

ORI NEWSLETTER

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ORI WEB PAGE REDESIGNED, REORGANIZED AND EXPANDED

A redesigned, reorganized and expanded ORI web page that is user-friendly and attractive was posted July 27 at <http://ori.dhhs.gov> to facilitate your access to information about scientific misconduct and research integrity.

The new format organizes the information in 10 sections: What's New, ORI Forms, Introduction to ORI, ORI Workshops and Conferences, ORI Publications, Regulations and Guidelines, Whistleblower Issues, Additional ORI Resources: Facts and Stats, PHS Administrative Actions, and Other Links.

"There is more information on the page and it is easier to find," Chris Pascal, Acting Director, ORI, said. "We intend to install a search engine to facilitate finding the information of interest and experiment with the format for presenting documents to permit faster retrieval of specific information. Eventually, we hope to make almost all documents accessible on line so that you do not have to download a document to see it."

The latest information on the page is posted under **What's New** before it is transferred to one of the other sections. The mission and organization of ORI, addresses and phone numbers, issues, and frequently asked questions are presented in **Introduction to ORI**.

The **PHS Administrative Actions** provides easy access to the bulletin board that lists the respondents who currently have PHS administrative actions imposed upon them for scientific misconduct. The *ORI Handbook for Institutional Research Integrity Officers* can be found in **Regulations and Guidelines** where Departmental Appeals Board decisions also are presented. The remaining sections are largely self-explanatory.

"The most underdeveloped section at this point is **Additional ORI Resources: Facts and Stats**," Pascal said. "We are developing some stats from the Annual Report of Possible Research Misconduct for that section. In addition, we are developing a report on investigations closed by ORI from 1993-1997 that will use the statistical profiles published in the ORI annual reports."

Pascal continued, "This is a work in progress. We would like to hear your suggestions for building the content of the page so that it is useful for researchers, teachers, administrators, institutional research integrity officers, respondents, whistleblowers, members of inquiry/investigation committees and others who have a stake in detecting, reporting, investigating, or preventing scientific misconduct or in promoting research integrity and the responsible conduct of research."

HOUSTON CONFERENCE TO EXAMINE RESEARCH ETHICS AND ACCOUNTABILITY

ORI is co-sponsoring a conference on March 11-12, 1999, with the University of Texas-Houston Health Science Center (UT-Houston) on "Research Integrity: A Professional, Ethical, and Social Obligation." The conference will focus on shared accountability among members of the scientific community and the general public. Additional co-sponsors include the University of Houston, Prairie View A&M University, Texas Southern University, and Texas Woman's University-Houston Center.

"This is part of a new series of conferences that ORI plans to co-sponsor with research institutions," said Chris Pascal, Acting Director, ORI. (For information on the next cycle of proposal deadlines, see page 8.)

The first day of the conference will discuss *scientific* community accountabilities, *i.e.*, the professional view of the ethical-social contract among researchers. Topics include PHS perspectives on research integrity, the roots and origins of scientific integrity, self-deception in research, ethics of authorship and publication, and ethics of randomized clinical trials.

The second day of the conference will specifically address *public* accountabilities for biomedical science, *i.e.*, the public or political view of the ethical-social contract with society. Topics include the public view of biomedical research, setting the biomedical research agenda, and industry sponsorship of research.

Speakers for the conference will include nationally-known research, industry, and public media experts from the Houston metropolitan area, ORI, NIH, NASA, and the mass media.

UT-Houston is located in the Texas Medical Center, the world's largest medical campus dedicated to the mission of biomedical research, education and patient care. The early-bird registration fee is \$100; after February 15, 1999, the registration fee will be \$150. Faculty, staff, and students from sponsoring institutions may register for \$50 before February 15th. Attendance is limited to 200 participants.

For more information about the conference, call the University of Texas-Houston Health Science Center at (713) 500-2028.

NEEDED CORRECTIONS VARY IN MISCONDUCT CASES

Two similar cases closed by ORI in 1997 demonstrated the need to consider all the forms of research reporting that must be corrected or retracted after a finding of scientific misconduct. In both cases, graduate students fabricated or falsified data related to their thesis research that required the retraction of multiple scientific publications (five original research articles and two review articles in one case; three research articles in the other case). In addition, both cases required the retraction of nucleotide sequences submitted to a national database, GenBank, which is maintained by the National Library of Medicine, NIH. In the second case, four sequences had been submitted both to GenBank and the European Molecular Biological Laboratory (EMBL) database. These cases were reported in the *ORI Annual Report - 1997* issued this month.

Research Integrity/Misconduct Conference or Workshop Proposals

Due February 1, 1999

Application Form and Instructions Available at <http://ori.dhhs.gov>

ORI ISSUES ANNUAL REPORT; REDUCES CASELOAD AGAIN IN 1997

In 1997, ORI reduced its active caseload to an all-time low of 35 open cases. Only six of these cases predate 1996. Of those six, one is pending before the Departmental Appeals Board, one is suspended pending final action by the Department of Justice, one is still under review by the institution, and two were in prelitigation review by OGC at the end of the year.

These are some of the facts published in the *ORI Annual Report - 1997* that was distributed in August to all institutions, except small businesses, that have an active assurance on file with ORI.

The report also discusses how ORI reactivated and restructured its conference and workshop program in 1997. A total of five workshops were held, and two of the extramural workshops were co-sponsored by the University of Florida and Tuskegee University. The program solicited institutional co-sponsors for the first time and added the promotion of research integrity and the prevention of scientific misconduct to the previous program goals-facilitating the handling of allegations of scientific misconduct and compliance with the PHS regulation. ORI staff gave a total of 46 presentations during the year, at the workshops it co-sponsored, as well as in response to invitations from outside organizations.

The annual report includes standard features such as summaries of all ORI cases, both misconduct and no misconduct, a description of ORI educational activities, and a statement of activities at the institutional level. It also includes a summary of scientific misconduct-related litigation handled by ORI (14 cases) and a summary of compliance and retaliation cases closed

in 1997 (11 cases).

The report also discusses major Federal policy issues such as a respondent filing a liability suit against an institution, various institutional officials, and several fact witnesses, including the whistleblower. The respondent is seeking damages on various grounds surrounding his employment dismissal.

STUDY OF INQUIRY REPORTS FINDS MAJOR DEFICIENCIES

A study of institutional inquiry reports not submitted to ORI for review because an investigation was not recommended found that more than half of the reports did not contain the detailed information required to support that recommendation.

The content analysis conducted by ORI was limited to the information contained in the reports. Additional information supporting the decision that an investigation was unwarranted may exist in other documents in the institutional file that were not submitted.

The study reviewed reports on 21 inquiries that were reported by institutions in their 1994 or 1995 Annual Report on Possible Research Misconduct. Because these inquiries did not proceed to an investigation, ORI did not previously request the reports and the institutions did not voluntarily submit them.

The study addressed the following questions: (1) Were the inquiries being reported by institutions on the Annual Report subject to PHS jurisdiction? (2) Did the institutions sufficiently document the rationale for deciding an investigation was unwarranted? (3) Did the conduct of the inquiries comply with the PHS regulation?

Twelve of the 21 inquiry reports (57%) did not contain allegations that fell under the PHS definition of scientific misconduct and/or did not document PHS support.

Thirty-three percent of the inquiry reports contained information on no more than four of the nine criteria used to determine whether an investigation was warranted and another 28 percent were marginal, covering only five criteria. Fifty-two percent of the reports did not contain a reasoned analysis that linked the evidence to the conclusion.

Seventy-one percent provided information on only three or fewer of the nine regulatory provisions with which institutions are required to comply in the conduct of inquiries.

Fifty-seven percent of the reports did not contain the detailed information required to justify the decision that an investigation was unwarranted. These reports were four pages or fewer; 33 percent of the reports were fewer than two pages. Five reports (24%) were 11 or more pages.

The complete report is available on the ORI home page; click on ORI publications and then on reports and special studies.

ATTORNEY WANTED

ORI is looking for an attorney with a few years experience either in administrative hearings or trial work (as opposed to motion practice) and who is willing to participate in litigation matters, has good writing and communication skills, and has either a background or interest in science and/or health law. The salary range is approximately \$39,270-47,066, depending on experience.

The Research Integrity Branch/Office of the General Counsel has a staff of approximately five attorneys. The Branch represents ORI in administrative hearings, provides legal advice and policy guidance for ORI oversight investigations and programs; acts as liaison to the Justice Department, other Federal departments, and extramural institutions in connection with legal matters; drafts or reviews ORI proposed and final regulations; and gives opinions to the Office of the Secretary on matters within the Branch's expertise.

The position is open until filled.

Contact: Gail Gibbons, ORI, Research Integrity Branch/Office of the General Counsel, 5515 Security Lane, Suite 700, Rockville, MD 20852-5003, (301) 443-3466, FAX: (301) 594-0041; e-mail: ggibbons@osophs.dhhs.gov.

MEETINGS

October 1-3, 1998 "Conference on the Management of Biomedical Research Laboratories" at University of Arizona in Tucson. Contact Noah Lopez, tel. (520) 626-9060; Fax (520) 621-3269; e-mail: noahl@u.arizona.edu.

November 8-9, 1998 "IRBs in the Shifting Sands of Public Opinion" at San Diego Paradise Point Resort in California. Contact PRIM&R/ARENA office, tel. (617) 423-4112; email: prmr@aol.com.

November 10, 1998 "IRBs: Motivating for Change" also at San Diego Paradise Point Resort. See above.

INTERNATIONAL CONFERENCE SLATED ON SCIENTIFIC MISCONDUCT

An international conference will be held in Poland on November 16, 1998, to explore the efforts of several countries to respond to scientific misconduct in their basic and clinical research

programs.

Eleven speakers from seven countries will make presentations during the conference, "Scientific Misconduct: An International Perspective," to be held at the Institute of Biocybernetics in Warsaw. The institute is located on the campus shared by The Medical University of Warsaw and the Polish Academy of Sciences.

Presenters will be researchers, administrators, and government officials from Denmark, England, France, Germany, Sweden, Poland, and the U.S. Proceedings will be published in *Science & Engineering Ethics*. The conference, organized by Andrew Gorski, M.D., Rector, The Medical University of Warsaw, is co-sponsored by the Ministry of Health and Human Services, S. Batory Foundation, ASTRA, and Nova Medical AB.

The registration fee is \$100 until October 30, \$150 thereafter. Contact Dr. Gorski by e-mail at agorski@ikp.atm.com.pl or by fax at (4822) 6256264.

E-MAIL NETWORK CREATED FROM ANNUAL REPORT RESPONSES

ORI will begin sending bulletins, announcements, and reminders to the more than 2,300 institutional officials who provided their e-mail address in the 1997 Annual Report on Possible Research Misconduct.

"We appreciate the willingness of institutional officials to give us their e-mail address because the electronic network will substantially expand our ability to communicate with them," Chris Pascal, Acting Director, ORI, said. "The network will give us the capability of communicating rapidly with responsible officials, either individually or en masse, at a lower cost. I urge all institutional officials who have not submitted their e-mail address to do so as soon as possible." Send e-mail message with address to dbrown@osophs.dhhs.gov.

Responses to the 1997 Annual Report indicate that a record number of responding institutions (2,772 or 92%) have established policies for handling allegations of scientific misconduct. Another 107 institutions that reported they did not have policies or they did not answer the pertinent policy question, have policies on file with ORI thereby raising the total to 96 percent. These institutions will be notified that they have policies on file with ORI. Policies were requested from 108 institutions that correctly indicated they did not have a policy or did not answer the policy question.

Four institutions reported conducting investigations in 1997 that were not reported to ORI as required by the PHS regulation. ORI has asked those institutions to submit reports on the investigations.

Only 69 percent of the institutions filed their Annual Report by the March 1 deadline, necessitating a second mailing that produced another 600 Annual Reports, a total return rate of 86 percent by March 31.

Institutional assurances were inactivated for 443 institutions that did not return their Annual Report by March 31, and 77 assurances were voluntarily withdrawn in lieu of submitting the Annual Report. Small businesses accounted for 63 percent of the 520 inactivated assurances, institutions of higher education accounted for 13 percent.

There continues to be a substantial turnover in responsible officials; 421 were new (14%). New addresses were submitted for 199 institutions. Thirty-nine of these made both changes. Forty-five Annual Reports were returned because they were unsigned.

ORI SEEKS STUDENT INTERNS & FACULTY FELLOWS

ORI is seeking undergraduate and graduate students in the biomedical sciences, social sciences, computer science, education and communications to serve as unpaid interns to provide assistance in the development of several projects.

The projects involve computer programming/database management; the preparation of educational materials; the development of the ORI home page; designing conferences and workshops; and conducting studies and literature reviews.

ORI also invites faculty members to serve as unpaid fellows during the summer or while on sabbatical to assist in devising a research agenda and develop a research group or invisible college focused on research integrity and scientific misconduct, establish a fellows program, and the projects listed above.

Prospective interns and fellows should send a résumé and a letter indicating their interests to Dr. Mary Scheetz, Division of Policy and Education, ORI. Phone: 301-443-5300. Fax: 301-443-5351. E-mail: mscheetz@osophs.dhhs.gov.

ASSURANCE MANAGER NAMED

John Butler has been named Assurance Program Manager succeeding Craig Fleischer, who resigned. Butler managed the program during its initial development. Doug Brown, with the assurance program since its inception, is expected to take on additional responsibilities. Butler will continue to serve as the Compliance Program Coordinator, a position he assumed in 1993.

CASE SUMMARIES

Benjamin S. Pender, Medical University of South Carolina (MUSC): Based on a report from MUSC, information obtained by the ORI during its oversight review, and Mr. Pender's own admission, ORI found that Mr. Pender, a former graduate student, Medical Science Training Program, MUSC, engaged in scientific misconduct in biomedical research supported by a grant from the National Institute of General Medical Sciences of NIH. Mr. Pender cooperated with MUSC's investigation.

Specifically, Mr. Pender presented to the MUSC Shock Research Group (1) a blank autoradiographic film, which he represented to be a Northern blot, as evidence that he had conducted an experiment that he had not done, and (2) a photographic slide representing a Western blot analysis that he had falsified by using a computer to duplicate two sets of bands to misrepresent oligonucleotide treatments at different times and by misrepresenting the identities of two bands in one of the sets. He also falsified data from experiments with thromboxane B2 and tumor necrosis factor alpha that were published and distributed in an abstract entitled "Antisense Oligonucleotide to G Protein Inhibits Endotoxin Stimulated Thromboxane (Tx) B2 production" (*Supplement to Shock* 7:20, 1997). This data also was reported as Figure 4 of a submitted, but unpublished and withdrawn, manuscript and in the Progress Report for an NIH grant.

Mr. Pender accepted the ORI finding and entered into a Voluntary Exclusion Agreement with ORI in which he voluntarily agreed, for the 3-year period beginning July 31, 1998, to exclude himself from any Federal grants, contracts or cooperative agreements and to exclude himself from serving in any advisory capacity to the PHS. No scientific publications were required to be corrected and the abstract was withdrawn before presentation.

Terry D. Reisine, Ph.D., University of Pennsylvania (UP): Based on material sent to ORI by UP, and ORI's oversight review, ORI found that Terry D. Reisine, Ph.D., former Professor, Department of Pharmacology, UP, engaged in scientific misconduct in biomedical research supported by PHS grants.

Specifically, ORI finds that Dr. Reisine falsified results related to the measurement of cyclic AMP in cultured, transfected cells by falsely representing in manuscripts and publications the number of experiments conducted, and by falsifying and/or fabricating some of the substantive data presented in those manuscripts and publications. Moreover, ORI found that Dr. Reisine attempted to falsify data by directing members of his laboratory to construct figures and tables with false values in the preparation of manuscripts.

Dr. Reisine entered into a Voluntary Exclusion Agreement with ORI, which is not an admission of liability by Dr. Reisine, and he denies having committed scientific misconduct. Dr. Reisine agreed to exclude himself voluntarily for a period of 3 years beginning June 11, 1998, from any Federal grants, contracts or cooperative agreements and to exclude himself from serving in any

advisory capacity to the PHS.

Additionally, Dr. Reisine agreed to request correction of the following articles:

Kong, H., Raynor, K., Yasuda, K., Moe, S.T., Portoghese, P.S., Bell, G.I., and Reisine, T. "A single residue, aspartic acid 95, in the gamma opioid receptor specifies selective high affinity agonist binding." *J. Biol. Chem.* 268:23055-23058, 1993. The results in Table 1 are stated in the table legend to be based on four experiments with calculated SEM values and Hill coefficients when, in fact, the majority of the listed compounds were tested only once, and Figure 2 data are stated in the figure legend to be the means of three different experiments when, in fact, most of the results were based on a single experiment.

Raynor, K., Kong, H., Hines, J., Kong, G., Benevoc, J., Yasuda, K., Bell, G.I., and Reisine, T. "Molecular mechanisms of agonist-induced desensitization of the cloned mouse kappa opioid receptor." *J. Pharmacol. Exp. Ther.* 270:1381-1386, 1994. The figure legend for Figures 3A, 3C, and 3D claimed that the values shown were the average of three different experiments when, in fact, the results were from only one experiment; the figure legend for Figure 4B claimed that the values shown were the average of four different experiments when, in fact, the results were from only three experiments; Figures 3A, 3C, and 3D each show several levels of adenylyl cyclase inhibition that do not reflect the actual results obtained in duplicate cyclic AMP assays.

Reisine, T., Kong, H., Raynor, K., Yano, H., Takeda, J., Yasuda, K., and Bell, G.I. "Splice variant of the somatostatin receptor 2 subtype, somatostatin receptor 2B, couples to adenylyl cyclase." *Mol. Pharmacol.* 44:1016-1020, 1994. The legend for Figure 3A claims that three experiments were performed when, in fact, only two experiments were performed for the SSTR2B mutants. The legend for Figure 3B claims that the values presented are the average of two different experiments when, in fact, the inhibition curve shown was based on a single experiment.

MEDICAL RESEARCH COUNCIL IN ENGLAND ESTABLISHES MISCONDUCT PROCEDURES

The Medical Research Council (MRC), the major source of support for biomedical research in England, adopted a policy and procedure for inquiring into allegations of scientific misconduct in December 1997 that applies to all employees, students, visiting researchers and fellows working within its establishments and teams.

The MRC policy and procedures are quite similar to the ORI policy and procedures. The similarities include three processing stages: preliminary action, assessment, and formal investigation; sequestration of data, notification to respondent, right to representation for respondent, maintenance of confidentiality, using appropriate expertise, guarding against conflicts-of-interest, challenge to committee members by respondent, preparation of written

reports, comments on reports by respondent, imposition of sanctions when misconduct is found, protection of whistleblowers against retaliation, the restoration of reputations for exonerated individuals, interim administrative actions to protect other employees and research subjects, and right to appeal.

But there are notable differences. MRC defines scientific misconduct as "fabrication, falsification, plagiarism or deception in proposing, carrying out or reporting results of research and deliberate, dangerous or negligent deviations from accepted practices in carrying out research. It includes failure to follow established protocols if this failure results in unreasonable risk or harm to humans, other vertebrates or the environment and facilitating of misconduct in research by collusion in, or concealment of, such actions by others." Also, a respondent will "have access to all material relevant to the allegation and its consideration at assessment, investigation and appeal stages."

The MRC will pursue disciplinary action against individuals who do not make an allegation in good faith, that is, who "recklessly disregard evidence that disproves an allegation." In addition, the MRC "will take action against individuals who victimize complainants" or witnesses.

The appeal process should begin within 20 calendar days after receipt of an appeal of the finding and/or sanctions by the respondent and be completed within 90 calendar days. The appeal "normally will include examination of all documentation called into question by the respondent." In addition, the respondent can provide oral evidence or submit relevant supplementary material.

ORI Introductory Workshop for Institutional Misconduct Officials

Proposed for February 1999

In San Diego, CA. Call Dr. Michael Kalichman at (619)822-2027;

e-mail:kalichman@ucsd.edu.

CALL FOR CONFERENCE PROPOSALS

ORI is seeking proposals from institutions, professional associations and scientific societies to collaborate with ORI in developing a conference or workshop dealing with scientific misconduct allegations or the promotion of research integrity. Generally, available funding would be from \$5,000 to \$20,000.

February 1, 1999, is the due date for conferences proposed for September 1999 to August 2000.

Proposal instructions are on ORI's home page (<http://ori.dhhs.gov>). Contact Dr. Alicia Dustira at (301) 443-5300, email:adustira@osophs.dhhs.gov.

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

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