

Insulin Gene Researchers Admit Breach of Rules

Through error or arrogance, researchers working on the insulin gene broke the National Institutes of Health guidelines on recombinant DNA research last winter. Scientists at the University of California in San Francisco prematurely used a specific ring of DNA (the plasmid pBR322) to carry rat genes into bacteria. That plasmid was not completely certified for use until July 7.

There is no issue of a public health problem. The same experiment would be acceptable if it were done today. Nor did the work give the researchers an edge on their competitors, since, according to a report in the Sept. 30 *SCIENCE*, the half-completed experiment was destroyed early in March when the scientists say they first learned that the plasmid had not been certified. The transfer of the rat insulin gene into bacteria, which was reported in May (SN: 5/28/77, p. 340) and which received worldwide acclaim, was done with a different plasmid, pMB9. That experiment did follow the NIH guidelines, the researchers emphasize. "The cloning and all the information in that [June 17] *SCIENCE* article were as stated. This incident has no relationship to that," William J. Rutter, one of the project leaders, said in a telephone interview.

The researchers are pleading confusion over the early NIH rules. Plasmid pBR322 had been tentatively approved by the NIH recombinant DNA committee on Jan. 15, but was not yet certified by the director of NIH. "If you read the guidelines carefully there is no mention of a distinction between approval and certification," Rutter says. "That was an unfortunate period of time when confusion reigned." However Herbert Boyer, the UCSF researcher who provided the plasmid, says that one individual from the insulin team did call repeatedly to ask the status of the certification procedures. "I was clear on it [the difference between approval and certification]. I just felt everybody knew and apparently that wasn't the case," Boyer says. According to the minutes of a meeting of the UCSF biosafety committee, the researchers said they had been verbally informed that the certification was imminent and that they should proceed with their experiments.

Neither NIH nor the local biosafety committee, which is charged with enforcing the rules, was immediately informed of the experiments. Rutter explains that approval for the plasmid pBR322 was considered imminent. He also points out that there was a tense political situation, with recombinant DNA legislation coming before Congress and with much public attention being given to rules and regulations. Eventually the researchers did call their breach of the rule to the local committee's attention.

Researchers in other laboratories and reporters suspected violations of the guidelines last May when the group announced in a press conference their surprisingly rapid success in transferring the gene using plasmid pMB9. That announcement occurred only three weeks after certification of the plasmid—barely enough time in which to do the work. Furthermore, an article in the June *SMITHSONIAN* by Janet L. Hopson, formerly of *SCIENCE NEWS*, described a careless attitude toward the guidelines among many young researchers working on recombinant DNA in the UCSF laboratories. Hopson quotes a researcher advising a foreign visiting scientist: "No one has to know if you go ahead a little early. You can repeat the experiments later and publish them from your own country."

The California researchers countered the suspicions by insisting that the experiment followed the guidelines completely and just went very well. "The major problem is getting the DNA. We had it all ready to go," Rutter and Howard M. Goodman told *SCIENCE NEWS* at that time. Because they had done the experiment from scratch with a certified vector, they did not mention their earlier experiment. Rutter now says, "We decided to not bring that up. True there had been confusion and we had discovered it. But we handled it appropriately; therefore it was not a thing we needed to make a great deal of publicity out of."

The researchers and the local biosafety committee attribute much of the trouble to communication problems between NIH and investigators. "At that time there was no formal means of communication with the investigators and either NIH or local safety committees," Rutter says.

"Most things were done by word of mouth." The NIH Office of Recombinant DNA Activities did not investigate the rumors at the time of the announcement that the insulin researchers had used an uncertified plasmid. "The first we heard of it was from Nicholas Wade [of *SCIENCE*]," says Daphne Kameley, assistant to the director. However James Cleaver, current chairman of the UCSF safety committee, says that NIH was informed of the experiment and the destruction of the material in June in a letter to DeWitt Stetton Jr., chairman of the NIH recombinant DNA committee and deputy director for science.

Another University of California researcher suggests the problem may lie in a lack of communication between the project leaders and the post-doctoral researchers who actually do most of the experiments. A spokesman for the university explained that the experiment with pBR322 was stopped when Goodman, who had been on sabbatical in Japan, returned to this country and first learned of the work with the plasmid and of the state of its NIH approval.

The researchers, NIH officials and a University of California statement emphasize that the experiments were done during a period when the guidelines were just being set up. "The system has improved and tightened up with experience both here and nationally. I think there is no likelihood of this type of confusion ever being repeated," says Cleaver. He reports a great deal more sensitivity among campus scientists to the necessity of following the regulations.

It is unlikely that any action will be taken against the researchers, although the local biosafety committee is continuing its investigation of the occurrence. □

Concorde rumbling may continue

Last week the Carter Administration announced that it would support permanent traffic of the Concorde, the controversial joint British and French supersonic jet, eventually with service possibly expanded to as many as 13 cities. The Concorde has undergone trial runs to Dulles International Airport, near Washington, since May 1976. Transportation Secretary Brock Adams described the federal decision on the Concorde as a difficult political compromise between the desires of environmentalists and the image of the United States and its aerospace industry as seen from abroad.

There is a loophole, however. The Administration has said that any city may set "reasonable" and "nondiscriminatory" noise standards that could, in effect, prohibit supersonic traffic. The Concorde was rated in a Government Accounting

Office study as twice as loud on takeoff as the loudest subsonic jet. The Federal Aviation Administration found the Concorde to be four to eight times noisier on takeoff than newer, wide-bodied jets. Before Concorde traffic is expanded, there will be public hearings and comments, although the Transportation Department is not yet saying where or when.

Another catch in the Concorde's approval is that only the 16 planes now in service or production would be allowed to operate at current noise levels; any future commercial supersonic aircraft would have to meet 1969 federal noise standards set for such wide-bodied jets as the Boeing 747 and McDonnell-Douglas DC-10—something that may well prove impossible for any supersonic commercial transport plane. □