Letters

FDA: Guidelines Chiseled in Stone

On 10 June, the Food and Drug Administration told the pharmaceutical industry that it intends to draw up detailed "guidelines" for the future clinical study of 25 classes of drugs. FDA invited industry's scientists to help.

Since then, the number of classes of drugs has grown to 29 (antianginal, anticholinergic, anabolic, anticonvulsant, and so forth) and guidelines are being drafted for publication by the end of 1970. Are clinical investigators aware of these plans? Lack of comment in the medical or scientific press leads me to believe they are not. They should be, as should all clinicians and bioscientists in related fields.

The drug industry is divided—nothing new about that. Those in favor of guidelines believe in them, or may really need them, or hope guidelines will prevent FDA's "recommending" last-minute studies.

Those opposed (I'm one) are not so much opposed as they are afraid the guidelines will become rigid checklists—"cookbooks" with the force of law, even if irrelevant scientifically. I'm afraid that resources will frequently be wasted on studies done to satisfy an obsolete guideline, done at the expense of work *more* relevant to safety and efficacy. Meanwhile, though, my company's scientists are serving on FDA-industry guideline committees. They're trying to write guidelines that will focus on the *questions* that should be asked about a new compound, not on every specific test to answer them.

FDA itself has been reluctant in the past to set clinical guidelines, probably realizing that guidelines can build impressive piles of unimpressive data, can even provide *false* assurance of safety and efficacy, while robbing investigators of judgment and deadening innovation in drug invention and development. But FDA's past reluctance doesn't reassure me now. Neither does this sentence in its model guideline (for antilipemics): "Some of the more esoteric tests above are optional under certain conditions. . . ." FDA's history repeatedly shows it cannot allow such options without fear of second-guessing and criticism. It is so much safer, easier, to ask the sponsoring drug company to do studies than it is to make a needed exception.

Who can blame FDA? The other day in Washington, I heard what can happen to FDA people who decide a guideline is obsolete. At a congressional hearing, they were asked sharply how this can happen in a country of law and order? How dared they waive a guideline? Shouldn't those who did so be disciplined? FDA answered, no, they should be *commended* for using their best scientific judgment. A brave answer. But all "guidelines" became a little more rigid that day.

I believe that those at FDA who must one day administer the guidelines for the clinical study of all of this nation's new drug products should be supported by panels of outside scientists when exceptions to the guidelines are indicated. Not that advisory groups are the answer to everything, nor can they ever remove from FDA its regulatory responsibility for proof of safety and efficacy. But their recommendations, openly arrived at after consulting both the sponsoring company's scientists and the FDA's, should provide the support FDA will need in dealing with studies of the truly innovative compounds I think are coming from drug research in the next few years.

Elements of this suggestion have been a part of several proposals from observers, friends, and critics of FDA over the past few years. So the suggestion is certainly not novel with me; but I think it deserves public airing and commentary—before guidelines and the way they are administered become chiseled in stone.

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Tektite: Expectations and Costs

With only limited resources to apply to an infinity of problems it seems imperative that value judgments be made in allocation of funds for research. The Tektite 1 program ("Tektite 1, man-in-the-sea project: Marine science program," 8 May, p. 659) cost $2.5 million according to Navy estimates. It was justified on the basis of technological development, biomedical and behavioral investigations, and marine science. Previously, shallow-water manned habitats have been utilized by Cousteau, Link, Perry, and MacInnis and in British, German, and Russian programs. For Tektite 1 the unlimited working time which was claimed as an advantage is misleading. It is possible with present technology to spend 6 to 8 hours per day at 50 feet and return to the surface with no time lost in decompression. The Tektite 1 divers averaged just over 2 hours per day in the water. Once inside the habitat there is no advantage and many disadvantages over a surface facility.

No serious biomedical problems have been encountered in other shallow-water habitats and there was no reason to expect any in Tektite 1. In fact there were none. The main justification seems to have been behavioral studies of an "isolated" group under the "stress" of a "hostile" environment.

John E. Randall previously spent several years studying the same area of St. John, supported by grants totaling about $60,000. He worked from a shore base with an outboard skiff and scuba. He published over 30 papers on the biology and systematics of marine life which were the result of his investigations. In terms of man-hours, his project was far smaller than Tektite 1—only three people were involved. As a marine biologist extensively employing diving in research, I am very much aware of the tremendous advantage of in situ studies, but I fail to see that the results of Tektite 1 justified such an expensive program.

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Starck is quite correct in saying that value judgments must be made with regard to awarding funds for research. In addition to program reviews by the Office of Naval Research, Department of the Interior, and General Electric, NASA awarded two independent small