pathological procedures at the laboratories concerned. One study cited in Goyan's judgement is discounted because the results are "not a credible dose-response" and another, carried out at the Fondation Curie in Paris, because an on-site investigation found the quality control to be inadequate.

Goyan himself is unrepentant. He acknowledges that his 1980 decision was conservative but says he still feels that Abbott Laboratories had not discharged their burden of proof and that, if errors are to be made in matters of public health, they should be on the side of caution. Goyan says also that he is "peeved" that FDA had not informed him of the questions being asked about his judgement. Goyan stresses that the mutagenicity data, which have not

been re-examined, would themselves have been sufficient to prevent a relicensing of cyclamates.

Goyan's judgement is supported by Dr Marvin Legator, an FDA scientist during the Carter Administration. Legator says there are no new data to alter the position since then. He points out that new understanding of tumour initiation argues for rather than against the combination of incidences from different sites. The argument that studies should be discounted because they fail to show a credible dose-response curve is, he says, "bunk": many carcinogens produce plateaus or peaked curves in crude tests. Legator also argues that manufacturers have failed to provide basic data on metabolism of cyclamates, which varies markedly between individuals and at different times of day. It is not enough, he says, simply to fail to demonstrate unequivocally raised incidence due to cyclamate and its primary metabolite cyclohexylamine; the metabolic pathway must be understood in its entirety.

The National Research Council launched its arbitration between the new and the old FDA last week with an extraordinary public hearing, a cross between a scientific meeting, a public protest and an evangelical conversion drive. Most of the witnesses enthusiastically supported the new FDA review of Goyan's decision, but there was also some fear that the research council would be manipulated if it ruled only on carcinogenicity and failed to examine evidence for chromosomal damage and possible teratogenic effects. The chairman of the special panel appointed by the National Research Council Dr Richard Havel, said that his panel possessed the expertise to examine such data but gave no commitment to tackle the question explicitly.

One of Abbott's supporters in the drive to get cyclamates back on the market in the United States is the Calorie Control Council, which wants would-be dieters to have the choice of as many artificial sweeteners as possible: the argument here is that synergism between sweeteners means that by using combinations it is possible to reduce intakes of any single compound. The director of the council gave a rousing speech pleading for the return of this "very useful" compound.

Meanwhile, many FDA scientists feel that cyclamates, if they are carcinogenic, are certainly much less so than saccharin. All the available epidemiological evidence argues against a carcinogenic effect for cyclamates. On the other hand, many are convinced that there will eventually have to be a ban on saccharin. The newer artificial sweetener, aspartame, has a clean bill of health so far, but cannot be used in cooking or food products intended to be stored for long periods.

Tim Beardsley

Materials science

Academy backs synchrotron

Washington

WHEN presidential science adviser George Keyworth tried last year to secure funding for a National Center for Advanced Materials at Lawrence Berkeley Laboratory in California (see *Nature* 301, 456 and 302, 645; 1983), he was met with a hail of protests from materials scientists and Congress for having short-circuited the proper channels of peer review. Partly in response, Keyworth's Office of Science and Technology Policy commissioned the National Academy of Sciences to produce a certified, peer-reviewed list of priorities for major materials science facilities; that

Priorities for new facilities

1. 6 GeV synchrotron	\$160 million
2. Steady state neutron source	\$260 million
3. 1-2 GeV synchrotron	\$ 70 million
4. High intensity pulsed neutron source	\$330 million

Priorities for upgrading existing facilities

1. Modifications to existing neutron sources at Brookhaven and National Bureau of Standards to exploit "cold" neutrons \$50-70 million
2. Incorporation where possible of insertion devices in existing synchrotron facilities (six facilities in all) \$20 million
3. Construction of an experiment hall and purchase of new instruments at the Los Alamos pulsed neutron source \$15 million
4. Improvements to the National Magnet Laboratory \$5 million
5. Development and installation of enriched targets for pulsed neutron sources, doubling the available neutron flux \$2-5 million

report* confirms what critics said at the time: there are more important things to do than build the synchrotron advanced light source that was to have been a major component of the Berkeley centre.

The good news for Keyworth is that now, armed with the academy report, he should face little opposition in pressing his materials science initiative — that is, so long as he modifies it to conform with the report's recommendations.

The 20-member academy committee that produced the report, after a reportedly gruelling effort to reach a consensus, gave its strongest endorsement to a new 6 GeV synchrotron radiation facility, estimated to cost \$160 million. This new generation synchrotron would, according to the committee, open up major new research

*Major Facilities for Materials Research and Related Disciplines, National Academy Press, Washington, DC, 1984.

areas by providing hard X-ray radiation at an intensity orders of magnitude greater than is now achievable. In particular, such a source could be used to detect elements in parts per million concentration and to identify their precise geometrical location in a molecule. One important application is in the discovery of geometric details of the active sites of catalysts and enzymes.

The 6 GeV synchrotron would be designed to take maximum advantage of the new "insertion devices" that can greatly boost the intensity of synchrotron radiation. Existing machines were designed and largely completed before the value of insertion devices was fully appreciated.

The committee's second-priority recommendation was for the construction of an advanced, steady-state neutron source that would provide perhaps ten times the intensity of present machines. Neutrons provide a unique probe of condensed matter by interacting weakly with atomic nuclei; neutron scattering has been used for example to determine the structure of magnetic superconductors and the spatial organization of macromolecules. US facilities are in the "dark ages" according to one committee member; by the mid-1990s, the earliest date

at which a new facility could be on-line, existing facilities in the United States will be nearly 30 years old.

The third-ranked priority is a synchrotron along the lines of the proposed advanced light source. This 1–2 GeV machine would be optimal for producing vacuum ultraviolet and soft X-ray radiation, of particular value in chemical physics and electron spectroscopy. Technological factors allow for radiation from such a machine to have a high coherence as well, favouring imaging applications such as microscopy and holography. (Although the administration has secured funding for the Berkeley centre — now known as the Center for Advanced Materials, without the prefix "National" — a decision on construction of the advanced light source was deferred.)

The committee also made a strong recommendation for upgrading existing facilities and for more money for small materials research programmes.

At least some of the committee's recommendations are expected to be incorporated into the fiscal year 1986 budget request now being formulated. It will be released by the President in January.

Stephen Budiansky

Computers

IBM in Europe

Brussels

Two giant US companies, IBM and ITT, are to participate in the European Community's Esprit programme. The avowed aim of this strategic programme in information technology research is to help European companies to catch up with the US and Japanese penetration of the European home market and the world at large.

The announcement comes in the same week as the results of an investigation by the Commission of an alleged abuse by IBM of its dominant position in the European computer market.

An EEC spokesman was quick to dispel any idea of a trade-off between the two events. In the Esprit programme, IBM and ITT will participate through their European branches and will share with a number of other companies the results obtained.

More than 440 companies and universities will be collaborating in the first part of the main Esprit programme; an average of four companies (but sometimes as many as ten) will join in each project. About 200 million ECU (European Currency Units) or about £120 million has been put aside for the projects agreed to this year.

In the long-running IBM anti-cartel case, the Commission has reached a no-winners compromise with IBM. The Community wanted IBM to announce the technical details of new products as soon as they were advertised, to enable smaller companies to make compatible equipment. IBM has now agreed that such technical information will be released within four months of a new product being announced.

David Price

US manpower

Shortages of specialists foreseen

Washington

A SHORTAGE of aeronautical engineers and computer specialists in the United States by the year 1987 but large surpluses of life scientists are predicted in a report published this week by the National Science Foundation (NSF).

NSF is a respected name in the difficult field of manpower planning and its figures are likely to be seized upon by a variety of special interest groups during financial planning exercises this fall. The study explicitly addresses the manpower shortages likely to follow from the current planned increase in defence expenditure of 45 per cent in real terms over the period 1982–1987.

The period covered is from 1982 to 1987, and a variety of assumptions about economic growth and military spending are considered. The main results are little affected by the assumptions, however, and show clearly that a serious shortage of specialized engineers — thought by many to have been overcome in the past year or so — is still in prospect. The new analysis suggests that it will be possible to fill vacancies by retraining engineers and scientists from other disciplines, but that this will require serious additional expense and impede progress through productivity and quality losses. NSF expresses particular concern that a large switch in supply could lead to students forgoing advanced degrees to capitalize on job opportunities, with consequent difficulties for university recruitment.

While growth of jobs in engineering is expected to continue apace, led by electrical and electronic engineering, growth of employment opportunities in science is expected to slow down markedly from the 8.7 per cent annual average between 1977 and 1982 to only 3 to 4 per cent per year. Growth will be most rapid for computer systems analysts and social scientists, including psychologists. Agricultural and biological sciences show the smallest projected growths, with agriculture barely keeping pace with the growth of overall employment. On a simple supply/demand analysis the number of biologists by 1987 will exceed requirements by over 60 per cent, but the surplus is dramatically reduced when inter-professional mobility is taken into account. Mathematicians, in contrast, are likely to be much in demand, especially if defence expenditure increases as quickly as is planned. Technicians will also not have to look too hard for jobs, as their job opportunities follow closely those for engineers and computer systems analysts, where the defence built-up again will increase demand.

NSF declines to comment on policy options for containing the projected shortfall of electronics and aeronautical engineers. It prefers to remain a source of factual information and leave it to others to argue about action.

Tim Beardsley

**Projected response of the science, engineering and technical labor market to defense and nondefense needs: 1982–87. National Science Foundation.*

Bombs and rockets

THE offices of the European Space Agency (ESA) in Paris were open again on Monday after a bomb explosion at the weekend destroyed its public relations department, which was empty at the time. *Action Directe*, a French terrorist organization, claimed responsibility.

Some speculate that the fact that Telecom-1, one of two satellites launched by the rocket Ariane-3 from Kourou, French Guiana, on Saturday, would carry French military communications systems, had raised terrorist ire.

However, the launch of Telecom-1 and the European Communications Satellite, ECS-2, into geostationary transfer orbit went perfectly. On Monday morning, ECS-2's apogee motor was fired, injecting it into true geostationary orbit. The satellites appear to be functioning perfectly, but nobody at ESA was making firm predictions until the last circuit was switched on — just in case *Action Directe* had perfected a high-technology sting.

Robert Walgate