FDA Reform: An Idea Whose Time Has Come

The political appeal of reforming the federal Food and Drug Administration (FDA) has repeatedly lured a swarm of politicians, scientists, and consumers to attack the agency for making one decision or another. Largely as a result of the strong influence of the drug industry lobby, however, Congress has approved major changes in the drug provisions of the 1906 Pure Food and Drug Act only twice—in 1938 and 1962.

Now, as the result of both consumer and industry disaffection with current law, there is a strong likelihood that Congress will pass major legislation to reform the FDA. In a speech on 5 October, Joseph A. Califano, Jr., Secretary of Health, Education, and Welfare (HEW), expressed strong support for FDA reform and announced that public hearings on Administration proposals will be held before Thanksgiving. In light of the observation common on Capitol Hill that such legislation will not be considered again for one to two decades, the current proposals assume great importance.

If successful, the legislation would check abuses in drug prescribing—pleasing consumers, get new drugs into the marketplace more rapidly—pleasing industry, and through a variety of measures, bolster the public's confidence in the soundness of FDA decisions—pleasing the agency. To accomplish these goals, the legislation would completely revamp the drug approval process, set up a new FDA advisory board of outside scientists, provide for tighter controls on drug testing, and open up more of the entire process to public scrutiny.

One of the more controversial proposals would enable the FDA to limit the distribution of an approved drug to specific groups of patients. Under current law, once a drug is approved, any physician may, at his discretion, prescribe it for any patient. The proposed change would give FDA new authority to put limits on the physicians' prescribing rights by saying, for example, that a given drug can be administered only in a hospital. Other controversial proposals would give the agency authority to require that drug packets include messages to patients spelling out the proper use and adverse effects of a drug, and to make industry data on drug safety available to the public for the first time.

Most of the issues addressed by these proposals first became the focus of public and congressional attention in 1974, during hearings sponsored by Senator Edward Kennedy (D–Mass.), chairman of the Health and Scientific Research subcommittee. Witnesses at the hearing testified that physicians were misprescribing drugs, that test data submitted by drug companies in new drug applications often were inaccurate, and that the FDA drug review process was too informal and secretive. In a litany of the criticism that has dogged the FDA for the last 5 years, witnesses from the pharmaceutical and scientific communities charged that overregulation by the FDA had led to a lag in the introduction of new drugs to this country, while a group of FDA employees backed by several consumer groups accused the FDA management of bending over backward to avoid disapproving a new drug.

The substantive result of the hearings was the creation by Caspar Weinberger, then Secretary of HEW, of the Review Panel on New Drug Regulation to investigate the FDA—the 19th formal review of the agency in the last 10 years. The panel's final report, which was released last May, offered few radically new suggestions for FDA reform, but it was well regarded for its thoroughness and careful conclusions. As a result, the report lent credence both to the need for reform and to many of the earlier complaints.

Vastly more important, however, was the widespread recognition in Congress after the well-publicized Kennedy hearings that the mixture of industry and consumer complaints had made serious efforts to reform FDA politically tenable. The agency had become a hot, popular issue, and both Kennedy and Representative Paul Rogers (D–Fla.), chairman of the Health and the Environment subcommittee in the House, recognized this. Kennedy introduced the first of a series of comprehensive drug bills while the review panel was still deliberating. Rogers introduced the first of his own bills soon afterward—partly, a staff aide told *Science*, because he was anxious to dilute charges of industry favoritism raised on a health issue several years earlier, and partly because "he realized that FDA is sexy; you can attract all sorts of press attention with hearings on it."

Both the Kennedy and Rogers bills now pending would enable drugs that represent significant medical improvements to enter the marketplace at a faster rate (a drug approval can now take up to 10 years) by giving the FDA authority to limit the drugs' distribution. This is referred to as the "sodium valproate" provision: it would enable the FDA to approve a drug such as sodium valproate—which is used widely in Europe for the treatment of epilepsy—for a limited patient population that would benefit greatly from it. The agency currently is reluctant to approve such drugs for the general population without thorough testing because the benefits do not as clearly outweigh the proven and potential risks in a group of that size. If a drug is distributed even to a limited population, however, enough additional data would be generated to more quickly satisfy a test of general safety, advocates of the bills claim.

Both bills also would authorize the use of package inserts to alert patients to drug risks and would increase the responsibility of clinical investigators to report evidence of drug carcinogenesis and toxicity. Clinics would also have to obtain the signed, informed, and voluntary consent of patients before they could use an experimental drug.

Other provisions of the Kennedy bill go further, to establish a National Drug Science Board of 11 scientific experts to assess the accuracy of testing conducted by drug companies. Supposedly, the board's imprimatur would boost the public's confidence in FDA decision-making. The bill would also establish a National Center for Pharmacology and attack the long-standing problem of FDA morale by setting aside one-third of the pharmacological, scientific, and medical positions for people rotating in from universities. One-third of the scientists could be on sabbatical at one time, and all of those working at any one time could spend 40 percent of their time at the National Institutes of Health in research unrelated to their FDA work. Officials at the FDA, of course, approve of the goals—to attract better scientists and maintain their expertise—but doubt that Congress would fund the 100 percent increase in manpower necessary under the plan to keep the current level of productivity. As one official said, "Morale and talent are problems that are not likely to ever disappear."

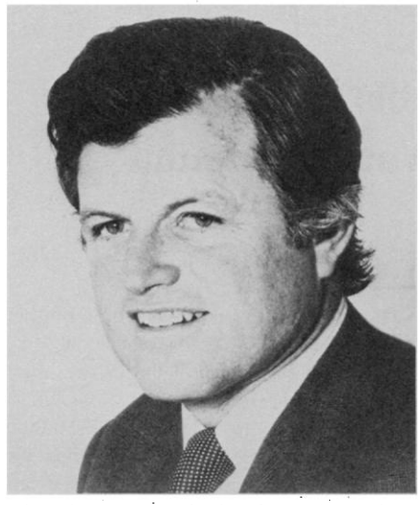
A third comprehensive drug bill, introduced by Senators Jacob Javits (R–N.Y.) and Harrison Williams (D–N.J.),

was added to the tangled thread of proposals in August. The explanation for the bill's introduction is a testament to the importance of congressional staff personnel to the outcome of this and probably other controversies: Alan Fox, who had worked for Kennedy and written the Kennedy bills introduced in previous sessions of Congress, became Javits' legislative assistant on 1 May. Fox was replaced by Gregory Spence, a former general counsel to the health and hospitals department of the city of Boston, who in less than 3 months wrote the Kennedy bill now pending. Fox was dissatisfied with the update of his bill wrought by Spence; bingo—Javits introduced a different bill. The Javits (Fox) bill is generally similar to Rogers', and differs from Kennedy's bill chiefly over the issue of trade secrets. The Javits bill requires disclosure of drug safety data, in exchange for a provision that gives the drug manufacturer patent protection beginning on the day of approval. Drug patents now take effect when the drug is first submitted to the FDA, even though the drug cannot be sold until it has been approved—a process that can take years. Manufacturers object that they're losing money as valuable patent time is eaten up during the approval process. The bill would require the manufacturer to license the patents after 8½ years for a reasonable fee, however.

[A more radical group of amendments has repeatedly been introduced by Senator Gaylord Nelson (D–Wisc.), including one provision that calls for the federal government to conduct all safety and efficacy testing of new drugs, at industry expense. His amendments would also prohibit the export of drugs not approved for use in the United States and strictly regulate drug promotion practices. None has ever been reported out of a committee.]

The massive publicity surrounding the FDA's recent involvement with saccharin and Laetrile has had mixed effects on the chances for reform legislation approval. In the House, the effect may have been to diminish the enthusiasm of Rogers and his companions on the subcommittee: an aide pointed recently to the quantity of other legislation pending there and said the drug bill may not be considered before next May, adding, "This is something that the members have to be thoughtful about. Rogers may not want to do anything to enhance the authority of the FDA while the public is highly critical of it."

Within the FDA itself, the publicity has made the agency more aggressive about changes it feels are needed to clarify its responsibility and authority. According to William Vodra, associate chief counsel for drugs, "The 1974 hearings caused a crisis at the agency: people here began to doubt whether we were doing what Congress really wanted us to do. Recently, we've been getting hit in public from both sides, and Congress has been holding 'drug-of-the-month' hearings. What we'd really like is for Congress to articulate exactly what our responsibilities are; we want the words, written into the law, to back up the actions we take."



Edward Kennedy: Calling for major legislative reform of the FDA.

FDA commissioner Donald Kennedy, who was sworn in while the saccharin battle raged on all sides, took that idea—an overhaul of federal drug legislation—to HEW Secretary Joseph Califano as one of three goals for which he needed Administration support. Califano immediately seized upon the idea, and directed the agency to begin preparation of an Administration bill.

Whether or not the bill, which Vodra has been preparing, will be ready in time for real consideration by Congress is doubtful. Vodra said that the complete Administration bill will not be ready until January, and Larry Horowitz, a Kennedy aide on the subcommittee staff, said that the FDA's proposals will be included informally in the markup of the Javits and Kennedy bills this fall.

Mostly, the FDA wants changes in the law that reflect the daily, practical exigencies of FDA rule-making, Vodra said. "We'd like to fine tune it to more accurately reflect reality." Provisions being considered now would ease the procedures for permanently removing a drug from the market as an "imminent hazard" to public health, and explicitly modify the definition of a "safe" drug to include some recognition of risks.

Opposition from manufacturers may hinge in part on the settlements of two challenges to critical parts of FDA regulation and of the proposed legislation: One is a challenge to the removal of the drug phenformin, which is used in the treatment of diabetes, from the marketplace as an "imminent hazard" to public health—the first time that the 15-year-old clause was invoked. The other is a legal suit challenging regulations that require the inclusion of patient warnings in birth control pills and other drugs that contain estrogen. If industry wins the suits, Vodra said, it will vigorously oppose legislation reestablishing FDA's authority in these areas; if it loses, it will fight for the most favorable legislative formula.

Other provisions in the legislation have been the subject of extensive comments by the Pharmaceutical Manufacturers Association (PMA), the American Medical Association, and an umbrella organization, the National Council of Drugs. Their chief target, aside from patient package inserts and the imminent hazard clause, appears to be provisions requiring the release of safety and efficacy data, which now are protected from disclosure as trade secrets. The drug companies worry that vital manufacturing data might be deduced from the safety information, particularly by foreign "drug pirates." Javits' aide Fox conceded that some pirating might occur, but said this would promote competition and lower prices. Bruce Brennan, vice president and general counsel for PMA, said that because industry believes such a view is the predominant one in Congress, it probably is willing to concede the release of some trade data even without a legislative trade-off.

Despite some reluctance in the House to act on the legislation during the current Congress, Kennedy's staff is pushing hard for passage of a bill in the Senate. Kennedy's aide Spence notes that "all the ingredients for major drug reform are here: Senate awareness, well-considered proposals, the interest of the Administration, and some industry willingness to change." In a reference to other occasions when comprehensive drug legislation was passed, however, he noted that a crisis was missing. In 1938, Congress passed drug safety rules in the wake of more than 100 deaths caused by a preparation of sulfanilamide; in 1962, drug efficacy rules were passed after congressional hearings on the thalidomide disaster.

"I only hope," Spence said, "that it doesn't take another disaster to get one of these bills through."

—R. JEFFREY SMITH