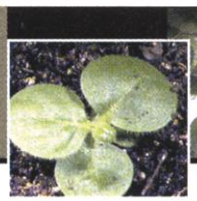

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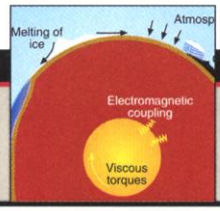
"Terminator" technology lives on



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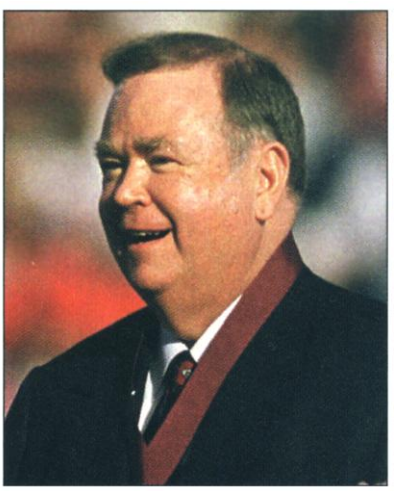
Why Earth wobbles

CLINICAL RESEARCH

Flawed Cancer Study Leads to Shake-Up at Univ. of Oklahoma

Allegations of lax safety procedures and flawed management in a clinical cancer trial have cost four researchers and administrators their jobs at the University of Oklahoma. They have also led to a temporary shutdown of 75 clinical trials at the university's Health Science Center in Tulsa and a sweeping overhaul of the school's process for approving human experiments. University officials emphasize that none of the roughly 100 patients involved in the 3-year-old study of an experimental cancer vaccine was known to have been harmed, and that most trials will soon be restarted.



Fresh start. University of Oklahoma president David Boren has raised the bar for human subjects protection.

Researchers and administrators around the country are closely watching the events at Oklahoma for clues to how a new federal office charged with overseeing human experimentation—the Office for Human Research Protections (OHRP)—is likely to operate (*Science*, 16 June, p. 1949). This is the first major case that the office, set up in May in the Department of Health and Human Services, has dealt with in public. The new administrative procedures, announced by university president David Boren on 21 July, could also provide a test-bed for other institutions, because they mirror tough rules for clinical trials that are being considered, but have not yet been approved, by Congress. Oklahoma has "chosen to be way ahead of the curve," says Jeffrey Kahn, director of the Center for Bioethics at the University of Minnesota, Twin Cities.

Oklahoma's troubles began last December, according to a chronology of the events outlined in a 17-page, 29 June letter from OHRP compliance chief Michael Carome to University of Oklahoma officials. A nurse coordinating the federally funded safety trial of a vaccine to treat melanoma, led by surgeon J. Michael McGee, told university officials and the Food and Drug Administration (FDA), which regulates vaccines, that she feared sloppy shipping practices might enable bacteria or viruses to contaminate the vaccine. The vaccine, which was made on the Tulsa campus, consisted of material extracted from specially grown cancer cells.

Carome's letter notes that on 31 January, McGee wrote to FDA acknowledging that the trial was "out of compliance" with federal regulations due to staffing and administrative problems. He said he would not enroll new patients until the problems were solved, but would continue providing vaccine to 28 patients already in the trial. On 9 March, however, McGee and Tulsa officials opted to shut down the trial after receiving a scathing consultant's report that was requested by the Tulsa science center. The report by Hausmann and Wynne Associates of Marlborough, Massachusetts, excerpted in the 14 July issue of *Tulsa World*, found numerous shortcomings. They included "egregious lack of control" in vaccine manufacture and record-keeping, lack of training for lab staff, and a database that identified patients by name, in violation of confidentiality rules. As a result, the consultants recommended that all remaining vaccine "either be destroyed or clearly labeled 'For research use only—Not for use in humans.' " According to OHRP, the report's conclusions were shared with McGee; his superior, Thomas Broughan, chair of Tulsa's surgery department; medical dean Harold Brooks; and Daniel Plunket, chair of the science center's eight-member Institutional Review Board (IRB), which oversees clinical trials.

In a 10 April letter to patients and collaborating physicians at eight sites around the country, however, McGee did not mention potential safety problems as a reason for the trial's closure. Instead, he wrote that due to "a great deal of interest in the study," he was "unable to provide material for further injections." According to the OHRP chronology, IRB members—who are supposed to be informed about any change in a trial—were also given a misleading explanation for the trial's end.

On 27 June, however, after OHRP officials informed the university that it would investigate and staffers prepared to interview IRB members by phone, the IRB panelists were finally given copies of the consultant's report. Two days later, OHRP's Carome sent Oklahoma officials his letter, which included the chronology and a summary of regulatory violations. Carome informed the university that OHRP had decided to suspend Tulsa's five remaining federally funded clinical trials until the university came up with "a satisfactory plan" for protecting human subjects.

Among many violations Carome cited in the melanoma trial are that 11 of the first 18 patients enrolled did not meet the study's approved criteria and that consent forms contained wording that was overly optimistic about the vaccine's potential benefits. Carome also wrote that Plunket's failure to share the consultant's report with his committee "un-

OKLAHOMA'S EIGHT-POINT PLAN

- Institutional Review Board (IRB) revamped
- IRB will be accredited by independent agency
- All projects approved by senior administrator and IRB
- A new independent research compliance office
- Unannounced spot checks of research
- Mandatory researcher education on procedures
- Researchers must sign conduct contracts
- "No fault" hotline for reporting potential violations

CREDIT: J. LAIZURE/AP

dermined the IRB's independence and authority in a manner that transcends this study." "In OHRP's experience," Carome wrote, correcting such problems "would necessarily include changes in leadership."

Boren, a former U.S. senator who has led the university since 1994, took the hint. He suspended another 70 university-sponsored trials, disbanded the Tulsa IRB, sent new letters to patients in the vaccine trial disclosing the real reason the study was halted, and appointed a six-member team to devise a scheme for approving and monitoring trials.

At a 21 July press conference, Boren announced that the four men most closely associated with the trial would be leaving the university: He had moved to terminate McGee; dean Brooks and director of research Edward Wortham had resigned; and Plunket had retired. (None of the four responded to interview requests by *Science*.) Boren also outlined an eight-point plan for overseeing clinical research at the university (see box) that closely follows rules, included in a bill introduced in Congress by Representative Diana DeGette (D–CO), that are considered likely to pass. "We have no choice but to demonstrate we're making a fresh start," Boren said. "The system failed because information about potential criticisms and irregularities did not make its way up the chain of command."

Some University of Oklahoma researchers worry that the new requirements are an "overreaction to an isolated incident," as one biochemist who has worked at the Tulsa center puts it. Minnesota's Kahn predicts that "we're going to see more of these kinds of requirements," although he questions whether "more levels of sign-off will protect human subjects." What's needed, he says, is greater attention to how researchers recruit and inform subjects "in the real world."

Meanwhile, researchers and patients who have worked with McGee, a former missionary to Nigeria who came to the Tulsa campus in 1989, say they are stunned by the developments. "He's the last person I know who would ever want to hurt a patient," says Joseph Price III, a biomedical researcher at Oklahoma State University in Tulsa who helped McGee design animal tests for the experimental vaccine. And three patients in McGee's trial have hired a lawyer—not to sue the embattled physician, but to help them petition FDA to release vaccine stocks that they believe will keep them alive.

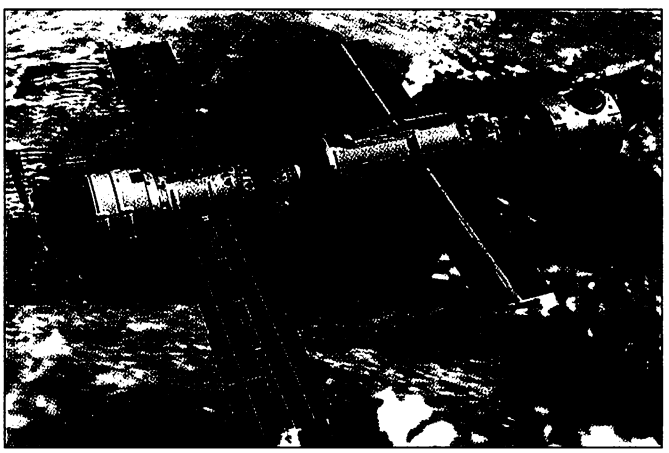
–DAVID MALAKOFF

CREDIT: NASA

NASA LIFE SCIENCES

An Improvement In Vital Signs

Life scientists hoping to conduct research in space finally have some good news. Last week a hefty Russian module with living and working quarters for astronauts docked with the pieces of the international space station already in orbit, a critical step in creating a full-time orbiting laboratory. Meanwhile, NASA bureaucrats put the finishing touches on a realignment of the agency's struggling biology effort that should bolster fundamental research and allow scientists to make better use of the facility, scheduled to be completed in 2005. The two events raise the hopes of U.S. academic space life scientists that their discipline is at last on the ascent at NASA (*Science*, 12 May, p. 938).



Coming together. The linkup of two Russian modules brings the space station closer to its goal of being an orbiting laboratory.

On 25 July Russian controllers at a mission control center outside Moscow guided the 20-ton Zvezda module into the U.S.-funded and Russian-built Zarya module. The maneuver formed a single spacecraft the length of an 11-story building. Although researchers must wait for the U.S. laboratory to arrive in late January, Vice President Al Gore praised the docking as a sign of the station's pending payoff for scientists, and NASA officials savored the opportunity to move beyond short, sporadic experiments on the space shuttle to more substantive projects. "We finally see the carrot at the end of that stick," says Julie Swain, deputy chief of NASA's life and microgravity sciences office, referring to the long and painful process of getting the station into orbit.

While engineers are putting the station through its paces, NASA managers are overhauling Swain's office in a way that will raise the profile of biological research. The new organization, due to be announced this week, will divide the current life sciences division into biomedical activity and fundamental biological research. The former, which will be run by NASA's Johnson Space Center in Houston, will focus on such human health problems as excessive bone loss from long-duration space travel. The latter, led by NASA's Ames Research Center in Mountain View, California, will include more fundamental research in such areas as cell biology. The two pieces, plus work in microgravity and other fields, will make up an office of fundamental space research.

The new arrangement reflects a shift in emphasis from a program centered on keeping astronauts healthy to one that will foster the exploration of fundamental biological processes. "This change is really necessary and long overdue," says Esther Chang, a genetics researcher at Georgetown University and a member of NASA's life and microgravity sciences advisory panel. "It has been very difficult to keep these two areas together and give each the attention it deserves." NASA now spends $57 million on biomedical research and countermeasures, not including health research and other related areas, and $39 million on fundamental biology.

Whether the new arrangement will translate into a bigger budget won't be clear until next year. "All of the professional societies involved have endorsed significantly increased funding for biological programs," says Norman Lewis, a biologist at Washington State University in Pullman and a former president of the American Society for Gravitational Space Biology. He would like to see a greater investment in Earth-based experiments to complement space-based missions, a view endorsed by agency officials.

NASA officials are looking for a prominent researcher with significant manage-