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WHERE HAVE ALL THE RESEARCHERS GONE?

The "researchers" referred to in the title of this editorial are the clinical research people who conduct the studies concerning safety and effectiveness of new drugs using human volunteers as test subjects.

Twenty-five years ago, it seemed that people conducting clinical trials were the proverbial "a-dime-a-dozen." Today, however, they are few and far between; and their number keeps shrinking at an alarming pace.

What has happened? What has caused this major shift? Is the net effect good or bad? And what impact will this have for the future of new drug development? A brief recapitulation and examination of this general phenomenon would appear to be in order.

Drug testing was an extremely lax business back in the 1950s. Furthermore, not only was it simple and easy for virtually any medical practitioner to begin conducting clinical experiments using human subjects—without their consent or even their knowledge—but it was also glamorous, exciting, and the "in thing" among many physicians. Not surprisingly, abuses were commonplace and the results and findings of these pseudoscientific studies by mostly untrained researchers were frequently of questionable validity and doubtful value.

Reform in the shape of the 1962 amendments to the Federal Food, Drug, and Cosmetic Act, coupled with related FDA regulations, changed this situation very abruptly by the mid-60s. "Experts qualified by scientific training and experience," "submission of preclinical test" protocols, "signed agreements from each such investigator," "the establishment and maintenance of records," "making of reports to the Secretary of HEW," certification of "informed human consent," and granting general authority for FDA inspectors to have "access to, to copy, and to verify all such records," were some of the new provisions of that legislation which directly related to the future operation of clinical investigators and their work.

In retrospect, that new law and its associated regulations had a very salutory effect. Most of the abuses were curbed, the amateur researchers were effectively weeded out, and the remaining people constituted a largely conscientious, qualified, and professional core of medical scientists. Indeed, almost overnight, clinical pharmacology came into its own, and this cadre of clinical investigators became regarded as a highly respectable sort of subdiscipline or specialty group.

But because some abuses continued, and because a few investigators were dishonest and got caught at it, increasingly stringent rules and regulations were subsequently promulgated to govern the operation of clinical investigators. Concurrently, other forces were at play that also impacted on the area of clinical investigations and on those who conduct such studies.

One of these was concern over the use of prisoners in human drug trials and the question of whether prisoners could participate in a truly voluntary fashion. A second development was the surge of malpractice cases and the soaring costs of settling liability claims and judgments. A third development was our growing sophistication as to what is needed to produce a valid drug investigation—including, for example, larger and better selected patient populations, adequate controls, and double-blind study designs.

More recently, there have been some other changes. Institutional review boards, or IRBs, have been established and have become a formal part of the clinical investigation process. They provide a broad perspective in reviewing the drug investigator's study plan, the suitability of its design, and the protection offered the patients participating. All of this is good, but it greatly lessens the feeling of freedom and hence the challenge that once attracted clinical investigators to such work.

The same can be said of FDA inspections which now are both more frequent and more thorough. They, too, give society greater confidence that patients' rights are protected and that society is being properly served; but concurrently, they also add greatly to the annoyance and frustration level of the clinical investigator who is subjected to this often intense scrutiny.

Increasingly, we are hearing reports that good people are dropping out of the pool of clinical researchers and that new people are reluctant to embark on careers in that field. Consequently, the field is giving signs that it is beginning to dry up, at least in this country. Partially, the impact has been dulled because many drug firms are now drawing upon foreign data to support their new drug applications. But that is no real or long-term solution for the problem.

If this country is to continue to benefit from the introduction of important new drugs, we need to find an answer that will somehow rejuvenate clinical testing in the United States, while continuing to afford reasonable protection for those who participate as test subjects in such studies. And the importance of this problem is such that it calls for prompt attention and serious consideration.