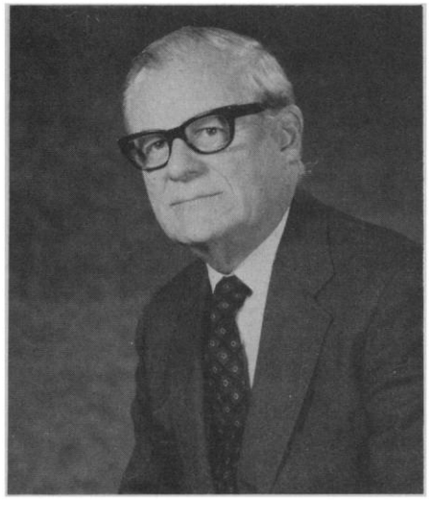
then determine the appropriate action according to newly available options. The choice would depend in part on the costs of replacing it or doing without it in the food supply.

The flexibility of the options and risk categories reflects a judgment by the panel that risks from food can be assessed qualitatively but not quantitatively. Robbins notes that "when we deal with issues where the science can only take you so far, whether you like it or not, you have to make judgments." (The panel's minority, on the other hand, deduced the opposite conclusion from the same premise. "The relative simplicities of our current food safety policy cannot be tampered with," the minority report reads, "because the structure of which it is a part can only support regulatory decisions no more complicated than a stop sign on a street corner.") The specific recommendation that risks be judged high, medium, or low was patterned on the different degrees of containment for recombinant DNA research, according to panel chairman Clifford Grobstein, a biology professor at the University of California, San Diego. "Foods that pose different risks would be contained in different degrees."



Frederick Robbins: Science goes only so far, and a subjective judgment must be made.

Though the panel took pains to avoid an undue emphasis on the saccharin issue, they found it a useful illustration. "Saccharin highlights the problems of a sharply defined and rigidly peremptory regulatory statute in a complex area such as food safety," the panel says. The statute mentioned is the Delaney clause, which was passed in 1957 and requires the banning of any additive shown to cause cancer in animals or humans.

To a minority of the panel as well as some outside consumer groups, the clause is worth retaining as a symbol because it strongly prohibits consideration of any benefits from a carcinogen. Moreover, the clause contains exact instructions for the FDA; it bars discretion that might be subjected to political pressure.

The panel's majority, however, concludes that the Delaney clause exemplifies the confusion that pervades the food laws. It exempts, for example, those substances sanctioned by the federal government prior to 1957, as well as those generally regarded as safe. Most of the recent controversy regarding the food laws stems from attempts by the FDA to ban or restrict the use of additives that come within these exemptions (for example, nitrites, cyclamates, saccharin). The Delaney clause also was enacted at a time when analytical chemists were able to detect carcinogens only in relatively large quantities in the food supply. Analytical abilities have been sufficiently refined to detect hazards of low magnitude that may not warrant a ban, the panel says. Although examples were mentioned only obliquely in the report, food packaging materials are said to be within this category. Richard Merrill, a former FDA general counsel, points out in an appendix that "many of these [packaging] materials are proving carcinogenic," in part because most are synthesized from hydrocarbons. Leaching of chemicals in minute amounts from packaging to food can now be detected, and many packaging materials may have to be banned under the Delaney clause, though the health risks may be slight. Merrill also claims that the Delaney amendment is redundant: serious carcinogenic hazards could be banned under a prohibition in the law against "unsafe" food additives.

Commissioner Kennedy is inclined to agree, and backs changes in the present clause. "I've never proposed the wholesale elimination of the Delaney clause because it isn't completely redundant; it does legislate something special about the dose-response curve for a carcinogen. But we need to get a definition in the law of unsafe additives that would permit trivial amounts to migrate into food. We could have a reasonably conservative and cautious approach by constructing a floor under the Delaney amendment; there is, however, no easy answer to where that floor would be set." Kennedy adds that the FDA will press its restriction of saccharin use, no matter what.

The Delaney amendment is not the only portion of the law that would be changed, nor is it the only example of

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Research Guidelines That MIT Can Live With

The final draft of an arcane but—to university research administrators—very important document known as circular A-21 was published by the federal government on 5 March. It is the revised version of a circular put out originally by the Office of Management and Budget (OMB) in 1973, setting the ground rules for the financing of government research in educational institutions. The new circular will take effect on 1 October.

This 45-page, single-spaced memo is billed by its authors as containing "tight new rules" designed to "improve accountability" for the $4 billion in federal funds spent each year on this kind of research. The reform is being undertaken, OMB officials are quick to point out, at the behest of congressmen and department officials who feel that universities have not been held to account as firmly as they should be.

"We are prepared to live with it," said Thomas F. Jones, vice president for research at the Massachusetts Institute of Technology (MIT). "We understand that the final document is more restrictive on recovery of indirect costs" by the university than the rules now in force, he said, but it is an improvement over a draft that was proposed in March 1978. The March version was so bad, in MIT's view, that MIT president Jerome Wiesner singled it out for scathing criticism in a long speech last fall on the crisis in relations between the government and academia (*Science*, 1 December, p. 955). He told reporters that it would be best if circular A-21 were buried.

Since then, the OMB has modified the language of the circular to appease the universities. According to OMB official John Lordan, the memo now states explicitly what was implied before: that universities may count students both as researchers (chargeable to government contracts) and as recipients of instruction (not chargeable). In the earlier document, students seemed to fall only into the second category. The new memo also permits greater flexibility in negotiating individual reimbursement rates, is more generous in accepting some of the costs of running libraries and other

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services, and includes a propitiatory note stating that the rules "should require no significant changes in the generally accepted accounting practices." It still requires some painful tightening of record-keeping, but an official at a major research university conceded that "these rules are not harmful at all."

Gene Splicers Simulate a "Disaster," Find No Risk

A team of biomedical researchers at the National Institutes of Health (NIH), interested in seeing federal restrictions on gene splicing relaxed, recently concluded a set of tests designed to assess the risk that such experiments would create a new, lethal microbe. The risk is negligible, they found.

To make the test, they inserted genetic material from a cancer virus into common microbes (*Escherichia coli*) and then put the microbes in mice. If the microbes containing the tumor virus DNA produced an infection in the mice, they theorized, some of the worst fears about recombinant DNA research would be confirmed. A destructive type of DNA would have been given a new route (*E. coli*) to invade mouse cells. If no infection occurred, they reasoned, many of the fears could be dismissed.

The five scientists, led by Malcolm Martin and Wallace Rowe of the National Institute of Allergy and Infectious Diseases, announced their findings on 1 March and published their papers in *Science* (2 March, pp. 883 and 887). The experiment, they said, confirmed their prediction that this form of recombinant DNA research will be perfectly safe. The microbes proved to be either noninfectious or far less infectious (by a factor of 10^9) than the tumor virus itself. The virus in question, polyoma, is highly infectious in mice, but not at all dangerous to humans, making it an ideal laboratory tool. Because of what is known about the similarity of infections in mice and men, the researchers believe that the laboratory results can be broadly applied to the human environment.

Rowe said, "It is enormously reassuring to find out that we know what we're doing. A few years ago we didn't." He was referring to the temporary moratorium on recombinant DNA research which scientists imposed on themselves while they considered the possibility that they might be creating new biological hazards. Rowe now says that his research shows that "there is nothing you could cut out of a smallpox virus" which, inserted in *E. coli*, would be dangerous to work on an open laboratory bench. The same applies to all the DNA tumor viruses and even to the lethal Lassa fever virus, he said.

The recent tests with polyoma were designed to mimic a worst-case hypothesis of what could happen if a recombinant DNA experiment went amok. They were meant to represent the possibility that DNA from a hazardous virus could be cloned accidentally in a common microbe and that the microbe could survive, escape the laboratory, establish itself in the environment, and ultimately provide a new route by which the DNA could infect mammalian cells.

There are a few caveats, however. The first comes from Martin and Rowe. They point out that their studies cover only one category of risks—those resulting from the cloning of a DNA virus. The findings cannot be extrapolated to the cloning of RNA tumor viruses, which are considered more hazardous. The scientists are planning to conduct tests in this area. They have not tested "positive strand" RNA viruses either, a category which no one has yet proposed to investigate.

Another caveat comes from a familiar critic of the government's DNA policy, the Coalition for Responsible Genetic Research (CRGR). Executive Director Francine Simring and a colleague pointed out that it is possible to see the Martin-Rowe test as a glass partly full rather than as one mostly empty. Although it is true that the recombinant molecules of polyoma were far less infectious than the naked polyoma virus, CRGR said, in at least one instance the recombinant polyoma DNA did move from a microbe into some mice and cause a polyoma infection. This happened in about half the mice that were injected with a bacteriophage containing a dimeric (two-copy) form of recombinant DNA. To Simring, this suggested that the experiment created a new vessel—however fragile—in which polyoma could attack mouse cells.

This fact is "of zero epidemiological importance," according to Rowe, because the new vessel is 10^9 times weaker than the naked virus. For his part, Martin suggested that some results may amount to an anomaly produced by the extreme conditions of the experiment.

Rowe brushed off another criticism, the observation that his mice were not examined to see whether any tumors were produced as a result of the exposure to infectious or noninfectious quantities of DNA. A test on tumorigenicity is still under way, and those results will be out in a year. He said, "We don't expect any surprises."

AIP Wins Case with IRS—Other Groups Seek Relief

The Internal Revenue Service (IRS) last year challenged the tax-exempt status of six scientific and engineering societies on the grounds that they seemed to be operating for the benefit of their members more than for the purposes of public education or charitable works. Two of them, after appealing from the district level to the national office in Washington, D.C., have won reversals and been told that their tax-exempt status is safe. The American Physical Society won its case in September 1978. The American Institute of Physics (AIP) learned in March that it had won its appeal because all of its activities, including publishing, are devoted to scientific and educational purposes or support other tax-exempt groups which have similar purposes.

The outlook is not so bright for the other four petitioners, the American Chemical Society, the American Institute of Chemical Engineers, the American Society of Civil Engineers, and the American Society of Mechanical Engineers. The Chemical Society has been told that it is in danger of losing its tax-exempt status altogether, and the other three may be reclassified from 501(c)(3) educational organizations to 501(c)(6) business leagues—putting them in a category with professional service groups such as the American Medical Association. All four have appealed and are awaiting decisions, which, the attorneys say, could come any time in the next 2 months.

Eliot Marshall