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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



## RRI Conference Abstracts Due April 28, 2006

ORI is planning to hold the 4th Research Conference on Research Integrity from December 1-3, 2006 in Tampa, Florida.

The biennial conference provides researchers with an opportunity to discuss crucial research problems, explore research methods, and share research results related to fostering research integrity and deterring research misconduct.

Preference will be given to original investigations that open new

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## Filing Annual Report Made Easier

Several procedural changes have been made to the Annual Report on Possible Research Misconduct to make it easier for institutional officials to file their 2005 report by the March 1, 2006 deadline.

Institutions are required by regulation to submit the Annual Report to maintain their research misconduct assurance. If that assurance is not maintained, the institution becomes ineligible to receive PHS support for research, research training, and related research activities.

In November and December, institutional officials were sent emails

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## RCR Resource Program Increases Funding

Increased support is available from the RCR Resource Development Program for the creation of interactive training material that facilitates the development of skills and competencies essential to the responsible conduct of research (RCR).

Applicants may request up to $50,000 in direct costs in this new round. Previously, funding was limited to $25,000 in direct costs. Indirect costs are not paid on these projects. The performance period is

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## RIO Video Being Produced By Michigan State Univ.

An orientation video that presents an overview of the main responsibilities of a Research Integrity Officer (RIO) is being produced at Michigan State University (MSU) under contract with ORI.

The RIO is the institutional official who is responsible for implementing the PHS Policies on Research Misconduct (42 CFR Part 93).

David Wright who served as the RIO at MSU for 11 years is serving as project director. Three other veteran RIOs are also participating in the video: Margaret Dale, Harvard University; Joe Corless, Duke

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## Focus on Skills and Competency Applications *(from page 1)*

from September 1, 2006 to September 28, 2007. Longer performance periods may be approved when appropriate. The new request for applications is available on the ORI home page. Submission deadline is February 24, 2006.

Persons planning to submit a proposal should contact Loc Nguyen-Khoa, Director, RCR Resource Development Program, before submitting a proposal to ensure that their submission meets program requirements.

"Over the last four years the RCR Resources program has focused on educational materials that disseminated information," Nguyen-Khoa said. "Now, we want interactive training materials that are designed to create the skills and competencies needed to be a successful researcher."

"In addition," he said, "we want the training materials to be presented as web-based or desktop applications that require hands-on involvement rather than as education modules aimed primarily at information transfer. The applications should include feedback to the learner."

Those training materials may address all aspects of data management including ensuring accuracy and integrity, laboratory management, developing research agendas, negotiating authorship, recognizing conflicts of interest, securing informed consent, creating and managing collaborations between researchers, developing proposals, and writing and submitting articles.

Training materials may also be developed for the handling of research misconduct allegations including the conduct of inquiries and/or investigations and the sequestration of data. Other resources which enhance research and administrative skills and competencies related to RCR will be considered.

Training material may be developed for graduate students, novice researchers, advanced researchers, research administrators, department heads, post-docs, clinical staff, international researchers and post-docs, technicians, and other personnel involved in research.

Awardees are expected to attend the 2006 RCR Expo in Quebec City, Canada and to exhibit their finished product at the 2007 RCR Expo in Nashville.

For further information contact Nguyen-Khoa at LNguyen-Khoa@osophs.dhhs.gov or at 240-453-8400.

## Video Expected to Be Available in Summer 2006 *(from page 1)*

University, and Todd Guttman, Ohio State University.

The video is being produced by Richard C. Tibbals and Brian Kusch, College of Communication Arts and Sciences, MSU, in collaboration with Ed Cheeney, Dennis Hart and Holly Giesman of Cheeney Media Concepts.

The one-hour video will be available on CD and the ORI web site when it is completed in summer 2006.

Wright said, "Institutions generally aspire to appoint new RIOs in sufficient time so that the outgoing RIOs can train them, but that doesn't happen often in practice. For this reason, ORI is developing educational materials to train and support new RIOs- professionalizing the role by defining essential functions and codifying best practices."

"The production of the video at this time is especially important," Wright continued, "because the first generation of RIOs, those that assumed the role shortly after 1989, is now starting to retire and we need to preserve their expertise for future generations."

The video will address administering institutional policies and procedures for handling allegations of misconduct; securing and safeguarding evidence; helping to protect whistleblowers; working with institutional counsel; liaison with those overseeing other regulatory areas, e.g. protection of human subjects, in complex cases that cross regulatory boundaries; and staffing and training inquiry and investigation committees.

The video will include interviews with experienced RIOs as well as senior ORI officials. Short scenarios of RIOs performing critical functions, e.g. sequestering data, may also be included.

## RCR in Graduate Training Supported by NSF

An effort to institutionalize responsible conduct of research education programs in graduate training begun by the Council of Graduate Schools (CGS) two years ago with ORI support will expand with funding from the National Science Foundation (NSF).

The award, *"Training Graduate Students in the Responsible Conduct of Research"*, made by the Ethics Program in Science and Engineering, NSF, began November 1, 2005 and ends December 31, 2007. The ORI award ends in May 2006.

The grant will enable CGS to make 8 awards at $15,000 each to institutions willing to develop RCR education programs. Submission deadline will probably be in August 2006. For further information click on RCR Program for Graduate Schools on the ORI home page.

## AAMC President Urges More Attention to Integrity

Jordan J. Cohen, M.D., President, Association of American Medical Colleges, urged his colleagues to "do a great deal more to fulfill our obligation to uphold the highest standards of scientific integrity" last September in his column in *The Reporter* in which he declared that "research integrity is job one" because "the general level of public trust in medical schools and teaching hospitals is, in large measure, the direct result of our reputation for scientific integrity."

"Conversely," he said, "few things are more damaging to the reputation of academic medicine than published instances of scientific misconduct." The full column is available at *http://www.aamc.org/newsroom/reporter/sept05/word.htm.*

"Even though only a tiny percentage of investigators appears to perpetrate frank scientific misconduct, each individual who does so tarnishes the reputation of the whole community and weakens public trust in medical science," he wrote. "That trust was damaged further last June when *Nature* published a survey of over 3,000 NIH-funded scientists in early and mid-career that purported to show that a substantial percentage had engaged in 'questionable research practices'."

He continued, "One can argue that the *Nature* survey had some serious shortcomings and should not be taken at face value. For sure, many questions were vaguely worded and produced ambiguous answers. Even so, some of the behaviors referenced, while not reaching the level of flagrantly outrageous misbehavior as codified in OSTP's definition of research misconduct, nevertheless pose serious threats to public trust. Whether caused by sloppiness, poor mentorship, inadequate training, or other factors, and whatever their 'true' incidence, the trustworthiness of the resulting 'science' is undermined."

## New Procedures Require Completion of All Data Fields *(from page 1)*

containing the password and IPF number for their institution to eliminate the need to call or email ORI to get them. If you have not received these notices, the contact information on your institution needs to be updated.

"Although officials may update their institutional information at any time by logging onto the Annual Report system on the ORI web site, " Randi Freedman, Manager, Assurance Program, said, "they will be required to verify their contact information - name of official and institution, mailing and email addresses, phone number—before they can complete the section on misconduct activity when filing the 2005 report."

ORI uses the contact information provided by institutions for mailing the *ORI Newsletter*, the *ORI Annual Report* and other publications, for emails announcing conferences, programs, and breaking news for referring research misconduct allegations to appropriate officials.

"All data fields in the institutional information and misconduct activity sections will have to be completed before the Annual Report can be submitted." Freedman said. "This is an effort to eliminate ambiguous and incomplete reports."

"Officials should determine whether their institution has a research misconduct policy before they indicate that it does not," Freedman continued. "About a third of the institutions that report they do not have a policy each year have already had their policy reviewed by ORI."

Bi-weekly reminders will be sent in January and February to institutions that have not already filed their 2005 Annual Report. Further information and assistance is available from Randi Freedman at rfreedman@osophs.dhhs.gov.

## Chinese NSF Makes 59 Misconduct Findings

The National Natural Science Foundation of China (NSFC), that country's leading basic research agency, has found 59 scientists guilty of research misconduct in the last two years, but has published detailed information including the names of the respondents in only three cases, according to *Science*. (9/16/05)

Falsification was found against 40 percent of the respondents, plagiarism against 34 percent, fabrication or theft of data against 7 percent, and other misconduct against 19 percent.

The NSFC formed a 19-member committee of distinguished scientists in December 1998 to investigate allegations of research misconduct. The committee has opened 542 cases based mostly on allegations made by anonymous whistleblowers.

Detailed information and the names of three respondents were announced for the first time in August 2005. In these three cases, the respondents were barred for up to four years from submitting new grant proposals to NSFC. No respondents appealed the findings.

The committee concluded that Su Bingyin, a neurologist at the Third Military Medical University in Chongqing, included ghost researchers in his grant proposal, plagiarized from other applications and altered biographical information; that Cui Jianwei, a postgraduate student in accounting at Jilin University, took a thesis from an American university web site, translated it into Chinese, and published it in a Chinese magazine; that Li Guibao, a lab director at the Institute of Water Resources and Hydropower Research, plagiarized material.

The 29-paragraph regulation published in April 2005 permits NSFC to decide whether to publicize its findings. No public announcements were made on 40 cases resolved in 2004. The general nature of the misconduct was announced in 16 cases resolved this year, but the respondents were not identified.

## Teaching Research Ethics Workshop

The thirteenth annual Teaching Research Ethics Workshop will be held at Indiana University from May 10-13, 2006. Session topics include an overview of ethical theory, trainee and authorship issues, conflicts of interest, using human subjects in clinical and non-clinical research, and responsible data management. Information and registration are available at *http://poynter.indiana.edu*.

## Abstracts *(from page 1)*

research areas, use new research methods, or provide new insights into recognized research problems. Proposals for theoretical or methodological presentations, historical analyses, and interpretive literature reviews will also be considered.

Abstracts for papers, poster sessions, panel discussions, and working groups should be submitted electronically by April 28, 2006. See the ORI web site for details on submitting abstracts and conference schedule as it develops at *http://ORI.hhs.gov*. Questions should be sent to Nick Steneck at nsteneck@umich.edu.

## ORI Intro to RCR Available In Three Languages

A Chinese translation of the *ORI Introduction to the Responsible Conduct of Research* was published in October making that publication available in three languages.

A Japanese translation of the booklet was published earlier this year by Maruzen Co., Ltd., Tokyo. The text was translated by Shigeaki Yamazaki, Department of Library & Information Science, Aichi Shukutoku University.

The Chinese version was translated by Nanyan Cao who teaches a course on research ethics at Tsinghua University. The booklet was published by Tsinghua University Press.

The English version is available for on-line reading or downloading on the ORI home page or may be purchased from the U. S. Government Printing Office at *http://bookstore.gpo.gov*. Cost is $14.00 per copy; a 25 percent discount is offered on purchases of every 100 copies sent to the same address.

The 178-page booklet, written by Nicholas H. Steneck, University of Michigan, with illustrations by David Zinn, Ann Arbor, introduces the reader to the nine RCR core instructional areas in four sections that follow the research process from inception to planning, conducting, reporting and reviewing. The publication features case studies, text-box inserts, discussion questions, and electronic and print resources.

## Missing Research Records Thwart Misconduct Investigations

Poor data management practices and the failure to sequester research records created serious problems in four investigations conducted by institutions and reviewed by ORI in 2005.

This problem is addressed in the new PHS regulation, 42 C.F.R. 93.106 (b)(1), which states the conditions under which institutions or ORI might consider the destruction of, absence of, or respondent's failure to provide research records as evidence of research misconduct.

"HHS grant regulations also require institutions to maintain research records for three years after the final annual or expenditure report is submitted to the funding agency," Alan Price, Director, Division of Investigative Oversight, said, "In the cases below, research records should have been available, but were not. It would seem prudent for institutional officials to make their scientists aware of these HHS record-keeping requirements, which may be needed to support their research whether or not it is challenged with allegations of research misconduct."

In one case, the investigation committee stated that if adequate research records had been available, the matter could have been readily substantiated or refuted. The postdoctoral fellow who was the respondent was known to be keeping very poor laboratory notebooks and other records, contrary to written institutional policy. The fellow was formally reprimanded for this by a supervisor three years ago and again one year before any allegations were made. The available records were insufficient for the institution to make a finding. ORI determined that the alleged false claims were not resolvable; they could have arisen from incompetence, error, or misconduct.

In another case, the institution found misconduct by a graduate student. However, it had been known by the mentor that this student had failed to keep laboratory notebooks or other organized records. Furthermore, many of the electronic research records were not sequestered for several weeks after the allegations were made and remained in the hands of the complainants; some records were presented as documents only in emails from the mentor back to the mentor. DIO found that, given the lack of records and the extensive problems between the mentor and student, the authenticity of the documentation could not be verified and used as a basis for any ORI misconduct findings.

In two other cases, records were also sequestered relatively late in the case, remaining with either the complainant or the respondent. The investigation committees basically deferred to the analysis by the complainant and did not carefully examine nor document the evidence for ORI. On receiving such a request for documentation from ORI, the institution had to spend many months trying to identify and collect appropriate records. In the end, they were insufficient for the institution or ORI to consider findings.

Several years ago, one institution had returned the sequestered research records to the respondent after finding evidence of research misconduct, before informing ORI of the outcome; when ORI asked for the records for its review, the institutional officials had to ask the respondent who had moved away to return them. When he did so, the key piece of evidence was absent. When challenged, he blamed the institution for losing it, claiming that he had returned everything that they had given back to him. And the institution had no copy or documentary record of that key evidence. Thus, ORI was unable to pursue a U.S. Public Health Service misconduct finding. In the present year, similar but much larger problems of missing records arose in four cases.

### FOURTH ANNUAL RCR EXPO

**October 16-17, 2006**
**Quebec City, Canada**

**Contact: LNguyen-Khoa@osophs.dhhs.gov**

### RCR PROGRAMS FOR ACADEMIC SOCIETIES

**Deadline: March 3, 2006**

**See ORI Home Page**

## Studies Report Behaviors That Adversely Impact Research

It is generally agreed that three major forms of dishonest behavior—fabrication, falsification, and plagiarism (FFP), violate the fundamental values of research and should be regulated by government. Other questionable practices are thought to be of lesser consequence and therefore left to the oversight of the research community. Two studies published earlier this year raise questions about the relative importance of improper behaviors that adversely impact research.

Brian Martinson of the HealthPartners Research Foundation in Minneapolis, MN, and colleagues are studying factors that can adversely impact research behavior. To assure their work looks at improper behaviors researchers themselves consider important, they interviewed 51 researchers during six focus-group sessions at several top-tier research universities and received additional input from six research compliance officers. The final "top-ten" list of improper behaviors is made up primarily of so-called questionable practices, suggesting that researchers regard these practices as important and potentially harmful to research as FFP. See Table 1. Martinson's study also found that researchers self-report engaging in these practices at alarmingly high rates.

Saana Al-Marzouki of the Department of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, England, and colleagues are interested not so much in the causes of improper behaviors as their impact. Using a Delphi survey rather than focus groups, they asked 32 clinical researchers to suggest ways "scientific misconduct . . . can arise in the design, conduct, analysis and reporting of a clinical trial." They then asked the same group to rate the potential impact and likely occurrence of the identified behaviors. Their final listing therefore contains improper behaviors that researchers believe will adversely impact the research process and are likely to occur. See Table 2. Interestingly, when the likelihood of occurring is factored in, improper behaviors equivalent to FFP drop off the list, leaving primarily behaviors that fall into the category of questionable practices.

Studies such as these are helpful in two ways. First, they suggest areas for future investigation. The perception that questionable practices may impact research more than FFP needs to be confirmed with empirical evidence. Methods also are needed to quantify the impact of different improper behaviors. Second, these and other similar studies suggest targets for responsible conduct of research (RCR) education. When no clear intent to deceive is evident, potential problems could be due to lack of proper training. Martinson's and Al-Marzouki's lists might therefore provide useful outlines for designing RCR education programs.

### Notes

Martinson, B. C., Anderson, M. S., et al. (2005). Scientists behaving badly. *Nature* 435(7043): 737-8.

Al-Marzouki, S., Roberts, I., et al. (2005). The effect of scientific misconduct on the results of clinical trials: a Delphi survey. *Contemp Clin Trials* 26(3): 331-7.

**Table 1. Partial List of Martinson's Ten Top Misbehaviors**

- Ignoring major aspects of human-subject requirements
- Using another's ideas without obtaining permission or giving due credit
- Unauthorized use of confidential information in connection with one's own research
- Failing to present data that contradict one's own previous research
- Overlooking others' use of flawed data or questionable interpretation of data
- Falsifying or 'cooking' research data

**Table 2. Partial List of Behaviors That Have an Adverse Impact and Are Likely to Occur According to Al-Marzouki's Study**

- Over-interpretation of "significant" findings in small trials
- Selective reporting of outcomes in the abstract
- Negative or detrimental studies not published
- Inappropriate subgroup analyses
- Selective reporting of positive results or omission of adverse events data
- Failure to report results or long delay in reporting
- Post-hoc analysis not admitted

## Case Summaries

**Randall Luce, University at Buffalo, State University of New York:** Based on the report of an investigation conducted by the University of Buffalo (UB), State University of New York (SUNY) (UB Report), and a conviction of the criminal offense of grand larceny, as defined in section 110-155.30 of the New York Penal Law, in the Buffalo City Court of Erie County, State of New York (Case 2004ER009612M), the Department of Health and Human Services (HHS) debarred Mr. Randall Luce, former research technician in the UB Research Institute for Addictions (RIA), for a period of three (3) years, beginning on July 26, 2005, and ending on July 25, 2008. Mr. Luce pled guilty to grand larceny and admitted to the misappropriation of funds and the fabrication of research subject interviews in the conduct of an RIA study supported by United States Public Health Service (PHS), National Institutes of Health (NIH), National Institute on Alcoholism and Alcohol Abuse (NIAAA) grant RO1 AA12452, "A harm reduction approach for reducing DWI recidivism." This action is taken pursuant to the HHS debarment and suspension regulation at 45 C.F.R. Part 76.

**Xiaowu Li, M.D., Ph.D., University of California at San Francisco:** On September 16, 2005, the U.S. Public Health Service (PHS) entered into a Voluntary Exclusion Agreement with the University of California at San Francisco (UCSF) and Xiaowu Li, M.D., Ph.D., former postdoctoral fellow at UCSF. Based on the UCSF report and additional analysis conducted by ORI in its oversight review, PHS found that Dr. Li engaged in scientific misconduct in reporting research supported by grants P01 DE13904, "Adhesion and proliferation in oral cancer progression," R01 DE12856, "Oral melanoma alpha v beta 3 expression and metastasis," and R01 DE011930, "Regulatory function of fyn in oral SCC invasion," all funded by the National Institute of Dental and Craniofacial Research (NIDCR), National Institutes of Health (NIH). Specifically, PHS found that Dr. Li falsified three images in Figure 5B of a paper, "Laminin-5 promotes cell motility by regulating the function of the integrin á6b1 in pancreatic cancer," published online in *Carcinogenesis Advance Access*, reporting studies on the role of integrin a6b1 and laminin on the invasiveness of pancreatic cancer cells and their ability to metastasize. In all three images, mouse melanoma cells were falsely represented as being human pancreatic carcinoma cells; the cancer cells were falsely represented as having been plated on medium with laminin-1, whereas they were in fact plated on medium with vitronectin; and for two of the three images, the cancer cells were falsely represented as having been stained with anti-integrin b1, whereas they were actually stained with anti-integrin b3. The misconduct was significant because pancreatic cancer has a poor prognosis for patients, since it tends to invade other tissues and to metastasize early in its course. Knowledge of the factors that facilitate cancer cell invasion and metastasis, which was the focus of the questioned figure and paper, is crucial to attempts to develop better treatments for pancreatic and other cancers. Thus, the falsified figure could have misled other investigators in this important area of medical research.

Dr. Li has entered into a Voluntary Exclusion Agreement (Agreement ) in which he has voluntarily agreed, for a period of three (3) years, beginning on September 16, 2005: (1) to exclude himself from any contracting or subcontracting with any agency of the United States Government and from eligibility or involvement in nonprocurement programs of the United States Government referred to as "covered transactions" as defined in the debarment regulations at 45 C.F.R. Part 76; and (2) 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 consultant.

## New Information Sources Issued on Human Protections

OHRP released a new set of Frequently Asked Questions to clarify issues related to research involving children at *http://www.hhs.gov/ohrp/policy/index.html#children*.

*The Universal Draft Declaration on Bioethics and Human Rights* was adopted by the UNESCO's General Conference. Available at *http://portal.unesco.org/shs/en/ev.php-URL_ID=1883&URL_DO=DO_TOPIC&URL_SECTION=201.html.*

A new directive on clinical trials that must be implemented by January 29, 2006 was issued by the European Union. Available at *http://pharmacos.eudra.org/F2/eudralex/vol-1/DIR_ 2005_28/DIR_2005_28_EN.pdf.*

## Conference, Workshop, and Meeting Proposals Due April 1, 2006.

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, 2006**. Proposal instructions and an application form are available on the ORI web site at http://ori.hhs.gov/html/programs/confworkshops.asp. Please submit your proposal electronically to stitus@osophs.dhhs.gov. Call Dr. Sandra Titus at 240-453-8400.

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