Division of AIDS, announced at the meeting, NIAID will conduct "a formal and thorough review" next spring of the field isolate issue and decide whether to launch efficacy trials in the United States by the end of 1994.

The hesitation may seem like appropriate scientific caution, but it has infuriated at least one major vaccine developer. Jack Obijeski, head of the AIDS vaccine project at South San Francisco's Genentech, says his company now has more than 200,000 doses of HIV vaccine ready to go because it thought NIAID was committed to moving forward. "To leave that vaccine on the shelf, something that might help someone, we think that's ridiculous," says Obijeski, who doesn't believe the primary isolate question should override other positive animal and human data from experiments with Genentech's vaccine. "If that's the case, this is a monumental disincentive for Genentech....What needs to be forthcoming is for NIH not to dwaddle about, one step forward, one step back. That's what makes CEOs nervous." He cautions there are many other projects competing with the AIDS vaccine work for company resources.

Jose Esparza, head of AIDS vaccine development at WHO, says developing countries, which will have more than 90% of the world's new HIV infections by 2000, cannot wait for a complete answer to the field isolate question. "Vaccine development is very empirical," says Esparza. "For every point you try to prove there's a counterpoint....I think a trial will give you more information than 1000 lab experiments." WHO, in fact, already is helping Brazil, Uganda, Rwanda, and Thailand prepare for efficacy trials and has run into what he sees as a much more formidable obstacle: Vaccine manufacturers have little interest in tailoring vaccines specifically for these countries—which have different strains of HIV—when the market is uncertain. "There's a need here to encourage manufacturers to make strain-specific vaccines," says Esparza.

The head of the United States military's AIDS vaccine program, Donald Burke, concurs with this view. For more than a year, Burke has been trying to find a company willing to make a vaccine for the strain of virus circulating in Northern Thailand, where he is helping to lay the groundwork with Thai officials for efficacy trials. "I don't want to close the door, but none of the manufacturers has made a commitment up to this point," says Burke.

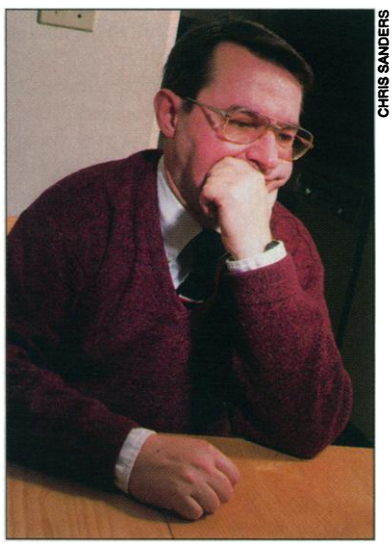
NIAID's Margaret Johnston ended the conference with the reminder that "none of us are willing to wait for the ideal vaccine" before starting efficacy trials. But if the field isolate findings hold up, expect a heated debate about the risk of jumping in versus the risk of standing still.

–Jon Cohen

SCIENTIFIC MISCONDUCT

Popovic Is Cleared on All Charges; Gallo Case in Doubt

A federal appeals board last week roundly criticized the government's 4-year effort to find scientific misconduct against AIDS researcher Mikulas Popovic—and, by implication, against his former boss, Robert Gallo of the National Institutes of Health (NIH). In clearing Popovic of any wrongdoing, the appeals board, which consists of three lawyers, also threw into question the government's case against Gallo (see box, p. 982). "One might anticipate," the appeals board wrote in a strongly worded, 79-page decision, "that from all this evidence, after all the sound and fury, there would be at least a residue of palpable wrongdoing. That is not the case."



CHRIS SANDERS

Nothing wrong. An appeals board rejected misconduct claims against Mikulas Popovic.

"How could it happen," the board asked itself, "that such a massive effort produced no substantial evidence of its premise?" Its answer: Investigators had initially concentrated on the big issues—allegations that Gallo's lab misappropriated the French LAV virus, a patent dispute, and disputes with other scientists. But the issue of misappropriation was dropped early in the investigation, and in the end, the board said, the items of alleged misconduct brought before it were "largely vestigial."

Popovic was a cell biologist in Gallo's laboratory in the early 1980s, a period marked by Gallo's attempt to identify and isolate the AIDS virus. The two scientists coauthored four groundbreaking papers in *Science* on the subject (4 May, 1984, p. 497). Since then, however, it has become clear that the virus Gallo and Popovic reported was virtually identical to a virus isolated by researchers at the Pasteur Institute, leading to allegations of misappropriation and deception. In the 4 years since those allegations were spelled out in a lengthy article by *Chicago Tribune* investigative reporter John Crewdson, two federal bodies—the NIH Office of Scientific Integrity (OSI), and its successor, the Office of Research Integrity (ORI), within the Department of Health and Human Services (HHS)—have conducted nearly continuous investigations of the two scientists. Early on, OSI determined that it lacked the evidence to conclude misappropriation rather than inadvertent contamination. OSI and later ORI issued reports on the case, the last of which

A SCORECARD ON POPOVIC

Charge	Board's Ruling
1. The sentence "The concentrated fluids [cell cultures from individual patients] were first shown to contain particle-associated RT [reverse transcriptase]" is false and misleading because Popovic did not test the individual fluids before pooling them.	1. ORI's charge assumes—without evidence—that Popovic concentrated the fluids before pooling them, despite Popovic's "reasonable" testimony to the contrary. ORI did not prove that Popovic actually drafted or approved the sentence, nor that he would have recognized that it could be misinterpreted. No misconduct.
2. Several experiments in Popovic's paper are marked "ND-not done" in a table, despite evidence that they were done.	2. ORI did not prove that "not done" can only reasonably mean "not performed." It could also mean not completed, not done properly, or not determinable, all of which would have been accurate reportings of the true results. No misconduct.
3.Popovic's "10%" entry in a table was improper considering that the only recorded data was a technician's reading of "very few cells" for the relevant slide.	3. Popovic's testimony that he had independently read the slide before inserting the 10% figure was "credible [and] corroborated" by the technician and other evidence. No misconduct.

found both Gallo and Popovic guilty of misconduct for making different, allegedly false statements in their papers (*Science*, 8 January, p. 168).

ORI's case against Popovic boiled down to his statement that certain experiments were "not done" when they had in fact been done, that a "10%" figure in a table was not supported by data, and that he claimed that certain fluids were "first shown" to contain signs of virus replication before they were mixed together, when that was not the case. The board noted that none of these alleged misrepresentations would have made any difference to the conclusions of the paper.

ORI had complained that its case was restricted by the board's requirement that they prove both intent and the "materiality" of the disputed statements to the entire paper (*Science*, 18 June, p. 1714). But the board concluded that the issue of intent was moot because "ORI did not prove that the *Science* paper contains untrue statements of data, much less that it contains intentional falsification." In each case, it concluded that Popovic's explanation was plausible.

Indeed, in instance after instance, the board criticized ORI for what it found to be shoddy work. It noted that ORI several times misquoted and misparaphrased key sentences in the *Science* paper. The board also rejected much of the testimony from ORI's expert witnesses, including Yale biochemist Frederic Richards, who headed a committee assembled in 1990 by the National Academy of Sciences to advise federal investigators. The board said that it gave "little weight" to Richards' testimony during the hearing because "his opinions were developed based on selected information given him by ORI." The board concluded that, because he is not a virologist or cell biologist, "he could not reliably comment on what 'not done' meant in these disciplines." Richards, in an interview, challenged the board's conclusion that one has to be a member of a scientific subspecialty to understand the meaning of common phrases. "Not done means not done and anybody who thinks otherwise is crazy," he says.

The Richards committee argued during the Gallo investigation that investigators were concentrating on specific allegations of wrongdoing rather than patterns of behavior. The appeals board ruled, however, that evidence purporting to show a pattern is inadmissible. Nevertheless, the board did review most of the additional charges that ORI had attempted to bring into the official appeals process, ranging from the allegation that there had never been a pool of cultures to the allegation that Popovic had improperly referred to some patients as "pre-AIDS" when they were not. Its conclusion: The additional arguments "would not make a difference in our decision."

The board was set up last year in part to address concerns that ORI investigations do not afford scientists full "due process," including the right to cross examine witnesses and evaluate evidence. Congressional critics had also argued that OSI, which was staffed largely by scientists, was too soft on research misconduct. In response, ORI added more lawyers, so that a process that started with a team of federal scientists investigating other scientists has evolved today to one of lawyers investigating scientists. Ironically, this has resulted in fewer misconduct convictions, as legal standards have proven more of a hurdle for ORI than issues of scientific fairness.

Neither Popovic (who is now working at

ORI Faces High Hurdle in Gallo Case

When a federal appeals board cleared cell biologist Mikulas Popovic of misconduct charges last week, it sent a strong signal that the government's Office of Research Integrity (ORI) will have a tough time making a similar case against Popovic's former boss, National Institutes of Health virologist Robert C. Gallo. The board was scheduled to begin hearings on 8 November on the charges against Gallo, but on 5 November, ORI requested a delay for at least a week.

Although the charges against Gallo are different from those faced by Popovic, the two cases face similar legal hurdles. In particular, the appeals board has made it clear that ORI must meet tough standards of proof, and in preliminary rulings it has narrowed the charges against Gallo.

ORI initially determined that Gallo had committed misconduct in a single instance: Stating in a 1984 *Science* paper that the French virus known as LAV "has not yet been transmitted to a permanently growing cell line" and had therefore been difficult to characterize. ORI says Gallo's lab had, in fact, grown LAV in a permanent cell line. ORI also identified four other instances of "inappropriate conduct," to provide a "context" in support of its misconduct finding. Gallo's lawyers asked that four allegations be upgraded to full misconduct charges so Gallo could rebut them during his appeals hearing. However, the board decided ORI had too little evidence on three of the charges to justify going ahead, thereby limiting the issues ORI would be allowed to raise at the appeals hearing.

The remaining allegation has two parts: ORI claims Gallo had failed to determine in a timely manner the origin of the cell line in which his laboratory grew the AIDS virus, depriving its inventor of due credit and retarding the efforts of others who sought to grow the virus, and that Gallo attempted to place unreasonable restrictions on the use of his cell line.

In response to the original misconduct charge, Gallo, through his attorney, says the context makes it clear the sentence means that the French themselves had been unable to grow LAV in a permanent cell line and were therefore unable to characterize the virus. To the two additional charges regarding the cell line, he says there was no time to identify the successful line in his laboratory's rush to find a line that would grow the virus. Subsequently, however, Gallo says he sent Popovic to compare it with its likely source, but the results were ambiguous. In any event, Gallo says, enough information about the cell line used was released to allow any skilled scientist to find a cell line that would work. Finally, Gallo says the only special restriction in the exchange agreements was a prohibition on comparing "his" virus, HTLV-IIIB, with the French virus LAV, an experiment he wanted to do himself in collaboration with the French.

The appeals board has made it clear both in the Popovic case and earlier rulings that ORI must prove not only that Gallo's statements were false but that he intended to deceive. Moreover, in a July preliminary ruling on the Gallo case, it also required ORI to preview its entire case in an "offer of proof." The defense was not required to do the same.

The board has also ruled that, in cases of alleged misconduct not involving outright fabrication, falsification or plagiarism, ORI must prove not only that the conduct "seriously deviates from the standards in the community," (the usual definition of misconduct) but also that "any reasonable researcher in [the defendant's] position would have considered [the conduct] to be misconduct at the time." That requirement will be difficult to meet in the Gallo case, which dates back more than a decade.

If the hearing is held, the board's three government lawyers will be joined by a scientist, Jules Younger, an emeritus virologist at the University of Pittsburgh. Both sides requested the addition of a scientist as a full voting member of the board.

–C.A.

a temporary position at the Karolinska Institute in Sweden after being unable to find a job in the United States) nor Gallo were talking last week, but their lawyers were jubilant. Barbara Mishkin, an attorney with the Washington firm Hogan and Hartson, declared Popovic "completely exonerated." Gallo's attorney, Joe Onek of Crowell and Moring, noted that many of the ORI witnesses criticized by the board are scheduled to testify against his client as well.

ORI director Lyle Bivens says staff attorneys will review the Popovic decision for its impact on the Gallo case. He says every option, "from changing the order of the witness list to revising our strategy to abandoning the case," is on the table. A decision on whether to go ahead was expected on 12 November.

Mishkin, meanwhile, has submitted a brief to the Appeals Board on behalf of Popovic asking HHS to reimburse his legal fees, which exceed $250,000. But his ultimate aim, she says, is to get back into science. Popovic "really hopes that NIH will now let him come back," she says. "That's where he really wants to be." Although Gallo had offered him a job in his lab several years ago, she says, NIH officials at the time said he should not return until the allegations of misconduct were laid to rest. For Popovic, the board's decision, the final step in the process, appears to have done just that.

–Christopher Anderson

NATIONAL SCIENCE FOUNDATION

Lane's Strategy on Strategic Research

Within days of taking over the reins at the National Science Foundation (NSF) last month, Neal Lane received a welcoming present from Congress—an 11% increase in the agency's 1994 budget. But the present came with some strings: an explicit directive from the Senate to work more closely with industry. This presents Lane with a dilemma. If he responds by moving NSF more toward applied research, he will please Congress but incur the wrath of the basic research community—a fact learned the hard way by Lane's predecessor, Walter Massey, who provoked a backlash when he suggested that NSF should do more research relevant to industry. Last week, in an interview with *Science*—his first one-on-one encounter with the media since taking office on 15 October—Lane made it clear that he will not follow Massey's approach. He said he will argue that NSF can make its biggest contribution to the nation's long-term economic health by strengthening basic, academic research.

Indeed, Lane said the best use of additional federal funds would be to buy more of the same type of fundamental research that NSF now supports, and he argued that likely benefits from so-called strategic research have been overstated. "I don't know what you gain by calling [research] strategic," Lane said. "It would be much easier if one could just talk about research, and leave it to whomever one is speaking with to determine if the work is of near-term, medium-term, or long-term significance to the problems facing society."

That argument will undoubtedly be applauded by academic scientists worried that the $3 billion agency may be changing direction. But in making it, Lane is swimming against the political tide. Last year Massey responded to congressional pressures by declaring it was time for NSF to "accept a major role in fostering the links between research and technology" by embracing programs "closely aligned with industry and other government agencies." This spring President Clinton requested $204 million more for NSF as part of his unsuccessful economic stimulus package, and in September the Senate appropriations committee said that 60% of NSF's budget should be devoted to research that is "strategic and applied in nature," threatening to impose cuts if it did not comply (*Science*, 17 September, p. 1512).

But Lane, a theoretical physicist and former provost of Rice University, warns that a larger budget isn't likely to result in research that is any more "applied" than what NSF now funds. In particular, he says one should not overestimate the short-term impact of half a dozen interagency programs, including such initiatives as global climate change and high-performance computing.

CATHALEEN CURTISS

Back to basics. Neal Lane says NSF's forte is "foundational" research.

"I would challenge anyone to walk into a laboratory funded by a program that fits within [such an initiative] and one that isn't and find any difference in how the investigator approaches the problem, what the students do, what the apparatus looks like, and so on," Lane says. "The key question to me is, 'What are the people doing in the lab?'" Although Lane says the areas in which they are working may be more closely connected to a particular problem facing society, what they are doing is basic—or what he calls "foundational"—research, now as always NSF's most important product.

Why is that so important? Although Presidents Reagan and Bush promised to double NSF's budget over 5 years in exchange for its contribution to the nation's economic well-being, the precise nature of the contribution has remained unclear. Lane and many researchers are arguing that NSF's contribution is to continue funding basic research, to train the next generation of scientists and to help improve scientific literacy among the population. The Senate, on the other hand, appears to be arguing that NSF's research portfolio should generate knowledge that can be used immediately to improve the nation's technological base.

Asked for his interpretation of the Senate's directive, the soft-spoken and thoughtful Lane chooses his words carefully. "There are many examples of research that falls under the category strategic that ends up never having an impact on an application. That's the nature of research; you can't know for sure." A short time later, he notes that "technology transfer is a buzz word that's got a lot of meanings. Knowledge transfer is a better word for what we do."

Lane says he recognizes that NSF may not be able to repeat its double-digit funding increases, and that he must set priorities among disciplines. But he says he would not reduce support for a particular field to the point where it can no longer make an important contribution to science. "The more we just cut off certain areas of science and say that it's somebody else's responsibility, the less able we will be to take advantage of opportunities that cut across disciplines."

Similarly, Lane holds the middle ground in the ongoing debate about the proper balance of NSF's portfolio between small grants to individuals and larger projects, which range from new facilities to multimillion-dollar centers. "If NSF is going to be in astronomy or play a role in high-energy physics or oceanography, there are going to be some big things that it will need to support," he says. "Now you might say that there are other agencies that can do the big lumps, and NSF can use them. But that never works.... Many of these instruments are themselves cutting-edge science, so if NSF is supporting the scientists and someone else is building the instrument, it really doesn't work."

–Jeffrey Mervis