withstanding the attacks that are now increasing in volume.

These attacks, it should be noted, suffer from lack of any common interest outside of preferences for spending Apollo's money on other enterprises. For a time the Air Force was doing its best to undermine NASA so that it could inherit a larger role in space. But since the Air Force has been unable to convince the civilian managers of the Defense Department that there is a military job, except for reconnaissance, that can be done better from space than from the air, it has, for the present at least, lost out in the battle over space jurisdiction. Accordingly, it has now ceased sniping at NASA and, presumably, is reconciled to NASA's developing the technology that it might ultimately take over.

Thus, what is happening in the politics of space is that space is now blending into the general national political scene. It has its friends and foes, its economic interests and a growing number of economic opponents, in space-poor states and, increasingly, among successful non-space industries that don't like to see their taxes going to a fully government-supported industrial effort. But the space establishment is now well founded, and those who would like to alter it in any substantial way have a formidable task ahead of them. The task is made all the more formidable by the fact that President Johnson has conspicuously and, probably, irretrievably lashed his prestige to the present program. And, though criticism of the moon program is increasing, in books, in newspaper editorials, and on the Senate floor, it would be well to remember that in American politics there is often a great disparity between the ability to make noise and the ability to control events. So far, despite the rising volume of anti-space sentiments, the forces behind the administration program remain so potent that the administration hasn't had to resort to even a bit of arm twisting to get its way. For window dressing purposes it is now often said that Congress is taking "hard looks" at NASA and trimming its budget, but when all is said and done, NASA will receive some $5.2 billion this year, which is quite close to what it sought. Doubts may exist about the wisdom of a manned lunar landing in this decade, but the doubts have not been reflected in money, which is the true measure of political power.

—D. S. GREENBERG

Drug Politics: Industry Seeks "Court of Appeals" To Challenge FDA Rulings on Drug Safety

The relationship between the federal government and the pharmaceutical industry is something like the relationship of a father and child on a seesaw: the child may have the illusion that they are perfectly balanced, or even, on occasion, that his weight has thrust his father in the air—but all along his father's feet are on the ground. The industry's periodic cries of pain suggest that it is being buffeted about by superior governmental forces, but the balance between industry and government is at best a tottering one, and for the most part the industry stays sturdily rooted to the ground.

For this reason it is hard to take too seriously proposals of the drug industry which would have the effect of insulating it still more against what it regards as the ravages of federal regulation. Nonetheless such a proposal is now afoot, and it appears to have the unanimous support of the industry as well as considerable backing from the medical profession and academic circles. Essentially the proposal calls for a scientific advisory board to which manufacturers could appeal unfavorable decisions of the Food and Drug Administration.

The proposal is in its early stages, and full details have not yet been considered by any of its proponents. Testifying before a House Government Operations subcommittee headed by Representative L. H. Fountain (D–N.C.) during an investigation of the safety of new drugs, Austin Smith, president of the drug industry trade group, the Pharmaceutical Manufacturers Association (PMA) said: "It is also our belief that a Council for Scientific Review should be established to provide an appeal mechanism for the review of drug evaluation problems. On purely legal matters the Food and Drug Administration can be challenged in the courts, but on scientific issues there is no formal or effective appeal. And yet in matters involving the toxicity and efficacy of drugs the agency is called upon to administer not only the laws of man but the laws of science as well. If the FDA makes a ruling or an interpretation on a scientific point, it is almost certain to stand, even though the ruling is considered unsound in the opinion of competent scientists." After going on to point out that an appeal mechanism exists for government decisions on pesticides and color additives, Smith concluded: "It seems anomalous that the manufacturers of pesticide chemicals and of color additives have the right of appeal to an independent body, while the drug industry—which surely is as vital to the health of the American people—has no such right."

There is no doubt that PMA's view is widely shared. Smith spoke for the industry as a whole; but representatives of several drug firms have recently made statements indicating their individual support for the group proposal. References to the desirability of an appeal procedure have appeared frequently in the drug and medical trade press in the past few months. In addition, a plan almost identical to Smith's was suggested by I. S. Ravdin, vice-president of the University of Pennsylvania for medical affairs, in a letter to the *AMA News* last April, and formally endorsed by the Great Philadelphia Committee for Medical-Pharmaceutical Sciences, which is composed of representatives of the area's medical schools and drug companies. Ravdin said last week that his letter had also drawn a considerable mail response from independent practicing and academic physicians.

The interest in a scientific "court of appeals" grows out of two things—the fundamental dissatisfaction of the drug industry with what it feels is its sometimes cavalier treatment by the FDA, and an apparently widespread indignation over the recent handling by the FDA of an antidepressant drug called Parnate.

Parnate Case

Parnate, a product of Smith, Kline & French Laboratories of Philadelphia, went on the market in February 1961 and quickly achieved considerable popularity for use in moderate to severe cases of mental depression. Although the drug's usual effect is to lower blood pressure, it was soon found that Parnate had the occasional "paradoxical" effect of raising blood pressure, and that it was associated with cases of arterial hypertension, with strokes, and with a small number of fatalities. In October 1963, the company and the government consulted and the company issued a warning letter to doctors which described the difficulties that had been encountered and cautioned physicians to be on the lookout for them. After the alert, reports of trouble continued to mount: by Feb-

ruary 1964 the FDA had reports of about 430 cases of arterial hypertension, about 50 strokes, and 15 or 16 fatalities. It was estimated that about 3½ million people had used the drug.

At this point the FDA concluded that Parnate should be taken off the market, and informed the company. The company disagreed. The two dickered a bit, with the company proposing an impartial scientific review, but FDA stood fast. In the end the company agreed to withdraw the drug voluntarily, "under protest," since the alternative—allowing it to remain on the market pending a hearing when the government had already marked it as dangerous—left the company open to charges of caring only about profit, and seemed unsatisfactory.

"With all due respect for the FDA," said the company's notice to physicians, "it is the opinion of the SK & F medical staff and the opinion of many eminent physicians whom they have consulted that the benefits of Parnate outweigh the risks; that it is a useful and valuable drug for the treatment of a serious illness and should remain available to the medical profession. . . . Nevertheless, under protest, we are withdrawing Parnate from the U.S. market. We are taking this step because under the present law and regulations, where there is an honest difference of medical opinion on scientific matters, there is no effective appeal to an impartial body of medical experts by whom the matter can be considered in a calm scientific manner. Such a procedure has been strongly advocated by leading medical authorities."

Already at odds over the fundamental issue, FDA antagonized the company still further by releasing news of the drug withdrawal to the press before the company's own announcement had time to reach the medical profession. Although presumably the result of mismanagement rather than malice, FDA's disclosure had the effect both of embarrassing the physicians who had prescribed the drug and of alarming their patients—a situation that the company and the doctors, understandably, hate.

Following the withdrawal, the company requested a hearing on the drug, and assembled a variety of medical experts who agreed to testify on its behalf. The hearing was postponed several times while both sides were gathering their evidence. Simultaneously, the two were negotiating about the possibility of putting Parnate back on the market on a more restricted basis.

During these preparations and negotiations the FDA was busily studying the drug, and on 15 June—the day before the hearing was to begin—the agency announced that it was permitting the drug to reenter the market, for use in reduced dosages in hospitalized cases of severe depression, or in cases outside the hospital in which other medication had failed. The FDA said that its decision was based "on study of the world's medical literature on the drug, evaluation of controlled studies conducted with the drug, and a consideration of the views of top experts in the field of psychotherapy." (Parnate will again be available on 1 August.)

Before or After?

To this not very edifying story the drug industry and other interested parties immediately appended the moral that if an appeal to a scientific panel had been possible when the FDA decision was first made, the agency would have saved face, the company would have protected its reputation as well as its earnings, and doctors and patients would have been spared a good deal of unnecessary confusion and alarm. Thus, *Medical Tribune*, a medical affairs newspaper distributed free to doctors, editorialized: "The steps taken to *restore* [Parnate] . . . to the market are precisely those that should have been taken *prior* to the *withdrawal*." To Walter Munns, president of Smith, Kline & French, "The whole episode emphasizes the benefit of close consultation by the FDA with the best qualified members of the medical profession when major administrative action is contemplated."

Attaching that moral to the Parnate story is vaguely reminiscent of the parody of popular quiz shows in which the answers are supplied and the questions have to be deduced from the answers. In this case, the answer is "establish a committee." But it is not clear whether the question is "How can you provide maximum security to the pharmaceutical industry?" or "How can you best promote drug safety?"

If a review board system were in existence, modeled after the pesticide review panels, Parnate might have been handled something like this: Following FDA's decision, Smith, Kline & French could have requested the appointment of an advisory panel. Candidates would then be nominated by the National Academy of Sciences–National Research Council, and chosen by the FDA commissioner from among the nominees. The committee would meet and make its recommendations to the commissioner, who would then make his ruling. This ruling might then be appealed still further in a public hearing. Again according to the pesticide model, the time scale for all this pondering would be the following. The company has 30 days after notification in which to request an advisory committee; the committee has an undesignated amount of time to get itself chosen and assembled, but must report to the commissioner within 60 days after it is formed; the commissioner could take 90 days to make up his mind; the company can take 60 more days to file objections and request a public hearing; and the commissioner could take another 90 days to make the final, binding, decision. Including the time involved in gathering a committee together, the procedure may easily take more than a year. By this measure, SK & F did very well in getting Parnate back on the market within a few months.

But suppose the drug in question were not Parnate, which was partially rehabilitated, but one of the several other drugs withdrawn from the market during the past few years whose reputations could not withstand the scrutiny of a committee. Suppose, to take an extreme example, the manufacturer had appealed FDA's decision on thalidomide? What would be gained by leaving a dangerous drug on the market for a year while a committee deliberated? If the drug were withdrawn during the committee's study, the manufacturer would be no better off than he is now. If the investigation were quietly handled and the drug remained on the market, the incidence of serious effects could be vastly multiplied.

Although it is a sensible principle of government that private parties should be able to appeal the frequently inconvenient and sometimes arbitrary decisions of the bureaucracy, there is also a strong argument that in matters so closely affecting public health the FDA should have the power to shoot first and ask questions afterward. Drug safety questions, seldom clear-cut, are susceptible to endless obfuscation (rare is the drug without fervent supporters), and in practice the FDA is usually more dilatory than swift. Whether its

caution should be institutionalized is a question deserving serious thought.

The proposal for a scientific court of appeals raises other difficulties. Who would serve on the committees? Impartial wisdom in drug evaluation is very hard to come by. It is no insult to the talented men who work in the field of pharmacology to point out that there are very few of them—a fact they themselves constantly bemoan. The largest cadre of experts in the drug field work for the pharmaceutical industry. Should they be permitted to serve on these committees? Should only representatives of the company making the appeal be disqualified? Surely company representatives should be heard at such an appeal, but what would the effect of the natural camaraderie of industry scientists be on the desired impartiality of the deliberations? Academic clinical pharmacologists are in very short supply, and it is in the nature of their work that their ties with industry are often very close. The reason is mutual dependence: drug companies need their advice and service in testing new drugs; the scientists frequently need facilities and financial aid available only from a company whose interests they share. What should their role on the court of appeals be? The problem of impartial advice is difficult in any field—as members of the government's grant-giving advisory panels well know. But in the field of drugs a supposedly pure "scientific" dispute can have terrific economic consequences for a manufacturer, and the problem of obtaining unbiased advice may be a crippling one. It is no secret that committees can be stacked, and it is some measure of the distrust and confusion apparently endemic to FDA-industry relations that while the agency, and some of its critics, worry about a committee being stacked *in favor of a company*, the industry has professed some worry that a committee would be stacked *in favor of the agency*.

Let NAS Do It

Faced with such sensitive dilemmas involving science policy, there has been an increasing tendency in recent years to turn to the pristine National Academy of Sciences, in the hope that the Academy would either agree to arbitrate the dispute itself or else suggest the members of an arbitrating committee. However, in a circumstance that has the aura of an attempt to evade a negative governmental decision, it is most unlikely that the Academy would agree to do the job itself. And, for that matter, although the Academy can name people to serve on such a committee, it cannot create them. The manpower problem remains.

Even if the mechanics of selection could be worked out, the problem of occasion remains. On this point it appears that industry's views are not entirely unified. A vice-president of Hoffman-La Roche, testifying at the Fountain hearings, seemed to envision a panel resolving very fundamental disputes between FDA and industry scientists. The example he gave was a current disagreement about whether adequate animal testing requires histological examinations of the organs of all animals used in a particular test or just of those receiving the highest dosages of a new drug. But most of the proponents of a court of appeals seem to envision it resolving controversies in which there is a more direct relationship of economic to scientific content. The position of PMA appears to be that an appeal should be allowed at any stage in which the FDA is empowered to turn down industry's work, either when approval is being sought for the initiating of clinical trials, when an application is submitted for permission to market a new drug, or when the question of withdrawal arises.

The effect of this intervention on the operation and morale of the Food and Drug Administration has to be considered, too. While admittedly the agency has gone through some bad times and made some mistaken decisions, it is not clear why the best way to reform it is to establish a prestigious committee over its head. One argument made in favor of the industry proposal is that it would bring the FDA into closer contact with top authorities in a given field. This is certainly desirable. But the FDA, somewhat belatedly, has already begun to establish links with outside experts. Last year it established a committee, headed by Walter Modell of Cornell, to advise the commissioner on general policy; in addition, the Medical Bureau, under its new director, Joseph Sadusk, has recently begun to acquire outside advisors to consult with it on a variety of problems connected with its evaluation of new drugs. The proposed court of appeals, instead of functioning cooperatively, would function only when the FDA staff was accused of being in error. While a decision of the scientific panel would not be binding legally, it could well be binding intellectually. The fear of being overruled by an outside panel, even if it did not actually encourage buck-passing, could easily reduce the incentive among much-harassed FDA staff members for firm commitment to agency decisions involving unpleasant consequences to the industry.

In the last analysis it seems clear that, although both the agency and the agency-industry relationships are in need of changes, the proposed court of appeals is not the change that is needed. If the agency is as wary as it ought to be, it will turn the proposal down. And if the industry is as anxious as it claims to promote safer drugs, it will come up with some more relevant suggestions.—ELINOR LANGER

Meeting Notes

The **American Institute of Biological Sciences** will hold its annual meeting 23–28 August at the University of Colorado, Boulder. Information is available from Gordon Alexander, Department of Biology, University of Colorado, Boulder, or from AIBS, Room 508, 2000 P St., NW, Washington, D.C. The societies scheduled to hold sessions in conjunction with the AIBS meeting are listed in the Forthcoming Events section, page 193.

Papers are being solicited for presentation at a symposium on **models for the perception of speech and visual form**, scheduled 11–14 November. The meeting will be sponsored by the data sciences laboratory, Air Force Cambridge Research Laboratories, and will take place in Boston. Emphasis will be placed on analysis of problems in current models for the perception of structured stimuli. Attendance at the meeting will be limited to 350 persons. Deadline for abstracts: *15 August*. (G. A. Cushman, Wentworth Institute, 550 Huntington Avenue, Boston, Mass. 02115)

The University of Washington, Seattle, will be the site of the fourth western national meeting of the American **Geophysical** Union, 28–30 December. Papers are invited on all the major areas of geophysical research. Deadline for submitting abstracts: *9 October*. (AGU, Suite 506, 1145 19th Street, NW, Washington, D.C. 20036)