FDA's Edict: Patients, Not Profits, Come First

It is not unprecedented for the chief of a government regulatory agency to criticize the industries under his jurisdiction, but it is unusual. The times are so rare that they tend to mark historic moments—Newton Minow's description of television broadcasting as a "vast wasteland" is a case in point. In the few months that he has been at the Food and Drug Administration, Commissioner James L. Goddard has made clear that he intends to be among the critics. Congress, the press, industry representatives and agency personnel have all been apprised that consumer-oriented firmness is to replace industry-oriented flexibility in dealing with complicated drug questions. Two top officials in FDA's Bureau of Medicine who are associated with the flexible approach—medical director Joseph Sadusk and deputy director Joseph Pisani—submitted their resignations within 2 months of Goddard's arrival. And the Commissioner has already taken action on nearly a dozen drug problems that affect not only the reputations but the fortunes of several major companies. (FDA's new consumer orientation will be discussed in detail in a future issue of Science.) *On 6 April Goddard carried the news straight to the lion's den in an extraordinary frank address to the annual meeting of the Pharmaceutical Manufacturers Association (PMA) in Boca Raton, Florida. The text of his speech, slightly abridged, appears below.*—E.L.

. . . Today I am not speaking to industry's physicians. I am speaking to its decision-makers. And I am asking you to consider the ramifications of some past decisions and the ramifications of your future decisions as company—and industry—leaders.

I ask this . . . because I am very uneasy about the way events are catching up with you.

I will be quite candid with you: there is a real danger that the pharmaceutical industry as you and I know it today may be altered significantly, altered beyond your present fears, and altered beyond recall.

If this sounds alarming, it is because—frankly—I am alarmed. Let me give you the basis for my feeling of alarm after only ten weeks in the Food and Drug Administration. During this brief but busy period I have seen evidence that too many drug manufacturers may well have obscured the prime mission of their industry: to help people get well.

Let us agree that every industry has to make a profit for its stockholders. I am not against profit in the drug or any other industry. The profit motive—as the Russians are finally discovering—stimulates beneficial activity: competitive research and marketing, mass education, and the rise of the general standard of living.

But each industry must have some deeper dynamic of its own, something that makes the drive for profit really worth the trouble. And I would submit that the central dynamic for the drug industry has been—and must continue to be—the maintenance of the health of all Americans through better pharmaceutical products.

Gentlemen, we must keep our eyes on the patient. For—once you get through the medical reports and the counselors' opinions, the advertising and the marketing data, the licensing and distribution agreements, the protocols and letters of credit, the labeling and packaging, and the report by the company treasurer—once you get through all that, you reach the physician who will administer your product to a human being.

At the end of the long line is a human life. Some of you seem to have forgotten this basic fact.

I cannot let you forget, as you cannot let me forget either. That is why I am genuinely concerned. Since becoming Commissioner, I have come upon situations that I did not expect. I know that many of you, were you to sit in my chair for a week, would be as troubled as I. Therefore, I am bringing to your attention some things that you must be made aware of, for only you know how to correct them.

And, for the health of the drug industry, I would hope you *would* rally together and correct them.

Let us begin with Investigational New Drugs. I can say that I have been shocked at the quality of many submissions to our IND staff. The hand of the amateur is evident too often for my comfort. So-called research and so-called studies are submitted by the carton-full and our medical officers are supposed to take all this very seriously.

I cannot, however.

As their chief, I have told them that unprofessional IND's should be cancelled immediately. If the sponsoring company is imprudent enough to waste stockholders' money on low-quality work, then that company must bear the consequences of such waste.

The Food and Drug Administration will not waste public money reviewing it.

In addition to the problem of quality, there is the problem of dishonesty in the Investigational New Drug stage. . . . Your medical staffs and legal staffs know the law and regulations as well as we do. Their failure to abide by law and regulation is a matter neither you nor I can take lightly.

Now, I will admit that Government employees do not have a corner on all wisdom. And I will admit that there are gray areas in the IND situation.

But the conscious withholding of unfavorable animal or clinical data is not a gray-area matter.

The deliberate choice of clinical investigators known to be more concerned about industry friendships than in developing good data is not a gray-area matter.

The planting in journals of articles that begin to commercialize what is still an Investigational New Drug is not a gray-area matter.

These actions run counter to the law and the ethics governing the drug industry.

I have already moved, as some of you know, to correct such action as soon as I see it. And I have instructed my medical staffs in all bureaus to follow my example. Will you, in your own organizations, protect the scientific integrity of the industry? Will you stand with me in this effort?

Let us move on to New Drug Applications. This is the take-off stage . . . for a new product of this industry. Now we must review the clinical evidence, the labeling and advertising, the promotional materials, package inserts—you are as familiar with the process as I.

But once again, I have been shocked at the materials that come in to us. I have been shocked at the clear at-

tempts to slip something by us. I am deeply disturbed at the constant, direct, personal pressure some industry representatives have placed upon our people. . . .

Here is one example of an NDA to be used for the treatment of cancer. It was submitted by a prominent member of the PMA. In its labeling, the company suggests the following language:

> Drug X is not recommended for use in children less than 15 years of age because of the lack of clinical experience with patients in this age group.

This is an interesting statement. Interesting—because the record shows that eleven children less than 15 years of age were in fact treated with Drug X and there were *no remissions.*

In other words . . . I must say that the drug hasn't been shown to work *at all* with children under 15—a fact based on the available clinical experience.

And *that* is why Drug X must not be recommended for use with children under 15.

. . . Here is another example, involving a diuretic. The label should be clearly marked: "WARNING—DANGEROUS DRUG." We suggested this to the company and added that they should reinforce the warning with the phrase "unparalleled potency."

The company returned with a label that used the phrase "unparalleled potency" with the phrase "unusual effectiveness" and produced an effect that was clearly promotional rather than precautionary. This is the language of advertising, not the language of danger. This is not in the spirit of science.

. . . The company forgot about the patient. But I cannot forget.

We have ruled, as you know, on several long-acting sulfonamides already available. We have an NDA for another long-acting sulfa in our Bureau of Medicine before us now. We have asked the sponsoring company to tighten its labeling language so that the physician will use it only for that part of the human system—the genitourinary tract —for which clinical evidence shows it would be effective.

The company, however, wants to tell physicians that clinical studies are still going on involving other uses.

It wants to include a reference to imply that the drug can be prescribed to treat acne.

And it has asked for other language that would leave the physician somewhat in doubt as to the full extent to which he might prescribe this drug . . . which even the most careful physician, given the proper warnings for restricted diseases, would use with some risk to his patients.

The company clearly wishes to promote—by subterfuge —wider therapeutic use for this drug. In the short run, this threatens the patient. And in the long run, it threatens the very fabric of your industry.

And what of advertising? Of the 8000 or so companies in the drug industry, about 1000 do some advertising. . . . A two-man medical advertising staff has, during the past year, passed on to our Bureau of Regulatory Compliance a number of complaints involving nearly one-third of the membership of the PMA.

Some advertising cases have been quite abusive of regulations. They have trumpeted results of favorable research and have not mentioned unfavorable research; they have puffed up what was insignificant clinical evidence; they have substituted emotional appeals for scientific ones.

Drug Industry Reaction

Following Goddard's speech, PMA president C. Joseph Stetler released the following comment:

"The general reaction to Dr. Goddard's address is that it might, unfortunately, be interpreted as an indictment of the entire drug industry, because of its overemphasis on isolated instances without acknowledging the integrity and responsibility which our industry has consistently demonstrated.

It is an unassailable fact that the scientific attainments and standards of performance of the American prescription drug industry have provided an immeasurable benefit to the improvement of health and the prolongation of life."

These cases are well-known among you. The FDA is moving against them.

But what of the less well-known cases? Why did they happen? I think I know the answer: I think some of you have been led to believe that facts don't sell drugs.

Gentlemen, if I'm right, then you have been led astray—astray of the law and astray of what physicians need and want to know. Facts do sell drugs—facts presented in a professional way for professional men to read with care and respect.

. . . I began my remarks by saying I was uneasy about the future of the pharmaceutical industry. The examples I have given—the poorly prepared IND's and NDA's, the improper labeling and advertising—these are all symptoms of a disease that drugs cannot cure—but which can undermine the industry as we know it.

That disease is irresponsibility.

Yon cannot afford to have it in your midst any longer. You as the leaders of this industry are capable of insuring that such irresponsibility is corrected. . . .

You are under pressure from a variety of quarters. You are under price pressure, patent pressures, generic-prescription pressures, as well as regulatory pressures. I am aware of these and I am sympathetic.

But I am also aware of other pressures far more dangerous to your industry than the ones I have mentioned. I am aware—and I know some of you are, too—of pressures to bring the drug industry under tighter Federal control.

Every time one company is caught falsifying IND or NDA data—this kind of pressure builds up.

Every time one company attempts to mislead the physician through its own poor advertising, additional regulatory pressure builds up against the advertising of all.

Every time the pharmaceutical manufacturers see a violation of law made by one of their number—and then look away—the pressure builds up even more for tougher, tighter, more sweeping regulatory action and legislative control over the drug industry.

Because lives are at stake.

. . . Government alone cannot serve all the health needs of the American people. This is a responsibility we gladly share with private industry.

But you cannot accept the partnership lightly. . . .