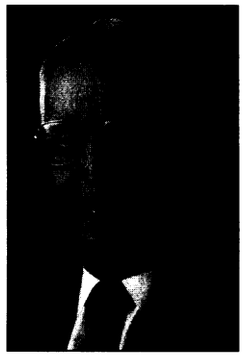
NASA

NRC Panel to Propose Station Institute

Researchers have long criticized NASA for giving scientists short shrift in funding facilities and experiments on the multibillion-dollar international space station now under construction. Now the space agency is about to get some controversial advice on how to fix the problem.

In a few weeks, *Science* has learned, a panel of the National Research Council (NRC) will recommend that NASA create a nongovernment institute to plan and manage science on the station. The report, requested by NASA, aims "to increase the visibility, voice, and clout of the research community" in the decade-long life of the station, says Cornelius Pings, president emeritus of the Association of American Universities and chair of the NRC panel drafting the document. Adds Michael Katovich, a physiologist at the University of Florida, Gainesville, and a panel member, "We scientists want to ensure that the best science gets done—that the station is used as a platform not for Mars exploration or for engineering goals, but for science." But the report's suggestion for an institute seems certain to spark opposition from NASA centers involved in the space station. It also presents a formidable challenge in trying to reconcile the competing research interests of scientists and engineers from different disciplines, sectors, and countries.



Shaky science? Pings, top, says institute would strengthen space station research, which includes vibration-reduction system.

CREDITS: (TOP TO BOTTOM) JAN JARECKI; NASA

Although Pings declined to discuss details, others familiar with the draft report said the new organization should be designed to circumvent NASA's notorious bureaucracy. "It's awful; every experiment on Spacelab required a couple of truckloads of paper," says New Jersey space consultant and panel member Judith Ambrus of the lab module designed to ride in the space shuttle bay. The new institute would give researchers a mechanism for access to NASA ground facilities, says one source, as well as financial and technical help in building experiments and planning and managing research time on the station. The NRC report will also suggest that crew members be specially trained to do primarily science during a tour on the orbiting base.

The NRC report proposes creating the institute by around 2002—3 years before the station is ready. But the panel is still wrestling with whether the new entity should be chartered and funded directly by Congress, and therefore be independent of NASA, or function like the Space Telescope Science Institute in Baltimore, which contracts with NASA to manage the Hubble Space Telescope. NASA recently examined more than a half-dozen ways to structure the institute—from a university and industry consortium to a government corporation like Comsat—without reaching a conclusion, says Mark Uhran, a NASA life and microgravity sciences manager who was instrumental in requesting the NRC report.

Although the idea of a separate organization has won early rave reviews from some officials at NASA headquarters, the reception at two centers with key roles in station management—Johnson Space Center in Houston and Marshall Space Flight Center in Huntsville, Alabama—is likely to be chillier. "We have a sense they won't like it," a panel member says. "But the [NASA] administrator wants this to happen." Katovich believes that the institute would relieve pressure on the centers by looking after scientific matters: "The centers clearly are critical for station development, but once everything is up and running, they can move on to other things."

Some center officials support the need for changing current practices. "Everyone is very eager to make it simpler to do research," says John David Bartoe, a former astronaut and solar physicist who heads the station's research program at Johnson. And Katovich and others say that the lengthy process to put experiments into space demands that NASA act as quickly as possible. "Part of the problem is that it takes so long to get something done—there are so many hoops," he says. "And while safety is still paramount, there are ways to do this less bureaucratically."

–ANDREW LAWLER

PCR

Taq Polymerase Patent Ruled Invalid

Be careful with whom you pick a fight. Seven years ago the Swiss pharmaceutical giant Hoffmann-La Roche took a swing at Promega Corp., a small biochemicals supplier based in Madison, Wisconsin, suing it for infringing a Roche patent on a key enzyme for molecular biology research. The enzyme, called Taq polymerase, is a crucial element of the polymerase chain reaction (PCR), the ubiquitous technique used to replicate snippets of DNA. But last week it was Promega that was still standing after a federal judge in San Francisco, California, ruled that the patent for Taq is invalid because its original holder, the now defunct Cetus Corp., obtained it by deliberately misleading the U.S. Patent and Trademark Office (PTO).

"We were very glad to see the ruling," says Promega chief technical officer Randall Dimond. "We felt for a long time that the only reason the patent was issued in the first place was due to a misrepresentation of the science." The ruling means that, for now, Promega can continue to sell Taq without paying royalties to Roche. But the war between the companies is far from over. The invalidated patent governs only one form of Taq and a small part of the current Taq market, but Promega is challenging Roche's patents on PCR itself and may do the same with other Taq patents Roche holds. And it claims this ruling makes these patents vulnerable. Roche, meanwhile, says it will appeal last week's ruling and is pressing on with a suit charging Promega with encouraging academic researchers to violate Roche's PCR patents.

This David vs. Goliath battle started shortly after Roche bought rights for the Taq and PCR patents from Cetus for $300 million in 1991. At that time Promega had a license from Cetus to sell "native" Taq enzyme, purified from the bacterium *Thermus aquaticus*, for uses other than PCR. Roche argued that Promega, which was undercutting Roche's price, was in fact marketing Taq for use in PCR and asked the company to renegotiate

its license. When Promega declined, Roche sued. But Promega lawyers fought back with a countersuit claiming that the original Taq patent should be disallowed. They argued that Taq had been purified earlier by others, but Cetus scientists had misrepresented their data to convince the PTO that the enzyme they had purified was different.

Three years ago Judge Vaughn R. Walker ruled that Cetus had indeed misled the patent office in obtaining the native Taq patent. But in order to decide whether to void the patent, the judge needed to determine whether it had been done intentionally. Last week, Walker said the evidence was clear: In a 65-page ruling, the judge outlined instances in which former Cetus scientists David Gelfand and Susanne Stoffel misstated or omitted data that "afford no inference other than that they were made to deceive."

In a written statement to *Science*, Gelfand and Stoffel maintained that the Taq they purified was different from previous versions. "We feel that the judge's ruling was both wrong and unfair to us," they state. "This situation ... puts all scientists at risk of having their raw data and good faith interpretations of it be misrepresented in court."

The ruling invalidates the patent only for the native Taq enzyme, or n-Taq. Roche has since patented a recombinant enzyme produced in *Escherichia coli*, which is licensed widely and now dominates the Taq market. The pharma giant also has several patents on the PCR process itself. So the new ruling is not likely to affect Roche's existing business immediately. But Brenda Furlow, Promega's general counsel, argues that because these patents are related and involve some of the same researchers, the judge could wind up invalidating other Taq or PCR patents as well. "There is a real possibility that additional patents could fall," says Furlow.

Melinda Griffith, head counsel for Roche Molecular Systems—the U.S. subsidiary that handles Roche's PCR business—flatly disagrees. "The fact of the matter is that this relates only to the n-Taq patent," says Griffith. "This does not or should not affect any other patents." Kate Murashige, a biotechnology patent expert at the Washington, D.C., law firm of Morrison and Foerster, agrees, calling the invalidation of related patents "conceivable but unlikely." Wall Street, too, seemed unworried: The stock price for Roche Holdings, AG, Hoffmann-La Roche's parent, dipped only a couple of points in end-of-the-week trading.

Despite Promega's victory in this round, Roche officials haven't thrown in the towel. "This decision has not changed the fact that Promega is infringing our PCR patents and inducing others to do it as well," says Griffith. Because of that, Griffith says, Roche plans to press its original case against Promega. Furlow counters that Promega will seek reimbursement for court costs as well as for royalties the company paid on Taq from 1991 to 1995. Judge Walker will map out the future the case is expected to take when he meets with the combatants at the end of next month. **–ROBERT F. SERVICE**

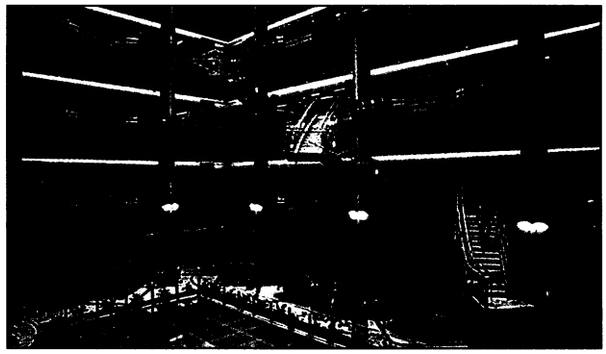
CREDIT: UNIVERSITY HEALTH NETWORK

LAB SAFETY

Licenses Suspended at 3 Toronto Hospitals

OTTAWA, CANADA—Citing violations of nuclear safety regulations, the government has blocked the use of radioisotopes for research at one of Canada's largest academic/medical hospital complexes. The action, taken on 2 December by the Atomic Energy Control Board (AECB), has halted all experiments involving radioactive compounds in 91 labs at the Toronto-based University Health Network (UHN). Although roughly 20 of the labs may be allowed to resume normal operations as early as this week, the AECB has said that patient care could be affected next spring if the network does not make the necessary improvements.

"They've been given a timeline," says AECB license assessment officer Richard Cawthorn. "If they don't meet that, they will have used [up] all of their get-out-of-jail-free cards." Although AECB's mandate covers only worker and public safety, Cawthorn says, it will have little choice but to take "further licensing action that will restrict the clinical areas" if the problems are not corrected by 1 April. UHN chief operating officer Michael Guerriere says he expects all 91 labs to be in compliance and operational within 3 to 4 weeks.



Inhospitable. The government found numerous safety lapses in research labs at Princess Margaret and two other Toronto hospitals.

The suspension follows a routine investigation of safety practices at UHN, which has a license to conduct experiments with radioactive materials at five buildings housing cardiac, neurosciences, organ transplant, and oncology programs. The inquiry found many deficiencies, including excessive contamination levels and unreported losses of sealed radioactive materials—problems that Cawthorn says indicated that the hospitals were exerting little control over the radioactive materials being used. Some 55 instances of noncompliance were discovered during site visits at the three hospitals in November. The occupational safety program "was essentially nonfunctional," according to a report from a site visit in October.

Guerriere attributes the lapses in safety practices to confusion caused by a merger in January 1998 of Toronto General Hospital, Toronto Western Hospital, and Princess Margaret Hospital that created UHN. "We had separate radiation safety programs at each of the three sites that were managed differently," says Guerriere. "We've also had the entire lab group that used to be at the Wellesley Hospital [in Toronto] moved across into our labs, and we've restructured them quite significantly. A lot of labs have moved around, and we didn't pay sufficient attention to these training issues during that process."

One bench scientist says that the shutdown has thus far been little more than a temporary inconvenience. "We're just going to go with the flow, follow the plan, and get recertified," says physician Michael Tymianski, whose research includes work on radiochemicals such as calcium-45. "The whole thing has been quite gentlemanly. Everybody has gotten reassessed and reevaluated, and our plan is to put things back together again."

The AECB has laid down nine directives that UHN must follow, including creation of a comprehensive radiation safety program covering all operations and facilities and adequate training of employees. "They basically have to build a program that has organization—a proper management structure, an oversight hazard control function, [and the ability] to control doses of radioactive materials," says Cawthorn. Guerriere says the UHN is already on the road to recovery by filling its vacant position of corporate radiation safety officer and reaching agreement with the control board on a "remedial training program."

Although no one on staff is known to have received an excessive dose of radiation, the board has ordered UHN to perform a thyroid bioassay on one worker. Cawthorn says he's unaware of any instances in which patients were exposed to excessive radiation, either, but adds that patient care is "not within the AECB mandate."

–WAYNE KONDRO

Wayne Kondro writes from Ottawa.