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Office of Research Integrity

NEWSLETTER

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.

IN THIS ISSUE

RCR Resources Program Identifies Priority Areas

The new request for applications (RFA) for the Responsible Conduct of Research (RCR) Resource Development Program stipulates priority instructional areas and emphasizes the need for more sophisticated and focused instructional materials that actively engage the learner in developing skills, abilities, and competencies.

ORI has allocated $260,000 to the program this round to fund 10 proposals. Additional awards may be made if funds are available. ORI funded 13 awards in the first round; and 17 in the second round. Submit applications electronically on or before February 27, 2004. See RFA Award Application on new ORI web site under Funding.

The awards were increased from $25,000 to $26,000 to cover attendance at the 2004 and 2005 RCR Expos. The 2004 RCR Expo will be held during the Society for Research Administrators annual meeting in Salt Lake City from October 23-27. Awards only cover direct costs; indirect costs are not paid.

Awards made under this program will be made through purchase orders, not grants. Awardees must provide a finished product to ORI at the end of the performance period which usually runs for 12 months beginning September 1. ORI will make the products available to the research community for free through its web site or at minimal cost when CD-ROMS, DVDs or videotapes are involved.

Loc Nguyen-Khoa, program director, said "We would like to move the production of the instructional materials from the 100 introductory survey course level to 400 to 500 upper level courses that are focused, in-depth, and intellectually stimulating."

High priority areas are data acquisition, retention, storage, custody, sharing, ownership, interpretation, and reporting; mentor-trainee responsibilities; collaborative science; and peer review.

See RCR Resources on page 5

Violation of Voluntary Exclusion Agreement Extends Exclusion Period

As noted in the September 2001 issue of this *Newsletter*, available at **http://ori.hhs.gov/html/publications/newsletters_vol9no4.asp**, Kuie-Fu (Tom) Lin, D.V.M., Ph.D., a former graduate student at the Medical University of South Carolina (MUSC), had been found in 2001 by both the University and ORI to have falsified research in two publications with his mentor on gene therapy models in which the introduced gene lowered blood pressure in hypertensive or salt-sensitive rats, in which Dr. Lin's falsifications greatly enhanced the apparent expression and effects of the introduced genes. He agreed voluntarily to exclude himself for 3 years beginning in June 2001 from any contracting, subcontracting, or involvement in grants and cooperative agreements with the U.S. Government and from serving in any advisory capacity to PHS.

See Voluntary on page 2

Submit Now !

Annual Report on Possible Research Misconduct - 2003

Due by **March 1, 2004**

Scientists Organizing Boycott Of 6 Prestigious Journals

Two scientists at UC-San Francisco are organizing a worldwide boycott of six prestigious journals in molecular biology because the journal publisher is demanding that the UC system pay more than $90,000 a year for electronic access to the journals, according to The Chronicle of Higher Education (10/31/03).

The scientists are Keith Yamamoto, chairman, department of cellular and molecular pharmacology, and Peter Walter, professor of biophysics and biochemistry. The target journals are *Cell, Cancer Cell, Developmental Cell, Immunity, Molecular Cell, and Neuron* published by Reed Elsevier which called the fee "an excellent value."

Librarians in the university system warned faculty members last October that the libraries may have to make "major reductions' in online journals. Faculty members must pay individually to view the journal articles online. Yamamoto and Walter circulated a letter last October urging their colleagues to take the following actions against the six journals: refuse to submit articles, resign from editorial boards and decline to review manuscripts.

RCR Intro Text

A copy of the *ORI Introduction to the Responsible Conduct of Research* is expected to be mailed in December 2003 to the responsible institutional official at each of the 4,000 institutions and organizations that have an active misconduct assurance on file with ORI.

The document will be posted on the RCR web page on the new ORI web site this spring. The Superintendent of Documents, U.S. Government Printing Office, will offer it for sale. Check the GPO on-line bookstore at **http://bookstore.gpo.gov/newpubs/index.html**

Nature Journals Broaden Financial Disclosure Policy

The Nature Publishing Group has broadened its competing financial interests policy to cover all Perspective, Analysis, Progress, Review, Brief Communication, Article, and Letters papers in *Nature* (including *Nature* Insights) and the *Nature* research journals following a controversy ignited by publication of a review article in *Nature Neuroscience* that did not disclose an author's competing financial interests including a patent, stock options, and consulting fees from companies whose products were favorably discussed in the review. Previously, disclosure was limited to authors of primary research articles.

The policy states, "Authors are required, before final acceptance of their contribution, to return a declaration of competing financial interests. A shortened version of this declaration is published as part of the paper, with a more detailed version, if appropriate, published online accompanying the paper. Authors may use the form to decline to disclose their financial interests, but *Nature* journals will publish the fact that they have declined to provide information."

The rationale for extending the policy to review articles (and presumably other secondary papers) was published in the October 2003 issue of *Nature Neuroscience:*

"The argument for extending our existing disclosure policy to reviews is strong. Studies of the clinical literature have concluded that industry funding is associated with pro-industry results, so there is a clear prima facie cause for concern. One can argue that because review articles are inherently selective and opinionated, they provide more scope for bias than do reports of research results. Moreover, there have been clear examples of abuse, in which academic authors have been paid by pharmaceutical companies to put their names and credibility to reviews produced by ghost writers employed to boost company products.

"The most compelling argument for disclosure, however, is to remove suspicion. When scientists (particularly those receiving public funding) offer their professional expertise without disclosing potential financial benefits to themselves, it threatens to undermine public trust, not simply in a particular paper or journal, but in the integrity of the scientific enterprise as a whole."

Voluntary (from page 1)

However, in April 2003, the Chair of the MUSC Research Integrity Committee happened to see a recent publication with National Institutes of Health (NIH) funding which listed Dr. Lin as the second author. This discovery triggered a further investigation that found Dr. Lin, his mentor, and the institutional officials who managed the mentor's grants, had not implemented the agreed upon exclusions. The principals were reprimanded by the University, Dr. Lin's postdoctoral appointment was terminated, and the University agreed to refund to NIH the more than $100,000 paid for Dr. Lin's salary and research support. Since Dr. Lin's exclusions were not implemented for these 2 years, ORI negotiated a supplemental agreement in which Dr. Lin admitted that he had not been debarred and voluntarily agreed to exclude himself for the next 4 years, through April 2007.

ORI reminds institutional officials that when they receive a notification letter from ORI regarding findings of misconduct and requirements, stating that an employee is excluded/debarred from receiving any Federal funding or is subject to special supervision or certification, that they should inform the appropriate program and financial administrators to ensure that these Federal actions are implemented. In the above case, the institutional integrity official is to be commended for discovery of the oversight.

Research = Responsible Conduct of Research

Columbia University Creates Comprehensive RCR Office

A comprehensive, central Office for the Responsible Conduct of Research (ORCR) has been established by Columbia University to foster a culture of integrity and compliance to ensure that participants in its research enterprise internalize and pursue the goal of self-directed responsible conduct of research.

The ORCR, created in June 2002 by the administration and the Trustees, reports directly to the Executive Vice President for Finance, who along with the Office of Internal Audit, initially recommended that an ORCR be developed. ORCR has assumed responsibilities such as:

- Coordinating research compliance and integrity procedures, communication, and training activities across campuses;
- Ensuring primarily through education that all participants in the conduct of research have a basic understanding of all research compliance issues;
- Acting as a principal source of guidance for researchers and administrators on the implementation and interpretation of research compliance and integrity requirements;
- Setting baseline standards for record keeping and documentation of research activities, procedures, and expenditures;
- Ensuring that training programs and materials for the responsible conduct of research are current, accurate, and comprehensive; and
- Managing the connections between research compliance and non-compliances issues, such as third-party billing administration.

The range of issues covered by the office is comprehensive, including the ethical conduct of research, mentor/trainee responsibilities, avoidance of conflicts of interest, responsible authorship, human subject protections, animal care, environmental health and safety as they relate to research, international research and financial responsibility in research.

Since it was established, ORCR has made presentations to faculty, staff, and students; created a web site (**http://orcr.columbia.edu**); developed E-seminars on 2 RCR core instructional areas (working on 9 others including environmental health and safety and financial responsibility); coordinated the organization of a national research integrity and human research protections conference, convened a committee to develop guidelines for international research; and participated in the founding of the RCR Education Consortium and the RCR Special Interest Group within the Society for Research Administrators.

Daniel R. Vasgird, Ph.D., CIP, directs the four-person office. Vasgird previously served as director of the Office of Research Conduct for The City University of New York and as director of the Health Research Training Program and chairperson of the Institutional Review Board for the New York City Department of Health. He received his doctorate in social psychology from Syracuse University. His assistant director is Ellen Hyman-Browne, JD, MPH, CIP.

The ORCR receives institutional guidance from an advisory committee composed of the provost, the executive vice presidents for health and biomedical sciences, research, and finance; several deans including the graduate school, and the general counsel.

Duke Requires RCR Training for All Doctoral Candidates

Duke University has broadened its responsible conduct of research (RCR) training program that focuses on the positive obligations graduate students have regarding research, rather than the avoidance of research misconduct, to include all incoming doctoral students beginning with the 2003-2004 academic year.

The program requires each Ph.D. candidate to attend a Fall Orientation RCR Workshop program and participate in at least three supplementary RCR Forums within the first 3 years of his or her program. Doctoral candidates in the basic medical science track are required to take 18 hours of training; candidates in the natural science and engineering track and the humanities and social science track are required to take 12 hours of training. See **http://www.gradschool.duke.edu/Regulations/rcr.htm**

"Although the push for RCR training began with pressure from NIH and NSF, the Executive Committee of the Graduate Faculty insisted from the beginning–over a decade ago–that such training should be provided for all doctoral students," Leigh DeNeef, associate dean of the graduate school, said. "Our own problem has simply been in finding the means to mount an institution-wide program that would include all incoming doctoral students." DeNeef created the program with Douglas James, administrative coordinator.

The program was developed by asking each department to identify one faculty member and one graduate student to facilitate RCR training. Then, each department was asked to select case studies suitable for its field.

"There has been virtually no objection from either graduate students or faculty," DeNeef said. "In the past, there was some resistance from faculty–not because they did not think such training was important, but because they did not feel competent to provide it."

See Duke RCR on page 5

ORI Annual Report - 2002

The ORI Annual Report - 2002 is available on the ORI web site. Copies of the report are available upon request while the supply lasts. Contact Robin Dorsey at 301-443-5300 or rdorsey@osophs.dhhs.gov.

New ORI Web Site Premiers in 2004

Beginning January 1, 2004, ORI will launch a new web site that employs cutting-edge technology to facilitate quicker access to information while maintaining the current web site during a transition period.

Powered by PHP technology, the new site boasts several web site administrative tools that allow ORI to easily add, delete, or change content, thereby simplifying the maintenance of the web site and ensuring the timeliness of the information provided.

"The Internet provides the most cost effective means of communication," Loc Nguyen-Khoa said, "ORI plans to use the growing web technology to provide the best possible service to the research community and the public." Nguyen-Khoa, a software engineer, joined ORI in 2002 to maximize ORI's web presence.

Users will find site navigation much easier because a "Folder" system allows visitors to find information quickly, without getting lost within the site. A robust site map permits users to view all folders and pages along with a short description of each page. Driven by a database, the site map will be updated automatically as ORI adds and updates pages. Using the site map, users may access their desired pages within 1-2 clicks.

A print version of each web page is available to users. Print pages are formatted without site graphics or web navigation bars, and is designed to fit on a 8½- by 11-inch sheet of paper.

A new on-line proposal system permits easy submission of proposals to fund workshops, conferences, RCR materials, and other activities. This comprehensive system will feature on-line submission, peer review, and award notification.

Several other features will be added throughout 2004 including an option that will enable users to customize their on-line experience. Using a log-in system, users will be able to design a personal "My ORI" page that will have fast links to ORI pages that are most relevant to them. Users will be able to add links (internal and external) to their customized page.

ORI Conferences and Workshops 2004

ORI is co-sponsoring 9 conferences and workshops with universities, medical schools, academic societies, and professional and institutional associations in 2004.

Information on the ORI conference and workshop program and proposal instructions are on the web site. Submission deadlines are April 1 and October 1. Contact Dr. Carolyn Fassi, Director, ORI Conference and Workshop Program, at 301-443-5300 or cfassi@osophs.dhhs.gov.

March 19-20. Promoting the Responsible Conduct of Research: What it Means to the Research Enterprise, Winston-Salem, NC
Co-Sponsors: Winston-Salem State University, Wake Forest University School of Medicine
March 22. Does Funding Source Influence Research Integrity? Baltimore, MD
Co-Sponsor: Society of Toxicology
April 13-14. Responsible Conduct of Research in Psychological Science, Washington, DC
Co-Sponsor: American Psychological Association
June 21-22. The RCR Summit: A National Dialogue on Future Directions of RCR, East Lansing, MI
Co-Sponsor: Michigan State University
October 14-15. Research Integrity and Financial Conflicts of Interest in Clinical Research: Legal Issues and Regulatory Requirements, Charlottesville, VA
Co-Sponsor: University of Virginia, School of Medicine, Center for Biomedical Ethics
October 23-27. RCR Expo, Salt Lake City, UT
Co-Sponsor: SRA International
November 12-14. ORI Research Conference on Research Integrity - 2004, San Diego, CA
Co-Sponsors: University of California - San Diego and AAAS
December 1-3. Developing Policy on Institutional Conflict of Interest, Las Vegas, NV
Co-Sponsor: University of Nevada - Las Vegas
December 8. Ethics and Responsible Conduct of Research Workshop, Washington, DC
Co-Sponsor: Council of Graduate Schools

Researchers Reprimanded For Cleaning Up Figures

A prominent German neuroscientist and a Swiss colleague were reprimanded by the German funding agency DFG for altering two figures in a paper published in 1998 in the *Journal of Neurochemistry,* according to *Science* (302:763).

Heinz Breer, University of Hohenheim, and Johannes Noe, University of Zurich, were found guilty of research misconduct by a DFG committee that investigated an allegation made by a former postdoc in Breer's lab. The committee concluded that the researchers committed misconduct because they failed to disclose that they had cleaned up the primer bands in the Southern Blots to make them look more dramatic. The alterations did not affect the paper's conclusions and the researchers remain eligible for DFG funding.

Naval Academy Historian Disciplined for Plagiarizing

An associate professor of history at the U.S. Naval Academy (USNA) had his tenure revoked, salary reduced, and rank lowered after an internal investigation concluded that he had published plagiarized material in his book on the development of the atomic bomb, according to *The Chronicle of Higher Education* (11/7/03).

The misconduct was alleged in an article last May in the *New York Times* on *Pandora's Keepers: Nine Men and the Atomic Bomb* by Brian VanDeMark. Five authors have charged that their works have been plagiarized; citing over 50 verbatim sentences used or rewritten only slightly. The publisher withdrew the first edition, but intends to produce a corrected version.

The USNA investigation concluded that the misconduct resulted from "gross carelessness" but did not "constitute a deliberate effort to pass off the works of other authors as his own," according to *The Chronicle*.

Duke RCR (from page 3)

The number of faculty and advanced graduate student facilitators have increased each year by providing some initial training to those who have attended the pre-orientation weekend retreat/workshops held when RCR was limited to students in the basic medical science track.

To further increase the supply of facilitators Duke University is applying for a collaborative NSF grant with RCR leaders at North Carolina State University, University of North Carolina -Chapel Hill, and North Carolina Central University to create a Triangle Consortium for Education in the Responsible Conduct of Research. "This consortium has as one of its central goals the training of faculty in various disciplines to conduct RCR training," DeNeef said.

Academic Societies Invited to Propose RCR Projects

A third funding category has been added to the RCR Program for Academic Societies that seeks to institutionalize commitments to the responsible conduct of research into the infrastructure of the academic societies and the cultures of the disciplines they represent.

The RCR Program, a collaborative effort between the Association of American Medical Colleges (AAMC) and ORI, funded 15 projects proposed by 13 academic societies in the first year. The program expects to fund 10-12 projects in the second year. Submission deadline is March 19, 2004. The request for applications (RFA) is on the ORI web site and **http://www.aamc.org/ori**.

"ORI would like to continue the program for a total of 5 years," Chris Pascal, Director, ORI, said, "but that will depend on the commitment demonstrated by academic societies and the availability of funds."

The new category provides awards up to $50,000 to support comprehensive society RCR/RI initiatives addressing one or more of the following: strategic planning; publication policy, committees or section structure, the annual meeting, RCR standards and competencies; training of postdocs, graduate and undergraduate students, or continuing education programs for members and impact and outcome evaluations.

The second category funds awards up to $25,000 for major RCR/RI program initiatives such as the use of leadership summits, focus groups, or needs assessments to identify RCR/RI educational gaps and members' interests, developing guidelines for one or more of the core RCR areas; integrating RCR training into one or more undergraduate or graduate courses; creating instructions for authors that include research integrity concerns; or producing a publication or module on mentoring, the responsible management of research laboratories, or data management issues, (e.g., data recording, storage, retention, access, custody, destruction, selection, reporting) or developing modules for teaching skills, abilities, and competencies.

The third category supports awards up to $5,000 to stimulate interest and discussion related to research misconduct, RCR, or research integrity by organizing a colloquium, symposium, meeting, session, workshop, or conference.

The program is open to nonprofit academic societies, headquartered in the U.S., and active in the fields of medicine, biomedical or the behavioral sciences, and whose primary missions include advancing medical education and/or biomedical or behavioral research. Proposals focused on bioethics and bioethical research will not be funded.

Awards under this program are contracts, not grants. No facilities and administrative (indirect) costs are provided. The performance period is up to 18 months, extension may be considered.

Contact Tony Mazzaschi, AAMC, at 202-828-0059 or tmazzaschi@aamc.org or Dr.Carolyn Fassi at 301-443-5300 or cfassi@osophs.dhhs.gov.

RCR Resources (from page 1)

Other high priority areas are assessment tools that allow institutians to evaluate their current RCR programs; materials specifically meeting the needs of international postdocs and researchers; and projects developing the technological backbone for interactive web-based tools for RCR such as online quizzes and games and decision tree approaches.

Moderate priority areas are publication practices and responsible authorship and research misconduct. Low priority areas are animal and human subjects and conflict of interest.

Direct inquiries to Loc Nguyen-Khoa at 301-443-5300 or lnguyen-khoa@osophs.dhhs.gov.

National Research Council Reports on Sharing Publication-Related Data and Materials

A new National Research Council report specifies "the uniform principle for sharing integral data and materials expeditiously (UPSIDE), plus 5 supporting principles and 10 recommendations on sharing publication-related data and materials.

The report, *Sharing Publication-Related Data and Materials,* was produced by the Committee on Responsibilities of Authorship in the Biological Sciences, chaired by Thomas R. Cech, President, Howard Hughes Medical Institute. The publication is available to read online on the National Academies Press Web site at **http://books.nap.edu/openbook/0309088593/html/index.html.**

The Uniform Principle

"Community standards for sharing publication-related data and materials should flow from the general principle that the fundamental purpose of publication of scientific information is to move science forward. More specifically, the act of publishing is a *quid pro quo* in which authors receive credit and acknowledgment in exchange for disclosure of their scientific findings.

"An author's obligation is not only to release data and materials to enable others to verify or replicate published findings (as journals already implicitly or explicitly require) but also to provide them in a form on which other scientists can build with further research. All members of the scientific community–whether working in academia, government, or commercial enterprise–share responsibility for upholding community standards as equal participants in the publication system, and all should be equally able to derive benefit from it."

Supporting Principles

Principle 1. Authors should include in their publications the data, algorithms, or other information that are central or integral to the publications–whatever is necessary to support the major claims of the paper and to enable someone skilled in the art to verify or replicate and build on the paper's claims.

Principle 2. If central or integral information cannot be included in a publication for practical reasons (for example, because a data set is too large), it should be made freely (without restriction on its use for research purposes and at no cost) and readily accessible through other means (for example, on-line). Moreover, when it is necessary to enable further research, central and integral information should be made available in a form that enables it to be manipulated, analyzed, and combined with other scientific data.

Principle 3. If publicly accessible repositories for data have been agreed on by a community of researchers and are in general use, the relevant data should be deposited in one of them by the time of publication.

Principle 4. Authors of scientific publications should anticipate which materials integral to their publications are likely to be requested and should state in the "Materials and Methods" section or elsewhere how to obtain them. If an MTA (material transfer agreement) is required, the URL of the Web site where the MTA can be viewed should be provided. If the authors do not have rights to distribute the material, they should supply contact information for their original source. A frequently requested reagent can be made reasonably available in the commercial market or by an author's laboratory for a modest fee to cover the costs of production, quality control, updating, and shipping.

Principle 5. If a material integral to a publication is patented, the provider of the material should make the material available under a license for research use.

Recommendations

1. The scientific community should continue to be involved in crafting appropriate terms of any legislation that provides additional database protection.

2. It is appropriate for scientific reviewers of a paper submitted for publication to help to identify materials that are integral to the publication and likely to be requested by others and to point out cases in which authors need to provide additional information on obtaining them.

3. It is not acceptable for the provider of a publication-related material to demand an exclusive license to commercialize a new substance that a recipient makes with the provider's material or to require collaboration or coauthorship of future publications.

4. The merits of adopting a standard MTA should be examined closely by all institutions engaged in technology transfer, and efforts to streamline the process should be championed at the highest levels of universities, private research centers, and commercial enterprises.

5. As a best practice, participants in the publication process should commit to a 60-day limit to complete the negotiation of publication-related MTAs and transmit the requested materials or data.

6. Scientific journals should clearly and prominently state (in their instructions for authors and on their Web sites) their policies for distribution of publication-related materials, data, and other information. Policies for sharing materials should include requirements for depositing materials in an appropriate repository. Policies for data sharing should include requirements for deposition of complex data sets in appropriate databases for the sharing of software and algorithms integral to the findings being reported. The policies should also clearly state the consequences for authors who do not adhere to the policies and the procedure for registering complaints about noncompliance.

See NRC Report on page 7

NRC Report (from page 6)

7. Sponsors of research should clearly and prominently state their policies for distribution of publication-related materials and data by their grant or contract recipients or employees.

8. If an author does not comply with a request for data or materials in a reasonable time period (60 days), and the requestor has contacted the author to determine if extenuating circumstances (travel, sabbatical, or other reasons) may have caused the delay, it is acceptable for the requestor to contact the journal in which the paper was published. If that course of action is not successful in due course (another 30 days), the requestor may reasonably contact the author's university or other institution or the funder of the research in question for assistance. Those entities should have a policy and process in place for responding to such requests for assistance in obtaining publication-related data or materials.

9. Funding organizations should provide the recipients of research grants and contracts with the financial resources needed to support dissemination of publication-related data and materials.

10. Authors who have received data or materials from other investigators that have contributed to the work published should appropriately and publicly acknowledge such contributions.

ORI Listservs

See ORI Web Site

Journal Will Publish RRI Conference Papers

Five articles based on presentations made at the second Research Conference on Research Integrity held in November 2002 will be published in Volume 10 Issue 4, *Accountability in Research.*

Two papers present conceptual and methodological frameworks for the critical assessment of integrity in research. The remaining papers present different approaches to the study of specific aspects of integrity in research.

Development of Two Measures of Climate for Scientific Organizations, Blaine H. Gaddis, Whitney Helton-Fauth, Ginamarie Scott, Amber Shaffer, Shane Connelly, and Michael D. Mumford, proposes two specific measures for assessing integrity, based on traditional climate and career assessment measures.

A New Approach to Assessing Ethical Conduct in Scientific Work, Whitney Helton-Fauth, Blaine Gaddis, Ginamarie Scott, Michael Mumford, Lynn Devenport, Shane Connelly, and Ryan Brown, takes a combined empirical/theoretical approach to develop a taxonomy of ethical events across a broad range of scientific disciplines and to identify proximate factors that can influence research behavior.

The Importance of the Preservation of the Ethical Principle of Equipoise in the Design of Clinical Trials: Relative Impact of the Methodological Quality Domains on the Treatment Effect in Randomized Controlled Trials, Benjamin Djulbegovic, Mike Clarke and Alan Cantor, applies statistical analysis to information compiled from 136 randomized clinical trials to detect possible bias and the use of inappropriate methods.

Two Postal Surveys of Different Methods of Communicating Rejection to Authors Submitting to a General Medical Journal, Helen Barratt, Sara Schroter, Richard Smith, compares two ways for communicating rejection notices to authors, with the goal of improving communication, the quality of publications, and general attitudes toward responsible publication practices.

Plagiarism in Academia: Trends And Implications, Sheldon Gelman and Margaret Gibelman, employs content analysis of media reports to study issues and trends in plagiarism.

2003 Annual Report Due March 1, 2004

Institutional officials will be asked to perform three distinct tasks when they file their 2003 Annual Report on Possible Research Misconduct using the new software developed for the ORI Assurance Program.

The tasks are (1) review and update the information already in the ORI assurance database about their institution; (2) submit their Annual Report, and (3) designate a unique password. Initially, the assigned IPF (Institutional Profile File) number serves as the User ID and password, and receipt of the new password will be a acknowledged. The program also will e-mail the User ID and password to the institutional official when the requested information is provided.

Institutional updates will be acknowledged on screen. Responses will be required in most data fields. In the two-part Annual Report, most officials will only see part one, which asks whether their institution has a research misconduct policy and whether any misconduct activity occurred. Part two asks for information on the misconduct activity. Receipt of the Annual Report will be acknowledged on screen.

RRI Research Applications Almost Double in 2003

The number of grant applications submitted to the Research on Research Integrity (RRI) Program by the November 14, 2003, deadline was considerably higher than the number of applications submitted in any of the previous 3 years.

Fifty-three applications were received in the fourth round compared to 31 in the third, 30 in the second, and 25 in the first.

Maximum direct costs were increased from $100,000 to $250,000 per year, and the project period was lengthened from 2 to 3 years in the fourth round.

The applications are expected to be reviewed in March or April 2004 and awards likely will be made in August 2004. The program currently supports 22 studies.

Case Summaries

Craig H. Gelband, Ph.D., University of Florida (UF): Based on the reports of two UF investigations and additional analysis conducted by ORI in its oversight review, the U.S. Public Health Service (PHS) found that Craig H. Gelband, Ph.D., Associate Professor, Department of Physiology, College of Medicine at UF, engaged in scientific misconduct in research. Publications and manuscripts containing the falsified data cited support from National Institutes of Health (NIH) grants, or falsified data was included in NIH grant applications, as follows: R29 HL52189-01A2 (then R01 HL52189-05), R01 HL56921, F32 HD08496, R01/R37 HL49254, F32 HL08531, P01 DK41315, and R01 HL69034-01. Specifically, PHS found that:

I. Dr. Craig H. Gelband falsified data based on contractile tension recording in antisense experiments on the angiotensin enzyme (ACE), purportedly using renal arteriolar smooth muscle tension preparation:

A. by falsely labeling the tension recordings in Figures 5, 6, and 7 in a publication by Wang, H., Reaves, P.Y., Gardon, M.L., Keene, K., Goldberg, D.S., Gelband, C.H., Katovich, M.J. & Raizada, M.K. "Angiotensin I-converting enzyme antisense gene therapy causes permanent antihypertensive effects in the SHR." *Hypertension* 35[part 2]:2002-208, 2000 ("*Hypertension* 2000 paper #1"), when he had earlier reported the same contractile records as being from experiments on the angiotensin receptor (not the enzyme), in Figures 6, 7, and 8 of an earlier mini-review by Martens, J.R. & Gelband, C.H. "Ion channels in vascular smooth muscle: Alterations in essential hypertension." *PSEBM* 218:192-200, 1998 (*PSEBM* paper);

B. by falsifying three of the four sets of the mean data that were in fact the same for both the F0 and F1 mean data in Figures 5 and 6 of the *Hypertension* 2000 paper #1. Dr. Gelband also dishonestly provided the institution with the falsified/fabricated tables of the mean data and the associated false standard error values as evidence that he had conducted the experiments for Figures 5 and 6; and

C. by falsifying EC_{50} values in Table 1 in NIH grant application HL52189-05; the EC_{50} values had been interpolated from the falsified mean and SEM data shown in Figures 5 and 6 in the *Hypertension* 2000 paper #1.

II. Dr. Gelband falsified data in the reporting of research, misrepresenting current/voltage (I/V) data to be results from totally different experimental models or preparations in six publications (including one manuscript "In-Press") and in NIH grant application HL52189-05, specifically:

A. as Figure 1A, in Gelband, C.H., Wang, H., Gardon, M.L., Keene, K., Goldberg, D.S., Reaves, P., Katovich, M.J., Raizada, M.K. "Angiotensin 1-converting enzyme antisense prevents altered renal vascular reactivity, but not high blood pressure, in spontaneously hypertensive rats." *Hypertension* 35 [part 2]:209-213, 2000 ("*Hypertension* 2000 paper #2").

B. as Figure 2, in Martens, J.R., Fergus, D.J., Tamkun, M.M., England, S.K., Gelband, C.H. "Identification of voltage-gated K^+ channel genes contributing to the decreased renal arteriolar K^+ current in hypertension." *J. Biol. Chem* (MS M01389200), online, in press ("*JBC* paper"). *J. Biol Chem Online* (submitted and withdrawn).

C. as Figure 4A, in Gelband, C.H. "Protein kinase C regulation of renal vascular K and Ca^{++} channels in hypertension." *Hypertension Online* paper, withdrawn ("*Hypertension Online* paper").

D. as Figure 3, in Gelband, C.H., Reaves, P.Y., Evans, J., Wang, H., Katovich, M.J., & Raizade, M.K. "Angiotensin II Type 1 receptor antisense gene therapy prevents altered renal vascular calcium homeostasis in hypertension." *Hypertension* 33[partII]:360-365, 1999 ("*Hypertension* 1999 paper").

E. as Figures 4A and 4B in Martens, J.R., Reaves, P.Y., Lu, D., Katovich, M.J., Berecek, K.H., Bishop, A.P., Raizade, M.K., & Gelband, C.H. "Preventions of renovascular and cardiac pathophysiological changes in hypertension by angiotensin II type 1 receptor antisense gene therapy." *Proc. Natl. Acad. Sci.* 95:2664-2669, 1998 ("*PNAS* paper").

F. as Figure 5A, in Reaves, P.Y., Gelband, C.H., Wang, H., Yang, H., Lu, D., Berecek, K.H., Katovich, M.J., Raizada, M.K. "Permanent cardiovascular protection from hypertension by the AT1 receptor antisense gene therapy in hypertensive rat offspring." *Circ. Res.* 85:344-350, 1999 ("*Circ. Res.* 1999 paper").

1. Dr. Gelband also falsified data in the proposing of research by submitting the above data as Figures 3, 14A, 14B, and 15 in NIH grant application HL52189-05.

III. Dr. Gelband falsified traces of potassium currents in Figure 4 of the *J. Biol. Chem* paper (see PHS Finding II) where they were claimed to have been recorded from smooth muscle cells from rats treated with antisense to potassium channels, and/or in Figure 3 of the *Hypertension Online* paper (see PHS Finding II) where they were claimed to have been records from rat renal cells treated with phorbol esters and PKC inhibitors. Furthermore, the potassium currents were recorded from neurons, not from smooth muscles as falsely reported in these publications.

A. Dr. Gelband falsified data in the proposing of research by submitting the falsified traces of potassium currents as Figure 9 in NIH grant application HL52189-05.

IV. Dr. Gelband falsified data by claiming in Figure 8 of NIH grant application HL52189-05 and in Figure 2 of the *Hypertension Online* paper (see PHS Finding II) to have generated in his laboratory Western blot data on protein kinase C isoenzymes in renal vascular smooth muscle cells, while in fact the data were actually from cultured neurons collected in another laboratory and published in Pan, S.J., Zhu, M., Raizada,

Case Summaries, Continued

M.K., Sumners, C., & Gelband, C.H. "Angiotensin II-mediated inhibition of neuronal delayed rectifier K^+ current: Role of protein kinase C-a." *American Journal of Physiology* 281:C17-C23, 2001 (*AJP* paper).

V. Dr. Gelband falsified data by misrepresenting experimental traces he provided as the unnumbered topmost figure on Page 26 of NIH grant application HL69034-01, as being recordings showing effect of indolactam inhibition in posterior cerebral arteriolar smooth muscle cells, while the identical tracings had been published by Dr. Gelband as Figures 2C and 7D of the *AJP* paper (see PHS Issue 4), where they had been reported as being tracings from neuronal cells.

VI. Dr. Gelband falsified data in the unnumbered rightmost figure on Page 25 of NIH grant application HL69034-01, by misrepresenting the data as showing potential changes induced in cerebral arterial myocytes by IP3 and heparin, while the same data were published by Dr. Gelband as Figure 5C in a 1997 publication: Gelband, C.H. & Gelband, H. "CA^{2+} release from intracellular stores is an initial step in hypoxic pulmonary vasoconstriction of rat pulmonary artery resistance vessels." *Circulation* 96:3647-3654, 1997 ("*Circulation* paper") as representing changes in intracellular calcium concentration of pulmonary artery cells induced by ryanodyne and hypoxia.

VII. Dr. Gelband falsified electro-physiological records by reusing the same current-voltage trace as the response of renal vascular cells exposed for 2 seconds to Angiotensin II (Figure 4C) and to Caffeine (Figure 4B) on p. 124 of the publication Gelband, C.H. & Hume J.R. "$[Ca^{2+}]_I$ Inhibition of K^+ Channels in Canine Renal Artery. A Novel Mechanism for Agonist-Induced Membrane Depolarization." *Circulation Research* 77(1):121-130, 1995 (*Circ. Res.* 1995 paper).

A. Dr. Gelband also submitted the falsified data above in Figure 4 in NIH grant application R29 JL52189-01A2.

VIII. Dr. Gelband fabricated laboratory research records for four Western blot experiments during the investigation, withholding form the institution his associate's notebook from which he had removed four labeled autoradiographic films from separate and different experiments, and using the removed films to fabricate a laboratory notebook containing falsified Western blots, which he provided to UF as evidence that he had conducted the experiments under investigation.

The terms of the Agreement between the U.S. Department of Health and Human Services and Dr. Gelband are as follows:

(1) Respondent agreed to exclude himself voluntarily from any contracting or subcontracting with any agency of the U.S. Government and from eligibility or involvement in nonprocurement programs of the U.S. Government referred to as "covered transactions" as defined in the debarment regulations at 45 C.F.R. Part 76, for 10 years, beginning on October 3, 2003.

(2) Respondent agreed to exclude himself voluntarily from serving in any advisory capacity to PHS including but not limited to service on any PHS advisory committee, board, and/or peer review committee, or as a consultant, for 10 years, beginning on October 3, 2003.

(3) Within 30 days of the effective date of the Agreement (October 3, 2003), Respondent agreed to submit letters of retraction to the following journals concerning the specified data in the listed articles:

A. *Hypertension* 2000 paper #1: Figures 5, 6, and 7 merited retraction. A retraction has been submitted relevant to this paper.

B. *Hypertension* 2000 paper #2: Figure 1A merited retraction. A retraction has been submitted relevant to this paper.

C. *JBC* paper: Figure 2 and Figure 4 merited retraction. It has already been withdrawn.

D. *Hypertension Online* paper: Figure 4A and Figure 3 merited retraction. It has already been withdrawn.

E. *Hypertension* 1999 paper: Figure 3 must be retracted.

F. *PNAS* paper: Figure 4A and 4B must be retracted.

G. *Circ. Res.* 1999 paper: Figure 5A must be retracted.

H. *Circ. Res.* 1995 paper: Figure 4C or 4B must be retracted.

Thonthi Karunakaran, Boston Medical Center (BMC): Based on the BMC investigation report and additional analysis performed by ORI in its oversight review, PHS found that Thonthi Karunakaran, Ph.D., former Research Scientist at BMC, engaged in scientific misconduct by plagiarizing, falsifying, and fabricating research that he reported to his supervisor for the project "Hemin Utilization by *Porphyromonas gingivalis*," funded by National Institute of Dental and Craniofacial Research, (NIDCR), NIH, grant R01 DE09161-11. Specifically, PHS found that Dr. Karunakaran engaged in scientific misconduct by: (1) plagiarizing a P. gingivalis strain W83 DNA sequence from an Internet database and misrepresenting to his supervisor that the Internet database printout represented his own cloning and sequencing of strain A7436 fur gene X; (2) fabricating the claim to have obtained sequence data for a strain A7436 cloned fur gene X from a sequencing facility at Massachusetts Institute of Technology (MIT); and (3) falsifying unrelated sequencing data from a graduate student's notebook in the laboratory by trimming off the identifying header and misrepresenting it to his supervisor as primary data from his sequencing of the A7436 fur gene X. There were no published papers that required correction or retraction.

The following administrative actions have been implemented for 3 years, beginning on July 17, 2003:
(1) Dr. Karunakaran is debarred from eligibility for or involvement in Federal covered transactions (i.e., any Federal

Case Summaries, Continued

transaction other than a procurement transaction) and from contracting or subcontracting with any Federal government agency; this action is being taken pursuant to the debarment regulation pertaining to grants and other forms of assistance (45 C.F.R. Part 76); and (2) Dr. Karunakaran is prohibited from serving in any advisory capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant.

Ilya Koltover, Ph.D., California Institute of Technology (CIT): Based on the CIT investigation report, an admission by the respondent, and additional analysis conducted by ORI in its oversight review, PHS found that Ilya Koltover, Ph.D., former postdoctoral fellow at CIT, engaged in scientific misconduct in research supported by PHS Postdoctoral Fellowship F32 GM20588 entitled "Design of targeted synthetic gene delivery vehicles." Specifically, PHS found that Dr. Koltover plagiarized a scanning micrograph (STM) from a graduate student, falsified it as an atomic force micrograph (AFM) of a separate molecule, and falsely represented it (1) to his research group at CIT; (2) in his grant application to the Petroleum Research Fund (PRF); and (3) to his mentor, who then included it as an AFM figure in a proposal to the National Science Foundation.

Dr. Koltover entered into a Voluntary Exclusion Agreement in which he voluntarily agreed for a period of 3 years, beginning on October 3, 2003: (1) to exclude himself from serving in any advisory capacity to PHS including but not limited to service on any PHS advisory committee, board, and/or peer review committee, or as a consultant; (2) that any institution which submits an application for PHS support for a research project on which Dr. Koltover's participation is proposed or which uses him in any capacity on PHS supported research, or that submits a report of PHS-funded research in which he is involved, must concurrently submit a plan for supervision of his duties to the funding agency for approval; the supervisory plan must be designed to ensure the scientific integrity of his research contribution; Dr. Koltover agreed to ensure that a copy of the supervisory plan is also submitted to ORI by the institution and that he will not participate in any PHS-supported research until such a supervision plan is submitted to ORI; and (3) that any institution employing Dr. Koltover submits, in conjunction with each application for PHS funds or report, manuscript, or abstract of PHS funded research in which he is involved, a certification that the data provided by Dr. Koltover are based on actual experiments or are otherwise legitimately derived, and that the data, procedures, and methodology are accurately reported in the application or report. Dr. Koltover must ensure that the institution sends a copy of the certification to ORI.

Timothy R. Smith, Ph.D., Michigan State University (MSU): Based on the findings of MSU, the respondent's admission, and analysis conducted by ORI in its oversight review, PHS found that Timothy R. Smith, Ph.D., former Postdoctoral Fellow, Department of Biochemistry and Molecular Biology at MSU, engaged in scientific misconduct in research supported by National Institute of General Medical Sciences (NIGMS), NIH grant P01 GM57323, entitled "Oxygen utilizing membrane heme proteins." Specifically, PHS found that Dr. Smith falsified and fabricated data involving research into the physical interaction of prostaglandin endoperoxide synthase-2 (PGHS-2) with cell membranes, and the effects of arachidonate and nonsteroidal anti-inflammatory drugs (NSAIDs) on PGHS-2 structure. Dr. Smith committed scientific misconduct by falsifying and fabricating data for the following tables and figures in his 2000 doctoral dissertation and in a paper in the *Journal of Biological Chemistry* (275:40407-40415, 2000) entitled "Arachidonic Acid and Nonsteroidal Anti-inflammatory Drugs Induce Conformational Changes in the Human Prostaglandin Endoperoxide H_2 Synthase-2 (Cyclooxygenase-2)" (*JBC* paper):

I. *JBC* paper Table II, entitled "Comparison of inter-residue distances as determined by EPR spectroscopy and as calculated from the x-ray crystal structures" (and corresponding Dissertation Table 6 entitled "EPR determined and X-ray crystal modeled inter-nitroxide distances of PGHS-2 MBD mutants");

II. *JBC* paper Table III entitled "Changes in inter-nitroxide differences between PGHS-2 holoenzyme and the apoenzyme, and the arachidonate, flurbiprofen, and SC58125 complexes" (and corresponding Dissertation Table 7), entitled "Relative changes in inter-nitroxide distances for NSAID and arachidonate complexes compared to the unliganded enzyme");

III. *JBC* paper Figure 4 (binding curves) (and corresponding Dissertation Figure 20 entitled "Binding curves for the association of heme, flurbiprofen and arachidonic acid with PGHS-2 double mutants");

IV. Dissertation Table 8 entitled "EPR determined inter-nitroxide distances for NSAID and arachidonate complexes of PGHS-2 MBD mutants;"

V. Dissertation Table 9 entitled "Relative changes in inter-nitroxide distances for NSAID and arachidonate complexes compared to the unliganded enzyme;"

VI. Dissertation Table 10 entitled "Kinetic properties and NSAID sensitivities of PGHS-2 active site mutants;"

VII. Dissertation Table 11 entitled "EPR determined inter-nitroxide distances for NSAID and arachidonate complexes of PGH-2 MBD mutants;"

VIII. Dissertation Table 12 entitled "Relative PGHS-2 protein incorporation of PGHS-2 into lipsomes of varying composition;"

IX. Dissertation Table 13 entitled "EPR determined inter-nitroxide distances for detergent solubilized and lipsome reconstituted PGHS-2 mutants;" and

X. Dissertation Figure 27 entitled "Lipid and activity profile of sucrose gradient fractions."

The research misconduct was significant for several reasons. First, the *JBC* paper was novel in that it reported that binding of arachidonate and NSAIDs induced structural changes in PHS-2. For the naturally occurring fatty acid arachidonate, this had not previously been shown. These results could be interpreted as having important implications for understanding the catalytic mechanism of this enzyme. In addition, a considerable expenditure of other researchers' time and resources was prompted by using results generated from the falsified and fabricated data in the *JBC* paper.

Dr. Smith entered into a Voluntary Exclusion Agreement in which he voluntarily agreed:

(1) to exclude himself from serving in any advisory capacity to PHS including but not limited to service on any PHS advisory committee, board, and/or peer review committee, or as a consultant for 3 years, beginning on October 27, 2003;

(2) to exclude himself voluntarily from any contracting or subcontracting with any agency of the U.S. Government and from eligibility or involvement in nonprocurement programs of the U.S. Government defined as "covered transactions" in the debarment regulations at 45 C.F.R. Part 76 for 3 years, beginning on October 27, 2003. During the 3-year period of voluntary exclusion, PHS grant funds may be used to pay for page charges for any written work currently being prepared for submission and/or publication on which Dr. Smith is listed as an author only if (i) such written work is unrelated to the misconduct findings described in the Agreement, (ii) Dr. Smith is not listed as first author, and (iii) the publication does not state that Dr. Smith was supported by a PHS grant. Dr. Smith must certify that all data supporting such written work is true and accurate to the best of his knowledge; and

(3) to submit a letter within 30 days of notification of this action to *JBC* requesting retraction of the following paper: Smith, T., McCracken, J., Shin, Y.K., & DeWitt, D. "Arachidonic Acid and Nonsteroidal Anti-inflammatory Drugs Induce Conformational Changes in the Human Prostaglandin Endoperoxide H_2 Synthase-2 (Cyclooxygenase-3)." *J. Biol. Chem.* 275:40407-40415, 2000. Dr. Smith agreed that the retraction will state that he alone was responsible for the falsification and fabrication of the results and will specifically list the falsified figures delineated on page 1 of the Agreement (Findings I, II, and III). Dr. Smith must submit a draft of the retraction letter for ORI approval prior to sending it to *JBC*. This requirement for retraction will be noted on the ALERT System until Dr. Smith sends a copy of the retraction letter to ORI.

Technical Assistance Available

Need help in handling a research misconduct allegation?

Call ORI Rapid Response Technical Assistance Program

301-443-5330

Cancer Researcher Indicted for Manslaughter

A cancer researcher who falsely claimed to be a doctor was indicted October 29, 2003 on manslaughter charges for causing a patient's death after fraudulently enrolling him and other veterans in drug studies at the Stratton Veterans Affairs Medical Center in Albany, New York, according to an article in the *Washington Post* (10/31/03).

Prosecutors said the researcher never completed his medical training at a school in the Caribbean island of Grenada. He worked as a chief research assistant at the medical center. The indictment alleges that the researcher altered the medical histories of dozens of patients over more than 3 years to get them into drug studies.

The patient's family filed a $20 million claim with the Department of Veterans Affairs in September.

German Agency Bolstering Approach to Misconduct

The German research funding agency DFG announced its intention last November to take additional steps to combat research misconduct because high-profile media coverage of misconduct cases may be lowering the reputation of science in that country, according to *Science Now* (11/18/03).

DFG plans to recruit two groups of experts to advise the agency on legal issues surrounding misconduct investigations and to suggest better ways to protect whistleblowers respectively. In addition, the agency plans to establish a database of misconduct cases to help estimate the size of the problem and identify recurring patterns of misconduct.

Legal issues are a concern because Germany's data- and employee-protection laws have interfered with investigations in several cases in recent years. Whistleblowers who frequently are graduate students or postdocs have little legal protection in Germany, where the hierarchical university system leaves young researchers especially vulnerable when they bring charges against a superior or colleague.

The concern for whistleblowers drew praise from a long-time critic of DFG's handling of misconduct cases. Peter Hans Hofschneider, Max Planck Institute for Biochemistry , Martinsried, said, "They are finally giving serious attention to the problem" by "acknowledging the important role they (whistleblowers) play in the system."

Notable Quote: "Universities should not rely upon formal complaints or scientific misconduct as the sole source of monitoring the integrity and quality of the research conducted under their auspices. They need continuing mechanisms to review and evaluate the research and training environment of their institution." *The Responsible Conduct of Research in the Health Sciences,* p. 31, IOM, 1989.

Conference, Workshop, and Meeting Proposals Due April 1, 2004

ORI is seeking proposals from institutions, scientific societies, and professional associations that wish to collaborate with ORI in developing conferences, workshops, symposia, colloquiums, seminars, and annual meeting sessions that address the responsible conduct of research, research integrity, or research misconduct. ORI will provide up to $20,000, depending on the event proposed.

The next target date for receipt of applications is **April 1, 2004**. Proposal instructions and an application form are available on the ORI web site at http://ori.dhhs.gov/html/programs/conf-workshops.asp. Please submit your proposal electronically to cfassi@osophs.dhhs.gov. Dr. Carolyn Fassi may be reached at 301-443-5300.

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