

# Dispute over Access to Reye's Study Data

*To defend itself in lawsuits, an aspirin manufacturer seeks the raw data from a government study; but the government says it cannot give them out*

A legal tussle is shaping up over access to raw data collected as part of a federal study of the potential hazards associated with the use of aspirin by children. Plough, Inc., the manufacturer of St. Joseph's Aspirin for Children, claims it needs to see the data to defend itself against lawsuits brought by parents of children allegedly harmed by taking aspirin. But federal agencies involved in the study argue that the data cannot be released without compromising the privacy of the patients.

At issue is a pilot study, sponsored by the Centers for Disease Control, whose results indicated that children and teenagers who take aspirin when they have influenza or chicken pox are more likely to develop Reye's syndrome—a very rare and potentially fatal disease (*Science*, 25 January, p. 391). The study figures prominently in a lawsuit brought by the family of a California boy, Larry Allen Bunch, Jr., who got Reye's syndrome 2 years ago when he was 10 years old and is now mentally impaired as a result of the disease.

Citing the CDC results in particular, the plaintiffs claim that there is scientific evidence linking aspirin use to Reye's syndrome and that Plough and other defendants, including Dow Chemical Company, which makes the salicylate, the active ingredient in aspirin tablets, have attempted to conceal the evidence. The suit seeks \$150 million in damages.

But, says Plough, this suit places the company in a quandary. In order to defend itself, the company would like to know whether the CDC's pilot study really did demonstrate a link between aspirin use and Reye's syndrome. Therefore, they would like to see the raw data and analyze them. But they have so far been unable to get those data because they reveal confidential information about the patients, their families, and the physicians who participated in the pilot study. The issue is, who owns the data from this federally funded study and to what extent must the privacy of the study participants be protected?

The company's quest for data also has led its lawyers to the Institute of Medicine, which has a contract from CDC to monitor and critique the study step-by-step for scientific and statistical validity.

Depositions have been taken from two IOM staff members, and the company is seeking information from committee members. Negotiations with the IOM and CDC are under way, but sources say it is unlikely that the data the company seeks will be released.

The first hints that aspirin use may be linked to Reye's syndrome arose in 1980 when the state health departments of Arizona, Michigan, and Ohio completed case-control studies comparing Reye's syndrome patients to children of similar ages and with similar initial illness who did not go on to get the syndrome. The states reported that one difference between the Reye's syndrome cases and the controls was that the cases were more likely to have taken aspirin. Later, Michigan conducted a case-control study that also linked aspirin to Reye's syndrome. Subsequently, these results, the Health Research Group, a consumer lobbying organization, called for warning labels on aspirin. But the states' studies were methodologically flawed—such studies are notoriously difficult—and the Food and Drug Administration sought more data before requiring warning labels. Thus the CDC began its pilot study.

The pilot study was not designed nor intended to resolve the question of whether aspirin use is associated with Reye's syndrome. It was meant to test the methodology that the CDC wanted to use for a subsequent full-scale study. But its results surprised everyone. The study indicated that children who take aspirin when they have influenza or chicken pox are 25 times more likely to develop Reye's syndrome. The CDC released the pilot study's results but cautioned that since it was just a small-scale study and not meant to be definitive, the larger study was still necessary to confirm the results. It is now being conducted, but the results will not be in until next year.

In the meantime, however, Plough is faced with what it anticipates to be the first of a number of lawsuits. The company has asked Seymour Grufferman, an epidemiologist and pediatrician at Duke University to look at the raw data from the pilot study to see how sound the conclusions from that study are. Grufferman explains that since most people are aware that aspirin use has been linked to

the development of Reye's syndrome, case-control studies can be very difficult. It could be that the parents of Reye's syndrome patients are more likely to recall giving their children aspirin when they are questioned, for example.

Grufferman wants to see the medical records of the cases and the controls and would like to know what the parents told the children's physicians about aspirin use before the children came down with Reye's syndrome. He wants to see the questionnaires administered to the parents of the cases and controls after the children had been diagnosed as having or not having Reye's syndrome. He also would like to know how the cases and controls were selected. "The issue is," he remarks, "were the methods adequate to say with some degree of certainty that this was a properly done study?" So far, however, he has been stymied in his attempts to see the raw data, most of which are in the hands of Westat, a Rockville, Maryland, consulting company which conducted the study under contract for the CDC, and the rest of which are in the hands of the Department of Health and Human Services.

Plough has had subpoenas issued for the raw data and has said it does not want the names, addresses, or any other identifying information. The company has offered to enter a protective order—a court order ensuring that Plough will not reveal any confidential information it may incidentally glean when examining the raw data.

Westat officials say they cannot release the data because the contract under which they did the study requires that the data be kept confidential. And HHS says it cannot give out much of its data because it is impossible to erase "indirect identifiers" which could reveal the identities of patients and physicians. These indirect identifiers include even such things as lot numbers of medications. Plough's attorney, Bryan Yolles of the Washington firm of Clifford and Warnke, explains that the ingredients in some "local medications" vary from state to state. "Some contain aspirin and some contain acetaminophen. We want the lot numbers so we can check the labels ourselves and verify what's in them," Yolles explains.

But the government argues that anyone with the lot numbers could trace where the medications were shipped and sold. Then, because Reye's syndrome is such a rare disease—only 204 cases were reported to the CDC in 1984—it would be possible to make a pretty accurate guess as to who was a subject in the pilot study. Other indirect identifiers include histories of chronic illnesses, the ages of the subjects, and their sexes—in short, much of what Plough considers essential to its analysis of the study's conclusions.

Michael Pietrangelo, who is a vice president for consumer operations at Plough, says he has been down this road before. Five years ago, when the results of the first of the state studies alleging an association between aspirin use and Reye's syndrome were reported, his company also sought raw data. At that time, they were trying to determine whether warning labels on aspirin were justified, he says. "We asked the CDC for the raw data, and the CDC advised us

that neither it nor the FDA had the data. The raw data were in the hands of the states. Yet the CDC was asking the FDA to require warning labels, and no one at the CDC had looked at the raw data."

The states refused the company's requests for the data, stating privacy and confidentiality considerations. So, says Pietrangelo, "We filed suits to get the data and we were successful. Then we gave the raw data to the CDC and the FDA. After analyzing the data, the government said there's not enough here and that a major study is needed." Pietrangelo emphasizes that when Plough looked at the raw data from the states' studies, it was entirely uninterested in identifying the patients or physicians involved. "We were actually given some names and we returned them," he says.

The Department of Justice and Westat decline to comment other than in their legal documents. The crux of their argument, however, is that, as the Justice Department says in one of its motions,

"The United States does have a compelling interest in preserving the privacy and confidentiality of information contained in those records and, in fact, required as much in its contract with Westat."

Walter Dowdle of the CDC says his agency has been meeting with aspirin industry representatives and trying to reach some sort of accommodation. The CDC gave Plough the information from the questionnaires, for example, but not the questionnaires themselves. "We provided raw data but not the rawest raw data," Dowdle remarks.

So the matter will be decided in the courts. And the decision is by no means clear-cut. Key information on the study's participants could indirectly identify them. Yet without such information, Plough says it will find it hard to defend itself in the current and future lawsuits. As Grufferman remarks, "It's a damned if you do, damned if you don't situation."—GINA KOLATA

## Stanford President Upholds Mosher Expulsion

*Kennedy criticizes the former anthropology graduate student for "lack of candor" and lying to him; Mosher plans rebuttal*

On 30 September, Stanford University president Donald Kennedy upheld the expulsion of graduate student Steven W. Mosher from the anthropology department, reaffirming an earlier faculty decision to dismiss him\*. Kennedy cited an alleged pattern of behavior by Mosher that "destroyed the confidence" of Stanford faculty in his ability to meet the requirements of the profession. Kennedy also accused Mosher of lying to him in the course of his investigation.

Mosher said in an interview with *Science* that he is preparing a detailed rebuttal to Kennedy's ruling and that he will sue the university.

In 1983, the Stanford anthropology department voted 11 to 0 to expel Mosher for engaging in "illegal and seriously unethical conduct" while doing research as a graduate student in China. In upholding the department's judgment against Mosher, Kennedy put great weight on what he called Mosher's "lack of candor" in dealing with his advisors

and the committee investigating charges against him.

However, Kennedy also noted that, on the basis of recently available information, it is not clear that allegations of illegal conduct can be sustained. Observing that from the beginning Mosher could have refuted the allegations against him by offering more than just a blanket denial, Kennedy said, "Had you been forthcoming with the committee, you could have availed yourself of many opportunities to raise doubts [about the charges], but by the attitude you adopted, you left a record that permitted no conclusion other than the one they reached."

The anthropology department has consistently refused to lay out the specific evidence against Mosher, which is contained in a report by an ad hoc Stanford committee that investigated the case, contending that disclosure might endanger Chinese villagers.

Mosher, who also has refused to release the report, has argued that the department bowed to political pressure from the Chinese and American Sinologists after he published an article in Taiwan about birth control practices in

China. The article was accompanied by photos of Chinese women, whose faces were not masked, undergoing abortion (*Science*, 24 June 1983, p. 1334; 13 May p. 692).

In his decision, Kennedy spoke to Mosher's charge that Stanford bowed to pressure from the Chinese government, which is displeased with Mosher's behavior. "I find no evidence that, prior to this review, anybody involved received any threats," Kennedy said. "The situation has changed, however, during my consideration of your appeal." On 22 July 1984, Kennedy received a letter from a Chinese official who said that Mosher's "behavior seriously damaged the cultural and scholastic exchange between China and the United States . . . I trust that you will make a correct judgment, based on the facts, and properly handle this matter."

Said Kennedy in reply to Mosher, "That does sound like a threat. . . . It is wrong to give in to a threat. It is equally wrong, however, to alter a decision in order to avoid the appearance of yielding to a threat."

Since the anthropology department decision in 1983, Mosher has unsuccessful-

\*Single copies of Kennedy's decision are available free upon request from Stanford News and Publications Service, Press Courtyard, Santa Teresa Street, Stanford, Calif. 94305.