Drug agency's research fails to make the grade

The US Food and Drug Administration "lacks a culture of science" and its in-house research suffers from fragmentation, poor internal communication and lack of leadership, according to a high-level review panel. The panel's critical report comes at a time when the dissatisfaction with the FDA in the pharmaceutical industry is already forcing it to cut back on its scientific program and when Congress is due to review its $190-million research budget.

The FDA has been struggling for decades to create a first-rate program of in-house research — the entirely plausible rationale being that it takes sharp, up-to-date researchers to make sound regulatory decisions about the plethora of new drugs and devices that come before the agency for approval. But the criticisms of the panel, headed by David Korn, former dean of Stanford University School of Medicine, echo those of more than half-a-dozen predecessors since the 1950s, suggesting that the agency's efforts have not succeeded.

The Korn committee concludes that the FDA currently lacks the culture and the "scientific communication that is essential for the nurture of high quality science." Its report says that the intramural science program "is uneven in quality, mission-relevance and efficiency." It is especially critical of what it calls a "pervasive disinclination among [the FDA's] centers to share data and expertise," and it finds that science management is generally poor.

The FDA can claim the credit for some important studies, for example, on vaccines for pertussis. But it has always had a hard time justifying its intramural research program. Although the agency can provide little hard data, it appears that, even though its best scientists publish respectable work in peer-reviewed journals, its research is not generally pioneering. Nor do its scientists publish regularly in first-ranked, highly competitive international journals. This performance compares poorly with that of intramural researchers at the nearby National Institutes of Health.

The biotechnology industry has already made clear, in Congress and elsewhere, that it is dissatisfied with the FDA. It has been particularly critical of the agency's inability to respond rapidly to therapeutic agents that do not fit the classic mold because its scientists allegedly do not understand clinically important nuances of new classes of drugs.

Since 1992, the pharmaceutical industry has been required by Congress to pay a "user fee" on applications for new drugs put before the FDA — in effect, a tax that has allowed the agency to hire more scientists in regulatory positions to speed the drug review process. In an effort to build up its research capacity, the agency has directed these new staff to spend about half their time in research.

But the pharmaceutical industry is now balking at what it sees as a useless tax. It is arguing that the FDA's intramural research adds little to its efficiency or skill in doing its regulatory job and that it is therefore not worth supporting. In response, the FDA has agreed to cut back on the amount of this tax that it spends on science. For example, in the Center for Biologics Evaluation and Research, where some of the FDA's vaccine work is done, the research budget will be cut by $10 million or more during the next couple of years. At the same time, as many as one-third of the center's 300 scientists will be transferred from dual duties in both research and regulation to regulatory work alone.

In this context, the timing of the Korn committee's report is particularly disturbing for the FDA. The committee, which was set up by the FDA itself and included prominent representatives of the National Institutes of Health, the research branches of the pharmaceutical industry and academia, concluded that much of the FDA's research inadequacy is due to its organizational Balkanization. Its different "territories" are organized according to regulatory requirements: for example, the biologics center includes divisions for bacterial products, vaccines research and a laboratory of bacterial polysaccharides.

One committee member offered this hypothetical example of the difficulties such a structure can cause: A new drug, only months on the market, appears to be cardiotoxic in combination with certain other drugs. "What you'd like to do is pull together all of the FDA's expertise on each of the drugs in question, all of the data it has on the ages and genders of patients, and whatever relevant expertise there may be in toxicology. And do it fast. But you can't because the agency is subdivided into various specialized 'centers' that don't share data and don't talk to each other."

The committee argues emphatically that the FDA should be conducting its own research. To improve its quality, the committee recommends that the FDA create what it calls a "virtual science center," headed by a chief scientist with the authority to cut across agency boundaries. This would cost little more than a top-level salary. The FDA's deputy commissioner for operations, Michael Friedman, says that he is already preparing a list of candidates for such a research czar once a new FDA commissioner is chosen to replace David Kessler, who recently resigned.

Friedman argues that it is important for the agency to be better equipped to make good scientific judgments during the early stages of drug and device development, when FDA and industry scientists are comparing the relative merits of different animal models or the appropriateness of certain types of statistical analysis. Much of this takes place before a formal application is submitted, he says. But the FDA's critics say it is up to the agency to justify by explicit example — and hard data — the potential value of better intramural science to the agency's regulatory job.

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