Briefing:

Lindow Microbe Test Delayed by Legal Action Until Spring

University of California pathologist Steven Lindow's effort to test altered bacteria designed to inhibit the formation of frost on potatoes, strawberries, and other crops has again been scuttled. The Berkeley-based scientist and the university are postponing the test pending the outcome of a new environmental assessment. It is being conducted as part of a court-supervised agreement with a coalition of citizens and environmentalists that contends the university and state failed to comply with the California Environmental Quality Act (CEQA).

After 2 years of delay, Lindow had hoped to finally initiate the experiments with strains of *Pseudomonas syringae* in early August at the university's research center near Tulelake in northern California. The Lindow field test is viewed by the biotechnology industry as a landmark trial that will ease public concern about the hazards of releasing genetically engineered organisms into the environment. Although Lindow had obtained the necessary federal and state permits to enable him to proceed last spring, the university postponed the experiment in the wake of local concerns about its potential effects on the farming community.

In the interim the university sought to convince residents that the experiments are harmless. Reviews conducted by the National Institutes of Health, Environmental Protection Agency, and the Food and Drug Administration have concluded that there is minimal risk since *Pseudomonas syringae* bacteria are commonly found in soils throughout the state. The difference in the Lindow strains is that a gene has been deleted to prevent the secretion of a protein that spurs the formation of ice crystals on plants. The alteration means some crops could be protected for short periods from damaging frosts when temperatures drop to as low as 25°.

Nevertheless, on 6 August, residents of Tulelake, Californians for Responsible Toxics Management, and social activist Jeremy Rifkin obtained a temporary restraining order from the California Superior Court blocking the experiment for 19 days. The plaintiffs asserted that the Department of Food and Agriculture wrongly issued the university a "transportation and use permit" for the bacteria. The agency, they argued, did not consider the state environmental quality act stipulations at the time. Officials of the department's plant industry division told *Science* that at the time they issued the Lindow permit, they were unaware that CEQA applied. The department, which typically screens applications for compliance with federal law, is now developing procedures to assure that the state law is taken into account.

Gary Morrison, an attorney for the University of California, contends that the university has met the letter of the law. Three years ago, Morrison notes, the university ruled that the experiment was not subject to CEQA. No one challenged the university declaration within 180 days as required by state law.

Morrison said the university and Lindow agreed to review and upgrade the existing environmental assessment where necessary to comply with state law because the restraining order threw off the test schedule. Regardless of the outcome of the legal challenge, by the time the isssue was resolved it would have been too late in the summer to initiate the experiment.

Under the negotiated settlement reached 19 August, the university will sit down with the Tulelake citizens and environmentalists to work out what issues need to be addressed in the assessment. Depending on the outcome, a more detailed "environmental impact review" could be required. In any event, says Morrison, Lindow should be able to proceed with his experiment next spring. As part of the agreement, he notes, the plaintiffs have agreed to file any new action in court within 30 days of the environmental review's completion.

It is not clear whether this latest legal wrangle means additional regulatory hurdles for researchers and companies seeking to conduct other tests of genetically altered bacteria and plants in California. Researchers and biotechnology companies have an estimated 15 applications to conduct outdoor experiments pending before the state Department of Food and Agriculture. The counsel for the plaintiffs, however, has asked the state attorney general to freeze these permits and permit applications pending the implementation of procedures by the department to assure that the California Environmental Quality Act is complied with.

Among the companies that could be affected is Advanced Genetic Sciences (AGS). The company's permit was revoked by the Environmental Protection Agency after it was disclosed that frost inhibiting bacteria had been injected into trees atop its Oakland headquarters building without federal approval. AGS hopes to have EPA reinstate its permit to proceed with the field test of its modified version of *Pseudomonas syringae*. Before that can happen, EPA officials say, the company must find an alternative to the proposed Monterey County site. ■

MARK CRAWFORD

PHS Invites Industry Collaboration on AIDS Vaccine

Assistant Secretary for Health Robert Windom recently released a notice* that solicits industry collaboration with the government " . . . for the development, testing, production and distribution of a vaccine for the prevention of acquired immune deficiency syndrome (AIDS)." Essentially, the document identifies the data and facilities that the Public Health Service (PHS) can provide to private industry, lists the patent applications held by the United States government that may be pertinent to vaccine development, and outlines the kind of information that should be included in a proposal to collaborate.

No vaccine for AIDS exists now but several pharmaceutical and biotechnology companies are working to produce one. Many, including Genentech in South San Francisco, Chiron in Emeryville, California, and RepliGen in Cambridge, Massachusetts, have already established vaccine collaborations with government scientists and researchers in university laboratories in the United States and other countries. According to Lowell Harmison, science advisor at PHS, the new PHS framework will "provide a more formal structure to develop collaborative efforts on the part of the public and private sectors."

Because scientists from many different private and government laboratories are already collaborating to develop a vaccine for AIDS, it is not readily apparent what additional opportunities the new PHS notice offers. In its statement, PHS says that it "may provide patent licensing, research results, scientific knowledge, laboratory facilities, animal models and animal testing, assistance in the formulation of clinical protocols and clinical trials, and other (appropriate) assistance" to private concerns that are selected for collaboration. Harmison indicates that by spelling out the variety of government data and services available to potential collaborators, industry may find them more directly accessible.

The PHS notice identifies 15 patent applications as available for licensing under the

*The PHS document "AIDS Vaccine Development: Private Sector/Government Collaborative Efforts" was published in the *Federal Register* 22 August.

Robert Windom *announces a framework for industry and government collaboration on an AIDS vaccine.*

collaborative program. These include: peptides isolated from or based on AIDS virus proteins that might be used in a potential vaccine, organisms such as vaccinia virus that can be genetically engineered to produce proteins normally made by the AIDS virus, methods for producing and dectecting the AIDS virus, isolation methods for proteins made by the AIDS virus, and molecular clones of the AIDS virus. The United States government owns the rights to these patents.

The PHS notice calls for collaborative plans from the private sector to be submitted by October 21, sixty days from the date of the notice. Each plan will be considered on a case-by-case basis, and final selection will be made by the agencies of the PHS including the National Institutes of Health and the Centers for Disease Control.

Harmison says that the concept for establishing a collaborative framework for AIDS vaccine development is not new. In 1984, the PHS issued an invitation for private industry to become involved in making test kits to detect AIDS virus antibodies in the blood (which were on the market by 1985), and the idea for vaccine development collaboration began then.

An AIDS vaccine is not likely to be available for general use until well into the 1990's. The primary reason for the expected delay in its development is the scientific complexity of the research problem, which necessitates large and equally complex research collaborations. Why did the PHS release its new notice now? Because the stage of scientific research warrants such collaborations at this point, says Harmison, and perhaps because the time is ripe for exercising some control over who has access to patent licenses. ■

DEBORAH M. BARNES

(A discussion of the different research strategies now being used to develop an AIDS vaccine will appear in the 12 September issue.)

Will an AIDS Vaccine Bankrupt the Company That Makes It?

In the present climate of richly rewarding lawsuits by individuals against manufacturers for product liability, U.S. pharmaceutical companies may be less than eager to invest large amounts of money and effort into producing a vaccine for AIDS. But an experimental AIDS vaccine should be available for initial clinical testing within the next decade, and individual scientists as well as drug companies recognize the need for legislation that will encourage rather than discourage vaccine production.

"The important legal issue is pretty clear," says Brian Cunningham, vice president and general counsel for Genentech in South San Francisco. "As the law stands today, manufacturers are held liable for injuries caused by a vaccine even though they were not negligent in designing it. In these circumstances, in my opinion, the legal system has simply run amuck. And for a small company like Genentech, we simply cannot take the financial risk." Genentech is now in the research phase of developing a potential AIDS vaccine, but the company has not decided whether it would move into full-scale vaccine development.

Currently, drug companies are subject to strict product liability, a legal term meaning that the manufacturer is liable for any injuries caused by the product, even though the product was made properly.

California is leading the legislative effort to lessen a manufacturer's liability for an AIDS vaccine with a bill, which is expected to pass before 1 September. Governor George Deukmejian has formally endorsed the vaccine legislation (as of this writing). His office projects that Californians will pay about $3.5 billion in medical costs alone for AIDS patients in 1990, making the need for a vaccine a financial as well as a health care issue.

Due in part to persistent lobbying efforts by Genentech and other pharmaceutical firms, the new bill would relieve drug companies from strict product liability. Introduced by assemblyman John Vasconcellos, it is designed specifically to apply to an AIDS vaccine once it has been approved by the Food and Drug Administration (FDA). The bill offers not only protection from two classes of liability claims, but also provides incentives for drug companies to make a vaccine for AIDS.

The California bill has four essential features. First, it leaves intact a person's right to sue because of injury due to manufacturing defects in an AIDS vaccine. At the same time, it eliminates strict product liability in a suit based on warning or design defects if the vaccine has been found to be "unavoidably dangerous" (defined on the basis of a California appellate court decision as a product with great public benefit that is unavailable in a less dangerous form). Second, it states that it is the intention of the state of California to purchase 750,000 doses of the vaccine for a maximum of $20 a dose, if this number is not sold in the 3-year period following FDA approval of a vaccine. Third, it provides for $6 million in grant money to be given to drug companies that do clinical testing of potential vaccines. And fourth, the bill guarantees compensation to individuals injured by an AIDS vaccine by paying their medical expenses, lost income, and a capped amount for pain and suffering. The money for this compensation fund will come primarily from a surcharge that the vaccine manufacturers will pay, with any future state appropriations to be decided later.

The California bill may prove to be model legislation for other states or perhaps for the federal government. The House of Representatives subcommittee on health and the environment has introduced bills that pertain to childhood vaccines. One of them, sponsored by subcommittee chairman Henry Waxman (D–CA), would protect pharmaceutical companies that make childhood vaccines which are already FDA-approved against strict product liability. It would also offer compensation to children who are injured by a properly made vaccine.

But any forthcoming vaccine for AIDS is admittedly experimental and will not have FDA approval until it is shown to be both safe and effective. Whether protective legislation will be introduced at the federal level for such an experimental vaccine is uncertain. Public Health Service scientists and representatives from private industry have been discussing these issues with congressional staff. ■ DEBORAH M. BARNES

NASA Council Sees Continued Erosion of Space Program

The advisory council of the National Aeronautics and Space Administration (NASA) has expressed "great concern" about the agency's ability to fulfill its mandate for national preeminence in space.

In a blunt letter to agency administrator James C. Fletcher, dated 14 August, council chairman Daniel J. Fink also says "that actions being taken by the U.S. to restore its