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The bill has other examples of overkill, provisions written for the past, when indeed there was no public participation, no postmarketing surveillance and no real give-and-take on study plans and protocols. Now all these procedures are developing well as a result of the hundreds of policy decisions, regulations and improvements to working relations that have filled the years from 1962 to 1978, especially the past few years.

* * *

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The FDA knows that the present system can work informally, but not in every FDA division, so the new law tries to create a standardized system. The trouble is that the proposed system standardizes things in the wrong direction, and it mandates by law what now sometimes works pretty well without it. And it deprives the agency of simple solutions. Often, now, technical points of difference about protocols, and just plain misunderstandings, can be settled by a telephone call.

Industry wonders, too, why a bill that so tightens the investigative phase in every respect, with prior approval of all protocols and even of changes in the protocols, must then insist on a 390-day period to consider the application. If nothing were being changed about regulating the investigational phase, I could understand doubling the approval phase, to reflect better the pace at which approval takes place now. Or the other way around, if the 180-day approval phase in the present law remained the same in the new law, I could see why we should have provisions for stretching out the investigative phase. But why make both changes?

The bill has other examples of overkill, provisions written for the past, when indeed there was no public participation, no postmarketing surveillance and no real give-and-take on study plans and protocols. Now all these procedures are developing well as a result of the hundreds of policy decisions, regulations and improvements to working relations that have filled the years from 1962 to 1978, especially the past few years.

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Well, those are the disincentives as the industry sees them. The question still is whether they are really important. The Administration thinks we are overconcerned about them, that we are overestimating them, and that in fact we may not be able to perceive what is good for us.

In one sense that opinion may be right; my industry may not understand as well as it should how incentives and disincentives work. The long, long process

declare themselves. Also, in those 60 days the Secretary must decide whether the overall study plan is adequate to meet objectives and whether the parts of the study plan — the proposed investigations — are adequate.

I can understand these latter provisions; the FDA has in the past seen study plans so flawed that they simply could not be expected to meet objectives. So they respond in the way that professional regulators must; they reach for a regulation to assure the ade-

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that brings an idea to the fruition of an active chemical compound, and then takes the compound through years of study to produce a new drug, is as complex as a natural ecosystem. You might as well ask a forest to explain how it replenishes its floor or a stream how it purifies itself as to ask the drug-development system how it works.

I'm not talking about the science of it; that's all well understood. I'm talking about the motivation behind the complex history of ups and downs that every research program goes through. Nothing is more impenetrable than the motivation of our actions; yet we must try to penetrate what motivates the search for new drugs, or we will lose our way and perhaps never find it again.

Every research program must have enthusiasts. That fact is well known. And, almost as inevitably, it must have detractors — scientists and managers in the same firm who are not as enthusiastic, who'd like to replace it with their program, their compound. The competition is for funds, for computer time and for a dozen other scarce resources.

Also, in the modern large firm, the decision to "take research overseas," as we used to say it, is different now. Research is now overseas as much as it is here. The United States is now the "overseas" to much of the research on new drugs.

Another consideration is that pharmaceutical companies are the world's greatest counters and measurers of things present and to come. By every method known to man, they research the potential market for new drug therapy. They try, in other words, to measure future economic incentive to decide present financial support.

And they try to measure *disincentives*. For the past 15 years the FDA new-drug-approval process has made up a large part of that effort. And if this bill is enacted, new worrisome questions will be asked at quarterly and annual reviews of research and development programs and of compounds in the laboratories of some 20 or 30 pharmaceutical companies. These questions will force a new compound to declare itself much too early, not just to the FDA, but to the managers of the money to be invested in it. It's as though the entire FDA approval process were moved up several years and previewed in each company by a whole new generation of nail-biting industry people guessing how many conferences, hearings, 60-day waits, formal rejections and unexplained delays lie ahead of a new compound. Everybody plays "What will FDA say?" and discouragement dominoes down through the organization.

It doesn't matter that industry may be misreading the FDA, or that it may be foolish to try to play "What will FDA say?" Experience tells the companies that the FDA will more frequently than now say, "no," or "not now," or "do more work."

So I predict that, with 20 or 30 companies trying constantly to measure research incentives and disincentives in quarterly budget reviews, fewer and fewer of the hundreds of risky, positive commitments needed will be made as companies opt for the surer and safer. The result will be a sort of cloning of the whole process as research programs, preclinical work, and clinical protocols hew close to the official, approved standard. And the change will be insidious — scarcely noticeable when it occurs.

I could be wrong. Things may work out. But that is not the modern way to decide on big changes. Ordinarily, in this age when the complexity of socioeconomic processes is well recognized, the burden is on those who would change a process to prove that they will do no harm. In this case, the process is complex and it does work, and those who are nearest to it, those who do make it work, are warning that it needs to be nurtured and cherished and can be hurt by the proposed changes. Those who do not make it work say it would not be hurt.

The question seems to be: Is the pharmaceutical industry standing up too close to its research process to understand it, or is the FDA standing back too far?

SmithKline Corporation
Philadelphia, PA 19101

ROBERT L. DEAN

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

Edited by
JONATHAN E. FIELDING, M.D., M.P.H., AND PEARL K. RUSSO

THE ECONOMIC COSTS OF STROKE IN MASSACHUSETTS

ELIZABETH MILLS, M.A., AND MARK THOMPSON, PH.D.

The morbid and mortal harm of strokes may be reduced by public-health programs addressed to the underlying risk factors — particularly the early diagnosis and control of hypertension — as well as by medical management of the condition. The benefits of such programs are alleviation of both the human and the economic costs of stroke. Although a consideration of both cost categories is critical to effective public-health policy, only the economic consequences can be measured. Of economic costs, the more evident and readily measured are the direct costs: hospital expenses, fees for physician visits, nursing-home charges

Further information may be obtained from Dr. Thompson at the Center for the Analysis of Health Practices, Harvard School of Public Health, 677 Huntington Ave., Boston, MA 02115 ([617] 732-1060).

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