Involving IRBs In The Drug Approval Process

Everyone knows that the Food and Drug Administration is slow, bureaucratic, inflexible, and unimaginative. After all, haven't we all heard and read such allegations on numerous occasions? Moreover, many of us in the pharmaceutical field have had some personal experiences that have confirmed—or at least seem to have supported—just such conclusions regarding that federal agency.

Consequently, it strikes us as strange that there is little notice or interest when the FDA advances a proposal that would be expected to (a) speed up drug approval, (b) reduce government involvement, (c) provide a major departure from current drug approval processing, and (d) represent innovative thinking on the entire regulation of early drug testing.

We refer to FDA's proposals to expand the role, function, and responsibility of Institutional Review Boards (IRBs). These are the local review committees which are now set up and operating in many private and public institutions, and which serve as a sort of peer review group to examine and pass upon the suitability of proposed research involving human subjects or patients prior to the start of such studies.

Evidently, the general track record to date of these IRBs has been quite satisfactory. Experience seems to have shown that they are effective and that they work rather well in accomplishing their objective of protecting human subjects from undue risks.

The FDA has taken note of this performance and has advanced the thought that IRBs might provide an excellent vehicle to expedite Phase I testing in the consideration of Investigational New Drugs (INDs). Phase I is the initial testing in humans that involves short-term studies in a small number of normal subjects or patients to test the properties of the drug and levels of toxicity, metabolism, and pharmacologic effects.

After basic information about the drug is obtained in these preliminary studies, and assuming the results are favorable and encouraging, the effectiveness and relative safety of the drug are then studied by larger and more detailed investigations in patients; this is referred to as Phase II. Finally, at Phase III, more extensive testing is performed on patients to systematically assess the drug's safety and effectiveness.

For various reasons, many compounds tested never get beyond Phase I. Moreover, this is a time-consuming process that requires practically the same degree of scientific review resources to evaluate as the subsequent phases which involve many more human subjects. Consequently, Phase I drains off a considerable, and perhaps disproportionate, fraction of FDA's available resources for conducting medical reviews.

And at the same time, a parallel process is being conducted by the IRBs. If not identical, the process is very similar and the ultimate objectives are comparable. Furthermore, it has been argued that due to local familiarity, the IRB is able to assess the situation far better than any agency hundreds of miles away with only a batch of papers on which to make its judgments and render a decision.

Consequently, certain officials within the FDA—along with a few outside clinical investigators—have raised the question of whether it might eliminate duplication, expedite drug approval processing, lower research costs, and conserve scarce resources if the FDA were to reduce its review functions during the Phase I/early-Phase II period of the IND, conditioned upon a willingness of the IRBs to accept increased responsibilities in this area. Such a transfer would not change the standards of human subject protection and, hence, would not put patients at any greater risk than under the present arrangement.

The FDA informally has been "floating" this idea for at least a year. And, in the *Federal Register* of September 11, FDA formally described its interest in pursuing such a possible arrangement by publishing a summary of the issue and inviting comments from all interested parties. The *FR* item asks for views on five specific points as well as inviting responses to the general proposition.

The FDA appears to be genuinely interested in achieving some positive result in this matter. FDA Commissioner Arthur Hull Hayes, Jr., has supplemented the *FR* notice with a personal mailing to a broad spectrum of individuals and groups to call their attention to this issue and to invite the widest possible response.

On the surface, this concept (of using local IRBs to a greater extent as a trade-off for reducing most FDA oversight during Phase I and early-Phase II drug studies) makes a good deal of sense to us. But, as noted above, for some strange reason the idea seems to have generated little interest or publicity among any of the usually vocal and active groups on the drug scene: the lay press, broadcast media, consumer advocates, pharmaceutical trade organizations, Congress, or special interest groups.

It would be most regrettable—indeed, even tragic—if one of the few real potential solutions to reducing government "red tape" and the so-called "drug lag" were allowed to die simply because of apathy and neglect on the part of all concerned.

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