BIOETHICS

Panel Faults Research Consent Process

A $5 million hunt through old files for signs of medical misconduct ended this week when a presidential panel handed in a 925-page report on radiation experiments conducted in the Cold War era. The exhaustive, 18-month inquiry confirmed that there had been serious ethical lapses, but turned up few surprises and few indications that U.S. citizens were physically harmed. President Clinton responded on 3 October by pledging to have the government review experiments that put people at risk and compensate the families of those who were wronged. He also promised to review federal oversight of current biomedical research and created a new, independent National Bioethics Advisory Committee to help guide the government in controversial areas.

The creation of the panel had been anticipated (*Science*, 29 September, p. 1807), but clinicians will find another message in the report that they may not have expected. It recommends that local review boards take a closer look at patient consent forms and weigh not just safety and ethics but also the scientific justification for projects involving human experimentation.

The report of the Advisory Committee on Human Radiation Experiments, chaired by ethicist Ruth Faden of Johns Hopkins University—whose inquiry was triggered by a series of shocking newspaper articles in 1993–94—focused on studies of ionizing radiation conducted between 1944 and 1974. And it noted that some government-sponsored studies had robbed vulnerable patients of their dignity, even when there is no evidence of physical harm. That was the case in notorious experiments during the 1940s in which doctors injected two dozen unwitting cancer patients with plutonium to learn what might happen to servicemen exposed to radiation in the line of duty.

The number of subjects who may have been harmed, the report says, was in the tens, not the tens of thousands suggested in some media reports, a finding that reassures some ethicists. "We are greatly relieved" at the numbers, says Gary Ellis, chief of the Office for Protection Against Research Risks, overseer of ethics at the National Institutes of Health (NIH) and of 3500 local review panels around the nation.

But the Faden panel didn't limit its critique to problems of the past. It also looked at ongoing biomedical research and found "evidence of serious deficiencies" in the current system (created in 1974) to protect human subjects. It based this conclusion on two quick surveys: a review of 125 randomly selected protocols for ionizing radiation studies from 1990 to 1993 and random interviews with 1900 patients in outpatient clinics. The committee found that patient consent forms often didn't jibe with descriptions of the same research in grant proposals. The version given to patients "appeared to overstate the therapeutic potential," the report says. The committee also felt that consent forms failed to distinguish between therapy and research and often gave patients too much technical information.

After reviewing these documents, one panel member—Jay Katz, a professor emeritus of law at Yale University—wrote an independent statement that was even more critical than that of the full panel. Katz was "stunned" by the extent of "obfuscation" in consent forms. He concluded that the government needs to create a new, "authoritative and highly visible body" to protect the rights of patients.

The full panel didn't go this far, but it did suggest a few reforms. It recommended that institutional review boards (IRBs)—small panels that meet at medical institutions around the country to screen and approve clinical studies—focus on big risks, try to handle routine issues more rapidly, and be certain that patients understand that they may not personally benefit from the treatment they receive. IRBs, it said, should ensure that patients realize that participating in research may at times bring more discomfort than benefit; that they always be told the sponsor and the purpose of research; and that they clearly understand the financial implications of participating (insurance often won't pay for experimental treatment). Finally, the panel said that IRBs should examine the scientific quality of all research proposals. "If the science is poor, it is unethical to impose even minimal risk or inconvenience on human subjects," the report says.

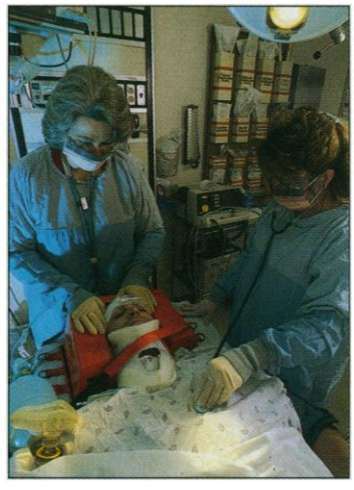
The NIH's Ellis says, "We are in complete agreement" with the recommendation that IRBs examine the quality of studies more closely. "Bad science," he says, "is bad ethics." But Ellis did not foresee any immediate change in the working of IRBs.

–Eliot Marshall

BIOETHICS

Waivers Proposed for Emergency Studies

Guy Clifton, chief of neurosurgery at the University of Texas, Houston's, medical school, ran into a roadblock last year in his efforts to determine the effectiveness of a new treatment for severe head injuries. Clifton wanted to learn whether chilling the patient's body in trauma cases might help prevent brain damage by stopping the biochemical processes that follow severe brain injury, causing additional damage. But his project was getting stalled because rules on informed consent—which require that subjects give their consent in advance—made it hard to enroll patients. Clifton says candidates for his hypothermia trial were unable to communicate. And family members who might have given consent by proxy were available only about half the time.



DAVID YORK/MEDICHROME

Fast track. New rule permits some research on emergency cases without prior consent.

After 10 months, Clifton had enrolled only 65 patients, although his plan called for a total of 500. Realizing it would take years to complete the trial, Clifton sought a waiver of informed consent from his funding source, the National Institutes of Health (NIH). Because he was persistent and armed with good data, Clifton says, officials at NIH and its parent organization, the Department of Health and Human Services (HHS), granted the waiver.

Now a new rule proposed by the FDA on 21 September may make it easier for other physicians to obtain waivers for similar studies. The FDA intends to loosen regulations that apply to research in its jurisdiction on medical emergency cases, and officials at HHS and NIH are planning to do likewise. The secretary of HHS is expected to issue an administrative waiver to match the FDA's final rule, so that all biomedical research will be held to the same standard. Mary Pendergast, FDA's deputy commissioner, says the reform would affect about 30 projects a year and that about six are already awaiting clearance.

This proposal "is of monumental importance," says Arthur Caplan, a bioethicist at the University of Pennsylvania. Although Caplan regards the informed consent rule as the "central dogma" of his field, he thinks the

FDA's proposal is justified. "You can assume that most people would approve of using investigational trials," he says, under the conditions FDA specifies.

Before any trial could receive a waiver, the FDA proposal calls for a review by an independent physician and a hospital's institutional review board (IRB)—a committee of experts and laypeople. They would have to agree on several points: that the trial addresses a life-threatening situation, that the experimental treatment is at least as good as conventional therapy, and that the condition of patients is likely to be such that it would be very difficult to obtain consent in advance. As added protection, the proposal requires consultation with representatives of the community from which the subjects will be drawn, advance public notice of all waived studies, an independent board to monitor the studies as they progress, and publication of all results.

While IRBs had authority to grant waivers in the past, the new rule will make such decisions easier by providing specific guidelines. One leading advocate of this change, Michelle Biros, research director of the department of emergency medicine at Hennepin County Hospital in Minneapolis, says she is pleased with the proposal. She says it incorporates many recommendations made by a coalition she heads that is made up of emergency medicine professionals, patient advocates, and bioethicists.

Although it has been well received so far, the new rule may have a practical drawback, according to Caplan: It may overburden the IRBs. "The FDA is requiring the IRB to take a close look at the research, justify a waiver, and monitor what's going on. That is asking a lot of a board that is already under tremendous workload pressure," he says. But Pendergast thinks that few studies will be eligible for a waiver under the FDA's guidelines, and few researchers will apply.

Unless it hears a strong objection, the FDA plans to finish collecting public comment on 6 November and put the new rule into effect shortly afterward.

–Lori Wolfgang

SPACE SCIENCE

Panel Critiques NASA Science

An 11-member independent panel of industry managers and academic researchers has come up with a litany of criticisms of how the National Aeronautics and Space Administration conducts science—but senior NASA officials will probably see it as a vindication. For starters, the panel says, the agency should give its chief scientist greater authority and come up with realistic priorities to match the agency's slowly declining budget. The panel also urges NASA managers to combat what it calls the "insular culture" at the agency's far-flung centers and to subject technology to more exacting peer review. But far from implying a new direction, agency officials say, most of those recommendations match the course that NASA Administrator Daniel Goldin had already set for the agency's $3 billion worth of research each year in astronomy, life science, and other fields.

Released last week, the 18-month study was spurred by the major reorganization of NASA science that Goldin undertook in 1992. Complaining that programs were taking too long, cost too much, and lacked thorough review from the scientific community, Goldin removed Lennard Fisk, the popular chief of NASA science programs, and chopped the single science office up into three pieces (*Science*, 23 October 1992, p. 540). The apparent downgrading of science angered Senator Barbara Mikulski (D–MD), a Fisk supporter whose appropriations subcommittee requested the NRC review of NASA's science the following year.

The NRC panel, chaired by former IBM research director John Armstrong, backs Goldin's revamped organization but calls for the chief scientist to have a greater say in formulating the agency's scientific direction. The chief scientist position has only rarely been filled in NASA's 37-year history, and then it was largely a ceremonial one. Last year, however, Goldin appointed Pennsylvania State University astronomer France Cordova to the job and elevated its status. "We have a more informal way of doing things, and they recommend we formalize that," Cordova told *Science*.

Another recommendation may also have a familiar ring to NASA managers: that Goldin improve the quality of science at the NASA centers by expanding their contacts with the outside community and promoting greater competition among research projects. "The administrator was very receptive to this," Armstrong says. At Goldin's request, a team of agency managers has been putting together a plan in recent months to set up independent institutes at the centers that would boost the quality of NASA science. "The whole business of these institutes [is] to make sure we're not insular," says Cordova.

NASA

Hot topic. Management of NASA science efforts, which include the recent Magellan mission that mapped the surface of Venus, is under scrutiny.

Armstrong warns, however, that the plan must be carefully put together to ensure that the institutes have a good measure of financial and managerial independence from the centers. "It's naive to think good intentions are all it takes," he says. His panel also emphasized that NASA headquarters should maintain a firm grip on peer review and overall science oversight, despite Goldin's push to downsize the Washington headquarters drastically in coming years.

Likely to be more controversial is the panel's advice that NASA be more strict in making awards for technologies that affect science programs—such as spacecraft design or propulsion. "This means peer review by engineers, not by scientists," says Armstrong. But one NASA official decries the recommendation as a "grab" by the scientific community to extend its control over technology efforts and budgets. "You don't go to the universities to develop a new propulsion system," he says. "You try and do it cooperatively with industry—and then you can't peer review it," as companies are nervous about giving away their technical secrets to potential competitors. Cordova says NASA will set a clear policy on technology peer review early next year.

On a broader scale, Armstrong's panel also calls for NASA to set up a more formal mechanism for choosing future missions in an era of tightening budgets. "The basic problem up to now is that [members of] the science community have been willing to choose what they believe are the most important projects within a discipline, but not across disciplines," he says. The study proposes a more open and structured process for making these choices that could avoid some bloodletting between disciplines.

Cordova was unwilling to discuss NASA's reaction to the report in detail until she discusses it in depth with Goldin and the agency's science managers, but she praises the report as "responsive to the issues" and full of some "creative suggestions." Of course, advice is especially welcome when it confirms what you are already doing.

–Andrew Lawler