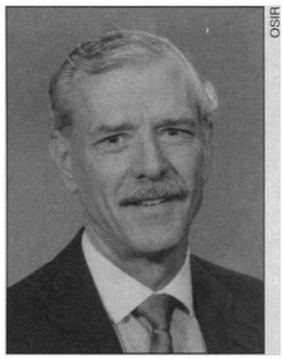
The Aftermath of the Gallo Case

An appeals board trounced the federal misconduct office in two recent cases and said it had misinterpreted its own definition of misconduct; in future, the office will be more selective in the cases it takes on

When the U.S. Office of Research Integrity (ORI) recently lost or abandoned four of its most prominent scientific misconduct cases, the recriminations quickly started flying. ORI director Lyle Bivens did what football coaches have long done to explain away an embarrassing loss: He blamed the referee. He accused a federal appeals board of changing the rules so that only the most clear-cut cases of misconduct can be prosecuted successfully. It was an understandable reaction by an office under fire. The appeals board, in two rulings, had slammed ORI for incompetence. And lawyers for the exonerated scientists said that overzealous investigators had subjected their clients to years of personal anguish in building their cases.



OSIR

Regrouping. ORI's Bivens wants to change rules.

Yet ORI's setbacks and the public brawling that ensued have left many researchers and university officials wondering what will happen to ORI, and to future scientific misconduct investigations. "If I were just an observer, I'd think the scientific misconduct process is in great disarray," says Patricia Woolf, a misconduct expert at Princeton University who has been an adviser to ORI.

In an effort to reduce the confusion, *Science* asked scientific misconduct experts —scientists, university administrators, and lawyers—to assess the impact of the four cases and their likely effects on future cases. Their almost universal conclusion: To make a charge of scientific misconduct stick, ORI will have to meet higher standards of proof than it has applied in the past. In particular, false or misleading statements by a researcher must have been deliberately designed to deceive other researchers. Most experts also agree that ORI should have been applying this standard all along, that in essence it has for years been misconstruing its own rules.

Bivens agrees that the consequence of the board's decisions is a tough new standard for ORI, but he argues that it is the board's "idiosyncratic" interpretations of the federal misconduct rules—rather than the rules themselves—that are to blame. Nevertheless, ORI will soon propose a new definition of misconduct that would make some cases easier to prosecute. But sources within ORI's parent agency, the Department of Health and Human Services (HHS), say ORI has little departmental support for such changes and may have to live within the legal framework spelled out in the board's decisions.

As for the four cases in which ORI suffered embarrassing reversals—involving AIDS researchers Robert Gallo and Mikulas Popovic of the National Institutes of Health (NIH), Georgetown University pediatrics researcher Margit Hamosh, and molecular biologist Rameshwar Sharma of the Cleveland Clinic Foundation—the initial decision to investigate was influenced by heavy media coverage and pressure from Congress. But when the cases came up for appeal, there was general agreement that ORI lacked the evidence to prove misconduct had occurred, in some cases even under its own standards of proof. The implication is clear, says Paul Friedman, dean for academic affairs at the University of California, San Diego, and a member of ORI's recently disbanded advisory board: ORI must be much more selective in deciding which cases to pursue. "If [ORI] would only have had the sense to go after the clear cases and leave the crap alone, they wouldn't have had these problems," he says. Adds Caltech vice provost David Goldstein, "The panel did exactly what should be done by holding a high standard. High legal standards chill investigative zealotry."

The bottom line, according to the experts *Science* consulted, is the emergence of a distinct, two-tiered system for handling misconduct. Academic institutions will continue to be primarily responsible for investigating such alleged misdeeds as improper claims of authorship or uncollegial behavior. ORI will intercede only in serious cases that may result in federal sanctions, such as debarment from receiving federal grants. Those cases will require a higher standard of proof and be handled more like criminal proceedings.

The trick to making a two-tiered system work, says C.K. Gunsalus, University of Illinois associate vice chancellor for research, "is to get a federal definition of misconduct that both explains what a federal offense is, and also drives what the institutional responsibilities are." Then "it's up to the universities to have the backbone to go beyond what constitutes a federal 'crime,'" she says. That won't be easy; she says some universities are already restricting the cases they prosecute to

ORI AT A GLANCE

ORIGIN
- Created in 1992 as an independent office within the Department of Health and Human Services (HHS);
- Replaced the Office of Scientific Integrity at the National Institutes of Health and the Office of Scientific Integrity Review at HHS.

STAFF
- 51 employees, including:
  6 full-time attorneys from the HHS General Counsel's office, which is attached to ORI;
  13 Ph.D.s or MDs with scientific backgrounds, working with a dozen other professional staff in the division of research investigations;
  13 staff members in the policy and education division.

BUDGET
- $4 million a year.

CASELOAD
- 15 ORI investigations under way.
- 36 institutional investigations under way or being reviewed by ORI.
- 21 inquiries (fact-finding exercises that may lead to an investigation) under way at ORI or institutions.
- 23 cases closed with no finding of misconduct.
- 22 cases closed with finding of misconduct (see graphic next page).

those ORI is likely to win under the newly clarified rules. But University of California, Berkeley, cell biologist Howard Schachman doesn't see such a hurdle. "It's simple," he says. "Universities have a responsibility to discipline unethical behavior. When that unethical behavior is fabrication, falsification, or plagiarism, it's time to turn it over to the feds."

From science to law

Some of the confusion among scientists over the current federal standards stems from the fact that the machinery for investigating allegations and determining sanctions has recently been transformed into a legalistic process. That's not what NIH had in mind when it set up the Office of Scientific Integrity (OSI) in 1989 to investigate alleged misconduct in NIH-funded research. The office was staffed largely by scientists, on the theory that researchers should be judged by their peers and their conduct measured against the norms of science. But the system didn't satisfy legislators and lawyers. And critics such as Representative John Dingell (D–MI) complained that some investigations—in particular, the Gallo case and an ongoing investigation of Tufts immunologist Thereza Imanishi-Kari, involving a paper coauthored by Nobel laureate David Baltimore—were not pursued vigorously enough. Dingell questioned whether universities and NIH are capable of investigating their own scientists. Several accused scientists and their lawyers also complained that OSI's misconduct procedures violated constitutional rights to due process because researchers had little opportunity to confront their accusers and rebut the evidence against them.

In response, HHS removed OSI from NIH in mid-1992 and merged it with the existing HHS-level Office of Scientific Integrity Review (OSIR) to create ORI. To allow for more due process, ORI later that year asked a standing HHS appeals board, consisting of lawyers, to review findings of misconduct in a court-like setting. If ORI determines that a scientist is guilty of misconduct, the accused can contest the evidence and cross-examine witnesses with the help of an attorney. In the 40% of ORI's misconduct findings that have so far been appealed, these changes turned the process from one of scientists investigating scientists to one driven largely by lawyers and offering all the checks and balances required for due process. Where OSI had no full-time lawyers, ORI has half a dozen (see box).

Ironically, although Dingell and his congressional investigative committee were leading advocates for this new system, ORI has lost some of the very cases Dingell cared most about. Dingell doubted scientists' willingness to police themselves, but it was ORI's scientific staff and its independent scientific advisers who pressed hardest for findings of misconduct in the four cases it recently lost. These cases collapsed only after lawyers revealed flaws and biases in the scientists' assumptions. Dingell has said little publicly about this turn of events, commenting only that the appeals board's decision in the Popovic case was "curious."

Failing the first tests

According to some measures, ORI has been quite successful in prosecuting cases under this new system. It has completed 45 investigations, finding misconduct in 22 cases. And the evidence was strong enough in 13 of those cases that the accused scientists declined to pursue an appeal (see chart). But the results are different for cases that have gone to the appeals board.

The first test was the Sharma case. Sharma had been accused of "anticipatory writing"—including data that he did not yet possess—in a grant application. Three separate panels looked into the case at the Cleveland Clinic and Sharma got a split decision: One panel found possible grounds for misconduct, the other two didn't. OSI took the case, but was forced to transfer it to OSIR when Dingell complained that NIH director Bernadine Healy had a potential conflict of interest because she had headed one of the Cleveland Clinic panels that exonerated Sharma. In April 1992, OSIR found no misconduct. But when ORI took over OSIR's caseload, it re-opened the case and reversed OSIR's conclusions, issuing a misconduct finding later that year.

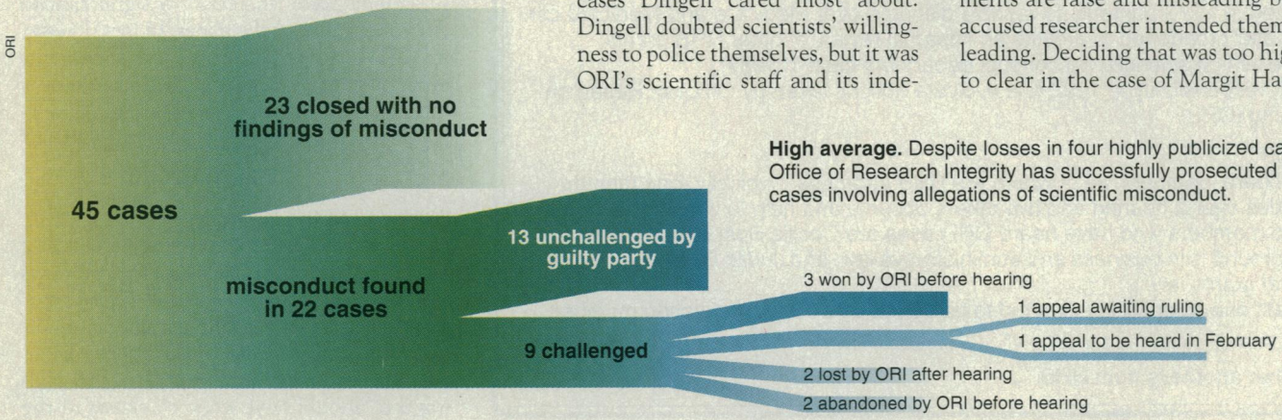
Enter the appeals board. Sharma's "misstatements," the board ruled in August 1993, boiled down to the use of an incorrect subscript in one instance of identifying a certain protein. The board concluded that the misstatement was most likely a typo and rejected ORI's conclusion of misconduct.

Losing a case that had been a focus of two widely publicized hearings before Dingell's committee was bad enough for ORI. But even worse was the board's ruling that, to win its cases, ORI must prove not only that statements are false and misleading but that the accused researcher intended them to be misleading. Deciding that was too high a hurdle to clear in the case of Margit Hamosh, who had been accused of making a false statement on a grant application, ORI dropped charges against her before the appeals board held a hearing (*Science*, 29 October 1993, p. 643).

The appeals board's second withering indictment of ORI's work came 3 months later, in the form of a thorough rejection of its case against Popovic. Gallo and Popovic had been under scrutiny for more than 4 years, starting with the sensational allegation that they had essentially stolen from a group at the Pasteur Institute the AIDS virus they claimed to have discovered in 1984. That charge was soon dropped when investigators concluded there was no evidence of misappropriation: Laboratory contamination was the most likely explanation for the fact that Gallo's virus was identical to the French isolate. Nevertheless, OSI continued to investigate allegations that Gallo's group had placed improper restrictions on reagents and included misleading statements in their scientific papers. And Dingell's committee turned up the heat on ORI by conducting a parallel investigation. Last year, ORI charged the two researchers with misconduct.

The appeals board took up the Popovic case first. It concluded that ORI had not even proved Popovic's statements were false—let alone that they constituted misconduct. And it criticized ORI for having pursued the case so long with so little evidence of wrongdoing (*Science*, 12 November

ORI's Track Record on Completed Cases



High average. Despite losses in four highly publicized cases, the Office of Research Integrity has successfully prosecuted most of its cases involving allegations of scientific misconduct.

1993, p. 981). Stunned by this rejection, ORI abandoned its prosecution of Gallo just 3 days before the appeals board was scheduled to hear the case (*Science*, 19 November 1993, p. 1202). That's when the recriminations started flying.

In a 12 November press release, ORI said the board's rejection of its case against Popovic had "established a new definition of scientific misconduct as well as a new and extremely difficult standard for proving misconduct." In an interview with *Science*, ORI's Bivens went further, implying that the board's definition of misconduct differed from that used by the scientific community. He noted in particular that a panel of scientists chosen by the National Academy of Sciences to review the Gallo case contended that Gallo had committed "intellectual appropriation" of the French AIDS virus by downplaying the French work in his public statements and published papers.

Defense attorneys for Gallo and Popovic protested ORI's statements in letters to Bivens' bosses at HHS. The implication that Gallo and Popovic got off on a technicality is patently false, they argue; the appeals board had simply stuck to the rules that ORI should have followed. In addition, ORI had been unable to demonstrate in the Popovic case that there were any false statements at all. Philip Lee, assistant secretary of health, apparently has some sympathy for this point of view, telling *Science* he has "concerns" about ORI's statements. ORI was under "tremendous pressure" to pursue these cases, he says, and in retrospect the board's rulings "do raise the question if [pursuing them] was a wise decision." Friedman puts it more bluntly: "Congress drove them into proving they're tough."

The intent of "intent"

Irrespective of the merits of ORI's cases against Sharma and Popovic, the board's rulings do spell out the standards ORI must meet in future cases. Perhaps the most controversial is the requirement to prove intent.

In both rulings, the board said ORI must prove "by the preponderance of evidence" that an accused researcher knew a statement was false and therefore intended it to be misleading. But Bivens says ORI has always operated on the assumption that it is enough to prove that the statement was false and the researcher "should have known" that was the case, and he says this was the standard Congress and HHS set when they drafted misconduct guidelines in the late 1980s.

Robert Charrow, a former HHS attorney who helped to draft the definition (and who served on Sharma's defense team), argues, however, that intent has always been implicit in the guidelines. He says HHS had planned to call misconduct "research fraud," a legal term that requires proof of intent. But common law also requires an injured party in a fraud case, something that might be difficult to obtain in the typical case of misstatements in a scientific paper. HHS eventually defined scientific misconduct as "fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community...[excluding] honest error or honest differences in interpretation or judgments of data." The inclusion of the "honest error" provision, says Charrow, now with Crowell & Moring in Washington, indicates "we intended intent to be implicit."

When ORI asked its own advisory panel for a clearer definition in early 1993, it recommended "...plagiarism; fabrication or intentional falsification of data, research procedures, or data analysis; or other deliberate misrepresentation in proposing, conducting, reporting, or reviewing research." Friedman, a panel member, says ORI "didn't want to hear" that most of the panel thought intent should be explicitly part of the definition (by the use of the word "deliberate"), and the panel's advice was ignored. Nevertheless, Friedman says, "I think that ORI is disingenuous in claiming that intent is a new requirement" imposed by the appeals board.

In interviews after the Popovic decision, ORI also contended that the board refused to hear evidence of a "pattern of behavior" to prove intent in the Popovic case. But Rebecca Dresser, a misconduct expert at the Case Western Reserve University law school who examined the appeals board decisions at *Science*'s request, says the board drew the line only when ORI tried to raise a serious charge not in its investigative report. ORI also claimed the board required it to prove that statements were "material" or significant to the conclusions of the paper. In fact, Dresser says, the board required only that statements be significant to form the basis of a claim of intent, on the grounds that it is hard to imagine a motive for fabricating an insignificant statement.

Working out the kinks

In the wake of its embarrassing defeats and its conflict with the appeals board, ORI plans to propose (through a Federal Register notice, which solicits public comment) modifications to the federal misconduct regulations. In particular, it intends to propose adding the "should have known" clause to the definition of misconduct. It also wants to make "materiality" an explicit factor in determining sanctions, but not in the finding of misconduct itself, and it hopes to clarify what evidence can be admitted in order to demonstrate a "pattern of behavior." Finally, it hopes to place the burden of proof on an accused scientist to demonstrate that a false statement was an honest error. One senior HHS official says, however, that ORI has little support within the department for most of these proposed changes.

The next round of debate over misconduct may be mediated by a congressionally mandated commission outside experts that ORI is assembling. In the meantime, ORI is likely to be much more selective in choosing which cases it will take up once a university has completed its investigation. Some researchers believe that faculty senates, traditionally conservative, may be reluctant to impose institutional standards more sweeping than those used by the federal government. But Schachman says "the machinery is there" for a two-tiered system in which universities deal with a broader range of research misdeeds than ORI can handle.

"There are a lot of transgressions of all sorts that are handled by universities even though they aren't federal offenses," he says. His advice to ORI is simple: Unless the case is strong enough to plausibly convince the federal appeals board, don't even take it.

–Christopher Anderson

APPEALS BOARD AT A GLANCE

ORIGIN
- Created in 1973 primarily to resolve disputes over Medicare and Medicaid contracts. Later broadened to provide an impartial review of other HHS grants;
- Heard its first scientific misconduct debarment case in 1987;
- Given responsibility in 1992 to adjudicate actions taken by Office of Research Integrity (ORI).

MAKEUP
- Five board members, all of whom are HHS attorneys. Typically, one member presides over a hearing and two others observe and help to write the decision.
- Board members who have heard ORI cases are Cecilia Sparks Ford, whose background is in business and administrative law, and Judith Ballard, an expert in federal grants law.
- At least one scientist is expected to be added as a temporary voting member.

STAFF
- 30 other attorneys from HHS.