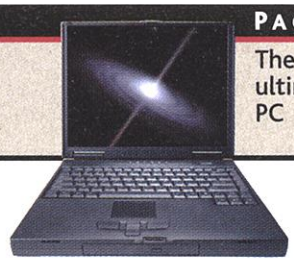

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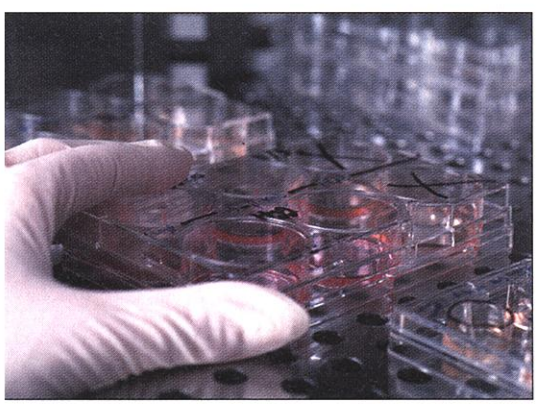
NIH GUIDELINES

Researchers Get Green Light For Work on Stem Cells

The biomedical community is moving quickly to take advantage of new guidelines from the National Institutes of Health (NIH) for use of human pluripotent stem cells. And so far there are no signs that opponents plan any immediate action to stop the first round of research proposals from being reviewed by an NIH panel.

The final guidelines, issued last week, allow NIH-funded researchers to derive pluripotent stem cells from fetal tissue, but not from embryos. Scientists may also work with embryonic stem cells, but may obtain them only from private sources and must ensure that derivation meets certain ethical conditions (see box). For example, embryos used to derive cell lines must be freely donated to research as excess embryos created during fertility treatments.



Lend a hand. New guidelines will allow publicly funded researchers to work with human embryonic stem cells like these from the University of Wisconsin.

The NIH spent nearly a year finalizing the guidelines, which researchers hope will allow work leading to the improved treatment of diabetes, Parkinson's, and other diseases. Because the cells are derived from human embryos or fetal tissue, groups who oppose fetal tissue research and abortion have lobbied to block federal funding for such research. NIH received 50,000 public comments on their draft—including thousands of preprinted postcards from opponents.

Indeed, federal law prohibits NIH from funding work that harms or destroys a human embryo, but a lawyer for the Department of Health and Human Services, NIH's parent agency, ruled in January 1999 that stem cell lines derived from embryos by privately funded scientists could be eligible for funding (*Science*, 22 January 1999, p. 465). The final guidelines, issued on 23 August, spell out the ethical requirements for scientists who hope to work with such cells.

Scientists will need to submit evidence to NIH that the cells they wish to use comply with the guidelines. A committee called the Human Pluripotent Stem Cell Review Group will decide whether the cells qualify for funding. At the same time, the grant application will be judged for scientific merit by a scientific review board. NIH officials say the stem cell committee will meet in December to review applications received by 15 November. Approved applications that receive high marks in peer review will be passed along to the appropriate institute for funding decisions. Despite the multiple layers of review, NIH associate director for science policy Lana Skirboll says that scientists who apply by November could receive funding as early as January.

Patient advocacy groups, many scientists, and even President Bill Clinton praised the new guidelines. In remarks to reporters last week, Clinton said stem cell research will have "potentially staggering benefits." Tim Leshan of the American Society for Cell Biology said the guidelines "will certainly allow federally funded scientists to do the work that they want to do." However, some legislators said they were appalled and vowed to fight the guidelines. Representative Jay Dickey (R–AR) said the guidelines show "obvious disregard of the moral consensus and the laws of our nation." The guidelines are illegal, he says, and will be opposed either through the courts or through legislation next year to block NIH from funding any research involving the cells.

The guidelines require researchers to present documentation with their grant application that the stem cells were derived properly. The embryo must have been left over after fertility treatments, the donors cannot receive any compensation for their donation, and they may not designate specific recipients of the cells. To ensure that embryos are surplus, eligible cell lines must be derived from embryos that were frozen. Donors must be informed that the cells derived from the donated embryo may be used indefinitely, possibly even for commercial purposes.

The new rules also address several problems raised by researchers reviewing the earlier draft, including a requirement that anything that might identify the donors of the embryo be removed from the records. Scientists pointed out that such cells would not pass Food and Drug Administration requirements for cell therapies, which require extensive documentation of a cell line's history. The new guidelines require the donors to be informed of whether identifiers will be kept with the cells.

James Thomson of the University of Wisconsin, Madison, the first to derive human embryonic stem cells, says his donations were anonymous. So there is no way

WHAT THE GUIDELINES SAY

NIH-funded researchers can work with pluripotent stem cells derived from embryos if privately funded researchers have established the cell line, provided that:

These conditions are met:

- Embryonic stem cell lines must be derived only from frozen embryos created for fertility treatment;
- The decision to donate embryos is separated from fertility treatment; and
- Embryo donors are told they cannot accept financial or other compensation.

And they avoid the following:

- Deriving pluripotent stem cells from embryos;
- Using stem cells from embryos created specifically for research;
- Using stem cells from nuclear transfer technology;
- Combining stem cells with an animal embryo;
- Using stem cells to create or contribute to an embryo.

CREDITS: (LEFT TO RIGHT) J. MILLER/UNIVERSITY OF WISCONSIN, MADISON; NIH

to trace the precise origins of the cells, some of which may have been derived from embryos that were not frozen. If his current cell lines are not approved, he says, he will derive new ones, a process that could take months. John Gearhart of the Johns Hopkins University in Baltimore, who derived pluripotent stem cells from fetal tissue concurrently with Thomson, says he also will ask NIH to approve his cell lines. He says he received more than 150 requests for collaboration on the day the guidelines were released. Both researchers derived their cells with funding from Geron Corp., a biotech company in Menlo Park, California.

The University of Wisconsin has set up a nonprofit institute called WiCell to distribute Thomson's cell lines (*Science*, 11 February, p. 948). However, in its first 10 months of existence, the institute has made only a "half-dozen" agreements with researchers, according to Carl Gulbrandsen, president of WiCell. He says the institute has about 60 agreements pending, which can take months to navigate through the recipient researcher's institution. Although contamination problems also slowed the process down at the beginning, Gulbrandsen says WiCell has sufficient stock on hand to meet the anticipated demand over the next few months.

WiCell may soon have company. In July, the Juvenile Diabetes Foundation (JDF) announced a request for applications for stem cell research, specifically including derivations of human stem cell lines from embryos. JDF's chief scientific officer, Robert Goldstein, says the foundation will also fund researchers who want to use cells from WiCell or Gearhart, but there is a chance that one cell line will work better for certain experiments than others.

Roger Pedersen of the University of California, San Francisco, who has been working on human embryonic stem cells with funding from Geron, calls NIH "courageous" for opening the door to further research. He notes that human cells are quite different from the mouse cells that have shown tantalizing promise—becoming pancreaslike cells and even dopamine-producing brain cells. No one has reported keeping the cells alive without a "feeder" layer of supporting cells, he notes, nor can anyone grow a cell line from a single pluripotent stem cell. "There's a lot of work to be done," he says—and apparently plenty of people eager to get started.

–GRETCHEN VOGEL

CREDIT: L. BLIZARD

NATIONAL ACADEMY

New Report Triggers Changes in the NRC

Shape up or risk losing customers. A panel of eminent science and engineering administrators has delivered that stern advice to the National Research Council (NRC), the operating arm of the National Academy of Sciences (NAS), in a report on how the council does its business.

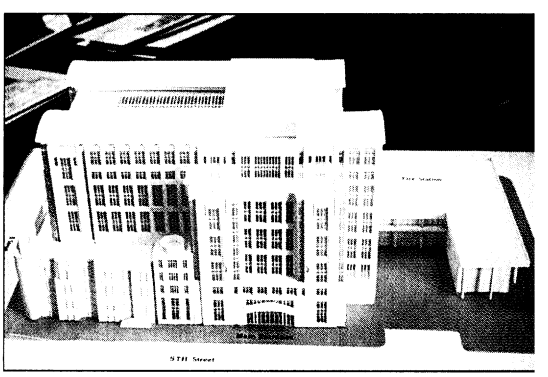
The review, led by Purnell Choppin, president emeritus of the Howard Hughes Medical Institute in Chevy Chase, Maryland, and Gerald Dinneen, a retired Honeywell manager, is the first hard look at the structure of the NRC in 2 decades (*Science*, 28 April, p. 587). It concludes that the council takes too long to produce many of its reports, is not responsive enough to its sponsors, lacks clear lines of authority, and its staff is too often frustrated and stressed. To fix these problems, the 15-member panel urges the academy "to reduce unnecessary layers of approval," delegate more authority, appoint a chief management officer, and create "a service-oriented culture." If NRC leaders don't act, the panel warns, "sponsors may look elsewhere for advice."

The academy's senior leaders don't quibble with the recommendations, which were blessed by the NRC's governing board at a meeting earlier this month in Woods Hole, Massachusetts. Indeed, "many of the recommendations are being followed through already," notes Mary Jane Osborn, a member of the panel and a biologist at the University of Connecticut Health Center in Farmington. "We want all of our reports to be done well, on time, and on budget," says NAS President Bruce Alberts.

The proposals would affect not only the 1000 NRC staffers but also the nearly 6000 outside scientists and engineers who serve each year as volunteers on the council's committees, boards, and commissions. The most radical idea would revamp the council's internal structure by merging the 11 commissions that oversee the boards, which in turn oversee the production of reports, into six new divisions. The commissions, arranged largely by clusters of discipline, have been criticized as a bottleneck in the arduous and complex process of approving NRC studies.

The new divisions would have more authority and responsibility and share one administrative system. They would be organized around broad themes: education and social matters; physics, astronomy, engineering, and energy; food and health; biology, earth sciences, and environment; policy; and transportation. That grouping, panel members say, will allow greater synergy among disciplines. The scores of boards and committees would remain the backbone of the organization, with NRC managers striving over time to reduce their overall number.

The task force is blunt in its assessment of the council's effectiveness at satisfying its customers—typically federal agencies. "Poor project management and delays in the review process," it notes, too often result in late delivery of the reports, which are the NRC's bread and butter. The solution, says the panel, is "a more service-oriented approach" reinforced by incentives to meet budget and time goals. One option is more fast-track studies, although Alberts says that reports done in 6 to 8 months "are unlikely to become routine." The panel also suggests that the council consider holding roundtables as a substitute for the lengthy review process.



Model organization. Changes at the National Research Council will precede completion of a new National Academy of Sciences headquarters, set to open in 2002.

The governing board should look at the bigger picture and leave the details to others, according to the panel. In particular, the panel says Alberts should shift some duties to his fellow presidents, who lead the National Academy of Engineering and Institute of Medicine, and give responsibility for daily operations to a chief management officer, who will be current Executive Officer William Colglazier. "As president, I plan to rely on a more focused staff management structure, reporting through [Colglazier]," says Alberts.

The panel had more trouble with the issue of broadening the pool of volunteers. It