THE OFFICE OF RESEARCH INTEGRITY®

NEWSLETTER

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QUEST FOR RESEARCH EXCELLENCE CONFERENCE

AUGUST 7–9, 2017
GEORGE WASHINGTON UNIVERSITY
WASHINGTON, DC

IN THIS ISSUE:

MESSAGE from the DIRECTOR

It has been a very great pleasure for the Office of Research Integrity (ORI) staff to welcome international visitors from far and wide to our office over the past few months. Since the year began, our staff has met with delegations from France, Japan, and South Korea. In previous years, we have met with delegations from these countries as well as from Australia, Ireland, and the Netherlands. Our visitors want to share information and ideas about how to promote research integrity and how to handle research misconduct. Through diversity of thought, interesting similarities and differences emerge in the approaches these countries take regarding research integrity.

They seem to have in common a growing concern about research misconduct, its negative impact on science, and increasing public pressure for an authority to protect the integrity of science. The research record, as reflected in scientific journals and publications, is equally important to all, and it appears that all of our international colleagues are working on ways to protect the research record from publications that lack integrity. Moreover, many are seeking ways to standardize the literature corrections process. There were discussions about how to distinguish between corrections made by honest scientists, who want to correct the record as a proactive, healthy act, and those who have committed misconduct and knowingly or intentionally falsified or fabricated the data in their papers, and therefore are forced to retract or correct their findings. I was delighted to read some of the plans, reports, and approaches that our international colleagues are taking in the research misconduct process.

It seems that each country has reached the same conclusion—education of research trainees is the foundation on which research integrity is built.

I have been struck by our shared commitment to the need for training and education on the responsible conduct of research (RCR). It seems that each country has reached the same conclusion—education of research trainees is the foundation on which research integrity is built. Yet there remain many questions about when to train, how to train, who to train, and what to include in the content of RCR training. Few of us feel confident that we have completely figured out how formal RCR education can more perfectly complement informal laboratory training and mentoring to produce investigators who are innovative, resilient, ethical, and successful.

MESSAGE from the DIRECTOR

We also noted some differences between international approaches to research integrity. Probably the most significant differences are in the implementation and legal authorities. There are also a range of perspectives about whether a government considers the oversight and enforcement of research integrity to be the responsibility of the funding agencies or the responsibility of academic or educational agencies. Various models seem to have their own strengths and weaknesses.

Virtually every international guest we have met agrees on the importance of activities that promote research integrity, both for protecting the research enterprise and for engendering public trust in their investments in science and education. The very nature of science is interdependent, and research integrity efforts must take into account the global nature of science. We all seem to agree, too, that this is an important moment in history when the public is genuinely concerned about research integrity, when steps must be taken to protect and promote research integrity. I think this will be emphasized at the 2017 World Conference on Research Integrity, to be held in Amsterdam this May. Although the United States, through ORI and other federal agencies, has been focused on these issues for only the past three decades, our research integrity infrastructure is more mature and established than that found in many other countries. As such, the U.S. Government is viewed as a thought leader in research integrity. This is both a source of pride and a reminder of our responsibilities, not only at home but also abroad. ORI is always pleased to welcome international visitors. The exchange between countries is important and always mutually beneficial.

RESEARCH INTEGRITY NEWS

Research Integrity and Regulatory Symposium

Thursday, May 25, 2017, to Friday, May 26, 2017, South Portland, ME

The Research Integrity and Compliance Symposium is a two-day event with focused workshops and plenary sessions on developing or improving compliance with and understanding of the regulations impacting today's businesses and academic institutions. From newcomers to experts, there is always something new to learn at the Symposium.

* This conference is funded by a grant from ORI, Grant #ORIIR160023.

Research Integrity Management Intensive (RIMI) Workshop

Thursday, June 22, 2017, to Friday, June 23, 2017, Arlington, VA

Sponsored by George Mason University and Society for Research Administrators International (SRA)

George Mason University and SRA are holding a two-day RIMI workshop that will provide research integrity leadership training for administrative leaders and will result in developing a guidance document and other resources for research administrators. Course curriculum will deal with RCR core content and explore the complex roles of grants administrators, research subject committee administrators, and research integrity and compliance officers, and how they interconnect to support and protect the research enterprise. For more information about the meeting, visit the conference website: http://srainternational.org/meeting/theme/research-integrity-management-intensive-workshop (link is external).

* This conference is funded by a grant from ORI, Grant #ORIIR160026.

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10 Questions to Robin Parker, ORI's Assurance Program Specialist

The first quarter of the year is a busy time for Robin Parker, ORI's assurance program specialist. Starting on January 1, institutions with active or pending research or research-training grants from the Public Health Service (PHS) have four months – until April 30 – to establish or maintain an assurance with ORI to be able to receive or continue to receive PHS funds, in accordance with the PHS Act and 42 CFR Part 93. Filing an assurance with ORI as a PHS awardee entails:

- completing an electronic Annual Report on Possible Research Misconduct (form PHS-6349), which states that the institution has developed and will comply with an administrative policy for responding to allegations of research misconduct that complies with 42 CFR Part 93 and documents all research misconduct activity for the previous calendar year.
- submitting the research misconduct policy for ORI's review.

Institutions complete this process by logging into ORI's Assurance Program Annual Report System. Over the years, ORI has developed several tools to help institutions establish and maintain an assurance with ORI. The latest one, a checklist developed to help institutions assess their policies for compliance with the regulatory requirements before submission to ORI, was just released on ORI's website. This release is an opportunity to ask Robin to clarify certain points regarding ORI's assurance program, and more specifically, the requirement for institutions to have a research misconduct policy on file with ORI.

1 Do institutions that file a federal-wide assurance (FWA) have to file an assurance with ORI?

YES. The FWA provides a guarantee that the institution will comply with the federal requirements for Protection of Human Subjects (PHS) regulations (45 CFR part 46).These requirements are distinct from those of the PHS regulation on research misconduct (42 CFR Part 93). Protecting human research subjects is different from protecting PHS research products and funds. Therefore, having an FWA does not exempt an institution from filing an assurance with ORI.

2 What requirements must a research misconduct policy meet to be considered compliant with the regulations?

The research misconduct policy of a PHS-funded institution has to comply with the requirements of the PHS Policies on Research Misconduct, as laid out in 42 CFR Part 93, in effect since June 16, 2005.

3 Does an IRB policy qualify as a research misconduct policy?

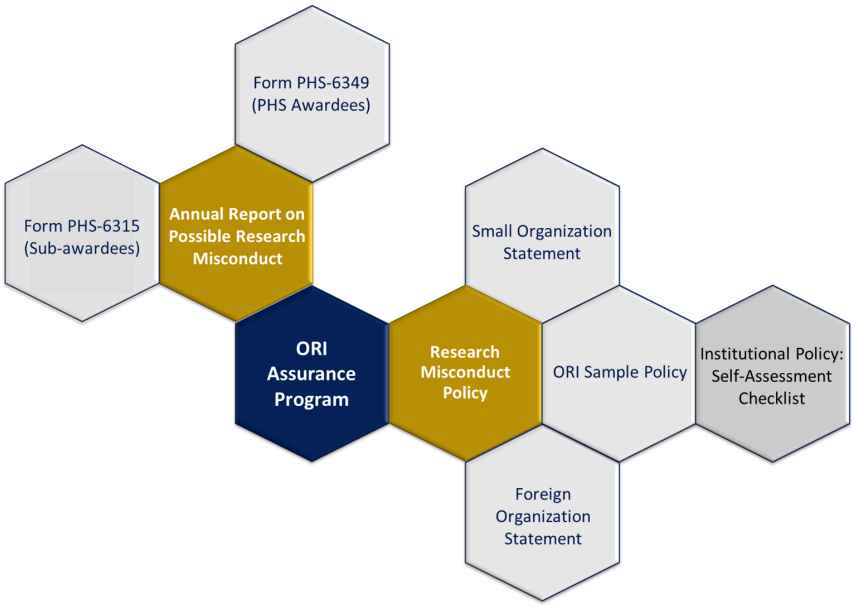
NO, unless the IRB policy includes additional elements that meet the requirements of 42 CFR Part 93, which is possible, if not the most practical solution (see also Question 1).

4 Are small organizations required to have policies and procedures for handling allegations of research misconduct?

YES, they are. However, a small organization may not be able to conduct an inquiry or investigation into an allegation of research misconduct without conflict of interest, as required by the PHS regulations. For this reason, small organizations meeting specific size criteria have the option to file a Small Organization Statement, a legally binding document that requires that the small organization notify ORI as soon as an allegation or evidence of possible research misconduct arises. The conditions of eligibility for filing this statement are detailed in the welcome letter that every first-time applicant for an NIH grant receives from ORI.

5 Are foreign institutions that apply for PHS funding exempt from filing a research misconduct policy with ORI?

NO, foreign institutions that apply for PHS funding must establish a research misconduct policy that complies with 42 CFR Part 93, just like their U.S.-based counterparts. To help foreign institutions fulfill this requirement without compromising their country's laws and procedures, ORI gives them the option to file a legally binding statement titled "Statement on Dealing with Allegations of Research Misconduct Under Public Health Service Research-related Activities for Foreign Institutions."



Requirements of the ORI Assurance Program and Tools Available to Institutions to Fulfill Them.

6 My organization will be receiving NIH funds from an NIH grantee organization, but not directly from NIH. Is it required to have its own policy on file with ORI?

YES, it is. Section 93.214 of the PHS regulation on research misconduct defines sub-awardees, contractors, and subcontractors as "institutional members." ORI de facto considers that an institutional member must comply with the same ORI assurance requirements as its PHS-funded parent institution, which includes filing a research misconduct policy with ORI.

7 Is the submission of the policies and procedures for handling allegations of research misconduct required each year with the Annual Report on Possible Research Misconduct?

NO, but you do need to re-submit the document if there has been any change made to it, especially if the original policy already has been reviewed and deemed acceptable by ORI. The best way to do this is to email the new policy to Robin Parker, mentioning "Policy Change" in the email subject line.

8 Is there guidance or a template for writing policies and procedures for handling allegations of research misconduct?

YES, ORI has developed a sample policy that U.S.-based institutions other than small organizations may file to comply with 42 CFR Part 93 if they do not have a research misconduct policy by the time they are asked to establish an assurance with ORI.

9 Do institutions need to file an Annual Report on Possible Research Misconduct if they no longer receive PHS research funding?

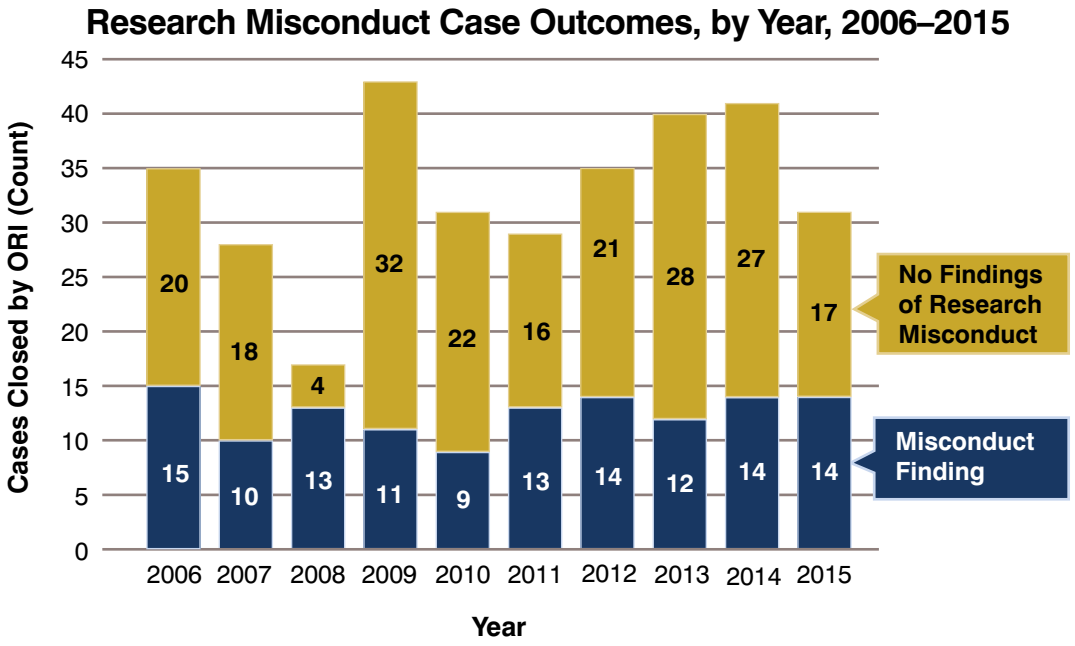
NO, you are not required to keep reporting on research misconduct to ORI unless you are still involved in PHS-funded research as a sub-awardee (see Question 6).

10 Who should be aware of the institution's research misconduct policy?

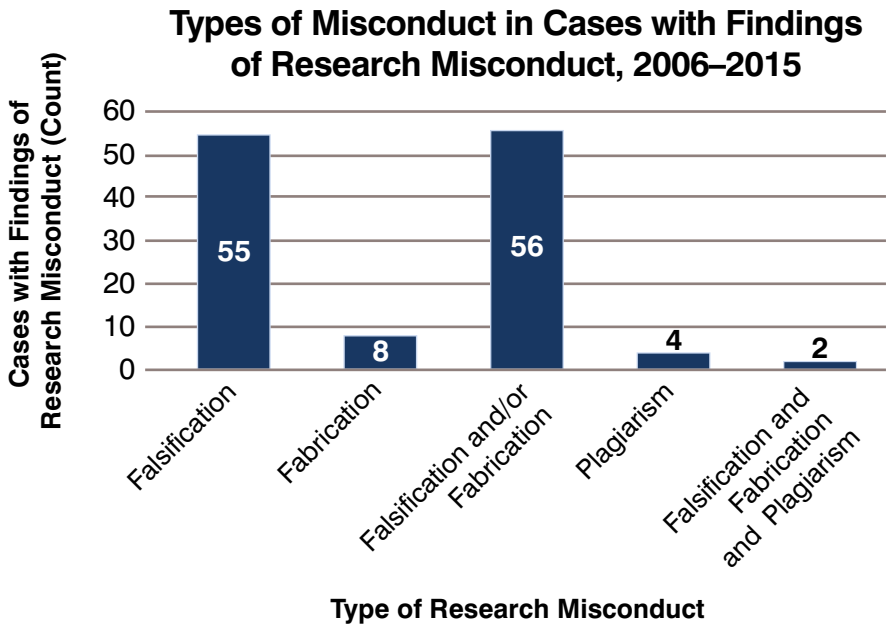
All of the institution's employees participating in or otherwise involved with PHS-funded research-related activities should be informed about the institution's policy for handling allegations of research misconduct. This is a requirement laid out in Section 93.302(a)(2)(i) of the PHS policies on research misconduct.

ORI Activity Summaries

You may have noticed that the ORI Annual Report has not been posted for the past few years. We have been working hard to remedy that. New plots and charts of both research misconduct and educational activity are being finalized now, and we hope to have lots of new data posted on the ORI website in the coming weeks. As we move forward, we will strive to post the previous year's data by July 1 each year. The data are interesting to look at, and we hope will be useful, particularly to RCR instructors. Here are a few of the plots we have been working on.

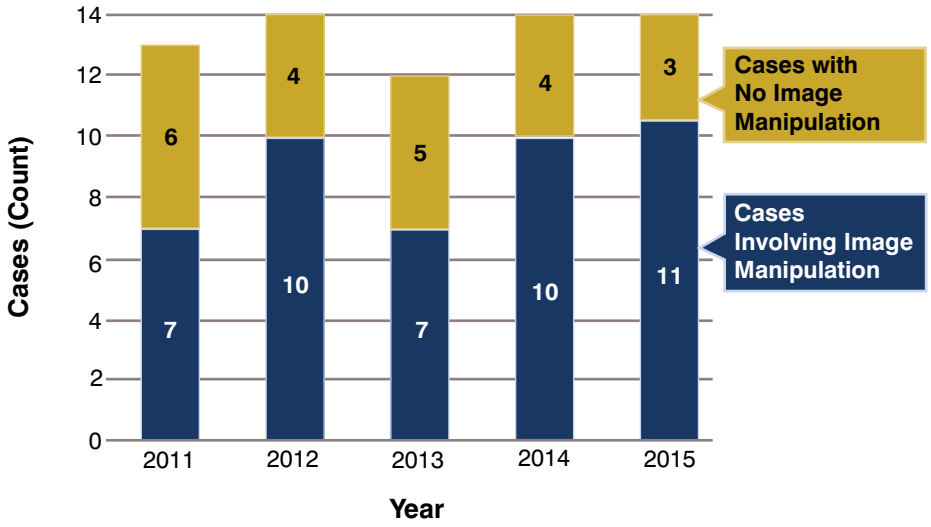


Research Misconduct Case Outcomes, by Year, for a 10-Year Period, 2006–2015. ORI closed 330 research misconduct cases between 2006 and 2015. Of these cases, 125 cases were closed with research misconduct findings, and 205 cases were closed with no findings of research misconduct.



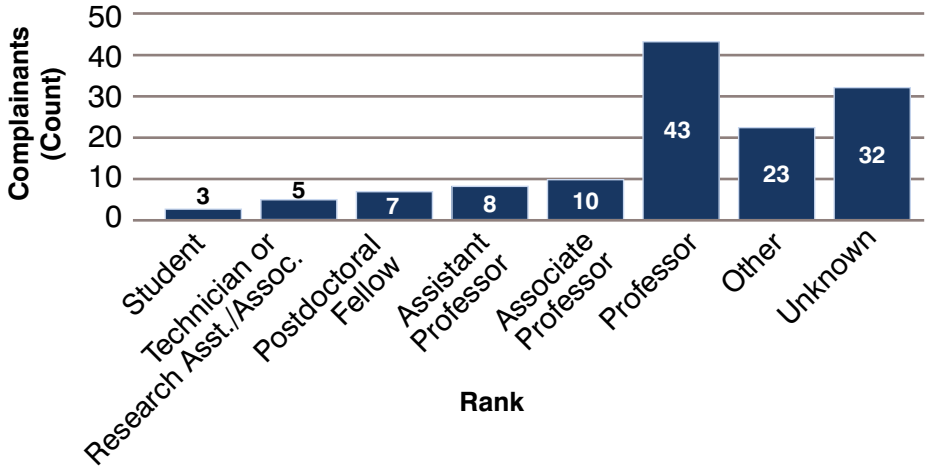
Types of Misconduct in Cases Closed with Findings of Research Misconduct for a 10-Year Period, 2006–2015. ORI closed 125 cases with findings or research misconduct between 2006 and 2015.

Cases with Research Misconduct Findings Involving Image Manipulation, by Year, 2011–2015



Cases with Research Misconduct Findings Involving Image Manipulation, by Year, for a 5-Year Period, 2011–2015. Out of a total of 67 cases closed with findings of research misconduct, 45 cases involved image manipulation. Examples of falsified images involved cutting and pasting bands from gels or western blots, deleting or inserting parts of micrographs, or reusing and relabeling unrelated images.

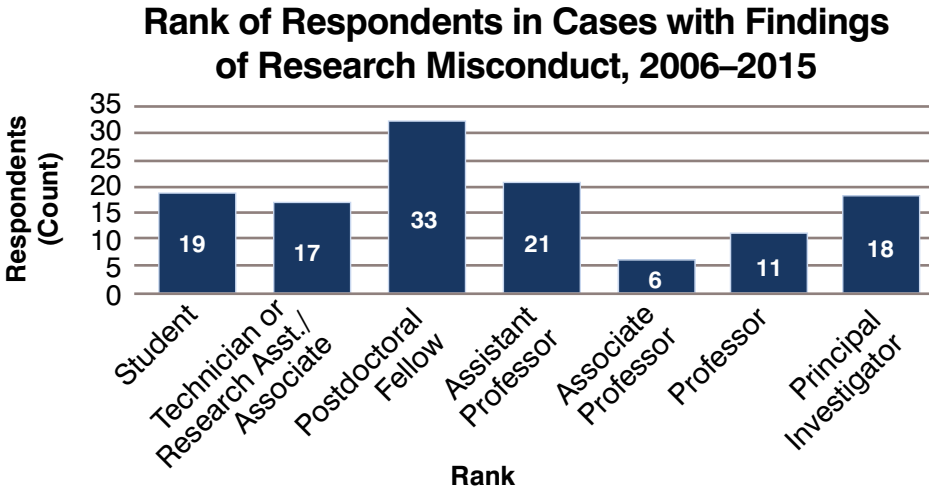
Rank of Complainants in Cases with Findings of Research Misconduct, 2006–2015



Rank of Complainants in Cases with Findings of Research Misconduct for a Ten-Year Period, 2006–2015. There were a total of 131* complainants in 125 cases with findings of research misconduct between 2006 and 2015.

* Six cases included two complainants. Each complainant was counted separately.

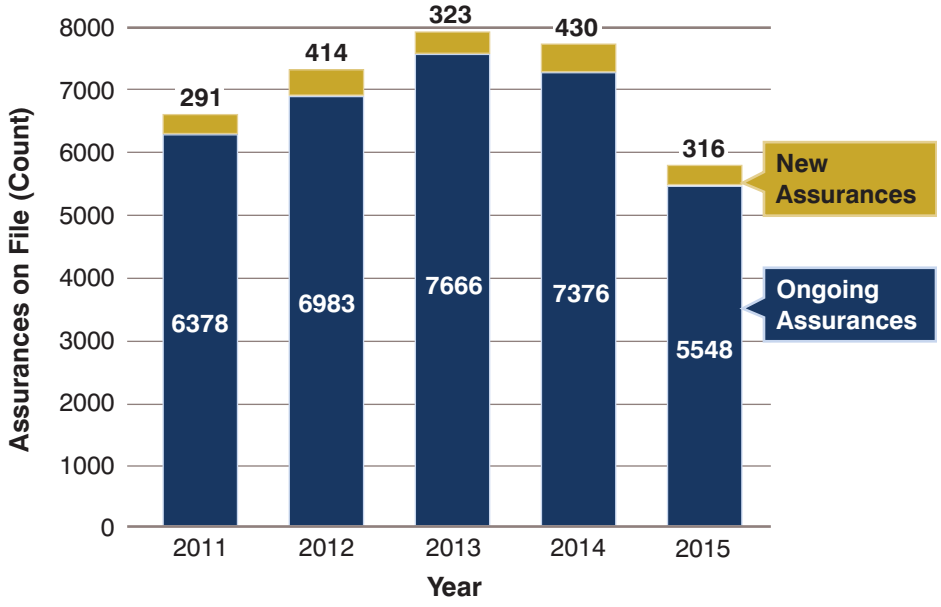
Rank of Respondents in Cases with Findings of Research Misconduct, 2006–2015



Rank of Respondents in Cases with Findings of Research Misconduct for a 10-Year Period, 2006–2015. There were a total of 125 respondents in 125 cases with findings of research misconduct between 2006 and 2015.

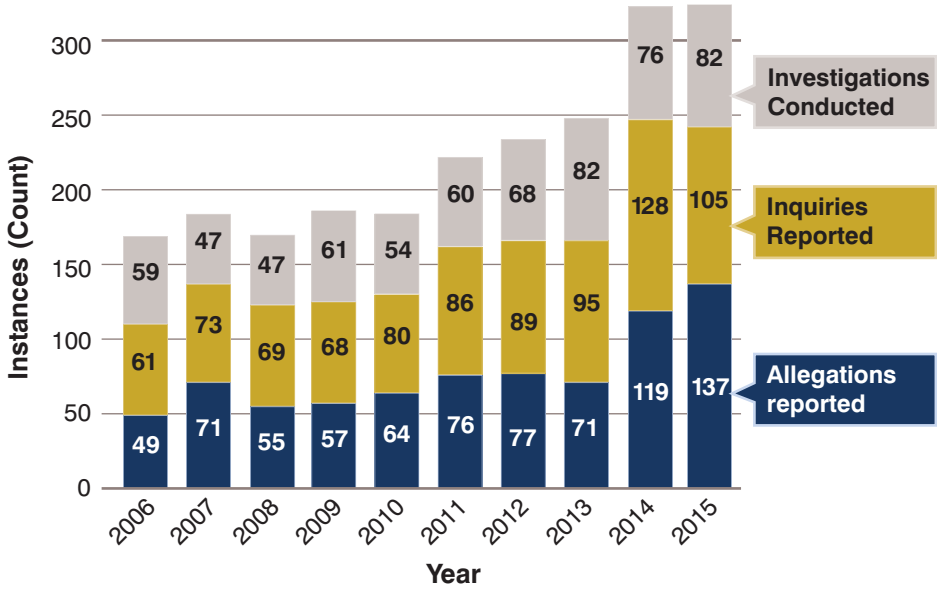
Institutional Assurances, by Year, for a 5-Year Period, 2011–2015. Between 2011 and 2015, ORI issued a combined total of 35,725 institutional assurances. All institutions receiving or applying to receive research funds from PHS agencies must have an assurance with ORI. This assurance means an institution promises ORI that it: (1) has the required policies and procedures in place for dealing with allegations of research misconduct (stipulated in 42 Code of Federal Regulations (CFR), Section 93); (2) has provided ORI with contact information for its assurance official; and (3) will submit an annual report to ORI, identifying any activity from the previous year that required inquiries and investigations into allegations of possible research misconduct involving research supported by PHS funds.

Institutional Assurances by Year, 2011–2015



Number of Allegations, Inquiries, and Investigations Reported by Higher Education Institutions by Year, 2006–2015. To keep its assurance active, each institution must submit to ORI an Annual Report on Possible Research Misconduct (PHS Form 6349) that provides aggregate information on allegations, inquiries, investigations, and other activities required by the PHS regulation. Over the 10-year period, 1,162 reports were submitted showing 776 allegations, 854 inquiries, and 636 investigations.

Allegations, Inquiries, and Investigations Reported by Institutions of Higher Education by Year, 2006–2015



It's All in the Planning

ORI is enthusiastically working with our planning committee and co-sponsors on developing the 2017 Quest for Research Excellence Conference, to be held in Washington, D.C., on August 7-9, 2017. ORI is grateful for the energy and ideas that are springing forth from our planning subcommittees and for the co-sponsorship of George Washington University and Public Responsibility in Medicine and Research (PRIM&R).

The overarching theme of the conference on research integrity is "breaking down the silos." The five tracks that will support that theme are:

- Responsible Conduct of Research
- Research Misconduct
- Communicating Science in 2017
- Open Science
- Legal Issues Related to Research Integrity

Instructions for registering and for submitting abstracts are now available. The conference website is https://ori.hhs.gov/Q4RE2017. Please check back to that site, as we will be updating it frequently over the next few months. Questions may be directed to Tracey.Randolph@hhs.gov. Stay tuned!

ORI's Newest Staff

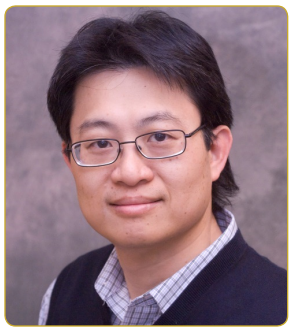
Lynn Powell-Hailey handles Freedom of Information Act (FOIA) requests and supports ORI investigators' case management, including research in using legal databases such as Westlaw and LexisNexis.

Before joining ORI, Lynn worked for approximately a decade at the Federal Mine Safety and Health Review Commission (FMSHRC), as a legal assistant to administrative law judges. Along with maintaining a caseload of about 500 case files, she processed FOIA requests, drafted decisions approving settlements, and managed a variety of databases, such as myCase, Credenza, Central Tracking System (CTS), and Electronic Computer Management System (e-CMS). She also handled monthly statistics and inventory reporting. Lynn received numerous performance and team awards during her tenure at FMSHRC.

Lynn has a master's degree in government, with a concentration in law and justice, from Johns Hopkins University; a certificate in paralegal studies from George Washington University; and a bachelor's degree in political science from Bennett College.

Lynn is a native Washingtonian and attended Woodrow Wilson High School in upper northwest Washington, D.C. Lynn is a member of a local paralegal association called the National Capital Area Paralegal Association (NCAPA). She served as a mentor to a high school student for three years through a non-profit organization, Mentors, Inc. Today, her mentee is a law school graduate and has a successful career.

Lynn and her husband, Shaun Hailey, reside in Laurel, MD. Although Lynn has gotten away from one of her most treasured hobbies, running/jogging, she finished the Marine Marathon in 2000. She continues to be very health conscious and currently is a member of a walking group called GirlTrek.



Technology is imperative to accomplishing ORI's mission efficiently and effectively. From our custom web-based database that tracks research misconduct investigation cases and institutional assurances to our fluid informational website, we depend on IT tools to get the job done.

It is no surprise that relying on IT has its challenges. Cybersecurity is a top priority for HHS and ORI. There are also ever-evolving policies promulgated by the White House and HHS to ensure all technology is updated and secure. Ensuring ORI's IT tools and infrastructure are maintained, updated, and secure is a full-time job.

To make sure our database and website are compliant, state-of-the-art, and secure, ORI recently hired **Wayne Wu** as its IT specialist. Wayne has extensive knowledge and experience in all things cyber, and is thoroughly knowledgeable about ORI's investigative database and website. As a previous contractor for ORI, he has the necessary historical background to best keep ORI's technological tools up-to-date and compliant.

In his new role, he is responsible for the maintenance, upgrade, and required certification of hardware and software, and for ensuring that ORI's IT infrastructure meets HHS cybersecurity requirements. He also is responsible for initiating, planning, executing, and evaluating new database functions as required by ORI to maintain records and evidence of investigations. Additionally, Wayne will be proactive in providing technical assistance to staff, continually assessing ORI's technological tools to identify potential cyber security weaknesses in real time and, when necessary, responding with plans of actions and remedies.

Welcome, Wayne!

SUGGESTED READINGS

Understanding the Pressures that Threaten Scientific Integrity at the Individual and Systemic Levels

Kathi E. Hanna

Two papers published in January 2017 focused on how incentives in academic science—for example, competition for funds and other resources, publication and authorship issues, and tenure and promotion policies—raise risks of misconduct and pose threats to research integrity.

In one paper, Trinkle et al. (1) asserted that responsible conduct of research (RCR) training might not be as effective as desired if the situational context and features of the research environment are not sufficiently understood and acknowledged. In an academic setting, professional and ethical values and standards can create conflicts that influence misconduct. Trinkle et al. reviewed the literature of the causal, predictive, and influencing factors for research misconduct and noted that little has been written about defects in the decision-making process; that is, how an individual might rationalize misconduct. They hypothesized that in many cases of misconduct, researchers know their behavior is wrong but find ways to justify it. This process allows the researchers to "neutralize" their undesirable behavior and even interpret it as permissible or appropriate.

In many cases of misconduct, researchers know their behavior is wrong but find ways to justify it.

To test this hypothesis, Trinkle et al. collected data from 233 U.S. graduate students. Participants were provided with vignettes in which authorship on a scientific paper was to be decided, and for which requests to be included were made by undeserving individuals. Participants answered questions about the appropriateness of adding authors, such as another student, an advisor, or another faculty member, under different scenarios. As suspected, students were more likely to add an undeserving author if the person making the request was a faculty member in their department and most likely to add an undeserving author if the faculty member was their advisor. A common neutralization technique used to justify this decision was the perception that adding an undeserving author does not harm anyone. Another neutralization technique was the students' perceptions that such a request from an advisor must be the norm in that field, and therefore ethical. The researchers found that participants who had received RCR training were no less likely to commit the ethical violation of adding an undeserving author to a paper. Trinkle et al. concluded that RCR training could benefit from a more holistic approach that addresses situational context and explores with trainees how neutralizing techniques can make scientists more vulnerable to misconduct.

In a second paper, Edwards and Roy contended that several factors in the past 50 years have perverted incentives in academic science; specifically, competition for funding, the development of quantitative metrics to measure performance, and a changing business model in higher education (2).

They wrote that the focus on measuring scientific productivity through quantitative performance metrics and using the results for hiring, promotion and tenure, awards, and funding, creates an environment in which incentives to manipulate the metrics for personal gain flourish. Edwards and Roy argued:

In a system overemphasizing quality, there is less incentive to cut corners because checks and balances allow problems to be discovered more easily, but in a system emphasizing quantity, productivity can be dramatically reduced by massive numbers of erroneous articles created by carelessness, subtle falsification (i.e., eliminating bad data), and substandard review if not outright fabrication (i.e., dry labbing) (p. 53).

They concluded that quantitative metrics have become a target of manipulation and therefore may now be counterproductive.

This focus on performance metrics also affects institutions as they increasingly rely on rankings for marketing, fundraising, and enrollment purposes. The authors cited examples of universities gaming the system by moving resources to places that are emphasized in ranking schema. Moreover, with research funding static or declining in the United States, more higher education institutions are focusing on becoming profit centers. This is set against a backdrop of a hypercompetitive grant environment that is susceptible to reviewer biases and overreliance on, yes, quantitative metrics.

The authors cited examples of universities gaming the system by moving resources to places that are emphasized in ranking schema.

Edwards and Roy also discussed the misconduct that can result from this mix of perverse incentives and its costs in terms of retractions and investigations. Although academic science claims to be self-policing, they argued that there are too many incentives across the scientific enterprise to "pretend misconduct does not happen" (p. 56). They further argued for resisting the normalization of corruption and cited Lance Armstrong and the culture of doping in professional cycling as an example of how unethical behavior can become normalized. They expressed concern that the current environment creates incentives to "cheat to compete." The paper concluded with a series of recommendations to address perverse incentives and hyper competitiveness, including surveying academic scientists' perspectives and experiences, developing best practices by expert panels, incorporating discussion of real world pressures and incentives at all levels of higher education, promoting graduate education as an exercise in character building as well as achieving quantitative metrics, and reducing perverse incentives in universities.

References

1. Trinkle B.S., Phillips T., Hall A., et al. "Neutralising fair credit: Factors that influence unethical authorship practices." *Journal of Medical Ethics*. Published Online January 31, 2017. DOI: 10.1136/medethics-2015-103365

2. Edwards M.A., & Siddhartha R. "Academic research in the 21st century: Maintaining scientific integrity in a climate of perverse incentives and hypercompetition." *Environmental Engineering Science* 34(1):1-61, January 2017. DOI:10.1089/ees.2016.0223.

New Analyses and Commentaries: No Simple Solution to Addressing the Reproducibility Challenge

Kathi E. Hanna

The issue of reproducibility of research, or irreproducibility, depending on one's perspective, has come into focus once again with the announcement of a first set of results from the Reproducibility Project: Cancer Biology (Project). In 2013, the Center for Open Science launched the Project with the aim of determining what portion of cancer biology studies can be replicated, and therefore considered sound. Originally, the Center selected 50 papers from *Nature*, *Science*, *Cell*, and other publications and hired independent laboratories to attempt to replicate their findings. On January 19, 2015, the Center published the results of five completed analyses (1). Of the five analyses, two substantially reproduced the initial results, two returned uninterpretable results, and one failed to reproduce the initial findings.

Not surprisingly, the results are being contested. Monya Baker and Elie Dolgin wrote in *Nature* that Erkki Ruoslahti, a California-based cancer biologist who authored the study that could not be

replicated, reported that at least ten laboratories around the world validated his 2010 study on the value of a peptide designed to infiltrate tumors and boost the strength of other chemotherapeutic agents (2). Although Reproducibility Project manager Tim Errington told *Nature* that "a single failure to replicate results does not prove that initial findings were wrong" (p. 269), Ruoslahti told *Nature* that this finding will hurt fundraising for the company he founded to develop the drug. Moreover, Baker and Dolgin wrote that the Project makes all its findings publicly available, which increases the discomfort level for those investigators whose work is under the microscope.

Nature also interviewed Atul Butte, a California-based computational biologist whose study was replicated, who nonetheless expressed concern that the project could put people's careers on the line. Of note, the two uninterpretable studies ran into issues concerning the pace of tumor cell growth in the original versus replication study (unforeseen spontaneous regression of tumors), highlighting the complexity of reproducing work with living cells.

[Flier] cautioned against stifling the spirit of science through increased professional fear of error, and urged finding an optimal balance.

In two recent commentaries about reproducibility, the authors discussed the problems of irreproducibility and the challenges of replication studies. In one, Professor John P.A. Ioannidis of Stanford University noted the intensive nature of replication studies, which require access to raw data, efforts to ensure the quality and uniformity of the materials used, and strict adherence to the experimental design (3). He noted that the early results from the Project demonstrate that when results do not align, it "is impossible to be 100% certain whether the original experiments, the subsequent experiment, both, or none are correct or wrong" (p. E1). He added that the complexity and multifactorial nature of biological processes can make it very difficult to control the background conditions that could affect results. Furthermore, basic and preclinical research can face greater challenges than clinical research because of smaller sample sizes and less regulatory oversight.

Ioannidis wrote that for reproducibility to be promoted, misaligned rewards and incentives as well as poor research methods and lack of transparency should be addressed. He concluded that we need better understanding of which disciplines have high consistency in their results and why. Moreover, he wrote that replication studies might be prioritized based on whether the study was pivotal and critical to many future investigations. Finally, he made the pointed remark, "[t]he research community should reassess whether it can have the luxury of continuing to fund so much research that is nonreproducible" (p. E2).

In the second commentary, Jeffrey S. Flier, dean of the faculty of medicine at Harvard University, reflected on what his 40-year career in biomedical research and academic medicine has taught him about irreproducibility of published bioscience research (4). Flier focused his commentary on reproducibility in basic and translational research. He defended the inevitable errors that will be made in science and noted that "a fundamental attribute of science is its capacity for 'self-correction'" (p. 2). He cautioned against stifling the spirit of science through increased professional fear of error and urged finding an optimal balance, "surely weighted in the direction of reliability, but appropriately tolerant of tentative conclusions and honest errors, while continuously seeking to reduce the latter" (p. 2).

Flier noted that no academic or financial incentives routinely reproduce the work of others. Rather, the expectation is that subsequent work builds on previous studies with an expectation that results will be "consistent with" the prior results, but not necessarily formally replicable. High-impact papers that are highly read are rarely found to be false, claimed Flier, but when they are found to be, corrections and/or retractions are published. Retractions can be easily tracked as an indicator of erroneous published

results. In addition, although the number of retractions is small, but increasing over time, the "majority of formal retractions today are related to scientific misconduct" (p. 4).

Flier reminded us that irreproducibility and contested results can arise from honest errors or incompetence as well as from research misconduct. The causes of irreproducibility are many, including poor methodology, poorly characterized agents, deficient oversight, training, mentorship, complex collaborative arrangements that diminish accountability, perverse incentives to obtain grants, tenure, and publications. ethical lapses and sociopathy, distortion in the grant making process that promotes expectation of a particular result, and shoddy or lax peer review policies and practices among journals.

Acknowledging that the irreproducibility problem is likely to be more of an issue for some disciplines and stages of bioscience research than others, Flier urged all fields to acknowledge its importance and find ways to confront it. He encouraged enhanced training in all aspects of the conduct of science, from experimental design to statistics, to use of reagents, to data measurement, to ethics. He also urged greater emphasis on the reproducibility and importance of published research, with less focus on the number of publications. Flier wrote that open data and transparency, more stringent publishing guidelines, increased willingness to publish negative and confirmatory studies, clarity in retractions, and changes to the peer review process are among the multiple approaches that journal publishers can adopt. Finally, he asked scientific leadership and the broader research community to take the steps needed to foster an environment that motivates scientists to search for and discover the truth.

These early reports from the Project and these commentaries seem to suggest that replication studies might be a useful, but complex and costly method for better understanding why studies can or cannot be reproduced. In fact, *Nature Reviews* reported that the Project has scaled back its goal of replicating 50 studies to instead assess 30 (5). The commentaries offered by Ioannidis and Flier suggested a multitude of approaches beyond replication studies that could be deployed to enhance reproducibility while replication studies evolve.

Rather than overreacting to criticisms regarding reproducibility, let's commit to the goal of making our scientific work careful, scholarly and impactful.

A recent statement by the American Society for Biochemistry and Molecular Biology offered another important perspective:

Nevertheless, rather than overreacting to criticisms regarding reproducibility, let's commit to the goal of making our scientific work careful, scholarly, and impactful. If we articulate this goal clearly, then the enterprise will be better protected against any future criticisms, and perhaps then we'll show the criticisms to be irreproducible.

Given the complexity of these issues, such discussions are expected to continue for some time.

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