DBS: Agency Contravenes Its Own Regulations

A major deviation from rules by a federal regulatory agency has been documented by the General Accounting Office (GAO), the investigatory arm of Congress. According to an 8-month GAO study released last week, more than half of the influenza vaccine lots certified by the Division of Biologics Standards (DBS) over a 3-year period were known to be less potent than the agency's own prescribed standard. The GAO study also indicates that the DBS director failed to order ineffective and potentially harmful vaccines off the market for fear that his bureaucratic domain would be threatened.

The GAO report is the first detached and independent study of the DBS since the agency was publicly criticized last September. DBS scientist J. Anthony Morris and consumer advocate James S. Turner charged that a major breakdown had occurred in the scientific integrity of the division (*Science*, 3 March). Robert Q. Marston, director of the National Institutes of Health (NIH), appointed a committee of vaccine experts to examine the indictment and announced on the basis of the committee's findings that "the Morris/Turner charges of scientific mismanagement are without merit." The GAO report confirms that in 2 of the 12 specific issues raised by Morris and Turner—influenza vaccine potency testing and the DBS's authority to require efficacy in the vaccines it licensed—the DBS was considerably at fault, although not precisely in the way described by Morris and Turner. The GAO report tends to corroborate the general theme of the Morris/Turner indictment, that the scientific management of the DBS has been less than outstanding. However, NIH officials contend that the GAO report seriously misrepresents the DBS's role in certifying influenza vaccines.

The GAO report was initiated last June at the request of Senator Abraham Ribicoff (D–Conn.), chairman of the subcommittee on executive reorganization. The GAO investigators discovered that on the evidence of the DBS's own records, 130 of the 221 lots of influenza vaccine released by the DBS in 1966–68 failed to meet the standards of potency required by the agency's own regulations. One hundred and fifteen of these lots were subpotent according to the test results submitted to the DBS by the manufacturers themselves. Another 15 lots were potent according to the manufacturers' tests and failed the tests conducted by DBS scientists, yet were released for public use by the DBS management.

Asked by *Science* on 2 March whether manufacturers had been submitting subpotent vaccines and why a manufacturer was given the benefit of the doubt with a particular lot that had failed the DBS's own tests, DBS director Roderick Murray stated in a written reply: "No lot of vaccine of low potency was knowingly released. . . . The suggestion that benefit of the doubt was given to manufacturers is untrue and is, in fact, reprehensible." The GAO study of the same question concludes: "We found, however, that DBS was releasing lots of influenza virus vaccines during 1966, 1967 and 1968 even when its tests showed the potency of the vaccines to be as low as 1 percent of the established standards."

A second area studied in the GAO report is the legal authority of the DBS to require that the products it licenses be effective. The GAO report states that according to Murray himself, 75 of the 263 products licensed by the DBS are generally not recognized as effective by most of the medical profession. Only 32 of these products are currently on sale to the public. Until recently the DBS claimed it had no legal authority to order these ineffective vaccines off the market (*Science*, 10 March). In November 1971 the Secretary of Health, Education, and Welfare (HEW) accepted an argument by Turner that the DBS did possess such authority under the Federal Food, Drug, and Cosmetic Act of 1962. The GAO report reveals that Murray was advised by HEW counsel in February 1969 that the DBS possessed authority under the 1962 act to enforce vaccine efficacy. Murray refused to use the act—which is the chief legal weapon of the Food and Drug Administration (FDA)—on the grounds that to do so would strengthen the argument of those who wished to merge the DBS with the FDA into a single control agency. As a result, the DBS has allowed to remain on the market vaccines which are not only ineffective but also potentially harmful. The GAO report notes that according to the package label on one of the ineffective vaccines, "there have been reports of children who have developed systemic reactions—consisting of fever, rash, abdominal cramps, and diarrhea —4 to 8 hours after injection."

Murray's memorandum declining to use the efficacy authority of the 1962 act was routed through the front office of the NIH. But until November 1971 the public position of the DBS and the NIH was that such authority did not exist. For example, the NIH committee of outside experts (the Benenson committee) stated in its report, which was endorsed by NIH director Marston, that "there is no legislative requirement that these products [licensed by DBS] be effective." This statement was based on a memorandum prepared by DBS assistant director Sam T. Gibson which, however, neglected to mention that HEW counsel had advised the DBS in 1969 that authority did exist to rule ineffective vaccines off the market.

According to Robert W. Berliner, NIH deputy director for science, the GAO report fails to make allowance for the variability of the test used to assess influenza vaccine potency. The vaccines the GAO describes as subpotent, Berliner told *Science*, were those that fell in the lower half of the statistical scatter about the mean and which may in fact have been potent. If the DBS had raised its potency standards significantly, the stronger vaccines in the statistical scatter would have caused unpleasant side effects. The DBS policy was thus reasonable scientifically, even though it contradicted the precise letter of the DBS's regulations. Asked why the GAO report should misrepresent the situation, Berliner said, "They're out to make a splash."

Morton A. Myers, an assistant GAO director who supervised the study, declined to comment on this remark but stated that Berliner's views had been considered earlier when the NIH was shown a draft copy of the report. The GAO position is that the DBS's own regulations required—and presumably for good reason—that all vaccines should equal or exceed the standard potency, hence vaccines which fell be-

low this precisely defined cut-off point should not have been released.

The precise effect of the DBS policy of releasing subpotent vaccines is hard to estimate but probably some 67 million doses of influenza vaccine were used in the United States during the 3 years covered by the GAO report. If half of these vaccines failed the DBS's own standards, and the cost to each recipient was $1 a head (a conservative estimate), then the DBS has allowed citizens to spend more than $30 million on subpotent vaccines.

On the question of efficacy of influenza vaccine, the GAO report records a difference of opinion between DBS officials, who estimate the vaccine is 50 to 60 percent effective, and studies conducted by the Center for Disease Control, one of which concluded the vaccine had "little if any effectiveness" and another that its efficacy was "20 to 25 percent at best."

The GAO auditors recommend in their report that the Secretary of HEW should require the NIH to establish milestones for implementing the efficacy provisions of the 1962 act and should monitor the NIH's progress in doing so. The report also advocates that the DBS should revise its philosophy of relying on the manufacturers to do the necessary tests. HEW should require the DBS to prevent vaccines from being released if either the manufacturers or the DBS shows the vaccines to be subpotent, the GAO report advises.

The fact that the GAO, not the NIH, discovered how the DBS went about certifying influenza vaccines raises the question of whether the NIH has exercised adequate supervision over the DBS. Not until last August, some 5 months after the DBS management had been crushingly overruled in a grievance hearing brought by Morris, formerly the DBS influenza control officer, did the NIH launch a formal inquiry to ascertain if all was well within the DBS. Despite the GAO report, however, NIH officials continue to maintain, as reported in *Science* (17 March), that Murray has a good record as a regulatory official.

Be this as it may, a committee chaired by NIH deputy director John F. Sherman has been appointed to search for a successor to Murray. The successor will assume office immediately rather than when Murray reaches mandatory retirement age in August 1973. NIH officials indicate that personnel problems in the DBS rather than any regulatory failing are the reason for this change.—NICHOLAS WADE

Navy F-14: New Fighter's Cost, Sophistication, Stir Controversy

Senate hearings are now in progress in advance of the fourth annual congressional debate over the future of the F-14, the Navy's costly, carrier-based, swing-wing fighter. The F-14 is intended to defend the fleet against air and missile attack, to provide aerial escort of carrier-based bombers, and to furnish air superiority over areas of ground combat. The Navy says the F-14 is essential to the national security. Others believe its contribution is out of line with its costs. The ostensible question before the Congress is whether to authorize procurement of 48 aircraft in addition to the 86 already funded. The underlying issue is whether limited government revenues should be spent here or elsewhere.

The F-14 controversy involves questions of cost, effectiveness, and need. Is the cost excessive? Are there more efficient means of protecting carriers from air attack? Is it more economical to use land-based bombers in situations where carriers might be employed, providing the F-14 were available for air defense? If so, should aircraft carriers be assigned a lesser role in the overall defense posture of the United States? Is the F-14 essential in order that certain commitments to allies be fulfilled? The argument is fueled by disparate estimates concerning the course of domestic and international affairs, military threats and capacities, and developments in science and technology.

So far, more than $2.5 billion has been appropriated for the F-14 program—$1.26 billion for research, development, testing, and engineering, and $1.47 billion for procurement. Eleven F-14's are in flying status, and 75 are in various stages of assembly.

By any standard, the F-14 is a major enterprise. It currently represents nearly 0.1 percent of the gross national product. It provides employment for at least 50,000 workers. It consumes approximately 1 percent of the entire Department of Defense appropriation, 3 percent of the total military procurement authorization, and about 7 percent of Navy procurement funds.

Support for the F-14 is shaky. Secretary of Defense Melvin Laird has expressed doubt. On 9 February, Senator John Stennis (D–Miss.), chairman of the Senate Armed Services Committee, stated his general concern that concentration on sophistication rather than numbers can leave American military forces inadequately equipped to perform their assigned missions.

The Senate Armed Services Committee tactical airpower subcommittee last week started hearings for the purpose of determining what the Navy's procurement plans were and how much the program was likely to cost. There is some concern that, if costs rise, appropriated funds will be used to procure a smaller number of aircraft than that specified in the original budget request. Senator William Proxmire (D–Wis.) has recommended that Members of Congress for Peace through Law, a bipartisan group of 30 senators and 97 congressmen, focus on the F-14 as one of four major weapons programs that should be cut back or terminated.

Adding to congressional and Executive skepticism is diminished public patience with cost overruns, delays, and technical problems inherent in undertakings of this type. In consequence, the F-14 is being pursued in an unsympathetic climate, where a lapse in management, design, or workmanship causing cost growth or a plane crash can lead directly to termination of the program.

The previous attempt to develop an aircraft to provide fleet air defense ended in failure with the cancellation