Medicinal Chemistry: GAO Chides NIH

The General Accounting Office, the government's chief auditor and roving critic of the bureaucracy's conduct, last week issued a report* which takes to task the National Institutes of Health. GAO says NIH policies inhibit researchers with grants in medicinal chemistry from obtaining adequate screening and testing services for new compounds that they synthesize.

As GAO reports go, this one is gentle, almost genial, in tone. Reactions to the report suggest that government agencies, researchers, and drug firms alike are deferring hope for major patent law reform and are striving to make the best of life under the existing law. (The crux of their problem is ownership of title to inventions.)

The report deals specifically with NIH research grants in medicinal chemistry, which, in 1967, amounted to about $13 million and between 1962 and 1967 totalled $53 million.

Until 1962, says the report, drug companies had "routinely made tests, at no extra charge, on compounds developed by grantees. . . . In general [drug firms] acquired certain rights to the development and marketing of promising compounds, without incurring the cost of synthesizing the compounds to be screened and tested." GAO says that a bottleneck was created in 1962 when the Department of Health, Education and Welfare revised its patent procedures.

When HEW revised its procedures, it meant that the government could step in and claim title to a compound if the investigator or any of his associates received federal funds or if equipment used in work on the compound had been bought with federal funds. The drug company reaction was to withdraw from cooperation with university investigators. Industry spokesmen argued that costs of screening and testing were very heavy, while chances of developing a useful drug were small and actual government contribution might be infinitesimal.

The GAO report says that grantees at eight of ten institutions visited had encountered serious difficulties in arranging for screening and testing. University researchers familiar with the subject told *Science* that, in practical terms, only drug firms have the full capability for testing compounds.

Screening and testing are terms used fairly interchangeably. Such services range from preliminary broad-scale screening of many compounds for "candidate" agents to testing on animals and humans to gather data required for an investigational new drug application to the FDA.

Alternative government testing services are available for cancer chemotherapeutic agents and for antimalarial agents. But neither these government services nor the commercial and nonprofit labs which also provide test services offer the broad-scale screening that could indicate whether compounds tested would be useful in other diseases.

Investigators discussed in the report are most often synthetic organic chemists. Also affected, but not mentioned in the report, are pharmacologists and other university scientists who before 1962 often did contract screening for compounds developed in drug firm laboratories.

The GAO report makes clear that HEW attitudes on patents have shown a tendency toward liberalization. Within government, patent policy has been far from monolithic. In 1963, President Kennedy issued a memorandum authorizing "flexibility" in administering the law, and this still stands. But attitudes range widely. The Atomic Energy Commission and Interior Department are usually strict in requiring that the government take title to inventions made under their grants. The Defense Department has a reputation for being more lenient in granting patent rights to industry.

Within HEW, a conflict over patent policy came to a showdown in 1966. Since then there has been a thaw, if a slow one. Interested outsiders say that more flexibility has been attained so far mainly by adjustment of individual cases, with officials in the higher reaches of HEW and in the top echelons of NIH taking a hand. There is not much to indicate this in memos or official correspondence, but, apparently, difficulties have often been eased by the timely telephone calls which figure large in the unwritten history of NIH under its retiring director James Shannon.

The GAO report, however, mentions four actions taken or contemplated by NIH which should make it easier for investigators to have compounds tested. Probably most important is the NIH plan to standardize its so-called institutional patent agreements and open them to more institutions than the 17 now participating. Under these agreements, universities are principal owners of rights to inventions made by their faculty under NIH grants. The government still retains the right to make use of the invention for its own purposes, and exclusive licensing rights are limited. Pharmaceutical firms, however, would rather deal with universities than with the government, and the opening up of the institutional agreements will probably increase a recent trend among drug firms to test compounds again.

GAO says that these innovations will all take time to work out, but the report indicates the investigators think prospects are encouraging.

Still looming, however, is the background problem of a patent law which has been made an anachronism by the impact of massive federal support of research since the war. So great is the complexity of the issue and so sharp the clash of interests that attempts to legislate changes (*Science*, 2 April 1965) in the law seem not to have moved very far.

Because of potential profits for drug firms, investigators, and their institutions, NIH faces problems of greater delicacy with its medicinal chemistry grants than with grants in other fields. Protecting the public interest by insisting on government ownership of title to new drugs had a logic, simplicity, and purity attractive to the official mind, but it seems to have blocked the development of useful new drugs. Pragmatism can be more difficult and dangerous, but NIH is trying, as the GAO report urges, to put the emphasis on results.

—JOHN WALSH

* Problem Areas Affecting Usefulness of Results of Government-Sponsored Research in Medicinal Chemistry B-164031(2).