Data falsification trial

Drug testing lab was "shambles"

Washington

FOUR scientists who held key positions at the major testing laboratory Industrial Bio-Test went on trial in Chicago last week on charges of falsifying safety data on drugs and other products submitted for government approval. In the government's opening statement, Assistant US Attorney William Spence painted a picture of a laboratory "in shambles", with mice escaping, watering equipment malfunctioning and flooding laboratories, large numbers of animals dying and left to rot in their cages, and too few trained technicians to carry out necessary tests. Spence charged that to hide its failings and to meet deadlines, the laboratory had fabricated results, cut tests short, and then, to cover its tracks, back-dated reports, destroyed records, and lied to investigators from the Food and Drug Administration (FDA).

The indictment names four specific products, all since retested and approved. FDA has begun reviewing 800 other tests carried out by the laboratory, however, and the Environmental Protection Agency is reviewing 200 tests performed on pesticides. According to the government, Industrial Bio-Test was one of the largest independent testing laboratories in the United States, until FDA began its investigation in 1976. At that time, it was carrying out as many as 2,000 tests a year.

The government's case will rely heavily on the testimony of employees who have been granted immunity from prosecution. One key witness will be Philip Smith, a technical writer whose job it was to write up reports on the studies carried out at the laboratory. In Smith's earlier testimony to a grand jury, he told how data from a test of the drug Naprosyn, an anti-inflammatory agent developed by Syntex Corporation, could not be found but nonetheless turned up — handwritten — in a final draft of the report. Smith and the laboratory's chief of clinical pathology had already concluded from a search of records that the work in question — blood and urine analyses — had never been done. Smith left that section of the report blank and told Paul Wright, director of rat toxicology and a defendant in the case, that he would not sign the report; several weeks later, Smith saw the final draft and saw not only the handwritten insertions but also found that a signature page from an unrelated study had been appended, making it appear that he had signed the report.

Smith also told the grand jury that he had been ordered by another defendant, Moreno Keplinger, previously the laboratory's manager of toxicology, to manipulate data reported on studies of two agricultural chemicals, Sencor and Nemacur, developed by Chemagro. According to Smith, Keplinger was dissatisfied with the data reported on the positive controls (animals fed a known carcinogen in order to demonstrate the susceptibility of the test strain to cancer) saying they did not show a high enough incidence of cancer. Keplinger is alleged then to have ordered Smith to incorporate into the final report a control group from an unrelated test, even though the controls had not been fed the carcinogen, as required by the Sencor and Nemacur studies, but had had it painted on the animals' skin. The government also claims the studies ran for only 14 months, not the 18 months required, and that records were doctored to conceal this.

The fourth substance mentioned in the indictment is TCC, an antibacterial agent used in deodorant soaps and manufactured by Monsanto. According to the government, Wright, who left Industrial Bio-Test to join Monsanto, brought pressure on the laboratory to change a pathology report which found harmful effects of TCC on the testicles of exposed rats. The government claims that the other unfavourable data were suppressed as well.

Spence, in his opening statement, dwelt at length on slipshod conditions at the laboratory. He described a chaotic scene of animals dying or escaping and being replaced in the middle of tests. Spence claimed that as many as 20 or 30 mice would escape from their cages each day (he said they were in rat cages and could slip through the bars) and would be periodically rounded up in "chloroform hunts" by employees armed with squeeze bottles of chloroform. The captured mice were returned to cages almost at random, he said, since there was no marking or numbering system.

As well as Wright and Keplinger, the company's president, Joseph Calandra, and the senior group leader for rat toxicology, James Plank, are also accused in the case.

The defence plans to question the government's use of immunity for its witnesses and what defence attorneys call the government's "bullying" and "brainwashing" to obtain evidence. Judge John Nordberg has already denied a pre-trial motion to dismiss the charges for this reason, but the defence will certainly focus on this in the trial. The defence attorneys have also accused the goverment of violating attorney–client privilege by offering immunity from prosecution to two attorneys who earlier represented the laboratory during the FDA investigation. The laboratory itself, however, is not charged in the case. Nordberger's denial of a motion to dismiss on this count is under appeal.

The defence will also argue that what the government calls "horror stories" about the laboratory's conditions in fact reflect acceptable laboratory practice at that time. The trial is expected to last three to four months.

Stephen Budiansky

Laboratory safety

Bending rules to aid research

ARE laboratory chemists more at risk than other people because many of the chemicals they handle are toxic, or does their competence give them immunity? This was the essence of the question discussed two weeks ago in London at a meeting organized by the Royal Society of Chemistry for the Federation of European Chemical Societies (FECS).

Insurance statistics from West Germany show that the accident and occupational health record of chemists compares very favourably with other research and industrial professions. And the evident longevity of members of the Royal Society of Chemistry was put forward as supporting evidence.

A view widely held was that the competence of the laboratory chemist in handling dangerous chemicals, and the fact that very small quantities are generally involved, should be taken into account when legislation on health and safety is formulated. Most of the regulations on the use of dangerous chemicals in European countries make no distinction between large-scale use of chemicals in industry and small-scale use in the laboratory. According to Professor M. Corn (School of Hygiene and Public Health, Johns Hopkins University, Baltimore), the US Occupational Health and Safety Administration is contemplating relaxing some of its more stringent requirements for specialized research laboratories.

Much of the discussion at the London meeting, however, centred on harmonizing legislation on an international scale. Recommendations included the standardization of statistics on the reporting of accidents and near misses, a research programme to establish what precisely constitutes a carcinogen, safety audits to be extended to universities (Dr N. H. Pearce of the University of Bristol reported a blackly humorous case of conflicting legislation which led the university first to install a door with two-hour fire resistance, and then, by adding mandatory view-panels and louvres, to reduce its efficacy to a few minutes), architectural research aimed at the better planning of laboratories (Dr Istvan Szentpeteri of the Chemical Engineering Centre, Budapest, pointed out the hazards of the high-rise laboratory blocks, popular among Hungarian planners for prestige reasons), and the incorporation of compulsory courses on toxicology and safety procedures into undergraduate studies in chemistry.

The media were subjects of one resolution, which called for less emotive reporting when discussing alleged carcinogens or other toxic chemicals.

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