"That letter disqualified them," he said. "If we'd tried to appoint them we'd have had resignations from half the committee."

The episode has led some participants to question the adequacy of the Academy's procedures for uncovering bias among prospective committee members. The list of names from which the committee was chosen was generated primarily by the Academy staff with help from relevant consultants, and Hastings added some names of his own. Then Hastings, after analyzing a list of the fields of expertise needed and the potential candidates from those fields, indicated whom he wanted as committee members. Hastings told *Science*, "I personally wasn't sensitive to any stands taken by these people."

Hastings' recommendations then had to gain the approval of other key figures in the Academy. But it was only *after* the committee members were appointed that they were asked to fill out bias statements indicating, among other things, any views they might have expressed publicly on the issues to be considered by the committee. By that time, it would have been embarrassing to ask anyone to withdraw, though Academy officials say they have done so on occasion in the past.

Some Academy representatives are suggesting that appointments should be made conditional upon review of the bias statement, but others consider it presumptious to ask scientists to reveal their stockholdings, commercial affiliations, grant support, and other such matters if they are not sure they will actually be appointed. And for every scientist who wants to tighten up the bias procedure, there is another who wants to weaken it. Schwan, for example, considers it "an awful thing" for the Academy to ask what stands he has taken on an issue. "It intimidates my freedom of expression," he said. "Where's the borderline between such things and what happens in Russia?"—PHILIP M. BOFFEY

Chemical Carcinogens: Industry Adopts Controversial "Quick" Tests

For generations, industry has been introducing new chemicals into the environment in staggering numbers without really knowing whether they might be hazardous. And the public, assuming there was nothing to be done, or not thinking about it, has passively tolerated the situation. But then the environmental movement came along, as did the calculations by epidemiologists that a large proportion of all cancers are environmentally caused. As a result, there has been growing pressure to force industry to evaluate new chemicals before they are released, on the theory that safety should be tested in the laboratory and not in the environment. And there is a good chance that Congress this year will pass the Toxic Substances Control Act that would mandate premarket testing (*Science*, 13 February).

The major impediment to premarket testing has been the lack of a test system that is reliable, fast, and cheap. However, during the past few years some progress has been made in that area, largely because of the leadership of biochemist Bruce Ames of the University of California, Berkeley. Ames developed a simple system for taking a quick look at the mutagenic, and by implication, carcinogenic, properties of chemicals.

No one yet is sure just how reliable a predictor the Ames test—a bacterial system—is, but it is generally thought to be the best available of its type. In view of the probable passage of the Toxic Substances Control Act, the chemical industry has begun, during the past year or so, to use the Ames, and other quick tests, on its own in order to get some idea of the safety of new products. In the process, industry itself may help to answer questions about the value of various types of screening systems by generating sufficient volume of data on which to base scientific judgments.

At present, the only officially recognized way to test a chemical for carcinogenicity is to see whether it causes cancer in laboratory animals, which takes 2 to 3 years and costs about $100,000 per chemical. Citing the time and money involved, industries have been notoriously reluctant to routinely screen new products in animals. On the other hand, they hesitate to invest huge sums of money in the development of new products without knowing whether those products will later be banned as carcinogens. Therefore, industries have seized on a variety of quick and inexpensive tests that, they hope, will tell them whether substances are carcinogens. This has led to a curious situation in which industries are implicitly endorsing the tests at the same time that scientists and legislators deliberate over whether companies should be forced to use them.

The extensive use by industries of these quick tests is hailed by many scientists as a change in the tradition of wanton release of chemicals into the environment even while debate continues on how to evaluate potentially harmful substances in accord with the pending Toxic Substances Control Act. Ames reports that 60 or 70 major companies, including such giants as American Cyanamid, Inc., Merck Sharp & Dohme, and Dupont have asked him to supply them with the strains of salmonella bacteria he uses in his system. Numerous other firms do not test their products themselves but send them to commercial laboratories for testing.

Companies are reluctant to discuss their uses of the quick tests, but Ames relates one story told to him by investigators at American Cyanamid's agricultural division. It seems that American Cyanamid found what looked like a promising new pesticide that turned out to be highly mutagenic when tested in Ames' bacterial strains. Not willing to just drop their new product the investigators of American Cyanamid took a second look and found that this mutagenic effect was due, not to the primary chemical but to an impurity in the pesticide. Now, Ames reports, the company has removed the mutagen from the pesticide and has decided that it is worthwhile to go the full route with the purified product by testing it in animals.

The Ames test is based on the presumption that many cancers are related to mutations or some sort of damage to the DNA of a cell and, therefore, that agents that are mutagenic are likely to be carcinogenic as well. After searching through innumerable bacterial strains, Ames hit upon some mutants of *Salmonella typhimurium* that have lost the ability to make the amino acid histidine. Consequently, in a histidine-free culture medium, these bacteria cannot grow. What Ames has shown is that, when these bacteria are exposed to mutagenic chemicals, they undergo additional muta-

tions that can have the effect of repairing the original defect. What it amounts to is that in the presence of a mutagenic chemical, the bacteria begin to grow again, forming colonies that show up as white spots. A particularly handy feature of the test is that powerful mutagens will cause a larger number of bacteria to revert than will less potent ones, thereby providing at least some indication of how potentially hazardous a suspect chemical may be. The test is cheap—it costs only $200 per chemical—and fast—it can be completed in 3 days.

Other quick assays for mutagenic chemicals are based on yeast, fruit flies, and mammalian cells grown in culture. At present, no other assay is as widely used as the Ames test, but each is being studied extensively.

Commercial laboratories report that the recent interest by industries in quick tests has provided them with a substantial increase in business. David Brusick of Litton Bionetics in Kensington, Maryland, says that his firm has had some contracts to screen chemicals for the past 2 years but that the vast majority of its clients have been signed up in the past few months. Now Litton Bionetics does the tests for about 50 companies. Clients include pharmaceutical companies, manufacturers of agricultural chemicals, producers of pigments and dyes, and other companies that may be marketing toxic substances.

Litton Bionetics, like most other commercial laboratories, offers its clients a range of quick tests, including the Ames test, which is almost always performed first. In many instances, a firm is told that its chemical is mutagenic in the Ames test and will then request other quick tests of the chemical before deciding what course of action to take. The cost of a whole battery of tests is less than one-tenth of the cost of a cancer test in which laboratory animals are used.

The widespread use of the Ames test is a tribute to the decade of work put in by Ames and his associates. They have

Medical Devices Law Is on the Books at Last

Congress has finally given the Food and Drug Administration explicit authority to regulate medical devices in a law signed by the President at the end of May. The event concluded 15 years of intermittent congressional efforts to fill a regulatory gap that was becoming ever more evident with leaping advances in medical technology.

Efforts to pass a devices law began in earnest following a 1970 report by a study group at the Department of Health, Education, and Welfare, which revealed that medical devices had been implicated in 10,000 injuries and 731 deaths between 1963 and 1969. Most of the deaths resulted from malfunctioning heart valves and pacemakers.

The new amendments to the Food, Drug and Cosmetic Act for the first time empower FDA to review and approve high-risk devices before they go on the market. The law puts all medical devices from tongue depressors to artificial organs into three categories. Classification, to be done by outside panels appointed by the secretary of HEW, will be made according to the potential danger of each device and the availability of information sufficient to formulate safe standards governing its design, manufacture, and use.

Devices put in class III, the most stringent category, will require FDA clearance before they are marketed. This applies to devices that are deemed to be life supporting or life sustaining or are implanted in the body. Class II devices must conform to standards to be promulgated either by groups from outside the government or by the government. Class I devices are subject to "general controls," which means they basically won't be regulated any more than they are now. This is equivalent to the "generally recognized as safe" designation for food additives.

Until now, the only explicit statutory authority the FDA has had to regulate devices has come from the 1938 drug law which permits the agency to take action against any device found to be "misbranded" or "adulterated." In 1969 the concept that devices could be regulated as drugs within the law was elaborated by a Supreme Court decision which ruled that Bacto-Unidisk, a paper disk used for testing bacterial sensitivity to drugs, should be classified as a drug. But since then, only a handful of devices, such as copper IUD's and soft contact lenses, have been regulated as drugs.

According to a lawyer on the staff of Senator Gaylord Nelson (D–Wis.), who is largely responsible for strengthening the bill from its earlier versions, what the new law does is shift the burden of proof that a device is safe and effective from the FDA (which only had the power to intervene after a device was on the market) to the manufacturer. The law requires that every "new" device—that is, every one that is introduced after passage of the law and is not "substantially equivalent" to something already in use—must be automatically put in class III. From there, panels have 6 months to decide whether to approve it and whether to reclassify it in class I or II. All "old" devices—those already on the market—that are implantable or life sustaining also go into class III. Their manufacturers are given 3 years from the date of the law's enactment to get marketing approval. Devices now covered by new drug applications would also probably go into class III.

Passage of the law has taken a remarkably long time considering the fact that some sort of legislation has been widely thought to be not only desirable but inevitable. Even device manufacturers have supported it as being far preferable to alternative and even more stringent regulatory procedures. Their main complaint about the new law, according to a spokesman from the Pharmaceutical Manufacturers' Association, is that class III is unnecessarily broad and that the restrictions in this class will impede the flow of new devices onto the market.

As for consumer advocates, the chief problem, according to attorney Anita Johnson of Ralph Nader's Health Research Group, is that the major classification decisions are to be made by committees of nongovernment personnel. Johnson believes outsiders are more lax and subject to conflicts of interest, and that the only way to ensure accountability is to keep all responsibility on the backs of public servants. "We must decide whether we want outsiders to be making basic public health decisions," she says. Johnson also calls the standards-setting procedures "a Rube Goldberg machine" that offers numerous opportunities for industry interests to create obstructions and delays.

The new law covers about 12,000 devices, products of a more than $3-billion-a-year industry. According to an FDA official, about 10 percent of all devices would go into the premarketing approval category and half would be allowed to stay under general controls.—C.H.

shown that 90 percent, or 156, of 174 known carcinogens cause mutations in their bacterial strains. By contrast, few of the 109 "noncarcinogens" that they have tested are mutagens. Because a wide variety of classes of chemical carcinogens are mutagens in his system, Ames argues that this bacterial test system provides a reliable screen for potentially harmful chemicals.

As an example of the usefulness of quick tests for carcinogenicity, Ames tells the story of a preservative (furofuramide) that was extensively used in Japan. It was tested in animals and found not to cause cancer. The chemical, however, did cause mutations in bacteria. It was subsequently retested in animals, found to be carcinogenic, and banned. Now, Ames reports, bacterial mutagenicity tests are extensively used in Japan. In particular, the Japanese require that all pesticides be shown not to cause mutations in bacteria. The Japanese are also taking very seriously the finding that hair dyes are potent bacterial mutagens and are currently trying to develop hair dyes that do not have this drawback, according to Ames.

Despite these arguments in favor of the Ames and similar tests, it is by no means clear how results of these tests are to be interpreted. One problem is that, with the data obtained so far, the logic behind the test evaluations goes the wrong way. Ames can say that 90 percent of all tested carcinogens are mutagens in his bacterial strains but he cannot say what the probability is that a chemical that is a mutagen will turn out to be a carcinogen.

Some investigators believe that this difficulty can be partially remedied by the use of more than one test system. A positive result in several quick tests might carry more weight than a positive result in the Ames test alone. Mammalian cell systems are of particular interest to some investigators who believe it would be intellectually more satisfying to detect DNA damage to these cells or transformation of them into tumor cells than to detect mutations in bacteria. Mammalian cell test systems are not yet extensively used, however, because these tests cost 5 to 10 times more than the Ames test and neither they nor the other quick tests have the data base or the sensitivity of the Ames test.

Legislators and officials at the National Cancer Institute have expressed interest in the quick tests but have hesitated to endorse any of them because of the difficulties in interpreting results. Yet rapid and inexpensive screens for harmful chemicals are needed if the Toxic Substances Control Act is to be economically feasible. The ultimate solution to the problem with the quick tests lies in obtaining more data. Then it will be possible to correlate results from quick tests with results from animal tests for carcinogens in a statistically convincing manner. By their recent extensive use of the quick tests, industries seem to be making a substantial contribution to the data base that must exist for these tests to be evaluated.—GINA BARI KOLATA

Nuclear Testing: U.S.–Soviet Treaties Viewed with Doubts and Misgivings

Control of nuclear arms is a matter about which the public, aware of the generally frustrating history of arms negotiations, has learned to lower its expectations. Accordingly, the treaties negotiated by U.S. and Soviet officials to limit underground weapons tests and peaceful nuclear explosions have not been awaited with much excitement or anticipation. But, now that the Ford Administration is finally ready to submit them to the Senate for ratification, these treaties give rise to so many doubts and objections that many senators will find it a close question whether they are marginally better than nothing or whether they are actually worse than nothing.

The treaties now subject to ratification go back to the Moscow summit of July 1974, Richard Nixon's last hurrah before he was forced to resign over Watergate. With the strategic arms limitations talks still at an impasse, the President seized the opportunity to sign a treaty limiting underground tests to a certain maximum yield or "threshold."

Had the treaty banned all underground tests or even all tests susceptible to unambiguous "verification" by seismic monitoring, it would have been applauded by the private arms control community that is made up in good part of groups such as the Federation of American Scientists (FAS) and the Arms Control Association (ACA). (A number of former government officials with responsibilities for arms control are active in both the FAS and the ACA.) But the treaty Nixon brought back from Moscow was instantly put down as a mockery by many of these arms controllers, who wanted a treaty that would effectively discourage further weapons development and inhibit nuclear proliferation.

By prohibiting testing in the atmosphere, in outer space, and under water, the Limited Test Ban Treaty (LTBT) of 1963 had stopped the dangerous radioactive contamination of the world environment. But the United States and the Soviet Union had simply moved their ambitious programs of testing underground, and, consequently, the LTBT had constrained the arms race little if at all.

The Threshold Test Ban Treaty (TTBT) signed by President Nixon and General Secretary L. I. Brezhnev in 1974 clearly would not do much to constrain the arms race, either. The threshold, set at 150 kilotons, would allow the testing of weapons 10 times more powerful than the one that destroyed Hiroshima. Also, this threshold would bear no relation to verification capabilities, which have been improved to the point that even explosions at yields of 10 kilotons or less may not escape detection.

Furthermore, many arms controllers objected strongly to the fact that, permissive as it was, the treaty would not take effect until 31 March 1976, thus leaving time for each of the two superpowers to carry out a series of tests at high yields. They objected, too, to a glaringly evident loophole in the TTBT—"peaceful" explosions, of whatever magnitude, were not covered even though such explosions can be indistinguishable from weapons tests.

Administration officials acknowledged that plugging this loophole was priority business. Assurances were given that the TTBT would not be submitted for ratification unless it was accompanied by an agreement on peaceful nuclear explosions, or "PNE's." And, sure enough, after a year and a half of hard negotiations, a PNE treaty (PNET) was signed on 28 May, in ceremonies conducted simultaneously in the White House and the Kremlin.

After its fashion, the PNET does address some of the concerns of the arms