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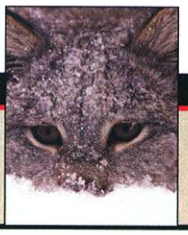
Evolution in action



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Lynx allegations prompt cat fight

CLINICAL TRIALS

Proposed Rules Aim to Curb Financial Conflicts of Interest

It doesn't go quite as far as "Just say no." But a new policy adopted by the Association of American Medical Colleges (AAMC) urges universities to disqualify investigators from conducting clinical trials if the scientists hold a significant financial interest in companies that could be affected by the results.

The guidelines,* issued last month, are the latest response to the 1999 death of Jesse Gelsinger, a volunteer in a clinical trial at the University of Pennsylvania in Philadelphia, in which the university and one of the scientists had equity in a company that was expected to benefit from the research. The incident rekindled public concern that ties between academia and industry are clouding the objectivity of clinical research and compromising patient safety. Since then, several journals and professional societies have weighed in, and the U.S. Department of Health and Human Services (HHS) has begun revising its 1995 rules designed to prevent conflicts of interest from influencing studies (see timeline). The HHS guidelines are expected to be finalized later this year.

But most universities would prefer to police themselves, and AAMC, which objected to the HHS draft proposal (*Science*, 16 March 2001, p. 2060), has now come up with guidelines that are an attempt to do just that. AAMC leaders are now encouraging members to incorporate the guidelines in their own rules. "The hope is that we have taken the issue on responsibly and that [HHS] won't be compelled to come up with more Draconian measures," says Harvard Medical School dean Joseph Martin, who in November 2000 convened a panel of academic leaders that fed into the findings of the task force.

The AAMC guidelines would apply to all human subjects research, not just studies funded by the National Institutes of Health or other federal agencies. They recommend that each institution establish a conflicts-of-interest committee—not just one official as the Public Health Service now requires—to review and "manage" financial ties of clinical researchers. AAMC says the committee should have "clear channels of communication" with an Institutional Review Board (IRB), the ethics review board that approves protocols, to which it should give summaries of its conflict-of-interest review. The policies should also require researchers to share the existence of significant financial conflicts with journal editors and research subjects on consent forms.

The task force's toughest call, says panel chair William Danforth, was to include the "rebuttable presumption" that individuals with a significant financial interest in the outcome of their work "may not conduct such research." "The wording of that was very careful and very much debated," says Danforth, chancellor emeritus of Washington University in St. Louis, Missouri. "This does represent a big shift," says Mildred Cho, a bioethicist at Stanford University. As for what constitutes a significant financial interest, the AAMC report adds a few new items, such as any equity in a non–publicly traded company, to the Public Health Service's threshold of $10,000 a year in payments or 5% equity. (The Food and Drug Administration's levels are higher.) The policy allows for narrow exceptions, says Danforth, such as studies of medical devices in which the involvement of surgeons is often crucial. Those cases would require "effective management of the conflict" and "credible oversight" by monitoring bodies, the report says.

Many universities already have such procedures, "but I'm not sure everybody does everything," says gene therapy researcher Savio Woo of Mount Sinai School of Medicine in New York City, a member of the AAMC task force. One major weakness, according to a recent critical report by the General Accounting Office, is that data are kept "in multiple offices, files, and formats" and not necessarily shared with the IRB that must make the final decision. "Our guidelines are very detailed about the process," says AAMC's Jennifer Kulynych.

Not everyone is happy about the proposed new guidelines, however. Task force member Susan Hellman, chief medical officer for Genentech in South San Francisco, declined to endorse them mostly on the grounds that they could impede innovation. And even supporters worry that im-

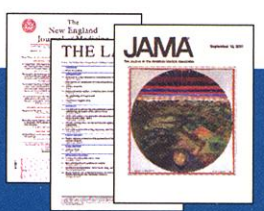
Avoiding Financial Conflicts in Clinical Trials

September 1999
Jesse Gelsinger dies in University of Pennsylvania trial.

DONNA SHALALA

April 2000
American Society for Gene Therapy says clinical researchers should hold no equity or stock options in sponsoring companies.

v June 2000
HHS begins policy review.



August 2000
NIH holds conference on topic.

December 2000
HHS issues draft interim guidelines.

< September 2001
Eleven major medical journals require authors to disclose financial role of sponsor.

October 2001
Association of American Universities issues report on financial conflicts.

December 2001
AAMC issues guidelines for individuals.

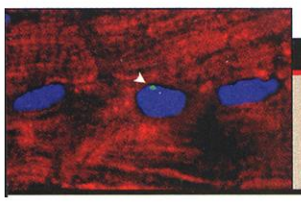
GREG KOSKI

< Early 2002
HHS guidelines expected.

Mid-2002
AAMC guidelines for institutional conflicts.

* Protecting Subjects, Preserving Trust, Promoting Progress: Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research, www.aamc.org/members/coitf

CREDIT: (LEFT) DENNIS COOK/AP



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Regenerating heart tissue?

LEAD STORY 256
Topographical history in grains of sand

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Women in China shun physics

plementing them will be expensive. "There's no doubt that institutions are going to need more resources and more bureaucracy," says Danforth. Adds Martin, "Nobody out here has proposed how to pay for this increased scrutiny."

The association plans to issue a second report this year on institutional conflicts. The next few months may also see guidelines from the HHS Office for Human Research Protections, whose chief, Greg Koski, says that AAMC's recommendations are "by and large very consistent" with what HHS is contemplating.

–JOCELYN KAISER

HIGH-ENERGY PHYSICS

Repairs Weakened Neutrino Detector

TOKYO—A single cracked photomultiplier tube apparently triggered the devastating accident on 12 November 2001 that has closed Japan's Super-Kamiokande neutrino detector for at least a year. An investigation into the accident has confirmed early suspicions about the sequence of events that destroyed about 7000 of the observatory's 11,000 light-detecting sensors (*Science*, 23 November 2001, p. 1630).

The $100 million detector has produced convincing evidence that neutrinos have mass, contrary to decades of theoretical predictions. The wispy particles cannot be observed directly, however, so the 39-meter-diameter, 41-meter-high observation tank is filled with water and lined with photomultiplier tubes that can catch a distinctive glow, known as Cerenkov radiation, produced when neutrinos smash into atomic particles in the water. Last summer, for the first time since the facility was completed in 1996, the water was drained so some 100 burned-out tubes could be replaced. The tank was being refilled when one of the tubes imploded and started a chain reaction that destroyed almost all of the submerged tubes.

By analyzing the sequence in which the sensors stopped sending signals, the investigators narrowed down the initial break to one of two tubes—one original, one a replacement—on the floor of the tank. To make the repairs, technicians stood on thick Styrofoam pads placed directly atop the tubes, after determining that the tubes were capable of withstanding the stress. Examining that assumption, investigators applied eight times the load calculated to have been imposed during the repair operation on an array of 12 tubes. One of these tubes subsequently broke at its neck when subjected to a water-pressure test. This result "hints" that the neck of the original tube could have been weakened by the repair work, the report concludes, although the replacement tube might also have been damaged during handling or installation.

To test the theory that a single imploding tube could destroy thousands of others, the investigating team three times submerged an array of nine tubes and deliberately punctured the central tube. Each time, the shock wave resulting from the implosion broke all the surrounding tubes. Yoji Totsuka, a professor at the University of Tokyo's Institute for Cosmic Ray Research and director of the observatory, says the team plans to test whether acrylic housings for the tubes will contain the shock wave and prevent a chain reaction. They are also working with the manufacturer to develop more shock-resistant tubes.

The Japanese and U.S. project scientists running the experiment must now convince a University of Tokyo committee that they understand the causes of the accident well enough to prevent it from recurring. If they do, scientists hope to resume some observations within a year using a limited number of photomultiplier tubes. But bringing the facility back to full strength could take 5 years and cost between $15 million and $25 million.

–DENNIS NORMILE

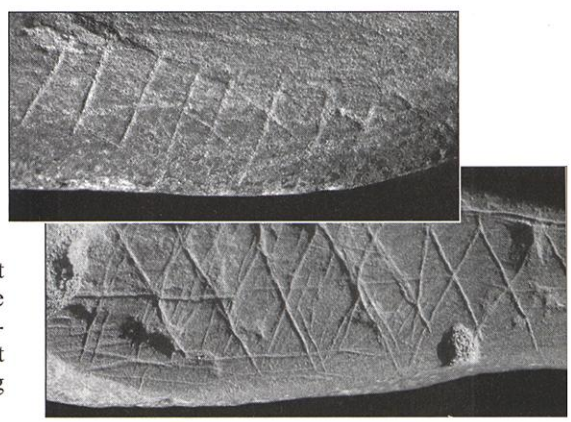
Fix-it fiasco. Repairs to the photomultiplier tubes triggered a costly accident when the tank was refilled.

CREDITS: (TOP) C. HENSHILWOOD *ET AL.*; (BOTTOM) ICRR

OLDEST ART

From a Modern Human's Brow—or Doodling?

Archaeologists in South Africa have found what may be the oldest known art, dated at least 40,000 years before the earliest cave paintings in Europe. The artifacts, two chunks of red ochre engraved with geometric crosshatches, were recovered from 77,000-year-old cave deposits. It's unclear what the ancient artist meant the marks to represent. Nevertheless, some researchers argue that the find in Blombos Cave, published online by *Science* on 10 January (www.sciencexpress.org), strengthens the case that modern human behavior arose much earlier than previously thought and that it took root in Africa long before spreading to Europe. Others caution against drawing sweeping conclusions from what may be a relatively rare find.



Ochre oeuvre? Researchers claim these engravings are evidence of symbolic representation.

Most experts believe that *Homo sapiens* arose about 130,000 years ago in Africa, when anatomically modern humans debut in the fossil record. But scientists have been puzzled by the seemingly long gap between when humans began looking modern and when they started acting modern. Until recently, there was little evidence of modern behavior—such as the use of advanced hunting and fishing techniques and the creation of elaborate tools and art or other symbolic expression—earlier than about 40,000 years ago, the start of Africa's Later Stone Age and Europe's Upper Paleolithic, when stunning cave paintings in France and Spain appeared.

Since 1993, however, a team led by ar-