a Washington, D.C., consumer organization. He claims what the Kennedy bill calls scientific review of a product can only be initiated after an outside panel of experts meets and decides that a certain product should be cleared before marketing and after a further determination by FDA that scientific review is really necessary. Said Wolfe, "These determinations could be made by FDA only if it had extensive evidence about the device. But it could not have extensive evidence about the device unless testing had already been conducted. This is the Kennedy bill Catch-22." And he argues that scientific review panels "cannot make recommendations for premarket testing because there is no mechanism to call their attention to the existence of recently developed or developing devices before they are on the market." Wolfe calls premarket clearance "an elementary mark of human decency."

The Kennedy and Administration bills emphasize standard setting as the primary means of regulating medical devices. A major issue here arises over the question of who should set standards—Nelson wants the bill to state that persons who have financial interests in medical devices are excluded from standard-setting panels—and whether standard-setting itself is reasonable in a field in which technology is rapidly changing. The inevitably cumbersome procedures, involving scientific panels and committees for establishing standards, could not possibly keep up with device technology, it is argued. Standards could be out of date before they are set.

Therefore, Nelson is adamant about wanting premarket clearance, although he is willing to leave the details of its implementation to the discretion of the FDA, largely to allow for the measure of flexibility that is said to be essential to workable device legislation. Indeed, none of the bills spells out just what premarket clearance should be, in contrast to the Food, Drug, and Cosmetic Act, which is quite explicit in setting forth requirements for new drugs.

FDA lawyer Hutt is not sympathetic to the scope of Nelson's premarket clearance amendment. "If it comes down to whether we should do premarket testing on all dental devices marketed during the last 50 years, or on all implantable steel pins, rather than on more sophisticated devices," Hutt says, "it is not hard to imagine where I stand." The FDA, he believes, simply is not able to undertake such a massive venture. Nor does he believe it necessary.

Whatever the final nature of the legislation, FDA will have to gear up in order to even attempt to implement it and forecasts of what will be required in terms of manpower and money have already been made. FDA figures it will have to take on 330 people and have a device budget of more than $12 million in 1975. By 1979, the agency anticipates needing 500 people and $15 million to carry out the medical device law.

—BARBARA J. CULLITON

Microbiology: Hazardous Profession Faces New Uncertainties

Since the turn of the century, some 3500 cases of laboratory-acquired infections have been reported, more than 150 of which resulted in death. Although with this accident rate it may still make more sense to be a microbiologist than a steeplejack, the profession is not entirely without risk. The risks are, if anything, increasing as more people take up work with viruses, including viruses suspected of causing cancer in man. Besides the risk to scientists themselves, there are also dangers posed by the new kinds of virus that can now be created in the laboratory and which, if they escaped, might constitute a threat to public health.

The degree to which people have become infected with the agents they work with depends on the care they take and the nature of the agent, but even under the most stringent safety conditions that can be devised, such as those at the former biological warfare laboratories at Fort Detrick, Maryland, infections do occur. During the quarter-century that the Fort Detrick laboratory was in operation, there were 423 cases of infection and three deaths. Since the cost of building even a moderate-sized laboratory to the same standards of safety is about $125,000, most civilian laboratories have to make do with less. One experienced virologist reckons that, when working with agents which infect man, about 5 percent of the laboratory staff may become infected each year. "Every microbiologist has inhaled or absorbed significant amounts of any organism he has worked with," says A. Wedum, former safety director at Fort Detrick.

Bacteria were once the most common cause of laboratory infections, a role that has now been taken over by viruses. According to Wallace Rowe of the National Institute of Allergy and Infectious Diseases (NIAID), the hazards to laboratory workers are probably on the increase. One reason is that many of the people now coming into virology are, for example, biochemists who do not have the safety instincts of the trained microbiologist and tend to regard viruses simply as another chemical reagent. Another is the trend to use viruses in more and more highly concentrated forms. Infection depends on the dose of virus to which a person is exposed, and solutions now in common laboratory use contain 100 to 1000 times more virus than they did a few years ago. A third kind of hazard is the creation of hybrid or otherwise new viruses, which pose unknown risks both to scientists who work with them and the population at large.

According to Wedum, about a quarter of all laboratory infections can be traced to accidents, such as self-inoculation with a syringe. For the rest, a precise cause is usually hard to find, but inhalation is often the reason. Many common laboratory operations, such as blending, sonicating, or simple spillage, can lead to the formation of an aerosol containing viral particles.

Probably the most dangerous single source of viruses is monkeys, in which occur a number of agents fatal to man. There have been 20 suspected cases of human infection with herpesvirus B, with only three possible survivors. Another monkey agent, Marburg virus,

infected 31 laboratory workers and others in an outbreak in Germany in 1967, resulting in seven deaths.

These are known dangers for which there are known precautions. Harder to assess is the degree of risk involved in dealing with tumor viruses. So far, the only known death from cancer caused by a laboratory accident is that of a French medical student, Henri Dadon, who in 1926 pricked his hand with a syringe containing fluid from a cancer patient; a nodule developed on his palm, and he died a year later from metastasized tumors. A different risk is presented by the numerous animal tumor viruses that have since been discovered and are now under intensive study. On the theoretical assumption that a species is able to combat its own tumor viruses quite well but may be more susceptible to those of other species, the animal tumor viruses may be just as hazardous to work with as a natural human tumor agent which, if it exists, is unlikely to be highly virulent. "I have no doubt that if you gave enough of some of these agents to a susceptible person he would get a tumor," says George J. Todaro of the National Cancer Institute. At the same time, Todaro does not rate the danger of working with animal tumor agents as very high—"It's entirely a guess as to risk, but my guess is that it is considerably less dangerous than smoking two packs of cigarettes a day." What if the guess is wrong? "We're in a pre-Hiroshima situation," says Robert Pollack of the Cold Spring Harbor Laboratory: "It would be a real disaster if one of the agents now being handled in research should in fact be a real human cancer agent."

James D. Watson, also of Cold Spring Harbor, is another who takes a serious view of the possibilities. "I'm afraid that the NCI avoids facing up to its moral, if not legal, responsibility by declaring almost all of the viruses we work with as unlikely to be of sufficient long-term danger to require [first grade safety equipment giving absolute control]," Watson said at a recent conference on laboratory biohazards.* W. Emmett Barkley, an NCI official concerned with safety, responds that, in the feeling of the NCI, the hazard of working with tumor viruses is not such as to require absolute control. In any case, 90 percent of safety comes from good technique on the part of the investigator, only 10 percent from the equipment and facilities, Barkley says.

Even more intractable than tumor viruses are the theoretical hazards posed by the creation in the laboratory of viruses that do not exist in nature. An empirical reason for believing such viruses would not be dangerous is that many millions of dollars were invested at Fort Detrick in trying to improve upon the lethality of viruses harmful to man, but, according to Wedum, they "never had much luck." Yet what Fort Detrick could not accomplish by design, others may achieve by accident. There is concern in virological circles with at least three kinds of study now in progress. One is the attempt to devise a better influenza vaccine by means of hybrid flu viruses. The danger here is that the ability to genetically manipulate flu viruses could lead to a new combination that might escape from the laboratory, by infecting an employee, say, and spread to the population at large. "This could recreate the conditions for an influenza pandemic like that of 1918," says Rowe of NIAID.

Tumorigenic Monkey Virus

Another kind of virus is a combination of the DNA of SV40, a monkey virus that causes tumors in lower animals, and certain bacterial genes. The hybrid DNA molecule was synthesized by Paul Berg and colleagues at the Stanford University School of Medicine for the purpose of studying how the bacterial genes work. One of the possible experiments with the hybrid virus calls for it to be made to infect *E. coli*, a bacterium that is a common inhabitant of the human gut. There is considerable concern that if an SV40-infected *E. coli* should escape from Berg's laboratory it might become established in the population at large, which would then forevermore be exposed to SV40 genes, the effects of which in man are unknown. "The Berg experiment scares the pants off a lot of people, including him," says Rowe. According to Todaro, the Berg experiment "is one of those which I think just shouldn't be done." Berg says he cannot prove the experiment to be absolutely safe and has decided not to do it for the time being.

The general issue of hybrid DNA molecules so concerned a group of scientists at the Gordon Research Conference this June that they sent a letter to the president of the National Academy of Sciences stating that such hybrid molecules "may prove hazardous to laboratory workers and the public" and suggesting that a committee be set up to study the problem (see *Science*, 21 September, p. 1114).

A third kind of virus that causes concern is the group of hybrids that occur between SV40 and some of the human adenoviruses. The hybrids were first created in the course of manufacturing adenovirus vaccine, which is produced in monkey cells. (The vaccine was received by military conscripts, but no follow-up study has been done to observe the effects, if any.) Certain of the adenovirus/SV40 viruses, known as non-defective hybrids, also happen to be a useful research tool for mapping the genes of SV40. Should the viruses escape, the risk they pose is that, like pure adenovirus, they could become established in the tonsils of young children and become part of the human experience for generations to come. Although some believe that concern about SV40 is a tempest in a teapot, at the same time it is impossible to know for certain what SV40 may do in man.

Because of these concerns, the virologist who developed the adenovirus-SV40 hybrids, Andrew M. Lewis of the NIAID, was uneasy about distributing the virus. It is now official NIAID policy that those wanting samples must sign a memorandum of understanding, in which they agree to take certain safety measures and not to pass the virus on to anyone who does not promise to do likewise.

Such a policy, moderate though it may seem, in fact cuts across the scientific ethic that materials should be freely exchanged with any fellow scientist who wants them—so much so, in fact, that Lewis has been suspected by some of raising public safety as a ploy to keep the viruses to himself. Lewis feels that an informal moral commitment is preferable to legal regulations.

"If the public feels the scientific community is acting irresponsibly, there will be an immediate reaction and the freedom of research will be curtailed. If we don't exercise due caution we are heading for trouble," Lewis believes.

It is probably true to say that virologists and other microbiologists are more safety conscious now than they used to be, but safety practices vary widely from one laboratory to another. The history of safety regulations in almost every field of activity is that it takes a disaster to arouse effective concern. Virology, maybe, will prove an exception.

—NICHOLAS WADE

* *Biohazards in Biological Research*, proceedings of a conference held at the Asilomar Conference Center, California, January 1973 (Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., 1973).