MICROGENESYS

Peer Review Triumphs Over Lobbying

One of Washington's longest-running scientific and political soap operas is broadcasting its final episode. After more than a year of outrage from AIDS researchers, arm wrestling among federal agencies, and pressure from the White House, the fate of a controversial $20 million congressional appropriation to test one company's therapeutic AIDS vaccine has been sealed. In letters to Congress on 4 January, officials of the Department of Defense (DOD), the National Institutes of Health (NIH), and the Food and Drug Administration (FDA) "certified" that the legislated large-scale trial of the gp160 vaccine, a therapeutic AIDS vaccine made by MicroGeneSys of Meriden, Connecticut, should not proceed.

Instead of a large-scale trial of a single product, which Congress ordered after an intense lobbying campaign by MicroGeneSys, the $20 million will be rolled into a fund for general research on HIV vaccine therapy. Unlike the aborted test of the MicroGeneSys vaccine, this research will all be subject to peer review. Edward Martin, acting assistant secretary of defense, explained in his letter that, "based on available data, it is premature" to start a large-scale efficacy trial with MicroGeneSys's gp160. Martin noted, however, that DOD "continues to believe" that vaccine therapy—which uses vaccine technology to treat, rather than prevent, HIV infection—"merits intense exploration." Hence the Army's new vaccine therapy development program.

This solution resolves the central scientific complaint about the $20 million appropriation: that by hiring a team of high-powered lobbyists—including former Senator Russell Long and former Reagan Administration officials—to convince Congress of gp160's merit, MicroGeneSys had done an end-run around peer review. That perception brought outraged responses from Bernadine Healy, then director of NIH, FDA head David Kessler, and many AIDS scientists who believed there was no scientific basis for singling out one company's therapeutic AIDS vaccine for a large-scale trial from at least a half-dozen competitors (*Science*, 23 October 1992, p. 536).

Lobbying will not draw much water in DOD's new vaccine therapy pool. Proposals for that pool, wrote Martin, "will be judged by peer review, and selections will be based on scientific excellence and potential for clinical impact." Martin also made it clear that scientists from both FDA and NIH will be brought into the peer-review process.

But DOD does not have the power to end the gp160 trial on its own. By law, the heads of NIH and FDA also had to notify Congress that they, too, objected to the test. Just such an objection was registered in a 4 January letter co-signed by NIH Director Harold Varmus and FDA commissioner David Kessler. "We feel that the funds in question could more appropriately be used to answer basic questions about the immune response and host defense mechanisms related to vaccines prior to initiating large-scale human trials of a therapeutic vaccine," wrote Varmus and Kessler.

Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, says he's thrilled by DOD's decision to spend the money on peer-reviewed research. "That sounds like an excellent solution. It serves the best interests of science," enthuses Fauci, who chaired a blue-ribbon panel that evaluated the $20 million appropriation. Col. Donald Burke, head of AIDS research for the military, says he is more than pleased: "I'm delighted that we're at the point where we should have been a year-and-a-half ago."

MicroGeneSys did not return repeated phone calls to discuss the impact that the decision will have on its plans. But the company's corporate partner in developing and marketing the vaccine, the American Home Products division of Wyeth-Ayerst Laboratories, has already weighed in with a verdict of sorts. On 14 January, Wyeth-Ayerst announced it will "terminate its involvement" in the development of the MicroGeneSys vaccine. A Wyeth-Ayerst spokeswoman would not comment on why they are ending their 3-year-old agreement.

DOD has not decided when it will begin soliciting researchers' proposals for what they would like to do with the $20 million, but Burke says that by September, the military will have decided which vaccine researchers will receive the windfall originally intended for MicroGeneSys.

–Jon Cohen

FRANCE

Researchers Nervous About Bioethics Bill

PARIS—The French Senate last week threatened a fragile consensus between legislators and medical researchers over the regulation of practices such as in vitro fertilization (IVF), genetic screening, and organ transplantation. On 21 January, the Senate, the upper house of France's parliament, approved by a large majority amendments to a sweeping bioethics bill that had been crafted to satisfy the concerns of both scientists and ethicists. The Senate's amendments would make some areas of research impossible to continue.

Many French medical researchers are horrified. The amendments "could stop all fundamental research, and halt all progress in medically assisted procreation," says Michelle Plachot, a researcher in the in vitro fertilization and reproductive biology laboratory at Paris's Necker Hospital. There may, however, be an opportunity to modify some of the worst aspects of the Senate's handiwork: The bill will now go back to the National Assembly, the parliament's lower house, for a second reading during the spring, and will probably not become law until May or June.

The ambitious law was originally drawn up by France's previous, socialist government with support from researchers. It passed its first reading by the National Assembly in November 1992. But since then, the political mood has changed in France and conservatives are now in power. If the Senate's amendments are retained, the donation and transplantation of organs, cells, and tissues would be strictly regulated, and menopausal women, single women, and widows would be barred from giving birth to "test-tube babies"—only couples married or living together for at least 2 years would be eligible (see box, p. 464).

From the point of view of France's research community, the thorniest features of the proposed law are two amendments, sponsored by the conservative government, that would severely limit what can be done with human embryos in the laboratory. The first forbids "experimentation" on human embryos, and prohibits their in vitro conception solely for research purposes. Yet "studies" of such embryos would be allowed in exceptional cases, with the permission of the couple and the approval of a special commission, as long as the "integrity" of the embryo is maintained and the research has a "medical end." The second amendment, a ban on preimplantation diagnosis—examination of embryos for genetic defects before they are transferred to the uterus—allows no exceptions.

These restrictions are bad news for many French scientists working in the field of human reproduction. "I respect those who say that the human embryo is too precious to destroy just to gain knowledge," says Plachot, but she argues that the bill would sharply curtail the development of improved culture media and other conservation techniques, particularly if the embryos studied were not intended for ultimate implantation. And most research into why some embryos are viable and others are not—which often requires dissection of the embryo into individual cells—would be proscribed.

Geneticist Axel Kahn, at the Cochin Institute of Molecular Genetics in Paris, says he accepts that human embryos should not be

conceived for research purposes, and that cloning of embryos should probably be prohibited. But he feels that the language of the bill does not give researchers clear guidance about what they can and cannot do. "What does it mean when research does not affect the integrity of the embryo?" "Are we simply to observe it with our eyes and nothing else?"

Most French researchers contacted by *Science* feel that some embryo research should be allowed, but they appear more divided on the question of preimplantation diagnosis. An outspoken opponent of these techniques is Jacques Testart, director of the IVF laboratory at the American Hospital, in the Paris suburb of Neuilly. Earlier this month, Testart—an IVF pioneer who has since become a leading advocate for strict regulation of the field—published an article in the French daily *Le Monde*, cosigned by more than 20 other scientists and academics, warning that genetic screening of embryos would lead to the "irreversible and unlimited" revival of eugenics.

THE AMENDED BIOETHICS BILL

The bill on biomedical ethics consists of three major texts:

Protection and respect of the human body:

- Bans eugenic practices, genetic screening for purposes other than medical research or judicial proceedings, and surrogate motherhood.
- Preserves the anonymity of gamete donors in medically assisted procreation.

Donation and utilization of organs, cells, and tissues, including medically assisted procreation:

- Detailed rules for giving consent for organ donations and transplants, and an absolute prohibition against trafficking in or profiting from such donations.
- Guidelines for infertility treatments, including in vitro fertilization, which are not permitted for single women, widows, or menopausal women.
- Prohibition on preimplantation diagnosis.
- Severe restrictions on embryo research.

Research and data banks:

- Permits the compilation of information on patients, particularly for epidemiological research, as long as informed consent is given and confidentiality is maintained.

Testart rejects the argument that there is no difference between such screening and conventional prenatal diagnosis, such as that resulting from amniocentesis. "Where prenatal diagnosis permits us to avoid the worst, by elimination," he says, "preimplantation diagnosis will elect the best, by selection." But this view is vigorously contested by Plachot. "The people working on this have no intention of doing eugenics," she says. "They simply want to avoid a child with genetic damage. The only difference between prenatal and preimplantation diagnosis is that the former can lead to an abortion, which is an assault on a woman's body, while the other cannot."

Kahn predicts that the law will be revised in the lower house, but the conservative government's strong majority will probably prevent a radical revision of the Senate version. "We have been badly served by the recent debates over menopausual women having babies," says Plachot. "The senators wanted to avoid such things, and so they have tried to forbid everything."

–Michael Balter

Michael Balter is a journalist based in Paris.

NATIONAL LABORATORIES

Another Shakeup at LBL Genome Center

The human genome center at the Lawrence Berkeley Laboratory (LBL) once again has posted an "under new management" sign on its door, following the abrupt departure earlier this month of its director, geneticist Jasper Rine. Rine's return to full-time research as a faculty member of the University of California (UC), Berkeley, comes as the center is moving toward production-scale genome sequencing, a transition that Rine feared could weaken its basic research.

The $10 million a year LBL center, one of three operated by the Department of Energy (DOE) at its national laboratories, has been plagued with management problems since its formation in 1988. Its first director, geneticist Charles Cantor, was forced out in 1990 after criticism that he was spending too much time away from the center promoting the government's overall human genome project (*Science*, 14 September 1990, p. 1238). LBL officials tried unsuccessfully to woo University of Washington geneticist Leroy Hood, then at Caltech, and finally resorted to collective leadership by a committee of local scientists (*Science*, 26 April 1991, p. 500). This approach lasted for 6 months until Rine, one of the members of the committee, agreed to take on the job alone.

Accounts differ on the reasons for Rine's departure. "We had a serious disagreement over which direction the center should take," says Mina Bissell, director of the life sciences division at LBL, which includes the genome center.

Bissell says the lab's top management and the center's scientific advisory committee thought the center should concentrate more on production-scale genome sequencing. Gerald Rubin, a UC Berkeley geneticist, is proposing to the National Institutes of Health (NIH) a $70 million, 5-year effort to complete the *Drosophila* sequence. Rubin's team has been collaborating with the LBL genome center on much of the *Drosophila* work to date, and Bissell says the lab hopes to be a major participant in the new effort.

But Rine, who says his departure was motivated primarily by his desire to get back to science, argued that the production sequencing effort should be spun off from the center to protect the center's basic research activities. "An expansion of the [*Drosophila*] project would be fine," Rine says, "But I chose a balance between production and basic research. Now that I'm leaving, the next person must decide which way to go."

Rine is credited with boosting the center's research program on genome informatics and laboratory automation. But management proved more of a challenge. Rubin, a long-time collaborator with the LBL center, says Rine's strengths "are scientific, not administrative." Directing the LBL genome center "was a large administrative job," Rubin says, and Rine "was miscast in this role."

Although Rine says he had already planned to leave in the fall, LBL asked him on 14 January to step down immediately to avoid having a "lame duck" director, according to Bissell. Mohandras Narla, who heads LBL's Cell and Molecular Biology Department, has been named acting director and a search is under way for a permanent successor.

Years of management turmoil have taken their toll on the center's research agenda. The mapping of human chromosome 21 was a priority during Cantor's tenure, and the administrative problems that led to his departure were a setback to the project, according to lab officials. In 1992, the LBL center was scooped on a map of the chromosome by a group at the French genome laboratory CEPH.

The current plan, says Bissell, is for LBL scientists to develop new sequencing technology while Rubin's team "gears up a sequencing factory" at the center. LBL's role would be unusual for a DOE genome center, which typically focuses on the human genome rather than those of model organisms. But Bissell says that the improvements in sequencing technology should be applicable to the human genome as well. With the LBL center experiencing yet another change in research direction, geneticists hope that the latest tack will finally provide smoother sailing for the troubled center.

–Christopher Anderson