Societies Submit 11 Proposals; Awards Set for January

Awards are expected to be announced in January 2003 in the first round of proposals submitted by academic societies to the AAMC/ORI program designed to encourage academic societies to take measures to promote the responsible conduct of research in their respective disciplines.

Eleven proposals were submitted by 10 academic societies before the November 15, 2002, deadline. The second round deadline is March 14, 2003. All academic societies whose members conduct biomedical or behavioral research are eligible to participate in the program.

“AAMC believes academic societies should play a crucial role in defining and promoting standards for the responsible conduct of research in their respective disciplines,” Anthony Mazzaschi, Director, Council of Academic Societies Affairs, AAMC, said. “We believe academic societies must be more active in fulfilling this role.”

Five proposals fell into the first award category that provides up to $5,000 to support single events or limited activities such as special meetings, national conferences or publications. The proposals request funds for workshops, annual meeting sessions, and a short course.

Six proposals were in the second category that provides up to $25,000 for major program initiatives aimed at promoting the responsible conduct of research such as the development of research guidelines, code of research ethics, instructions for authors, curriculum module, and so on. The proposals request funds for a symposium, creation of guidelines, an ethics curriculum, a code of research ethics, and a clinical trials training program.

Proposals on Research Integrity Arrive; Review Next

Over 30 applications, received in the third round of the Research Program on Research Integrity, will be reviewed this spring; awards will be made by September 30, 2003.

Among the topics proposed for study are statistical practices, preliminary studies, neurosurgical clinical research, text appropriation, and the responsible conduct of research education received by medical residents and registered nurses.

A new request for applications will be published this spring; the submission deadline will most likely be in November 2003. The research program currently funds 16 studies with support from the National Institute of Neurological Disorders and Stroke, the National Institute of Nursing Research, and ORI.

New Look!

The ORI Newsletter begins its second decade of publication with a new look featuring a three-column format, which permits more flexibility in presentation and improves readability.
Second Round RCR Proposals Due Feb. 28

The next deadline for submitting proposals for the development of instructional materials that may be used in responsible conduct of research education programs at various institutions under the Responsible Conduct of Research (RCR) Resource Development Program is February 28, 2003.

ORI has committed $200,000 in FY 2003 to fund about eight projects. More projects will be supported if funds are available. Seventy-eight applications were received in FY 2002; 13 awards were made. Funding for each project is limited to $25,000 in direct costs; indirect costs are not covered. For more information see http://ori.dhhs.gov/html/programs/RCR_2nd_RFA.asp.

ORI launched the program last year because three reports issued by the Institute of Medicine and the National Academy of Sciences since 1989 have recommended that research institutions develop educational programs for their faculty and students to promote the responsible conduct of research.

IOM Report Available From ORI

Copies of the Institute of Medicine report, *Integrity in Scientific Research: Creating an Environment That Promotes Responsible Conduct*, are available in complete or summary form from ORI while the supply lasts. Call Robin Dorsey at 301-443-5300 or email her at rdorsey@osophs.dhhs.gov.

ORI/NIH Evaluate RCR Training

ORI is collaborating with the National Institutes of Health to develop an evaluation plan for the responsible conduct of research (RCR) requirement included in National Research Service Award (NRSA) institutional research training grants since 1990.

The contractor, American Institutes for Research, will conduct a literature review, perform a descriptive analysis of a representative sample of NRSA research training programs, organize an invitational workshop that includes individuals who are experts in RCR training, scientific integrity, bioethics, and evaluation methodology, and prepare a plan for a comprehensive evaluation of the RCR requirement.

RCR Instruction

The provision of instruction in the responsible conduct of research need not be driven by federal mandates, for it derives from a premise fundamental to doing science; the responsible conduct of research is not distinct from research; on the contrary, competency in research encompasses the responsible conduct of that research and the capacity for ethical decision making. *Integrity in Scientific Research: Creating an Environment That Promotes Responsible Conduct*. Institute of Medicine, 2002, p. 9.

2002 Annual Report Due Now!

Please take a few minutes to electronically submit the 2002 Annual Report on Possible Research Misconduct to smoothly continue your institution’s eligibility to receive PHS research funds beyond March 1, 2003. Instructions are available under Featured Attraction on the ORI homepage at http://ori.hhs.gov.

Doctoral Student Sues Over First Authorship

A lawsuit over first authorship ended with a former doctoral student in molecular biology winning over his professor when a German judge ruled that an implicit contract was breached when the professor substituted herself as first author on the final draft according to *Nature*.

The judge said the original verbal agreement bestowing first authorship on the doctoral candidate constituted an implicit contract because first authorship was not disputed in the 14 months of paper preparation.

The doctoral candidate sued the professor before the paper was submitted for publication, alleging that the professor had substituted herself as first author on the final draft without reasonable cause. The court immediately issued an injunction preventing publication.

The professor said the contribution by the doctoral candidate did not warrant first authorship. The doctoral student replied that he had independently carried out experiments and helped to write the paper.
ORI Investigator Positions Open

The Division of Investigative Oversight (DIO), Office of Research Integrity, is losing at least one senior staff scientist-investigator to retirement in early 2003. DIO welcomes calls, e-mails, or letters of interest from persons with experience at research institutions in handling allegations and investigations of research misconduct, or serving as a scientific expert in analyzing data, images, notebooks, printouts, or clinical files as evidence in trying to prove or disprove allegations of research misconduct. If you, or one of your colleagues, is interested in being considered for a GS-14 Health Scientist Administrator position as a Scientist-Investigator in DIO/ORI, contact Dr. Alan Price, Director, DIO, ORI: phone 301-443-5330, aprice@osophs.dhhs.gov, 5515 Security Lane, Suite 700, Rockville, Maryland 20852. The official job announcement is expected to be posted soon. Please check the ORI web site.

Two Conferences Slated For 2003

ORI will co-sponsor two conferences/workshops with a professional association and a university so far in 2003.

ORI will co-sponsor a meeting to discuss the research integrity issues related to Building a Research Agenda in Communication Sciences and Disorders: Lessons for Success with the American Speech-Language-Hearing Association from May 1-3, 2003, in Savannah, Georgia.

In fall 2003, ORI will co-sponsor an Introductory Workshop for Institutional Research Integrity Officers at the University of Connecticut Health Center.

New Staff Members Focus On Research and Education

Three new staff members—Sandra L. Titus, Carolyn R. Fassi, and Loc Nguyen-Khoa—joined the Division of Education and Integrity (DEI) this fall strengthening the capability of ORI to focus its mission on research and education.

Dr. Titus will serve as Director, Intramural Research Program. She has served as the associate director of research for the Minneapolis Children’s Medical Center, as an assistant professor at the University of Minnesota Medical School where she taught research skills to physician faculty, and as an assistant professor of sociology at St. Olaf College. In addition, Dr. Titus held research positions at the Institute of Child Development, the Center for Health Services Research, and the Family Social Science Department at the University of Minnesota. Before coming to ORI she worked extensively with IRBs and advisory committees at the FDA. Dr. Titus earned her doctorate in family social science, her master’s in public health from the University of Minnesota, and her bachelor’s in nursing from Wagner College.

Dr. Fassi and Nguyen-Khoa are educational specialists. Dr. Fassi helped establish an information network for public health officials, assisted the development of the first Master in Public Health education program in Nevada, created education programs for health care professionals and collaborated on distance learning program development for NASA-Ames employees. She has served as a health specialist at the National Institute of Allergy and Infectious Disease; as Nevada state coordinator for AIDS programs supported by the Centers for Disease Control and Prevention; as a consultant for the Nevada State Division of Health, and as administrative adjunct faculty at the University of Nevada, School of Medicine. Dr. Fassi holds a doctorate in public administration from the University of Southern California; a master of public health degree in community health education from San Jose State University, and a bachelor degree in fine arts with course work for a teaching credential from Webster College.

Mr. Nguyen-Khoa has extensive experience in graphic art, web design, and the development of software, health programs, web sites, and interactive health education CD-ROMs having worked for several years with web design firms. He received clinical training in occupational therapy at Johns Hopkins Hospital, University of Pittsburgh Medical Center-Rehabilitation Hospital, and the Maryland General Rehabilitation Hospital. Mr. Nguyen-Khoa is a doctoral candidate in public health and health education at the University of Maryland. He holds a masters in occupational therapy from Duquesne University and a bachelors in psychology from the University of Maryland, Baltimore County.

Three employees left DEI in the last year. Barbara Bullman retired, and Alicia Dustira and Anita Ousley moved to the National Institute of Mental Health and the National Cancer Institute, respectively.

Listservs Available

ORI operates listservs for RCR instructors, research integrity researchers, and research integrity officers. Subscribe to one or all by accessing the NIH listserv web site at http://list.nih.gov, then click on Browse, select the name of the listserv, and provide your e-mail address and full name. That’s all there is to it.
ORI Conference Explores Integrity in Clinical Research

The Conference “Enhancing Integrity in Clinical Research at Academic Medical Centers: A Practical Approach to Effectively Administering Clinical Research and Enhancing Integrity,” sponsored by the Office of Research Integrity (ORI), the Office for Human Research Protections (OHRP), and the Association of American Medical Colleges (AAMC), on September 9-10, in Baltimore, Maryland, drew 140 officials and 30 speakers.

As keynote speaker, Eve E. Slater, M.D., Assistant Secretary for Health, DHHS, emphasized the current need to increase the infrastructure to support the human research enterprise at institutions. This was followed by a session of talks by top research administrators from four leading clinical research institutions describing their experiences in shutting down and then reopening clinical research at their institutions; each agreed that they increased substantially, as much as three times, their institutional management infrastructure to support their clinical research. The Conference included talks on specific management issues such as dealing with conflicts of interest and privacy issues in clinical research, on-line and goal-oriented training for research ethics, and very practical matters in building a coherent compliance system within an institution.

The next day, the emphasis changed to research misconduct issues. One speaker emphasized and elicited discussion about the responsibility of Principal Investigators as trainers and mentors of young clinical research staff within their mentoring and academic setting.

Others illustrated specific issues and ways of enhancing research integrity in clinical trials by detecting research misconduct and specific data-handling measures. Preliminary data on many clinically-related research misconduct cases, including the respondents’ views on their training, supervision, and admissions, were presented. The focus shifted to descriptions of specific quality control measures used to monitor research from the several perspectives of a data coordinating center, external audits, funding program audits, and various Federal oversight audits. One speaker emphasized the need for continuing to develop unique data collection forms (rather than making them more standard), and another described the differences in quality control conducted by external audits.

The concluding keynote speaker, Barbara Mishkin, J.D., Hogan & Hartson, L.L.P., Washington, D.C., related the costs of protecting the research enterprise and the ethical and legal obligations for doing so. She summarized the meeting and her perceptions as counsel to universities and to respondents as they react to misconduct in phases using terms analogous to the Kubler-Ross model for dying. She emphasized the necessity for institutions to foresee the need to have an effective process for completely resolving a full range of research issues, including the responsibilities of individual investigators in human subject matters, with protections in place for all parties.

ORI Moving To New Quarters

ORI will move to a new building adjacent to Route 270 in Rockville this spring as part of an effort to consolidate housing for several units in the Office of Public Health and Science.

The new ORI address is the Tower Oaks Building, 7th Floor, 1101 Wootton Parkway, Rockville, MD 20852. Phone and fax numbers will remain the same.

Notable Quotes: Causes of Research Misconduct

“We need to know more about what motivates scientific misconduct and what can protect against it. Alas, the thin database on the etiology of fraud yields only a few hints.” Donald Kennedy, Science 289:1137, 2000.

“A broad range of factors in the research environment have been suggested as possible causes of misconduct in science. Such factors include (a) funding and career pressures of the contemporary research environment.; (b) inadequate institutional oversight; (c) inappropriate forms of collaborative arrangements between academic scientists and commercial firms; (d) inadequate training in the methods and traditions of science; (e) the increasing scale and complexity of the research environment, leading to the erosion of peer review, mentorship, and educational processes in science; and (f) the possibility that misconduct in science is an expression of a broader social pattern of deviation from traditional norms.” Responsible Science: Ensuring the Integrity of the Research Process. Vol. 1:30, NAS, 1992.

“One area where carelessness or dishonesty is particularly likely to occur is in the misuse of statistical techniques. No scientist can avoid the use of such techniques, and all scientists have an obligation to be aware of the limitations of the techniques they use, just as they are expected to know how to protect samples from contamination or to recognize inadequacies in their equipment.” Honor in Science, p. 18. Sigma Xi, The Scientific Research Society, 1997.
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Heather J. Muenchen, Ph.D., University of Michigan (UM): Based on the UM investigation report, Dr. Muenchen’s admissions, and additional analysis conducted by ORI in its oversight review, the U.S. Public Health Service (PHS) found that Dr. Muenchen, former UM postdoctoral fellow, engaged in scientific misconduct in research funded by National Institutes of Health (NIH) Urology Research Training Grant T32 DK07758 and SPORE grant PS0 CA69568. Dr. Muenchen falsified and fabricated research data by computer manipulation of 12 Western blot analyses in 3 publications and 2 draft manuscripts. Specifically, PHS found that Dr. Muenchen: (1) falsified Western blot data in Figures 3, 4A, and 4B in Muenchen, et al., “Tumor necrosis factor-alpha-induced apoptosis in prostate cancer cells through inhibition of nuclear factor-6B by an I6B ‘super-repressor’” Clinical Cancer Research 6(5):1969-1977, 2000; (2) falsified Western blot data in Figures 2 and 3 in Muenchen, H.J., Poncza, P.J., and Pienta, K.J. “Different docetaxel-induced apoptotic pathways are present in prostate cancer cell lines LNCaP and PC-3.” Urology 57(2):366-370, 2001; (3) falsified Western blots and associated claims for Figures 1, 5A, 5B, and 8 in Muenchen, et al., “Re-expression of functional androgen receptor in androgen-independent prostate cancer cells.” which was published electronically on November 13, 2000, in the Journal of Biological Chemistry (JBC) (withdrawn January 16, 2001); and (4) falsified Western blot analyses in Figures 4A, 4B, and 7 of the original draft submitted for publication on September 29, 2000, and the corresponding Figures 5A, 5B, and 8 in the second draft of the JBC manuscript. Dr. Muenchen was the first and corresponding author on the above publications, which were supported in part by the above-cited grants. These falsifications are significant because they misrepresent the expression of the androgen receptor, the necessary control data, the evidence for “super-repressor” binding and its effect, and the control data for assaying apoptosis. These misrepresentations occurred through a series of separate and specific deceptions in an attempt to obviate the legitimate criticisms of publication reviewers. These falsifications were designed to be misleading about the experiments’ true results and to wrongfully induce publication of the experiments. Dr. Muenchen’s work could have provided tools for understanding metastasis in prostate cancer and ultimately impact on treatment of this disease.

Dr. Muenchen entered into a Voluntary Exclusion Agreement in which she voluntarily agreed for 5 years beginning September 5, 2002, to exclude herself from any contracting, subcontracting, or involvement in grants and cooperative agreements with the U.S. Government, and to exclude herself from serving in any advisory capacity to PHS. In addition, within 30 days of September 5, 2002, she agreed to submit letters to the editor of Urology retracting the published paper, and to the editor of Clinical Cancer Research, identifying and retracting the falsified or fabricated data in Figure 3 and Figures 4A and 4B. Dr. Muenchen submitted retraction letters to both journals.

M. Renuka Prasad, Ph.D., University of Kentucky School of Medicine (UK): Based on the University of Kentucky School of Medicine investigation report, Dr. Prasad is prohibited from supervising other research staff; and (b) any institution employing him is required to submit a certification that the data he provided are based on actual experiments.

Dr. Prasad entered into a Voluntary Exclusion Agreement in which he voluntarily agreed: (1) that for 3 years beginning August 19, 2002: (a) any institution that submits an application for PHS support for a research project on which Dr. Prasad’s participation is proposed or that 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 certify in every PHS research application or report that Dr. Prasad is prohibited from supervising other research staff; and (b) any institution employing him is required to submit a certification that the data he provided are based on actual experiments.

JBC, 832:7-12, 1999.
Case Summaries

or are otherwise legitimately derived, and that the data, procedures, and methodology are accurately reported in the application or report; (2) to exclude himself from serving in any advisory capacity to PHS; and (3) within 30 days, Dr. Prasad must submit a letter to the journal *Brain Research* requesting retraction of the paper, stating that some of the data for the reported effects of kynurenate are falsified. Dr. Prasad sent a copy of the retraction letter to ORI.

Zhenhai Yao, M.D., Ph.D., The University of North Carolina at Chapel Hill (UNC): On August 20, 2002, PHS entered into a Voluntary Exclusion Agreement with UNC and Zhenhai Yao, M.D., Ph.D., an Associate Professor of Anesthesiology, School of Medicine at UNC. Based on the UNC Report, the respondent’s admissions, and additional analysis conducted by ORI in its oversight review, PHS found that Dr. Yao engaged in scientific misconduct in research funded by the National Heart, Lung, and Blood Institute, NIH. Specifically, PHS and UNC found that Dr. Yao:

1. Falsified two fluorescent micrographs for figures presented in three NIH grant applications:

   Dr. Yao falsely claimed that two fluorescent micrographs in the figure represented neonatal rat cells transfected with an adenovirus-derived vector, when the cells actually were chick cells transfected with a cytomegalovirus-based vector, taken from another scientist at the University of Chicago.

2. Falsified the same two fluorescence micrographs of CMV-transfected chick cells described in (1) above, by misrepresenting their description as embryonic chick cells transfected with pcDNA, with and without green fluorescent protein in an NIH grant application.

3. Falsified a flow cytometry histogram in Figure 1B on p. 22 of NIH application R01 HL66230-01A1, by claiming the histogram represented results with rat cardiomyocyte cultures treated with an opiate antagonist (staurosporine).

   However, this histogram had been published by Liu, H., McPherson, B.C., & Yao, Z. “Preconditioning Attenuates Apoptosis and Necrosis: Role of Protein Kinase Cε and δ Isoforms.” *Am. J. Physiology Heart Circ Physiol.* 281:H404-H410, 2001, as Figure 1f showing the result from embryonic chick cells treated for 12 hours with deoxy-glucose in the absence of oxygen (simulated ischemia).

4. Falsified claims about research results in NIH grant application R01 HL66230-01A1, by claiming that data in Figure 3 on p. 23 represented experiments on cultures of neonatal rat cardiomyocytes as an *in vitro* model of hypoxia-reoxygenation, shown as data from four separate experiments measuring apoptosis by different means.

   The data in the four separate experiments portrayed in Figure 3 are identical to Figure 1, p. 2009, in the publication by Liu, H., Zhang, H.Y., McPherson, B.C., Baman, T., Roth, S., Shao, Z., Zhu, X., & Yao, Z. “Role of Opioid δ1 Receptors, Mitochondrial KATP Channels, and Protein Kinase C during Cardiocyte Apoptosis.” *J. Mol. Cell. Cardiol.* 33:2007-2014, 2001, which were reported as the results from experiments on cultures of embryonic chick cardiocytes.

5. Falsified the micrographs in panels a and d, Figure 1, p. 2009, in the publication by Liu, H. et al., *J. Mol. Cell. Cardiol.* 33:2007-2014, 2001, by claiming they represented TUNEL data showing normal media and opioid antagonist (TUNEL) data showing normal media and opioid antagonist (BTNX)-treated cultures of chick cardiocytes, respectively.

   The same micrographs had been reported by Liu, H. et al., *Am. J. Physiology Heart Circ Physiol.* 281:H404-H410, 2001, in Figure 1 (panels a and e) and in Figure 2 (panels a and b), as representing cardiocyte cultures exposed for 24 hours to deoxy-glucose and no oxygen (simulated ischemia).

6. Falsified the physiological effects of gene transduction into hearts, by copying and re-using the same pressure tracing for untreated rates as he did for rats purportedly treated by intracardial injection with adenovirus (AdEGFP) in 4 NIH grant applications.

7. Falsified data in panels c and d in Figure 13, p. 26, in NIH grant application R01 HL66230-01A1. Dr. Yao claimed that panel c represented a TUNEL assay on histological sections of myocardium from a rat transfected with Ad.βgal and subjected to ischemia-reperfusion and that panel d represented a tissue section from a rat transfected with Ad.PKδ-FL.

   Panel c is a horizontally compressed copy of panel b, purported to be a non-transfected rat subjected to ischemia-reperfusion, and panel d is a horizontally expanded version of panel a, purported to be a sham-operated, non-transfected control.

8. Falsified claims about the micrograph of ischemic data in (7) above.

In both examples, the figures, which are identical, consist of two panels purported to be TUNEL data showing sham operated controls (panel a) and the effect...
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of transient ischemia for 30 minutes (panel b). However, these data are identical to Figure 10, p. 32, in NIH application K08 HL03881-01, reported a control and the effect of nontransient ischemia, i.e., 20 hours of ischemia followed by 24 hours of reperfusion.

(9) Falsified data in Figure 14 on p. 27 in NIH grant application R01 HL66230-01A1, as representing a gel electrophoresis data from an in vivo experiment on rat myocardial ischemia. However, the same data was represented as Figure 3, p. 23, of the application (and also as in Figure 1, J. Cell. Mol. Cardiol. 33:2007-2014, 2001), as results from a study of embryonic chick heart cell cultures for the effect of preconditioning on opioid receptors. Furthermore, Dr. Yao falsified the stated size of the fragments in the DNA marker ladder by altering the position of the molecular weight markers in Figure 14.

(10) Falsified Figure 3, p. 27, in 1 R01 HL67416-01, a DNA-laddering gel electrophoresis experiment, showing that apoptosis in cardiocyte cultures is significantly increased by staurosporin and by 12 hours of simulated ischemia. The same data was shown in Figure 1, p. 26, in application HL03881-07 showing that apoptosis is significantly increased by 10 μNE and by 15 nM TNF-α. The research misconduct was significant because Dr. Yao’s research involved the fundamental mechanisms for cardiac cell injury and pathogenesis after a heart attack. The falsified data were significant to reviewers’ opinions on funding because they were advanced as preliminary results showing successful new experiments extending his experimental model to adult rat hearts.

Dr. Yao entered into a Voluntary Exclusion Agreement in which he voluntarily agreed for 5 years beginning August 20, 2002, to exclude himself from any contracting, subcontracting, or involvement in grants and cooperative agreements with the U.S. Government, and to exclude himself from serving in any advisory capacity to PHS. Additionally, he agreed to submit a letter to the Journal of Molecular and Cellular Cardiology requesting retraction of Figure 1 in the article by Hui Liu, et al., J. Mol. Cell. Cardiol. 33:2007-2014, 2001, within 30 days of August 20, 2002. This requirement will be noted on the ALERT System until Dr. Yao sends a copy of the retraction letter to ORI.

New Lawyer Joins Research Integrity Branch

A lawyer experienced in federal and state health care fraud investigations and regulatory compliance issues has joined the Research Integrity Branch, Office of the General Counsel.

Jo An Rochez Leonce worked for a Washington law firm since she graduated from the University of Maryland Law School, Baltimore, in May 1997 where she was a member of the Maryland Law Review. Besides the issues noted above, Ms. Leonce focused on the corporate practice of medicine, Medicare and Medicaid reimbursement, and fraud and abuse counseling. She is a member of the bar in Maryland and the District of Columbia.

While in law school, Ms. Leonce interned as a legislative analyst in communications, patent and copyright law at the Congressional Research Service, Library of Congress, and at a Washington law firm where she did legal research for attorneys in the employment, health, business, and federal practice departments.

Ms. Leonce attended Howard University on full-scholarship, graduating magna cum laude with a bachelor’s degree in journalism. She was elected to the Golden Key National Honor Society and the Frederick Douglass Honor Society.

Watch for RFA on Research on Research Integrity
### UPComing Events

**Meeting Proposals**  
**Due June 1**

ORI is seeking proposals from institutions, professional associations, and scientific societies that wish to collaborate with ORI in developing a conference or workshop on promoting research integrity or handling scientific misconduct allegations. The amount of funding available generally would be from $5,000 to $20,000.

Proposals are welcome any time, with **June 1, 2003**, serving as the next target date for the receipt of applications. Proposal instructions and an application form are available on ORI’s web site ([http://ori.dhhs.gov](http://ori.dhhs.gov)), by calling (301) 443-5300, or by sending e-mail to askori@osophs.dhhs.gov.