

## ORI NEWSLETTER

Volume 2, No. 3, Office of Research Integrity, U.S. Public Health Service, June 1994

### COMMISSION ON RESEARCH INTEGRITY MEMBERS APPOINTED

Donna Shalala, the Secretary of the Department of Health and Human Services (HHS), recently appointed the members to the newly chartered Commission on Research Integrity.

The Commission, mandated by the NIH Revitalization Act of 1993, is to make recommendations to HHS and Congress on how the PHS should deal with research misconduct in federally-funded research.

The Commission is composed of twelve members representing science, academic administration, law, and ethics. Several members have direct experience in conducting investigations of research misconduct.

Meetings of the Commission will be open to the public, and will usually be held in the Washington, D.C. area. The first meeting has not yet been scheduled, but is likely to be in late spring or early summer of this year.

#### **The members are:**

**Kenneth John Ryan, M.D.**, who will chair the Commission. He is the Distinguished Kate Macy Ladd Professor in the Department of Obstetrics, Gynecology and Reproductive Biology, Harvard Medical School. He is a past Member of the President's Committee on Mental Retardation. He has been Chairman of the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research; Chairman of the Ethics Committee, American College of Obstetrics and Gynecology; and Chairman of the Scientific Issues Human Transplantation Research Panel. He was President of the American Gynecological and Obstetrical Society from 1990 to 1991.

**Carol Ann Kemp Aschenbrener, M.D.**, is Chancellor of the Medical Center, University of Nebraska, Omaha, NE, and Professor of Pathology at the University of Nebraska, NE.

**Eugene H. Cota-Robles, Ph.D.**, is Professor Emeritus, Biology, at the University of California, Santa Cruz, CA.

**Thomas Michael Devine, J.D.**, is Legal Director of the Government Accountability Project, Washington, DC.

**Linda L. Emanuel, M.D., Ph.D.**, is Assistant Director of the Division of Medical Ethics, Harvard Medical School; and Faculty Associate in the Program in Ethics and the Professions at Harvard University, Cambridge, MA.

**C. Kristina Gunsalus, J.D.**, is Associate Vice Chancellor for Research and Research Standards Officer at the University of Illinois at Urbana-Champaign, IL.

**Karl J. Hittelman, Ph.D.**, is Associate Vice Chancellor for

Academic Affairs at the University of California at San Francisco, CA.

**Drummond Rennie, M.D.**, is Adjunct Professor of Medicine, at the Institute for Health Policy Studies, at the University of California at San Francisco, CA and Deputy Editor (West) of the *Journal of the American Medical Association*, Chicago, IL.

**Priscilla Ann Schaffer, Ph.D.**, is Professor in the Department of Microbiology and Molecular Genetics at the Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA.

**S. Andrew Schaffer, LL.B.**, is Vice President, General Counsel, and Secretary of the University, New York University, New York, NY.

**Judith P. Swazey, Ph.D.**, is President, The Acadia Institute, and Executive Director, Medicine in the Public Interest, Bar Harbor, ME.

**Carolyn Dickson Whitfield, Ph.D.**, is Associate Professor in the Department of Biochemistry and Molecular Biology, Howard University, Washington, D.C.

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#### DAB AFFIRMS ORI RECOMMENDED DEBARMENT AGAINST HISERODT

The Office of Research Integrity's findings of scientific misconduct against John C. Hiserodt, M.D., Ph.D., have been affirmed by the Departmental Appeals Board (DAB) of the Department of Health and Human Services. As a result of an intensive investigation, Dr. Hiserodt, a former assistant professor and researcher at the Pittsburgh Cancer Institute, was found to have deliberately falsified critical data and fabricated experimental results in several figures and tables in two grant applications submitted to the National Institutes of Health (NIH).

In reporting research results on antigen recognition by natural killer (NK) cells, Dr. Hiserodt falsely reported the discovery of a purportedly unique protein with a molecular weight of 48 kilodaltons by altering photographs of autoradiograms. He falsely reported that this protein has been found on the surface of human NK cells, falsely reported the methodology and materials used in several experiments, and deliberately failed to include relevant information on the results of a gene sequence submitted in response to questions raised by NIH grant reviewers about his experimental findings. He also deliberately fabricated a laboratory notebook presented to officials at the University of Pittsburgh, the grantee institution, in an attempt to conceal his actions and to persuade the officials to continue to support the applications.

The DAB affirmed the administrative actions against Dr. Hiserodt, which include a prohibition from serving on Public Health Service (PHS) advisory committees, boards, or peer review groups

monitoring PHS-sponsored research for seven years, the required correction of a published article, and a five-year debarment from receipt of any Federal funding. Dr. Hiserodt's subsequent motion for reconsideration of the debarment was denied by the Deputy Assistant Secretary for Grants and Acquisition Management.

The ORI argued to the DAB that had Dr. Hiserodt succeeded in his deception, he would have obtained more than \$1,000,000 of public funds. In affirming the ORI misconduct findings, the DAB stated that Dr. Hiserodt violated fundamental standards of conduct and that the government had an obligation to award its limited Federal research monies only to those individuals it determines will use those funds responsibly. In reaching this determination, the DAB stated that Dr. Hiserodt's actions constituted scientific misconduct under the 1989 regulations. In addition, the DAB found that those actions occurring prior to the effective date of the regulations were scientific misconduct under the applicable and widely-recognized professional standard which predated the regulations. It noted that both prior to and subsequent to the adoption of the 1989 regulations, applicants for research funds have had a duty to honestly and truthfully report the experimental results on which they premise their applications. The DAB stated that Dr. Hiserodt "engaged in an unremitting pattern of behavior evidencing indifference to the truth."

Dr. Hiserodt's contention that there was no PHS jurisdiction because both applications were unfunded was also rejected by the DAB. The DAB noted that the broad purpose of the scientific misconduct statute is to protect the integrity of the grant programs and that the event which triggered the authority to investigate was the filing of the applications. Additionally, Dr. Hiserodt's actions fell within the debarment regulations because his conduct demonstrated a lack of present responsibility. The DAB found that ORI has jurisdiction over the fabricated notebook because it was an integral component of Dr. Hiserodt's attempt to persuade NIH to fund the grant applications, since he had prepared it to convince the University of Pittsburgh that allegations of scientific misconduct against him were unfounded. The fabrication of the notebook was also relevant to the question of Dr. Hiserodt's integrity with respect to whether he is presently responsible to receive Federal funds. Debarment, the DAB stated, is not a punishment but a remedy which is designed to protect federally-funded programs from individuals who have shown by their conduct that they are not trustworthy to deal with program funds. Thus, Dr. Hiserodt's argument that the term of debarment should be shortened because he had been "effectively debarred" during the investigation was rejected.

Please call Gail Gibbons, ORI Investigative Counsel, at (301) 443-3466, for more information on this case. Copies of the ORI Investigation Report and the DAB decision may be requested from

ORI.

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#### FORMER STUDENT COMMITTED MISCONDUCT

An inquiry conducted by Cornell University Medical College found that Dr. Keith A. Caruso, while a medical student in the Department of Psychiatry, altered, fabricated, and destroyed primary laboratory data while learning techniques for insulin receptor binding on erythrocytes at the Columbia College of Physicians and Surgeons; this work was supported by grants from the National Institute of Mental Health. Dr. Caruso admitted to these acts of alteration, falsification and destruction of primary data. ORI has accepted the university's findings, and the administrative actions previously imposed by Cornell University. Dr. Caruso has signed an agreement with ORI not to appeal the finding of scientific misconduct. This agreement was made final on April 6, 1994. ORI has determined that the university's administrative actions were sufficient, and has not imposed any further Public Health Service actions. The fabricated data did not appear in any scientific publications.

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#### MISCONDUCT CASE PRODUCES CHANGES IN MONITORING OF CLINICAL TRIALS

The National Cancer Institute (NCI) has changed its procedures for monitoring clinical trials and taken significant actions against the National Surgical Adjuvant Breast and Bowel Project (NSABP) at the University of Pittsburgh as a result of its experience in a scientific misconduct case involving Dr. Roger Poisson at St. Luc's Hospital in Montreal. Dr. Poisson was found to have committed scientific misconduct by ORI in a report dated March 1993.

Dr. Samuel Broder, Director, NCI, announced the changes and actions during a hearing in April before the Subcommittee on Oversight and Investigations, House Committee on Energy and Commerce, chaired by Representative John D. Dingell, to "bolster the confidence of the Congress, the public, and the medical community in our clinical trials program."

During the hearing, lawmakers, activists, and patients chastised the NCI and NSABP officials for their handling of the case, particularly the long delay in publishing a reanalysis of the data that showed that a lumpectomy followed by radiation treatment is a safe alternative to a mastectomy.

The ORI was criticized for not adequately publicizing its finding of scientific misconduct in this case. Dr. Lyle W. Bivens, Director, ORI, told the Subcommittee that ORI will issue a press release when scientific misconduct is found in clinical trials.

In his opening statement, Representative Dingell said, "Many in the scientific community have resisted outside scrutiny, and others have sought to minimize the problem. But, as we see today, scientific misconduct is a very real problem that requires an aggressive response by the scientific community and the Federal government. The case before us is a vivid reminder of how poor the response of the scientific community can be, and how serious the consequences may be when the scientific community and Federal government fall down on the job."

Mr. Dingell continued, "One of the reasons we are here today is that no one followed the direction of the Director of the NCI. Top NCI officials ignored the Director's instructions, and Pittsburgh ignored the directions of its funding institution. In fact, top NCI officials have complained to the Subcommittee staff that they could not even get Dr. Fisher [head of NSABP] to return their phone calls, let alone take any direction from the NCI."

Mr. Dingell concluded, "This illustrates a central problem identified in numerous Subcommittee investigations of scientific misconduct: who is in charge--the NIH funding institutions or the prominent investigators? NIH's capability and willingness to manage and oversee federally-funded research continues to be the key question."

In his testimony, Dr. Broder clearly indicated that NCI has taken charge of its clinical trials: "We have created a new unit, the Clinical Trials Monitoring Branch, to monitor compliance in our Cooperative Groups, and we will take swift and uninhibited action in the event of lack of compliance. New procedures are in place to report and track audits, and we are initiating a system of NCI-directed site visits to validate the cooperative group audit findings, with sites selected at random. We are developing a new internal NCI operations manual for situations involving fraud and scientific misconduct. This new manual will be in place within days. The measures also include automatic notification of journals when falsified data have been published and informing other financial sponsors of projects affected by scientific misconduct."

Addressing actions taken against NSABP, Dr. Broder stated, "We are trying to learn from this experience to ensure that our response to episodes of fraud in clinical trials is prompt and effective. Thus, recently NCI personnel have taken possession of NSABP's computer data-file; analyzed and disseminated the results; and initiated a government-run, on-site audit of clinical research conducted by NSABP. In doing so, NCI has clearly confirmed the principle that the granting agency can demand, distribute, and disclose a grantee's data in response to pressing public health needs. Fraud will by definition always constitute such a need. We will not ever again hesitate to exercise this authority whenever necessary."

Dr. Broder continued, "We have learned a great deal about the process and pitfalls of dealing with scientific misconduct. We clearly understand the principle that we cannot allow a grantee's formidable reputation, history of prior accomplishments, or service in science to stand in the way of prompt, corrective action and oversight. We cannot, and will not ever again, defer or appear to defer to the timetable of a grantee in reporting fraud and fabrication to the public. We have taken steps to make this the explicit policy of the NCI." Dr. Fisher has been replaced as head of NSABP at the request of NCI.

Dr. Broder reported, "The Group has been placed on probation and has until the end of June 1994 to initiate programs to bring its auditing and reporting procedures into compliance. Accrual to clinical trials has been temporarily suspended until these deficiencies are corrected and a quality auditing system is in place. The terms of award of the NSABP grant have been modified to require immediate re-publication of any trials affected by fraud. Similar grant modifications are being made for all of NCI's Clinical Trials Cooperative Groups. Our own NCI-run audits of various hospitals and academic centers affiliated with NSABP continues. We are attempting to recover funds expended at the fraudulent data site. We consider the entire data-set from St. Luc to be a total loss to the American taxpayer."

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#### ORI COMPLETES NEEDLEMAN INVESTIGATION OVERSIGHT

The ORI has accepted the University of Pittsburgh finding that Dr. Herbert Needleman's reports on the effects of low levels of lead on the intellectual abilities of children did not constitute misconduct in science as defined in the Federal regulation. However, both the university and ORI found numerous problems, errors, and inaccuracies in Dr. Needleman's reports and presentations of his research.

Because of the number and magnitude of these problems, ORI notified NIH (the funding agency), the Centers for Disease Control and Prevention (involved in lead poisoning issues), and the Environmental Protection Agency (set lead standards based in part on Needleman's data).

In addition to notifying the agencies involved, ORI concurred with the university's proposed actions, in particular, that Dr. Needleman correct the scientific literature and allow researchers access to the data that support his reports so that they may be independently assessed.

ORI also made its oversight report of the university's investigation available to the public upon request. Although this is unusual in a case of no misconduct, the investigation had already become a public matter. Because the research affected

significant public issues, ORI strongly believes that the public has a right to know the results of the investigation.

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#### AAMC TEACHING HANDBOOK AVAILABLE

The Association of American Medical Colleges (AAMC) has just published a new resource in research ethics titled *Teaching the Responsible Conduct of Research Through a Case Study Approach: A Handbook for Instructors*. This book is oriented to those directing courses on this topic and provides some basic materials that should prove useful when either initiating or augmenting such programs.

At the core of the handbook are a series of case scenarios organized topically. The cases present various dilemmas and are accompanied by questions designed to facilitate discussion of data selection, authorship and attribution standards, peer review, sharing research materials and information, misconduct and conflicts of interest in research, the use of animal and human subjects, and the ethical implications of genetic research.

Each topical section concludes with an annotated list of references and audiovisual materials that will give students and instructors appropriate background information for evaluating the cases. The handbook also includes a chapter on the case-based approach to teaching, which discusses some of the goals and techniques associated with this method of instruction. In the appendices, readers will find a survey for evaluating the cases, a table of sample institutional approaches to teaching research ethics, and a consolidated bibliography.

Since 1990, all institutions receiving NIH training grants have been required to provide some form of organized instruction in the responsible conduct of research. This handbook should prove particularly useful for individuals charged with oversight of those programs. The NIH, which provided support for the development of this resource, will be distributing single copies of the handbook to all institutional training program directors.

Copies may be ordered by contacting AAMC Publications Sales, 2450 N St., N.W., Washington, D.C. 20037, (202) 828-0416.

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#### INTRAMURAL PROCEDURES, INSTRUCTIONS ISSUED

In April, ORI issued explicit instructions on how to conduct an inquiry within the PHS. These instructions are designed for use by PHS officials who have operational responsibility for conducting or overseeing the conduct of an inquiry. This step-by-step guide is designed to assist the intramural official

in the detailed steps involved in an appropriate inquiry.

At the same time, ORI issued general procedures for PHS agencies to follow when handling allegations of possible scientific misconduct in intramural research programs. These procedures establish a uniform approach to dealing with misconduct issues and should facilitate efficient and effective handling of misconduct issues in PHS.

The procedures and explicit instructions for conducting intramural inquiries also formed the basis for a workshop for PHS personnel. The workshop was designed to reinforce the written instructions and to ensure that those who have responsibility for assessing allegations and conducting inquiries are fully aware of the requirements.

In the workshop, the ORI provided detailed guidance for assessing allegations and conducting inquiries in alleged cases of misconduct within the intramural program. The following issues were discussed:

Allegations: The chain of reporting and preliminary assessment of allegations.

Inquiries: Notification of those involved in the allegation; prompt sequestration of data and evidence; appointment of a formal inquiry committee that precludes possible conflict of interest; documentation and feedback on interviews; and development and review of the inquiry committee's report.

ORI intramural investigations: How ORI conducts an investigation and the possible role of intramural staff; notification of an impending investigation; and findings of an investigation and possible administrative actions.

Hearings: The availability of hearings through the Departmental Appeals Board and debarment hearings; publication of final report summaries; and notification of complainants.

Protection of reputations: Efforts to restore the reputations of respondents when no scientific misconduct was found as well as protection of whistleblowers, witnesses, etc.

The workshop provided a step-by-step approach for assessing an allegation of scientific misconduct, conducting an inquiry, and applying administrative actions. By sponsoring such workshops, the ORI hopes to train individuals in each research agency to take appropriate action when scientific misconduct is alleged and to make the intramural scientific community aware of the seriousness and potential consequences of scientific misconduct.

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## EXTRAMURAL GUIDES BEING DEVELOPED

Work has begun on developing "How To" guides that will provide institutions with practical guidance on how to handle the nuts and bolts of an inquiry or an investigation. ORI recognizes that there is a considerable difference between reading Federal law and regulations and handling real problem situations. This guidance will be in the form of technical assistance and will contain strictly non-regulatory suggestions to help institutional officials who lack practical knowledge and experience in dealing with scientific misconduct.

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## PUBLICATIONS

"Perspectives on Research Misconduct" is the subject of the May/June special issue of the *Journal of Higher Education*. Edited by John M. Braxton, Vanderbilt University. To order copies of special issue, contact Margaret Starbuck, Ohio State University Press, 1070 Carmack Rd., Columbus, OH 43210-1002; Tel: (614) 292-3666.

"Ethical Problems in Academic Research" is an article describing surveys of graduate students and faculty that raise important questions about the ethical environment of graduate education and research by Judith P. Swazey, Melissa S. Anderson, and Karen Seashore Lewis. In *American Scientist* November-December 1993, Vol. 81 (6), 542-553.

Based on the work reported in *American Scientist*, an opinion piece entitled "The Ethical Training of Graduate Students Requires Serious and Continuing Attention" by Judith Swazey, Karen Lewis, and Melissa Anderson was published in *The Chronicle of Higher Education* in the March 9, 1994 issue, pages B1-2.

"The Contributions of Authors to Multiauthored Biomedical Research Papers" reports on a study by David Shapiro, Neil Wenger, and Martin Shapiro which was designed to determine the contributions of each author to multiauthored biomedical research papers. *JAMA*, February 9, 1994, Vol. 271 (6), pages 438-442.

"Authorship! Authorship! Guests, Ghosts, Grafters, and the Two-Sided Coin," is an editorial by Drummond Rennie and Annette Flanagan related to the above article, Vol. 271 (6), pages 469-471.

"Teaching the Responsible Conduct of Research Through a Case Study Approach: A Handbook for Instructors" [Also see article on page 5 in this newsletter.] Copies may be ordered by contacting AAMC Publications Sales, 2450 N St., N.W., Washington, D.C. 20037, (202) 828-0416.

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DrFarrahCancerCenter.com

## SYLLABUS EXCHANGE PROJECT

The National Reference Center for Bioethics Literature at the Kennedy Institute of Ethics has established the Syllabus Exchange Project as part of its curriculum development clearinghouse. The Syllabus Exchange Project serves as a means to exchange information regarding bioethics course and workshop design and content. For further information, contact Mary Carrington Coutts, Reference Librarian, National Reference Center for Bioethics Literature, Kennedy Institute of Ethics, Georgetown University, Washington, D.C. 20057; Tel: (800) MED-ETHX or (202) 687-6779; Fax: (202) 687-6770.

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## ETHICAL ISSUES VIDEOTAPE AVAILABLE

"Ethical Issues in Scientific Research" is an hour-long videotape program available from the Research Triangle Park Club of Sigma Xi, The Scientific Research Society. It presents a panel of distinguished scientists and administrators from industries and universities in and around Research Triangle Park, N.C. The purpose of the tape is to alert viewers to the kinds of problems which sometimes arise, and encourage open discussions of the issues involved. The scenarios include issues related to authorship of research articles, use of information obtained in peer review for one's own research, data reporting and biasing of data, intellectual property, industrial data recording practices, and the media's role in informing the public of new developments in research. Copies of the videotape may be obtained by contacting Dr. Harvey Krasny at P.O. Box 13416, RTP, NC 27709-3416. To purchase a copy or site license, call (800) 768-4336 or (803) 269-7744.

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## ORI TO NOTIFY JOURNAL EDITORS

ORI has begun to notify the editors of scientific journals containing publications that might require correction or retraction as a result of confirmed scientific misconduct. Such notification is made at the time of publication of the *Federal Register* notice announcing the ORI findings and administrative actions. The notice and a copy of the ORI report on the case is provided to the editor(s).

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\*List of Publications are neither exhaustive nor all inclusive. Nor, should any of the items listed or described be even remotely construed as being favored or endorsed by the Government.

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Please Duplicate and Circulate this Newsletter to Offices, Departments, Committees, and Labs. Thank You.

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#### ORI NEWSLETTER

The ORI Newsletter is published quarterly by the Office of Research Integrity, U.S. Public Health Service, and distributed to applicant or awardee institutions to facilitate pursuit of a common interest in handling allegations of misconduct and promoting integrity in PHS-supported research.

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