to the increasing difficulties that the United States faces in operating a foreign aid program mainly on its original bilateral lines in a world that has changed profoundly in the quarter century since the U.S. foreign aid effort was shaped.

In a key concluding paragraph of its recommendations, the Peterson report says "With this new institutional framework, the U.S. government should need fewer advisers and other personnel abroad. It could assume a supporting rather than a direct role in international development."

AID Administrator Hannah is a proponent of research and of greater university involvement in development problems, and he is said to be sympathetic to the Peterson blueprint. Hannah is also said to have firmer standing at the White House than his predecessors.

But the foreign aid program has been reorganized many times before without being changed very much. And the Nixon Administration could implement the Peterson recommendations to the letter and still miss the spirit.—JOHN WALSH

FDA: Efficiency Drive Stumbles over the Issue of Drug Efficacy

The Food and Drug Administration has long been one of the most overworked, understaffed, and universally criticized of all federal regulatory agencies. Since 1962, when the Kefauver-Harris Drug Act was passed in response to the thalidomide scandal, the agency has had the responsibility for ensuring the safety and effectiveness of some 7100 drugs already on the market and all new drugs that are proposed for marketing.

The drug industry has kept up an unrelenting attack on the FDA both for delay in approving new drugs for marketing and for allegedly hasty action in removing harmful drugs from the market. Congressional critics and consumer groups at the same time have accused the FDA of being lackadaisical in protecting the public from dangerous drugs. Under fire from both sides, the agency has gone through a number of changes in both operating procedures and personnel during recent years. Three commissioners have served in the last 4 years. Yet the central problem of adequate financial backing remains. Budgetary limitations have hindered the FDA in hiring the number of trained personnel that it needs to review data concerning drug safety and have opened the way for charges that its drug review procedures take too long and are often inadequate.

The most recent attempt to revitalize the FDA was initiated last year by the then Secretary of Health, Education, and Welfare Robert H. Finch. Finch ordered several structural changes in the agency and appointed a new commissioner, Charles O. Edwards. Edwards came to the FDA from the management consultant firm of Booz, Allen & Hamilton. The 46-year-old surgeon is typical of the cool, efficient managers who have filled the top posts in the Nixon Administration.

Edwards describes himself as a man who is "impatient with bureaucratic nonsense." His zeal in cutting through red tape has speeded the process of approving new drugs for marketing and softened industry criticism of the agency. At the same time it has opened the way for charges by Congress and consumer groups that the FDA is circumventing the law and its own regulations in a rush for an efficiency that is helping industry but is of doubtful value in protecting the public.

On 15–17 July, the House Subcommittee on Intergovernmental Relations, whose chairman is Representative L. H. Fountain (D–N.C.), conducted hearings to examine the "new-look" FDA's streamlined methods of reviewing the safety and effiacy of new drugs. The subcommittee, which has a reputation as a sharp-eyed watchdog of federal agencies, spent 2 of its 3 days of hearings investigating FDA's approval for marketing of a new drug called Demulen, an oral contraceptive which allegedly has a relatively low dose of estrogen. Recent studies have shown that low-estrogen pills cause fewer hazardous side effects than do pills which have larger amounts of estrogen in them.

Under the law, when a manufacturer develops a new drug it must be approved by the FDA before it can be marketed. To obtain FDA approval, the manufacturer is required to submit adequate evidence of the safety and efficacy of the drug. This evidence is submitted in the form of a New Drug Application (NDA). The FDA then examines the evidence and either approves or rejects the NDA.

In submitting the NDA for Demulen, G. D. Searle & Company, of Chicago, included two pieces of evidence—a 40-volume British study of the drug and an American study which compared some effects of Demulen with Ovulen, an oral contraceptive then on the market.

According to Delphis Goldberg, professional staff member of the Fountain subcommittee, neither study adequately demonstrated the efficacy of Demulen as defined by FDA regulations. The British study was designed to test only the safety of the drug. The American study provided a comparison of certain effects of Demulen with Ovulen but did not provide a controlled study of Demulen itself. In addition, the American study represented an examination of only 80 women over a period of about 2 years or 24 menstrual cycles. Under questioning from Goldberg during the hearings, Edwards conceded that normal FDA procedures call for the study of at least 200 women. But he said that this is one of the procedures that is "being reviewed."

The FDA approved Demulen for marketing after a 7-day review of the evidence. Normal FDA reviews take an average of 15 months. In defending FDA's decision on Demulen, Edwards cited a recent report by the FDA, which advised doctors that, in view of the evidence that high doses of estrogen cause hazardous side effects, doctors should prescribe, where possible, pills that contain a lower amount of estrogen. After this report was issued, Edwards says that he called in a group of drug manufacturers and, in an unrecorded meeting, told them that if they had any low-estrogen pills ready for marketing, FDA would "expedite" the review of their NDA's. "The Demulen review was expedited in view of my meeting with the drug manufacturers and because of my feeling that

there could be a shortage of low-estrogen pills on the market," Edwards told the Fountain subcommittee.

The decision to expedite the review of Demulen was made despite the following:

1) Several companies already had low-estrogen pills on the market.

2) When Representative Benjamin S. Rosenthal (D–N.Y.), a member of the Fountain subcommittee, asked Edwards "Is it your position that you are to be guided in your priorities according to market conditions and the availability of drugs?," Edwards answered, "Absolutely not."

3) The New Drug Application, according to Fountain's subcommittee staff members, did not adequately demonstrate the efficacy of the drug as required by law.

After several hours of questioning by the Fountain subcommittee, Henry Simmons, director of the FDA's Bureau of Drugs, explained the problem with Demulen and other similar cases, which the agency faces. "We have a difficulty here in being damned if we do and damned if we don't. If we try to be logical about the regulations and use good sense we get tripped up because we haven't followed the letter of the law," he said.

Goldberg had a different view of the case: 'What we are dealing with here is not hard science but the making of decisions on the basis of hypotheses, without the evidence required by law."

The Demulen approval was not the only instance of the new FDA efficiency in speeding the process of getting a new drug on the market. The approval of L-dopa, which is used in treating Parkinson's disease, came after Edwards characterized as "an extraordinary effort by the FDA to make the drug available as quickly as possible." In announcing its approval, Edwards noted that clinical tests showed that one-third of the patients treated wih L-dopa did no respond favorably and that there was a high incidence of side effects. Also cited by the commissioner was the lack of information on the long-term effects of L-dopa. Because of these considerations, the FDA required the drug's manufacturer to continue clinical testing of the drug while it is on the market, an unprecedented requirement by the FDA. According to Simmons, the agency would not in the past have approved the drug until the completion of long-term clinical studies.

Yet while the FDA's new efficiency has speeded up the process of approving new drugs for marketing, it has not appreciably expedited the removal of ineffective drugs from the market. For example, the agency has, to date, published only about one-third of the National Academy of Sciences–National Research Council study of the safety and efficacy of all drugs on the market. This study, undertaken to implement the Kefauver-Harris Drug Act, was completed in 1968. Edwards has promised that all the findings will be made public by the end of this fiscal year and blames the delay on the need to formulate guidelines for relabeling and other changes which the FDA says must accompany the release of the findings, but which the overburdened FDA staff has not yet found the time to compile.

Lawsuit to Compel Release

The commissioner's promises and explanations do not carry much weight with FDA critics. Robert McCleery, for example, a former chief of the Medical Advertising section of the FDA's Bureau of Medicine and now a consultant to Nader's Center for the Study of Responsive Law, believes that economic considerations have played a part in delaying the release of the NAS–NRC reports. He helped initiate a recent lawsuit to obtain immediate release of all the reports.

FDA officials deny that economic considerations play any part in their operations and insist that their only criterion in making decisions is the safety and efficacy of drugs.

Yet the drug industry, which is one that has consistently enjoyed high profits, is certainly given ample opportunity to collaborate with and influence FDA decisions. When an NDA is submitted to the FDA, the manufacturer is advised which FDA official will review the case and is permitted to meet continually with that official to answer any questions and allay any doubts he may have. When this reporter tried to find out the names of the officers who reviewed the Demulen evidence, however, he was informed by Simmons that such information is not normally made public.

In opposing FDA decisions the drug industry is also a powerful force, often employing legal delaying tactics to force long intervals between an FDA ruling against an ineffective drug and the actual removal of the drug from the market (*Science*, 29 August 1969).

FDA critics accuse the agency of inviting such proceedings and delays by failing to declare ineffective drugs "imminent hazards to public health." Such a labeling would eliminate the court proceedings and force the drug off the market immediately. The FDA claims that it cannot evoke the ruling against drugs which are merely ineffective, but FDA critics contend that ineffective drugs can be hazardous because a patient can be jeopardized by an ineffective drug. "Apparently people have to be dropping like flies all over the country before the FDA will employ the imminent hazard procedure," McCleery said.

Under the new management, then, criticism of the FDA has not appreciably decreased. In addition the agency's financial outlook remains bleak. Edwards has asked Congress for a substantial increase in the FDA budget for fiscal year 1972. The increase would more than double the FDA budget, bringing it to $150 million from its current $72-million level. A belt-tightening administration, however, has been reluctant to back Edwards fully in his request, and it appears unlikely that Congress will grant more than a small increase.

Thus while the new-look FDA has speeded the approval of new drugs for marketing and reduced criticism from industry, many of its basic problems remain to be solved, and criticism from Congress and consumer groups has, if anything, increased. Edwards still has a long way to go before he convinces these critics that the FDA's new-found efficiency is not more in the interest of the drug industry than in the interest of the public—THOMAS P. SOUTHWICK

APPOINTMENTS

W. J. Tietz, chairman, physiology and biophysics department, Colorado State University, to vice president of student and university relations at the university. . . . **Roger F. Palmer**, director, clinical pharmacology division, department of medicine, University of Miami School of Medicine, to chairman, pharmacology department in the school. . . . **Lionel E. Mawdesley-Thomas**, director of pathology, Huntingdon Research Centre, England, to director of research at the centre. . . . **Victor H. Hutchison**, professor of zoology and director, Institute of Environmental Biology, University of Rhode Island, Kingston, to chairman, zoology department, University of Oklahoma.