FUSION RESEARCH

European Report Champions ITER

While the scientific underpinnings of the International Thermonuclear Experimental Reactor (ITER) program are under attack in the United States (see previous story), the $10 billion project continues to gather momentum in Europe. A panel of scientists and industrialists has given the European arm of the effort a resounding pat on the back.

"We have really been very much impressed by progress that has been achieved in the last 5 years," says Sergio Barabaschi, science adviser to the Italian government and chair of the panel. The European Commission, the executive arm of the European Union (EU), last year appointed the eight-strong panel to assess both scientific progress and ITER's management. According to the panel's report, expected to be published soon, its members were impressed by research progress since the previous evaluation in 1990.

The report endorses the ITER concept as it stands now, stating that a smaller reactor than currently planned—a strategy favored by some scientists—would be a poor choice because the aim is to build a reactor as close to a commercial, power-generating machine as possible. The board also believed that the demonstration reactor should be based in Europe, which would require an increase of at least 50% in EU funding for its fusion programs, now at $285 million a year, in the first decade of the next century. Italy is the only European country that has expressed a desire to host ITER.

On the technical side, the board suggests that the collaboration investigate stellarator technology as a possible alternative to the currently favored magnetic-confinement option, as scientists cannot be certain which will work best in a large reactor. Both techniques confine the plasma in a toroid-shaped vessel with magnetic fields, but in the current ITER design, the fields are pulsed and the confinement aided by a current circulating within the plasma. A stellarator operates in a steady state, and all the heating and confinement comes from outside.

On the management side, the board was impressed at how well the EU's fusion program has coordinated research in different member states, says Barabaschi. But the board admits that ITER has an image problem: Because of its huge cost and technical complexity, the project constitutes a "democratic dilemma." The board suggested that some money be spent on research on the economic and political aspects of fusion and public awareness.

–Alexander Hellemans

Alexander Hellemans is a science writer in Paris.

FDA SCIENCE

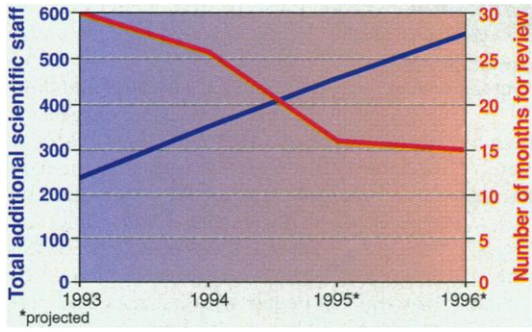
Kessler's Legacy: Unfinished Reform

At first blush, this month's third annual conference on in-house research at the Food and Drug Administration (FDA) will look like a typical scientific gathering. But accompanying the presentations and posters will be a new slate of awards for innovative research—an attempt to raise the spirits of a group that some critics in Congress and elsewhere say shouldn't exist, and which FDA Commissioner David Kessler has fought hard to strengthen. Now, the issue is one that Kessler's successor will have to face: Last week, Kessler announced that he would step down after six hectic years as FDA commissioner as soon as his replacement is chosen and confirmed.

Kessler, who will probably be remembered most for his campaigns to regulate nicotine as an addictive drug and to improve food labeling, admits that the job of improving the agency's science remains unfinished. Indeed, the agency has just embarked on a 5-year plan that would consolidate research at its 19 labs scattered across the country into as few as five. Still, his colleagues praise his efforts to define and elevate agency research. "He has had more impact on science than any of his predecessors," says Philip Noguchi, a 16-year veteran of the agency and current director of the cellular and gene-therapies division at FDA's Center for Biologics Evaluation and Research.

Kessler's departure comes at a time when FDA's $190 million research portfolio is under scrutiny by a Congress intent on reforming the entire agency. "It's a basic question of whether research is really FDA's role," says Carl Feldbaum, president of the Biotechnology Industry Organization (BIO). Feldbaum maintains that many of FDA's activities, including research, should be contracted out. Kessler argues, however, that FDA scientists will be better regulators if they also conduct cutting-edge research.

When Kessler arrived at FDA during the Bush Administration, he faced widespread criticism that neither FDA's science nor its regulatory machinery were working well and that the agency was too slow in approving new drugs. After lengthy talks between industry groups and FDA, Congress authorized the agency to collect fees from companies that file new drug applications. These "user fees" have been spent on hiring more than 500 new scientific staff—from microbiologists to statisticians—to review applications.



SOURCE: FDA/BIO

Helping hands. User fees have allowed FDA to hire more scientists and speed up the drug approval process.

The additional staff have helped lower the time needed to act on a new drug application from an average of 30 months in 1992 to 17 months in 1995. This is a "major accomplishment," says Louis Lasagna, dean of the Sackler School of Graduate Biomedical Sciences at Tufts University. For anti-cancer and AIDS drugs, it's a brisk 6 months.

Another key issue confronting Kessler was how to bring research at the agency's National Center for Toxicological Research (NCTR) in Jefferson, Arkansas, in line with agency needs. "It used to be out there doing its own work that wasn't relevant to the agency," Kessler says. His response: Every proposed project at NCTR must contain a statement justifying its relevance to FDA's mission. He also brought in toxicologist Bernard Schwetz from the National Institutes of Health as NCTR director and, later, also named him to the new position of associate commissioner for science. Schwetz helped to forge scientific collaborations across FDA's five product centers in suburban Maryland on subjects ranging from tissue engineering to emerging infectious diseases. "We have a lot of very good scientists, but what we haven't had is a common framework to work from," says Noguchi. Last year, Kessler lured Michael Friedman from the National Cancer Institute to become deputy commissioner for operations and to revive the agency's moribund science board, which coordinates the agency's in-house research.

Kessler has had less success in improving communication between agency reviewers and drug-company representatives. Although approval times have shrunk, companies see the FDA as part of the reason for the increasing cost and time spent on R&D, now estimated at 10 years and $500 million per drug. Company officials complain of poor commu-

nication with FDA reviewers, who often ask for additional time-consuming tests late in the approval process. The fear of such requirements, says Lasagna, leads to "real or imagined perceptions of what FDA will demand," which in turn lengthen the process.

Lasagna praises Kessler "for moving the agency in the direction of a collegial relationship with the regulated communities." Kessler calls this change "one of the most important things the agency has done" to try to shorten drug development times. But the real test of this relationship is whether drug companies will still be required to provide data on demand. The FDA is not known for its flexibility in arguments over data requirements. "It's like fighting a 600-pound gorilla in its cage," Lasagna says. "You aren't going to win."

The next commissioner must balance the need to keep FDA's staff scientifically up to date with the need to review new drugs even more quickly. Friedman says the agency can do a better job in seeking advice from scientists at universities and other government branches, such as the National Institutes of Health, adding that "we need more effective linkages with scientists outside the agency."

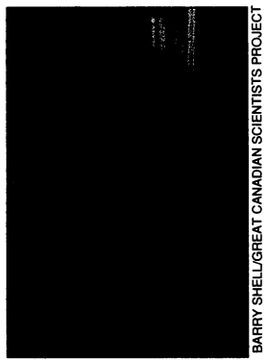
Those who support FDA's research program realize that they must find new ways to demonstrate why science is vital to a regulatory agency. "It's hard to show that better science is giving the public more bang for the buck," says Noguchi. But Friedman thinks the case can be made. "These are very difficult times for science and regulatory activities," he says. "What's essential is that we find more effective ways for science to be the engine that drives the agency."

–Richard Stone

ETHICS

Draft Research Code Raises Hackles

Scientists in Canada who do research with human subjects have spent the past several months worrying—and complaining—about a proposed new ethics code that many say would needlessly restrict good research while making funding decisions more vulnerable to political pressures. The proposal, first unveiled in the spring, was put together by the Tri-Council Working Group on Ethics, formed by the country's three top research funding agencies* to devise a uniform code for government-funded research with human subjects. Made up mostly of doctors, ethicists, and lawyers, the group originally set a 15 July deadline for feedback from the professional community. But that has gone by the boards. The committee's chair, Jean Joly, an infectious-diseases expert at the University of Montreal, says the mail is still arriving. About 260 letters, "most [of them] single-spaced," have come in, he says. Although many are "laudatory," some are "absolutely explosive." A second draft now isn't expected to be ready until spring.



BARRY SHELL/GREAT CANADIAN SCIENTISTS PROJECT

Concerned psychologist. Doreen Kimura.

One major sticking point for the critics, who include many experimental psychologists, is a redefinition of the role of an institution's Research Ethics Board (REB). Under the new guidelines, REBs would review not just the ethics but the "scientific validity" of proposed studies with human subjects. This sets up a process that threatens to "confuse ethics with experimental design," argues psychologist John Furedy, president of Canada's Society for Academic Freedom and Scholarship (SAFS). Because only two of the five board members would be required to be knowledgeable about the science, board decisions on sensitive research—such as a study comparing AIDS prevalence and promiscuity in different ethnic groups—could be swayed by local political sensibilities, critics say.

Critics have also reacted to the draft's emphasis on ensuring a "subject-centered perspective" in research. One provision in particular stipulates that in studies where at the outset subjects are either deceived or not fully informed about the purpose of the research, "If the subject decides he or she does not want to participate following [a postexperiment] debriefing, the subject's data must be removed from the study." Doreen Kimura, a psychologist at the University of Western Ontario in London, Ontario, and a founding member of SAFS, says that allowing subjects to back out of a research project after the data have been collected would complicate the type of research she does. For example, she says, the results of a study comparing old and young people on a cognitive task could be biased if old people who felt they had performed poorly often withdrew.

Both SAFS and the Canadian Society for Brain, Behaviour, and Cognitive Science also say that the working group has put too much emphasis on the need for research to be of moral benefit to society. "What are the 'moral benefits' of knowing whether a particular configuration of lines on paper produces a visual illusion?" asks the brain society in a draft response to the proposed code. The society's president, psychologist Vincent DiLollo of the University of British Columbia (UBC) in Vancouver, also says that the working group's concern about avoiding "coercion" of research subjects is so extreme that many psychologists worry that the final version of the code will prohibit them from paying or giving course credit to students for being research subjects.

The draft code has also raised a shower of objections from historians and social scientists with a proposal that in research with people who belong to a "collectivity," such as a family or community, "the researcher may not begin until permission has been obtained from the appropriate authorities for that collectivity." Critics maintain that this could be interpreted to mean, for example, that one would have to get permission from the head of a neo-Nazi gang to interview a disaffected member.

Tricouncil group members acknowledge that they have gotten some people very rattled, but insist that they are listening to all comments. Indeed, in some instances—including the matter of consent for members of collectivities, and a proposal that would prohibit clinicians from recruiting their own patients into their trials—the working group is promising to back off. In other cases, members say that their critics have overreacted. For instance, Michael McDonald, director of the Center for Applied Ethics at UBC, says that there is no need to worry about the REBs turning down good science for political reasons: Because funding agencies do scientific reviews of proposals, "I don't expect REBs themselves to be really much concerned about scientific validity other than making sure some kind of review has taken place."

Chair Joly admits that the working group has a "very, very difficult" task before it. Ultimately, he says, "the document that we produce we hope will be a living document ... always under revision." Furedy, for one, is not reassured. "That ... is always the case with vague, totalitarian documents," he claims.

But as McDonald points out, most reactions to the draft have been positive. "This is the first time we've had a discussion all across the country on the subject of research ethics," he says. "I think it's marvelous ... terrific."

–Constance Holden

* The Medical Research Council, the Social Sciences and Humanities Research Council, and the Natural Sciences and Engineering Research Council. The draft report can be found on the Internet at http://www.ethics.ubc.ca/code/