ORI Newsletter

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NEW RESEARCH GRANT PROGRAM ANNOUNCED

The Office of Research Integrity (ORI) and the National Institute of Neurological Disorders and Stroke invite R01 applications to conduct research on "research integrity," which is understood as "adherence to rules, regulations, guidelines, and commonly accepted professional codes or norms" related to research.

The grant program is designed to foster research on the institutions, processes, and values that positively and/or negatively influence integrity in research. Sponsors are particularly interested in studies that will inform policymakers and research institutions on effective ways to foster integrity in publicly-funded research programs.

Little is known about the causes, significance of, or remedies for practices that fall short of professional standards of research conduct. There is little empirical evidence to determine whether intentional research misconduct is rare or widespread. Therefore, proposals are encouraged that will provide data that can be generalized about the ways researchers and research institutions meet, or fail to meet, their professional responsibilities in the conduct, evaluation, and reporting of research. For this grant program, "research" is defined broadly to include societal, institutional, and individual aspects of the enterprise.

ORI intends to commit approximately $500,000 in Fiscal Year (FY) 2001 to fund three to five new grants. Applicants may request up to a 2-year project period and direct costs up to $100,000 per year. This Request for Applications (RFA) is contingent on funding availability and meritorious applications.

By November 17, 2000, applicants are asked, but not required, to submit a letter of intent. Application deadline is December 15, 2000. For specific information, see the ORI web site, **http:\\ori.dhhs.gov**, or **http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-01-008.html**.

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CONFERENCE ON RESEARCH INTEGRITY NOVEMBER 18-20, 2000

Join your colleagues at the Bethesda Hyatt Regency for the first Research Conference on Research Integrity where participants will have an opportunity to present and exchange scholarly information on research integrity, the responsible conduct of research, and scientific misconduct. Over 70 researchers from a wide variety of disciplines will present research concerning various aspects of research integrity. Plenary, concurrent, and poster sessions are planned to encourage interaction among attendees.

Over the past 2 decades, research integrity in publicly funded research has become a national

concern, increasing the need for more and better information. Hardly any evidence exists to guide government, research institutions, scientists, and professional societies in policy- and decisionmaking related to integrity in research. Moreover, the lack of research has prevented the creation of a knowledge base upon which to build policies and programs to ensure integrity in research and to assess the impact on the public health when good research practices are not followed.

The goal of the conference is to provide a forum for scholarly debate and to encourage research on the sociological, psychological, educational, institutional, organizational, and cultural factors that positively or negatively influence integrity in research.

See the ORI web site for further meeting details.

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INDIVIDUALS CANNOT FILE QUI TAM SUITS AGAINST STATE INSTITUTIONS

On May 22, 2000, the Supreme Court held that private individuals may not bring suits against a State or a State agency on behalf of the United States under the False Claims Act (FCA). *Vermont Agency of Natural Resources* v. *U.S. ex rel. Stevens*. The FCA permits the Federal Government to bring a suit alleging that someone submitted a false claim for payment to the United States. A section of the FCA also permits private individuals ("relators") to file FCA suits on behalf of the United States, which are referred to as *qui tam* actions. The U.S. Attorney General reviews *qui tam* claims, and decides whether to intervene. If the Attorney General decides not to intervene, the FCA then permits the relator to pursue the case independently. The Supreme Court decision does not affect the ability of a relator or the United States to bring a FCA suit against a private institution or individual.

For more details about this ruling and predicted effects on pending suits involving NIH grants, see "Legal" section under "Programs" on the ORI web site.

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INSTITUTIONAL COMPLIANCE CONFERENCE SLATED FOR MAY 2001

ORI expects to co-sponsor a national meeting with the Johns Hopkins University (JHU) School of Medicine on creating effective research compliance programs within academic institutions in Baltimore, MD, May 6-8, 2001.

The conference is expected to cover issues such as training in the responsible conduct of research, use of human subjects in research, managing possible conflicts of interest, managing a research integrity program, and the use of animals in research. A committee of Federal and JHU officials will be meeting this fall to prepare the conference agenda.

For further information, contact Julie Gottlieb, Senior Dir., Office of Policy Coordination, JHU School of Medicine, Phone 410-955-9545; Fax 410-955-3890.

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PHYSICIAN HEADS NEW OFFICE FOR HUMAN RESEARCH PROTECTIONS

Greg Koski, Ph.D., M.D., became director this month of the new Office for Human Research Protections (OHRP), which is located in the Office of Public Health and Science that is headed by the Assistant Secretary for Health and Surgeon General. OHRP replaces the Office for Protection from Research Risks.

Dr. Koski previously was an associate professor of anesthesia at the Harvard Medical School and director of human research affairs at Partners HealthCare System, Inc., in Boston. Dr. Koski and OHRP plan to work with NIH and FDA on a variety of new initiatives for protection of patients and research subjects. These initiatives include:

- Efforts to educate IRB members and staff and clinical investigators about protection of patients and research subjects;
- New guidance and procedures on informed consent for research participants;
- Improved safety monitoring by investigators, FDA, and sponsors so problems can be detected early and corrected; and
- Clarification of policies on conflicts of interest affecting researchers and institutions.

ORI expects to collaborate with OHRP in developing ORI's education and research integrity program.

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NEW REQUIREMENT FOR HUMAN SUBJECTS RESEARCH

Beginning October 1, 2000, NIH will require education for all investigators submitting applications for grants or contracts, or receiving noncompetitive awards for research involving human subjects. Before awards are made, investigators will need to provide a description of the education completed by each of the key personnel identified in the proposed research. The information is to be submitted with other requirements, according to Just-in-Time procedures. See **http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html**.

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SELF-INSTRUCTION BOOKLET BEING DEVELOPED FOR RESPONSIBLE CONDUCT OF RESEARCH

A self-instruction booklet designed to meet the minimal training requirement on the

responsible conduct of research (RCR) for individuals supported by PHS research or research training funds will be developed by next spring with support from ORI.

"The booklet will provide immediate assistance to small and mid-sized institutions with no current RCR capabilities," Chris Pascal, Director, ORI, said. "But, the booklet could be used at any institution. Institutions, however, may provide more detailed and intensive training in their effort to foster integrity in their research environments."

Pascal continued, "ORI also is exploring funding possibilities for the development of investigator-initiated web-based resources, CD-ROMs, videotapes, teleconferences, and other resources to facilitate RCR training."

An RCR web site developed with support from ORI is expected to go online this year. ORI also is planning to hold a series of regional workshops in 2001 to promote a collaborative approach to the implementation of the RCR requirement.

The booklet is expected to be developed by Michael Kalichman, Director, Research Ethics Program, UC-San Diego, with the assistance of an advisory board composed of:

- Stephanie Bird, Special Assistant, Provost's Office, M. I. T., and Editor, *Science and Engineering Ethics*;

- Susan Eastwood, Principal Analyst, Publication, UC-San Francisco, and Past President of Council of Biology Editors;

- Paul Friedman, Professor of Radiology, UC-San Diego, and member of the IOM Committee for the Study on the Responsible Conduct of Research;

- Stanley Korenman, Associate Dean for Ethics and Medical Scientist Training, UCLA Medical Center, and co-author of *Teaching the Responsible Conduct of Research through a Case Study Approach*;

- Marky Pitts, Director, Animal Subject Program, UC-San Diego, and co-organizer of IACUC 101 course for PRIM&R; and

- Ada Sue Selwitz, Office of Research Integrity, University of Kentucky, and organizer of IRB 101 course for PRIM&R.

The booklet is designed to cover each of the core instructional areas that will be listed in the final RCR policy scheduled to be announced this year. Besides the text, each unit will contain exercises, resources, and a test. Core topics currently under consideration are:

- Data acquisition, management, sharing, and ownership.
- Mentor/trainee responsibilities
- Publication practices and responsible authorship
- Peer review
- Collaborative science
- Human subjects
- Research involving animals
- Research misconduct
- Conflict of interest and commitment
- Compliance with existing PHS and institutional policies

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ETHICS COURSE

October 12-14, 2000 "Extreme Ethics: Unusually Difficult Challenges in Epidemiology and Human Subjects Research," will be held on Oct. 12-14 in Miami, FL. The NIH-sponsored short course will feature review and discussion of issues for which standard models of valid consent and scientific practice may be inadequate. A limited number of scholarships are available to minority students. For more information, please contact University of Miami Ethics Programs at 305-243-5723, ethics@miami.edu or **http://www.miami.edu/ethics** and click on "Bioethics" Programs.

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WHEN INSTITUTIONS MISTAKENLY REPORT "ADMISSIONS" TO ORI

ORI has found that failure to follow an appropriate investigation process led to reaching incorrect conclusions in two different cases during the past year. In one case, institutional officials informed ORI that they were closing the case because the respondent had made an "admission" of scientific misconduct. In another case, officials said they were closing the case because a former employee was probably responsible for the alleged misconduct.

In these cases, initial conclusions by research staff, principal investigators (PIs), and/or institutional officials that the respondents had made "admissions" or were "responsible for misconduct" were largely undocumented and ultimately were found to be unsupportable. In each case, ORI asked the institutions to provide a more formal investigative process to address the questions raised during ORI's oversight review.

To concur with an institution's finding of scientific misconduct, and decide that no further investigation is necessary with an "admission," ORI not only needs a well-documented (preferably written or transcribed) admission containing language such as "I falsified results" or "I admit to scientific misconduct," but also sufficient substantive evidence to support the admission. In addition, the PHS regulation requires that the respondent be

notified of the allegations and findings and be allowed to respond to them, or to waive that opportunity under the institution's policies for investigations.

Case 1

A research manager for a behavioral research study found discrepancies in records by a staff interviewer. The manager checked with a few of the research subjects, who said they did not remember getting any calls in the past year. When the principal investigator (PI) confronted the interviewer, he denied any wrongdoing and subsequently resigned without explanation. The institutional officials then notified ORI that the interviewer had "committed" scientific misconduct.

As part of its oversight process, however, ORI required the institution to notify the respondent of the proposed findings and offer him the opportunity for an interview with an inquiry committee. During the respondent's interview, he again denied any falsification of data, stating that he had called the subjects from home, as allowed by the protocol. The respondent told the committee that he had resigned simply because he thought the PI no longer trusted him. The committee ultimately found there was insufficient documentary evidence to warrant an investigation or a finding of scientific misconduct.

Case 2

An institution investigated allegations that a PI had falsified research records in a clinical trial. The committee exonerated the PI, but its report found the nurse coordinator to be the most likely person responsible for the discrepancies (possible falsifications) between the primary records and those sent to the trial's data coordinating center. However, the institution had closed the case without contacting the nurse coordinator, who had left the institution.

ORI required the institution to open a new investigation with the nurse coordinator as respondent in this case. While the nurse coordinator was not available for an interview, she provided written comments. After interviewing several witnesses and reviewing the records, the new investigation committee found one change in the data was not significant. For the other discrepancies, the committee found insufficient evidence that the respondent had changed the records. Thus, the institution made no finding of misconduct in this case.

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SES JOB VACANCY

The Office of the General Counsel, HHS, has announced a vacancy for the NIH Legal Advisor as a Senior Executive Service position. The vacancy announcement closes

October 10, 2000. For more information, phone Richard Riseberg, Chief Counsel for the Public Health Service, at 301-443-2644.

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INQUIRY VERSUS INVESTIGATION STAGES IN SCIENTIFIC MISCONDUCT CASES

When examining allegations of scientific misconduct, institutions have an obligation to conduct an initial inquiry, and, if warranted, a thorough investigation in accordance with Public Health Service (PHS) standards. 42 C.F.R. Part 50, Subpart A. This article discusses some procedural and substantive considerations in examining allegations of scientific misconduct in inquiries and investigations.

After receiving a good faith allegation of scientific misconduct, an institution will usually open an inquiry to gather general information and make initial findings of fact to determine whether the allegation has substance and there is sufficient evidence to warrant an investigation. Sometimes, however, when there is sufficient evidence already at hand, for example as the result of an audit of a clinical trial, the institution may move directly to the investigation stage. If the inquiry uncovers evidence of "fabrication, falsification or other practices that seriously deviate from those that are commonly accepted within the scientific community," the institution should move quickly to a full investigation. See 42 C.F.R. § 50.102. In general, absent full admissions, inquiries should not be used to make findings on whether scientific misconduct itself has occurred.

On occasion, ORI receives an inquiry report in which either the committee has conducted the equivalent of an investigation and made specific findings or which is obviously the result of a negotiated agreement. These reports may violate the PHS regulation and cause substantial difficulties for ORI's oversight. Findings made at the inquiry stage are all too frequently incomplete because the record has not been fully developed, and negotiated agreements violate the PHS regulation, if made without ORI's advance approval. Both instances may deprive ORI of the facts necessary to determine whether there has been an adverse effect on the PHS sponsored research, and the institution may need to reopen its case and initiate an investigation.

Instead of short circuiting the process, once an institution has determined that there is some evidence of possible misconduct, a thorough investigation should be conducted to analyze "all documentation, including but not necessarily limited to relevant research data and proposals, publications, correspondence, and memoranda of telephone calls." 42 C.F.R. §50.103. Only after this process is complete should the investigation committee turn to an analysis of whether the charges meet the burden of proof under the PHS definition of scientific misconduct.

Even if the record is relatively complete at the inquiry stage, the PHS regulation normally gives respondents the opportunity to have a full investigation before any findings are made against them. Most institutional policies have this same requirement. This multiple stage process has also been endorsed by the Federal Office of Science and Technology Policy which has stated that the investigation is "the formal examination and evaluation of the relevant facts leading either to dismissal of the case or a recommendation for a finding of research misconduct." Proposed Federal Policy on Research Misconduct To Protect the Integrity of the Research Record, 64 Fed. Reg. 55722, 55724 (Oct. 14, 1999).

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NIH ANNOUNCES STREAMLINING OF IRB APPROVAL FOR PROPOSALS

Starting with the June/July 2000 proposal receipt date, NIH no longer requires institutions to obtain Institutional Review Board (IRB) approval for research involving human subjects before peer review of an application by NIH. The NIH study section will consider whether the application includes appropriate protections for human subjects as part of its review process. This policy change gives institutions flexibility in deferring IRB review until after peer review.

Until now, applications submitted to NIH involving human subjects research were required to have IRB approval at submission, or within 60 days after receipt.

Although NIH no longer requires IRB review prior to application submission, an institution may require it, or may determine that certain types of research or mechanisms should receive IRB review at the institution before the application is submitted to NIH. No NIH award will be made without IRB approval. After review, if an application is within the support range, the institution should see that the IRB review is conducted and IRB approval submitted in a timely fashion.

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ORI CONTINUES IMPROVING CASE MANAGEMENT IN 1999

According to the ORI *Annual Report - 1999* published last month, ORI opened 30 new cases in 1999 and closed 33 cases. At the end of the calendar year, 32 cases remained open. Thirteen of the thirty-three closed cases resulted in sustained findings of scientific misconduct. Historically, ORI has made a finding of misconduct in about one third of its cases.

ORI continues reducing its backlog of older cases. During 1999, there were 13 cases that had been open for over 2 years. As of December 1999, there were just five such cases. ORI offered Rapid Response Technical Assistance on four cases, and two were accepted by novice institutions for assistance with sequestration of evidence or

investigative strategy.

In 1999, 10 cases were closed in less than 6 months, 16 cases were closed within 6 to 12 months and 7 cases were closed after more than 12 months. The average processing time for misconduct cases was 14.2 months, and the average processing time for no misconduct cases was 6.2 months. Seventy-nine percent of all cases were closed within 12 months, which approximated ORI's goal for the year, closure of 80 percent of cases within 12 months.

Copies of the report are available upon request or from ORI's web site **http://ori.dhhs.gov**.

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NEW, EASY ORI WEB SITE ACCESS

Visitors to the new, redesigned ORI web site that will go on-line this month should find it easier to access the information they seek because numerous routes have been built into the home page to quickly identify the location of the desired information.

Five buttons at the top of the home page access information **about ORI** including its mission, history, professional staff, and contact numbers; provide the latest **news**; allow **searches**; present a **site map**, and permit a return to the **home** page from anywhere in the site.

Four additional buttons along the left side of the page address the process for **handling misconduct**, describe ORI **programs**, list **publications** available from ORI, and identify additional **resources**. Each of these buttons have drop-down menus that further specify the content of the category.

In addition, the home page text provides direct links to information on 18 topics that frequently draw individuals to the web site.

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CONFERENCE PROPOSALS DUE FEBRUARY 1

ORI is seeking proposals from institutions, professional associations, and scientific societies that wish to collaborate with ORI in developing a conference or workshop on promoting research integrity or handling scientific misconduct allegations. The available funding generally ranges from $5,000 to $20,000. ORI intends to hold four to six regional conferences or workshops each year in strategic locations around the country.

February 1, 2001, is the next target date for receipt of applications. Instructions and an

application form are available on ORI's web site (http://ori.dhhs.gov), by calling 301-443-5300, or by e-mail to **requests@osophs.dhhs.gov**.
For questions about the application process, to discuss a possible proposal, or to work with ORI staff in planning an event, contact Dr. Dustira at ORI.

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ORI DIRECTOR CHOSEN AND OTHER SENIOR APPOINTMENTS MADE

Chris B. Pascal, J. D., Acting Director, ORI, for more than 4 years, was appointed Director, ORI, by the Dr. David Satcher, Assistant Secretary for Health and Surgeon General (ASH/SG) on August 14, 2000, following a national search that produced 17 candidates.

Following his appointment, Mr. Pascal named Alan R. Price, Ph.D., as the Director, Division of Investigative Oversight (DIO), and Barbara Williams, Ph.D., as Deputy Director, DIO. Each held their respective positions in an acting capacity since May 1999.

In addition, Mr. Pascal named Dr. Price and Lawrence J. Rhoades, Ph.D., Director, Division of Education and Integrity (DEI), as Associate Directors, ORI.

In announcing his selection, Dr. Satcher said Mr. Pascal "has extensive knowledge of the challenges and opportunities facing the Public Health Service and the research community in promoting research integrity and ensuring public confidence in the results of the scientific enterprise."

Dr. Satcher continued, "During his tenure as Acting Director, ORI evolved from an office almost solely focused on scientific misconduct to an office with a much broader mission of education in the responsible conduct of research, prevention of misconduct, research on research integrity issues, and the promotion of research integrity in collaboration with the PHS agencies, research institutions, and the scientific community."

Mr. Pascal served ORI since 1992 as Chief, Research Integrity Branch, OGC, and later as Director, Division of Research Investigations. Previously, he was Legal Advisor to the Alcohol, Drug Abuse, and Mental Health Administration.

Dr. Price served as Chief, Investigations Branch A, ORI, since 1992. Prior to joining the Office of Scientific Integrity (OSI) in 1989 where he was a senior scientist and assistant director, Dr. Price worked as the AIDS Unit Assurance Coordinator in the Office for Protection from Research Risks and as a program officer for genetics in the National Institute on Aging. Before joining the government, Dr. Price was associate professor of biological chemistry and Assistant Vice President, University of Michigan.

Dr. Williams served as Chief, Investigations Branch B, ORI, since 1992. Before joining the OSI in 1989 as a senior scientist, she was a staff fellow at the National Institute of Dental Research and an extramural program officer in the genetics program at the National Institute of General Medical Sciences. Before entering the government, Dr. Williams was a fellow in medical genetics at Johns Hopkins University.

Dr. Rhoades has served as Director, DEI, since January 1993. Previously he was the Deputy Director of the Office of Scientific Integrity Review. From 1981-89, Dr. Rhoades held various research policy, planning, and evaluation positions at the National Institute of Mental Health. Before joining the government, he served as an executive associate at the American Sociological Association and an assistant professor of sociology at North Carolina State University.

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COMMON FEDERAL DEFINITION AND POLICY

The Office of Science and Technology Policy (OSTP) is reviewing all the comments received in response to its proposed common Federal definition of research misconduct and procedures for responding to misconduct allegations that were published for public comment last fall. "Proposed Federal Policy on Research Misconduct To Protect the Integrity of the Research Record," 64 Fed. Reg. 55722, 55724 (Oct. 14, 1999). ORI supports this effort to bring the Federal agencies together and to develop a common definition.

However, until OSTP has finalized the common policy and definition and the U.S. Department of Health and Human Services formally adopts them by amending its regulation, ORI and institutions must continue to use the current regulation and definition at 42 C.F.R. Part 50, Subpart A.

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CASE SUMMARIES

Lingxun Duan, M.D., Thomas Jefferson University (TJU): In a case related to a Global Settlement Agreement in a *qui tam* suit between the United States and TJU, and based on an oversight review conducted by the Office of Research Integrity (ORI), the U.S. Public Health Service (PHS) entered into a Voluntary Exclusion Agreement with Dr. Duan, former Research Assistant Professor of Medicine, Division of Infectious Diseases, Department of Medicine, TJU. The PHS alleged that Dr. Duan engaged in scientific misconduct by reporting research that was inconsistent with original data or could not be supported because original data were not retained. Dr. Duan denied all allegations of scientific misconduct and contended that some of his original data is missing. The research in question was supported by a National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), grant, R01 AI36552,

entitled "Intracellular antibodies and HIV 1." Specifically, the research in question was reported in an NIAID, NIH, grant application; in an FDA-approved phase I gene therapy investigational new drug (IND) application entitled "Intracellular immunization against HIV-1 infection using an anti-rev single chain variable fragment (SFV);" and in two publications: (1) Duan, L., Bagasra, O., Laughlin, M.A., Oakes, J.W., & Pomerantz, R.J., "Potent inhibition of human immunodeficiency virus type I replication by an intracellular anti-Rev single chain antibody," *Proc. Natl. Acad. Sci*. USA 91:5075-5079, 1994; and (2) Levy-Mintz, P., Duan, L., Zhang, H., Hu, B., Dornadula, G., Zhu, M., Kulkosky, J., Bizub-Bender, D., Skalka, A.M., and Pomerantz, R.J., "Intracellular expression of single-chain variable fragments to inhibit early stages of the viral life cycle by targeting human immunodeficiency virus type 1 integrase," *J. Virol*. 70:8821-8823, 1996.

Under the terms of the Agreement, Dr. Duan voluntarily agreed, beginning June 7, 2000: (1) to exclude himself from any contracting, subcontracting, or involvement in grants and cooperative agreements with the U.S. Government for a period of 2 years; (2) that for 1 year after the conclusion of the voluntary exclusion period, his participation in any PHS-funded research is subject to supervision requirements; and (3) to exclude himself from serving in any advisory capacity to PHS, for a period of 2 years. Dr. Duan also agreed that he will not oppose the submission to journals of a statement summarizing the current state of the science with respect to the scientific matters at issue relating to grant R01 AI36552, which was jointly agreed to by TJU and the United States in the Global Settlement Agreement.

Mr. Jin Qian, New Dimensions Research and Instrument, Inc. (NDRI): Based on an investigation by ORI, the PHS made a final finding of scientific misconduct against Mr. Qian, Executive Manager for Corporate Planning and Research, NDRI. Mr. Qian committed scientific misconduct by plagiarizing research results and text from other investigators in an application to the National Institute of Neurological Disorders and Stroke (NINDS), NIH, for a Small Business Innovation Research award, "Glass-based neurochip system," 1 R43 NS39266-01. Specifically, based on ORI's analysis, the PHS found that Mr. Qian: (1) used research images and descriptions posted on the Internet to create seven figures in the application and used that material, its associated text, and text from other publications obtained from the Internet without attribution; (2) misrepresented research results in two of the plagiarized figures as exemplar applications of NDRI's proprietary technology; and (3) misrepresented his research bibliography in that application and to ORI staff during the investigation. These actions constitute falsification in proposing research because their collective effect was to falsify the basis on which NIH reviewers determine whether NDRI could achieve the goals of the proposed project.

Mr. Qian accepted the PHS finding and entered into a Voluntary Exclusion Agreement with PHS in which he has voluntarily agreed for a 3-year period, beginning June 12,

2000, to exclude himself from any Federal grants, cooperative agreements, and from serving in any advisory capacity to PHS.

William A. Simmons, Ph.D., University of Texas Southwestern Medical Center (UTSW): Based on a report of an investigation by UTSW, and extensive additional analysis conducted by ORI during its oversight review, the PHS made a final finding of scientific misconduct against Dr. Simmons. The PHS found that he engaged in scientific misconduct by falsifying research supported by NIH grants R01 DK47692, R01 AR38319, R01 AI42860, P01 AR09989, and T32 CA9082. While he was a graduate student and postdoctoral fellow at UTSW, Dr. Simmons manipulated results of cytotoxic T-lymphocyte (CTL) assays by adding predetermined amounts of radioactivity to scintillation counting vials rather than carrying out the assays as claimed. As a result of falsifying these assays over a minimum of 5 years, none of Dr. Simmons' research can be considered reliable and the publications identified below have been, or soon will be, retracted or corrected. The falsified research was also reported in the 1 R01 AI42860-01 grant application ("A new MHC locus influencing class I peptide display"). Additionally, Dr. Simmons was responsible for falsifying Figure 3 published in *J. Immunol*. 159:2750-2759, 1997 (see below), by substituting preparations of chemically synthesized oligopeptide for natural peptides obtained from T cells isolated from B27 transgenic rats. These actions adversely and materially affected the laboratory's ongoing research into the role that human histocompatibility leukocyte antigens play in the development of disease.

Publications affected:

- Simmons, W.A, Summerfield, S.G., Roopenian, D.C., Slaughter, C.A., Suberi, A.R., Gaskell, S.J., Bordoli, R.S., Hoyes, J., Moomaw, C.R., Colbert, R.A., Leong, L.Y., Butcher, C.W., Hammer, R.E., and Taurog, J.D. "Novel HY peptide antigens presented by HLA-B27," *J. Immunol*. 159:2750-2759, 1997 (being retracted).

- Simmons, W.A., Leong, L.Y., Satumtira, N, Butcher, G.W., Howard, J.C., Richardson, J.A., Slaugher, C.A., Hammer, R.F., and Taurog, J.D. "Rat MHC-linked peptide transporter alleles strongly influence peptide binding by HLA-B27 but not B27-associated inflammatory disease," *J. Immunol*. 156:1661-1667, 1996 (being retracted).

- Simmons, W.A., Roopenian, D.C., Summerfield, S.G., Jones, R.C., Galocha, B., Christianson, G.J., Maika, S.D., Zhou, M., Gaskell, S.J., Bordoli, R.S., Ploegh, H.L., Slaughter, C.A., Lindahl, K.F., Hammer, R.E., and Taurog, J.D. "A new MHC locus that influences class I peptide presentation," *Immunity* 7:641-651, 1997 (retracted).

- Simmons, W.A., Taurog, J.D., Hammer, R.E., and Breban, M., "Sharing of an HLA-B27-restricted H-Y antigen between rat and mouse," *Immunogenetics* 38:351-358, 1993 (retracted).
- Zhou, M., Sayad, A, Simmons, W.A., Jones, R.C., Maika, S.D., Satumtira, N., Dorris, M.L., Gaskell, S.J., Bordoli, R.S., Sartor, R.B, Slaughter, C.A., Richardson, J.A., Hammer, R.F, and Taurog, J.D. "The specificity of peptides bound to human histocompatibility leukocyte antigen (HLA)-B27 influences the prevalence of arthritis in HLA-B27 transgenic rats," *J. Exp. Med*. 188:877-886, 1998 (published erratum).

Dr. Simmons entered into a Voluntary Exclusion Agreement with PHS in which he voluntarily agreed, for the 5-year period beginning August 22, 2000, to exclude himself from any contracting or subcontracting and from nonprocurement transactions with the United States Government, and to exclude himself from serving in any advisory capacity to PHS.

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NIH PUBLISHES ADDITIONAL GUIDANCE FOR MANAGING CONFLICTS OF INTEREST

Because of some recently highly publicized cases and the potential threats they can pose to the integrity of research, NIH issued an announcement on June 5, 2000, that provided institutions with some additional points to consider when reviewing potential financial conflicts of interest.

The notice encouraged Institutional Review Boards (IRBs) to consult their own institutional policies and procedures for identifying and managing conflicts of interest. To deal with the potential that financial holdings might interfere with objectivity in research, specific examples of approaches used by IRBs to identify and respond to perceived conflicts of interest were described in the notice. These approaches were: (1) including a statement in the informed consent form that all clinical investigators comply with institutional guidelines on conflict of interest; (2) asking investigators to complete a short questionnaire about whether anyone on the project has economic or financial interests that might be affected by the research; and (3) instructing IRB members about identifying and responding to perceived financial, academic or other conflict of interest.

The full text of the notice is at:
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-040.html. The conflict of interest regulation promulgated in 1995 is at
http://grants.nih.gov/grants/guide/notice-files/not95-179.html.

The roles of investigators and IRBs in this process were also considered during a public

consultation process held at NIH on August 15-16, 2000.

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WORKSHOP FOR NEW INVESTIGATORS

ORI expects to co-sponsor a national meeting with the American Speech-Language-Hearing Association (ASHA) on the responsible conduct of research in 2001. Tentatively titled "Promoting Research Integrity in Communication Sciences and Disorders and Related Disciplines," the workshop will focus on educating advanced doctoral students, post-doctoral fellows, junior faculty and others in the early stages of their research careers.

For more information, visit the ORI web site, **http://ori.dhhs.gov** and click on Upcoming Conferences and Workshops.

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GERMAN MISCONDUCT CASE ADDING RESPONDENTS

A research misconduct case that began in 1997 with allegations against a well-known and decorated member of the German research establishment and a colleague has expanded to include the department chief and four other co-authors, according to published reports.

A recently-completed 2-year investigation of 347 scientific articles authored by Friedhelm Herrmann, former hematologist and cancer researcher, found that 52 articles "contained falsifications"; 42 contained suspected data; and 121 were placed in a "grey category" because the investigators could not get access to original data. The remaining 132 papers are deemed valid. Of the 94 suspected papers, 53 were published with his accused colleague, Marion Brach.

The investigation, jointly sponsored by Germany's main granting agency and its largest cancer charity, was expanded to cover three of Herrmann's most frequent co-authors besides Brach, all of whom were in the same department. The investigation examined over 600 articles published by the quintet.

The department chief said he was only an honorary author on the 59 suspected articles that contain his name. An examination of a paper published by the department chief without Herrmann, however, indicated many "irregularities and indications that data had been improperly handled." Two researchers who were co-authors on that paper were added to the investigation.

Evidence of improper data manipulation has also been found in three habilitations, the uniquely German post-Ph.D. qualification for aspiring professors, submitted by three of

Herrmann's frequent co-authors, including Brach.

Four universities and a research center have conducted investigations into the case. In June, the university where Herrmann and four of his co-authors worked reactivated its fraud panel to investigate the department that employed the respondents. Both funding sources are considering legal action to recover research funds.

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ORI ACCEPTS 298 INSTITUTIONAL POLICIES DURING 1999

According to the *ORI Annual Report - 1999* published last month, ORI processed a total of 374 institutional policies during 1999, closing 258 reviews and carrying 116 into 2000. ORI requests copies of institutional policies, and reviews whether they comply with the PHS regulation. The closed reviews included 225 accepted policies and 33 inactivated assurances because policies were not submitted. Of the 116 open reviews, 78 required institutional action, such as modification of the existing policy. A total of 1,279 reviews have been completed since ORI began its systematic policy review in 1996.

In 1999, ORI also completed a study of the policies and procedures created by parent institutions and their affiliates to determine whether viable systems for responding to allegations of scientific misconduct exist. The report analyzed the assurances of 251 institutions in 73 parent/affiliate units composed of 73 parents and 178 affiliates to determine whether (1) the parent policy complied with the regulation, (2) the affiliate policy (if different than parent) complied with the regulation, (3) the parent policy acknowledged responsibility for responding to allegations at the affiliates, and (4) the affiliates accepted the parent policy. The study found that only 10 of the 73 units (14%) initially met all 4 of these criteria. After requesting that their policies be modified or other appropriate actions be taken, all 73 units met the 4 criteria by the end of the study.

Copies of the *ORI Annual Report - 1999* are available by request or from **http://ori.dhhs.gov**.

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IMPROVED DATA SAFETY MONITORING FOR EARLY CLINICAL TRIALS ANNOUNCED

NIH recently announced a new policy that requires a data safety monitoring plan, but not necessarily an independent Data Safety Monitoring Board for Phase I and Phase II clinical trials. The nature of the monitoring can vary depending on the trial.

- The NIH policy is that for Phase I and II clinical trials, investigators must submit a description of the data safety and monitoring plan as part of the research application.

- The plan will be reviewed by the NIH study section. Comments and concerns about the plan will be included as an administrative note in the summary statement.

- After review but before the trial begins, a detailed monitoring plan must be included as part of the protocol and it must be submitted to the Institutional Review Board (IRB) and to the funding NIH institute or center before the trial starts. The detailed plan must describe how adverse events will be reported to the IRB, FDA and NIH.

- Each NIH institute/center must have a system for overseeing and monitoring the conduct of clinical trials for safety of participants and validity and integrity of data.

- The funding institute/center must be informed of recommendations resulting from monitoring activities.

For multi-site Phase I and II trials, it is expected that investigators will organize a central reporting group that will prepare timely reports of adverse events, if any, and distribute the reports to all sites and IRBs.

NIH guidance for reporting adverse events for multi-site clinical trials can be seen at **http://grants.nih.gov/grants/guide/notice-files/not99-107.html**.

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SAVE THIS DATE

March 1-4, 2001

ORI is negotiating with a contractor to hold a national conference in the DC area on the new Federal requirements for education in the responsible conduct of research. ORI expects to follow this conference with a series of regional meetings around the U.S.

More information will be posted on the ORI web site as it becomes available.

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