dozen members of Universities Associated for Research and Education in Pathology. In response to earlier criticisms of his study Newberne has said that "I have no apologies and no doubt that the implications my diagnoses delineated are indeed correct." In a statement prepared last week Newberne describes the differences in diagnosis as subjective but says that "In principle, I agree that [the FDA working group] did an excellent job with a difficult task."

The effect of FDA's reversal is to vindicate the congressional and scientific critics of its phaseout proposal and to validate the argument of the meat and poultry industry, that no regulation of nitrite should proceed unless the results of an animal test have been duplicated. C. Manly Molpus, president of the American Meat Institute, says that "certainly the government's attempt . . . to halt the use of nitrite was ill-advised, and the need for peer review of studies of this type should be an essential element of the process."

Several FDA scientists claim that if Kennedy had followed ordinary procedures for the in-house review of a study such as Newberne's that the flaws would have been caught before the agency stuck its neck out. Albert Kolbye, associate director for toxicology in the Bureau of Foods, has complained to the General Accounting Office and the Congressional Research Service that he and other employees in the bureau were excluded from decision-making before the first public announcement.

Kennedy, now president of Stanford University, insists that "the procedure for review we followed was correct. In the first place, there is no *ordinary* procedure, and I was perfectly satisfied that the people on that task force were competent." Asked if it would have been better to withhold a regulatory proposal until after a more lengthy scientific review had been completed, Kennedy replied, "You can't simply analyze the results and then say no option suggests itself when in fact one does."

Top officials at FDA say they are inclined to act more deliberately and seek more review in light of the nitrite reversal. "You can't handle an issue like this privately," says one official, "even though you pay a price for handling it publicly."

Where does this leave the consumer of hams, hot dogs, and bacon? The FDA says it has asked the National Academy of Sciences to search the literature on nitrite and investigate alternative ways of preserving meats. Privately, FDA officials see the study as a device for getting both Congress and consumer activist groups off the backs of both FDA and USDA.

William Lijinsky, an expert in cancer-causing nitrosamines at the Frederick (Md.) Cancer Research Center, says that nitrites still pose a risk of cancer because they might combine with amines after consumption to form nitrosamines. "Even though we've been given the impression that nitrites are now safe, this risk remains." Jere Goyan, current FDA Commissioner, agrees that "nitrites are not home-free by any means. There are still questions, and I'm sure they will eventually be phased out of the food supply because of the nitrosamine problem."—R. JEFFREY SMITH

DNA: Chapter of Accidents at San Diego

Not sabotage, but cross-contamination, was the most likely cause of the wrong virus being cloned

Events have conspired to cast an air of drama around the case of the miscloned virus at the University of California, San Diego.

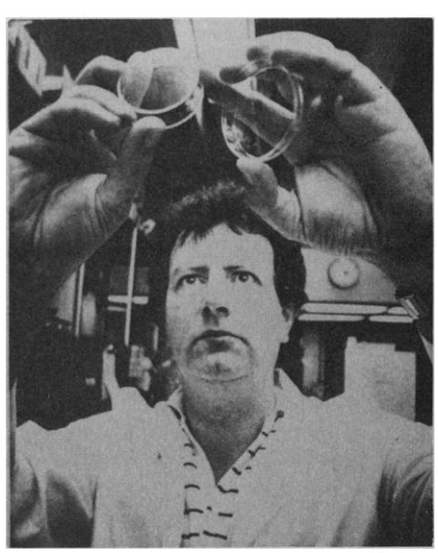
The first such event was a sudden announcement from the University's Institutional Biosafety Committee. There had been a violation of the recombinant DNA safety rules in the laboratory of Ian T. Kennedy, the committee reported in a letter of 31 July to the National Institutes of Health.

Students in Kennedy's laboratory had informed the chairman of their department of ambiguities in Kennedy's results. Tests by the California State Department of Health confirmed that cloned material meant to contain the mosquito-borne Sindbis virus seemed to be instead the closely related Semliki forest virus, which was also under study in Kennedy's laboratory.

Semliki forest virus is classified, along with smallpox and yellow fever, as a class 3 agent. Class 3 agents, according to the January 1980 version of the NIH safety rules, may not be cloned. Concluding it had a violation on its hands, the Institutional Biosafety Committee confiscated all Kennedy's cloning materials and rescinded permission for further cloning. Kennedy was himself a member of the committee.

Kennedy's sudden disbarment from the cloning fraternity was followed by the theft of a bottle of rabies vaccine from the laboratory Kennedy works in. Kennedy then revealed that over the past 6 months he has received several anonymous calls from a person objecting to recombinant DNA research. Sabotage, he suggested in press interviews, might have been the cause of his cloning the wrong virus, although before the rabies incident he had suggested contamination of virus stocks in transit as the cause.

This mountainous drama has not yet been resolved, but the outlines of several molehills are already discernible. The University of California, San Diego, has some $1.8 million worth of recombinant DNA research grants at stake, so that the biosafety committee's quick reaction to a possible violation is understandable. But the committee may have acted al-



AP photo

Ian Kennedy

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most too promptly in the Kennedy case. It is not yet beyond dispute that he infringed the safety rules in the sense stated by the committee, although it is clear that he cloned a virus different from the one he intended.

The safety rules in force at the time of the cloning experiment state that Semliki forest virus, though a class 3 agent, "may be classified up or down, depending upon the conditions of use and the geographical location of the laboratory." If the NIH considered the virus as class 2, and Kennedy believes there is some evidence that it did, the mistaken cloning would not even at that time have been a forbidden experiment. Through a rule change that came into force on 29 July, class 3 viruses may now be cloned.

Even if there were no infraction of the rules, it is still apparently the case that the wrong virus was cloned. Kennedy, who now thinks the sabotage hypothesis less likely, considers that cross-contamination may have occurred when he shipped both Sindbis and Semliki forest virus from the University of Warwick, England, where he was working, to San Diego.

Despite assurances given by the air freight company, Kennedy explains, the Dry Ice surrounding the viruses had melted on arrival and a vial containing Semliki forest virus had broken. The virus may have contaminated a screw-top bottle of Sindbis virus and outgrown it in subsequent culture—hence the mistaken cloning.

Best microbiological practice calls for viruses to be shipped in flame-sealed vials so as to prevent the possibility of contamination. Kennedy explains that he was transferring seed stocks, which had been frozen down originally in screw-top bottles, and which he did not wish to thaw and refreeze. Best practice would perhaps call for all bottles to be tested for contamination after such an accident: Kennedy states that he did retest all but one of his bottles containing Sindbis virus; it was presumably this bottle that was contaminated.

The fingerprint of the cloned material seemed more like that of Semliki forest virus than Sindbis.

In a test to characterize the cloned virus, Kennedy says he found a fingerprint that seemed more characteristic of Semliki forest virus than of Sindbis. He decided to carry out further tests to resolve the confusion, but his students felt the department chairman should be informed of the problem at once. Kennedy agreed, and a decision was made to send the cloned material out for testing. But before he could finish his own tests to resolve what happened, the results came back from the California State Department of Health and the biosafety committee halted all further work.

Could Kennedy have been trying to steal a march on competitors by cloning Semliki forest virus in anticipation of the experiment becoming legal? Kennedy's response is that he had no need to since few if any other researchers in the United States are working with the virus.

The cloning experiment was performed in a P3-level laboratory. Although Semliki forest virus is at present assigned to the same category as smallpox, it usually produces only a mild fever in man and has caused only one known death, says Kennedy.

As with the two previous infractions of the NIH rules, which occurred at the University of California, San Francisco, and at the Harvard Medical School, the UCSD incident posed no threat to public health. Contrary to the case with the other two incidents, the infraction seems on present showing to have been purely accidental, and the institutional biosafety committee reported it promptly to the NIH.—NICHOLAS WADE

Gene Splicer Goes Public

The gene tailoring company Genentech has announced plans to go public next month, the first of the new genetic engineering companies to do so.

Founded in 1976 by Robert Swanson, and by Herbert Boyer of the University of California, San Francisco, Genentech now employs a staff of 126, including 40 Ph.D.'s. It is not yet a gold mine. In the first 6 months of this year the company earned $81,000 on a revenue of $3.5 million. But Genentech officials say they expect the million shares to be offered to the public next month to sell for $25 to $30 each.

The basis for this unusual price-to-earnings ratio is Genentech's hope of substantial revenues after its products reach the market. The three major recombinant DNA-made products so far announced are interferon, under contract to Hoffmann-La Roche, insulin, prepared for Eli Lilly, and growth hormone, made for Kabi.

A possible cloud overhanging the interferon project is a claim against Genentech's partner Hoffmann-La Roche by the University of California. The prospectus issued by Genentech says only that there exists a claim against Roche which, if a law suit is filed, could be expanded to Genentech. But in that event, the prospectus continues, there would be no effect on Genentech's earnings because Roche has agreed to protect Genentech against loss.

The claim concerns a cell line developed by H. Phillip Koeffler and David W. Golde of the University of California, Los Angeles, in 1978. The interest of the cell line is that it produces interferon, the wonder substance hoped, but not yet proved, to be of relevance to the treatment of cancer.

Both Golde and Koeffler, under instructions from their attorney, refuse to discuss the claim against Roche, and Roche officials stick tight-lipped to a statement that they "acted properly with regard to the cell line," which the company obtained from the National Cancer Institute. The dispute seems to center around the terms under which the cell line was received by Roche.

Genentech is going public earlier than generally expected. An investment analyst who follows the gene splicing industry, Nelson Schneider of E. F. Hutton, said only in May that "None of these companies has any thought of going public and if they were we would tell them not to because there is no guarantee as yet that this technology will produce anything."

Now is an appropriate time for Genentech to go public, says vice president Thomas D. Kiley: it has shown it can make useful products and needs money to build a manufacturing plant. Public, not private, capital is being sought "because we want to maintain our independence and freedom of action," says Kiley.—N.W.

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