A CASE STUDY APPROACH TO ESTIMATING THE BURDEN OF RESEARCH MISCONDUCT IN PUBLICLY FUNDED MEDICAL RESEARCH

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Abstract:

The economic impact of research misconduct in medical research has been unexplored. While research misconduct in publicly funded medical research has increasingly been the object of discussion, public policy debate, government and institutional action, and scientific research, the costs of research misconduct have been unexamined. The author develops a model to estimate the per case cost of research misconduct, specifically the costs of fabrication, falsification, and plagiarism, in publicly funded medical research. Using the database of Research Misconduct Findings maintained by the Office of Research Integrity, Department of Health and Human Services, the model is used to estimate costs of research misconduct in public funded medical research among faculty during the period 2000-2005.

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INTRODUCTION

Background and Rationale

The economic impact of research misconduct in medical research has been unexplored. While research misconduct in publicly funded medical research has increasingly been the object of discussion, public policy debate, government and institutional action, and scientific research, the costs of research misconduct have been unexamined. Using Summaries of Closed Investigations Resulting in Findings of Scientific Misconduct or Administrative Actions for 2000-2001 and Summaries of Closed Investigations Resulting in Findings of Research Misconduct or Administrative Actions for 2002-2005 from the Office of Research Integrity Annual Report published by the Office of Research Integrity (ORI), Department of Health and Human Services, the author develops a model to estimate the burden of research misconduct, specifically the costs of fabrication, falsification, and plagiarism, in publicly funded medical research and uses the model to estimate a cost of research misconduct among faculty.

Evolution of the Research Misconduct Concept

The fact of research misconduct has generated focused debate and scrutiny from various perspectives for decades. Woolf (1991) notes that prior to the 1980's instances of irregularities in science were considered "rare" and individual instances of scientific misconduct regarded as a "hoax". But beginning in the late twentieth century reports of "fraud" tempered the promise of science. Both Steneck (1994) and LaFollette (2000) chronicle the impact of several high profile cases. They explore the stream of events transforming questions about scientific integrity from a matter handled among individual

scientists, to an issue addressed in a sequestered academic institutional venue, and, finally, to a public policy issue. Both point to two cases at prestigious academic institutions as seminal incidents. Summerlin's "painted mice" case in the 1970s raised questions about research integrity at an institution as prominent as Memorial Sloan-Kettering Cancer Hospital (Steneck, 1994; LaFolette, 2000). John Darsee's fabricated research in cardiac medicine at Harvard Medical School and the slow response of NIH and Harvard investigations appeared to tarnish public confidence that the scientific community could respond promptly in self-policing. In addition to individual cases of scientific misconduct, Steneck (1994) highlights the impact of the 1983 publication of *Betrayers of the Truth* on flagging public confidence in science and notes that university policies in the 1970s and 1980s governing academic conduct did not cover scientific misconduct.

In 1981 Congressional scrutiny opened the black box of publicly funded research and peer reviewed funding. The ensuing two decades altered the landscape of oversight of scientific misconduct (Heinz & Chubin, 1988; Bick, 1988; Tangney, 1988). Then Senator Al Gore, Jr., Chair of the House subcommittee investigating several high profile cases in 1981, summed up the Congressional intent when he observed, "We need to discover whether recent incidents are merely episodes that will drift into the history of science as footnotes, or whether we are creating situations and incentives in the biomedical sciences, and in all Big Science, that make such cases as these the tip of the iceberg" (USHR, 1981). Congressional attention was the stimulus for a regulatory agenda established through public law mechanisms based in the United States Code (U.S.C). Scientific misconduct, increasingly used interchangeably with the phrase research misconduct, became subject to public policy

oversight through a series of administrative law provisions (1) considering and settling upon definitions of misconduct and (2) creating and implementing policies and procedures for policing research misconduct (Dresser, 1993; Steneck, 1994; LaFollette, 2000). ORI documents the historical background of its creation and the key administrative laws which define public policy and procedures for handling research misconduct (ORI-About ORI, 2008). The Health Research Extension Act (HREA) of 1985 called for both government and academia to investigate scientific misconduct then referred to as "scientific fraud" (ORI-About ORI, 2008). HREA created a framework with administrative oversight of allegations of misconduct and mandated reporting of investigations to the Secretary of Health and Human Services (HHS). During this time period beginning in 1986, whistle-blowers in cases of scientific misconduct were allowed to access the False Claims Act of 1865 via the courts to seek a portion of recovered grant funds rather than taking a potentially less public and less lucrative route of institutional investigation (Rennie & Gunsalus, 1993; ORI-About ORI, 2008; Palca, 1990). Published guidelines to operationalize the HREA were incorporated in the *NIH Guide for Grants and Contracts* in 1986. The framework was developed further with 42 CFR Part 50, Subpart A - the Final Rule "Responsibilities of Awardee and Application Institutions for Dealing With and Reporting Possible Misconduct" codified by the *Federal Register* in 1989. That same year the Office of Scientific Integrity (OSI) was born to oversee investigations of misconduct (Hamilton, 1992). With the NIH Revitalization Act of 1993, OSI would be replaced by ORI, an independent agency within HHS, and ORI charged with oversight of "research misconduct". Beginning with 1993, ORI began publishing an Annual Report which, among other topics, reports on investigations resulting

in findings of scientific misconduct and resultant administrative actions, such as effectively restricting the person's access to public funding. Going beyond investigating and reporting duties, ORI, effective 2001, implemented a federally funded research program on research integrity and granted its first awards for research in this area (ORI, 2000). LaFollette (2000) believes research misconduct became a "controversial policy issue in part because of failures in communication and a lack of a spirit of cooperation between the scientific community and the federal government that supported its work". At the end of the twentieth century, with the integrity of publicly funded research formally challenged, the resultant regulatory agenda was in place to address these failures. The subject of research misconduct had come full circle from denial about incidence to validation as a topic for funded research support. Table 1 provides a time line of the major milestones of U.S. public and policy responses.

The full implications of the regulatory agenda set in place became apparent when, in 1995, the Department of Justice filed suit in the Superior Court of Quebec seeking $518,175 from St. Luc Hospital on behalf of the National Cancer Institute (U.S. DOJ, 1995). The suit alleged breach of funding agreement terms due to falsification of data on 99 patients and sought recovery of funds provided through National Institutes of Health (NIH) grants. While this case signaled a willingness to recover public funds, during the next decade only two cases brought under the umbrella of this Federal law would seek financial restitution for research misconduct. In 2000, Thomas Jefferson University In 2005, the Department of Justice (DOJ) concluded its investigation of Eric Poehlman, a former tenured research professor funded by NIH. Poehlman was assessed criminal, civil and administrative penalties for falsifying and fabricating research data in publications and grant applications

totaling $11.6 million in federal funding spanning research in menopausal women, obesity and hormone replacement therapy, metabolism in Alzheimer's patients and the effect of endurance training on metabolism (Kintisch, 2005; ORI-Press Release, 2005).

Table 1. Timeline of Major Milestones of Response to Research Misconduct in the United States

Time Period	Milestone
Pre-1980s	Scientific misconduct regarded as rare and characterized as "hoax" not fraud (Wolfe, 1991)
1981	Subcommittee on Investigations and Oversight of the Committee on Science & Technology U.S House of Representatives Fraud in Biomedical Research 97th Congress, 1st Session Scientific "fraud" common general descriptor includes falsification and fabrication
1985	USC 289b requires NIH funded institutions to adopt policies & procedures to address scientific misconduct allegations Health Research Extension Act –Applicant and awardee institutions required to have "an administrative process to review reports of scientific fraud" and to report alleged substantial "scientific fraud"
1986	PHS Interim Policy provides first formal definition of "research misconduct" and scientific misconduct replaces scientific "fraud" as general descriptor False Claims Act of 1865 court access extended to whistle-blowers in scientific misconduct cases
1988	Congressional Investigation of research misconduct
1989	42 CFR Part 50, Subpart A - the Final Rule "Responsibilities of Awardee and Application Institutions for Dealing With and Reporting Possible Misconduct" codified by the *Federal Register* Office of Scientific Integrity (OSI) and Office of Scientific Integrity Review (OSIR) legislated within NIH
1992	OSI and OSIR re- organized into Office of Research Integrity (ORI)
1993	NIH Revitalization Act codifies ORI First ORI Annual Report published. Scientific misconduct section includes "Investigations Resulting in Findings of Scientific Misconduct or Administrative Actions"
1994	Model Policy and Procedures developed for responding to research misconduct allegations
1998	ORI reports that 174 institutions reported 432 allegations of research misconduct from 1991-1996. ORI investigations from 1993-1997 resulted in 76 misconduct findings and 74 no-misconduct findings
1999	Investigation of research misconduct allegations transferred from ORI to institutions, PHS agencies, Office of the Inspector General and research institutions. ORI's mission refocused on oversight, including continued reporting of misconduct findings in the ORI Annual Report, education, and prevention
2000	Legal definitions for falsification and fabrication revised in Public Health Service Policies on Research Misconduct - 42 CFR Part 50, Subpart A PHS publishes Policy on Instruction in Responsible Conduct of Research
2001	ORI initiates Research Program on Research integrity
2005	PHS Policies on Research Misconduct, 42 C.F.R. Part 93, becomes effective on June 16, 2005, replacing Public Health Service Policies on Research Misconduct - 42 CFR Part 50, Subpart A

Source: Adapted from About ORI – History and Integrity in Scientific Research, IOM.

These two cases demonstrating the government's willingness to assess penalties for research misconduct beyond the administrative actions imposed through administrative law and reported by the ORI signal that the evolution of research misconduct, one aspect of scientific misconduct, is complete.

Literature on Research Misconduct and Estimated Burden

The literature on research misconduct reflects the major milestones of the public policy issues: motivations to commit research misconduct, various forms of research misconduct and definitions, conduct of investigations, and consequences of research misconduct (National Academy of Sciencies, 1992; Swazey, Anderson, & Lewis, 1993; Anonymous, 1996; Grayson, 1997; Weed, 1998; Shamoo & Resnik, 2003; Fuchs & Westerfelt, 1996; Wible, 1998; Lock & Wells, 1993; Eisenman, 1996; LaFollette, 2000; Mirowski and Sent, 2002). Dresser (1993) characterizes the debate around the integrity of science as "protection of society from harmful wrongdoing and protection of individuals from undeserved punishment." Steneck (1994) provides a comprehensive reasoned summary and review of the progress toward examining scientific misconduct. He begins with the 1981 Congressional Hearings, reviews progress to date, and sets an agenda for reform. However, his agenda overlooks economic consequences. Bulger, Heitman and Reiser (2002) include "Preventing Scientific Misconduct" in a collection of essays meant to serve as a standard text on ethics in the biological and health sciences. Such a prevention agenda acknowledges the nature and extent of the problem of scientific/research misconduct and suggests that by 2002 debate over its existence has concluded. Interestingly, Piantadosi, in Clinical Trials: A Methodologic Perspective (2005), includes a final chapter on "Misconduct and Fraud in

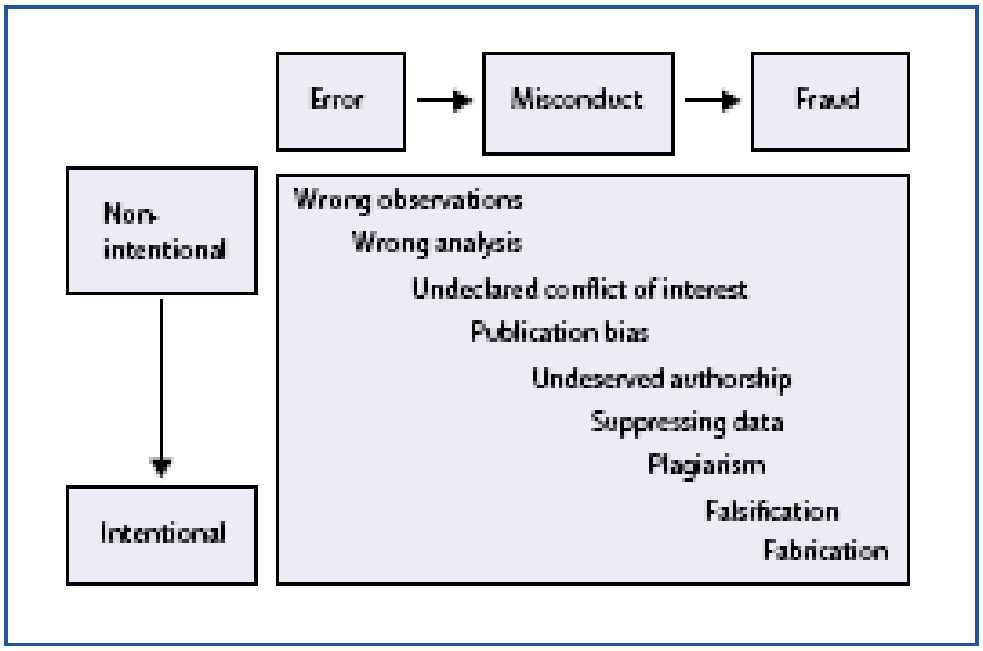
Clinical Research" to bookend a guide to clinical researchers. The chapter introduces the "fraud" issue, using that phrase, rather than the more generally accepted legal descriptor of research misconduct, and grapples with the definition, reviews regulatory agencies and handling of misconduct allegations, summarizes several high profile cases, as well as outlining researcher and sponsor responsibilities. In 2006, the impact of research misconduct on scientific literature was explored in an *Annals of Internal Medicine* article which argued that the scientific community must go beyond retraction of ORI identified articles and examine each published article assuming that it is "suspect until proven otherwise" (Sox and Rennie, 2006). By 2006, the existence of research misconduct is no longer debated, but fully integrated into scientific methodology, literature and oversight. Yet financial aspects, costs, or issues of public funding and scarce resources and other economic dimensions of research misconduct remain unexamined.

Incidence and Prevalence of Research Misconduct

Incidence and prevalence statistics for research misconduct bedevil the scientific community and the public. Two issues obfuscate measurements, a clear consistent definition of the concept and agreement of how the denominator is measured. The question of a generally accepted and agreed upon definition permeates the literature on scientific integrity and confounds attempts to estimate incidence and prevalence. Figure 1 illustrates what one author has labeled the "slippery slope between honest errors and intentional fraud, with examples in the middle" (Nylenna & Simonsen, 2006). This rendering concisely conveys much of the discussion about the general topic of research integrity, including the problems

with labels and definitions. The boxes for error, misconduct and fraud are organizing cut points for categorizing deviation from scientific methods, while the boxes to address

Figure 1. Slippery Slope between Honest Errors and Intentional Fraud According to Nylenna.



intentionality attempt to clarify researchers' motivation. The Nylenna graphic suggests that plagiarism, falsification and fabrication fall into the intentional fraud category. However, the word "fraud", while it appeared in the literature on scientific misconduct during the 1980's and early 1990's, is generally out of favor. Further in 1989, nearly twenty years prior to Nylenna's publication date, the Public Health Service Policies on Research Misconduct, 42 CFR Part 50, Subpart A, adopted a formal definition of misconduct:

> Misconduct or Misconduct in Science means fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research. It does not include honest error or honest differences in interpretations or judgments of data.
> (See Appendix A for complete Federal guidelines)

ORI provides a clarification for the three types of misconduct in science (http://ori.dhhs.gov/misconduct/definition_misconduct.shtml):

> (a) Fabrication is making up data or results and recording or reporting them.
>
> (b) Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
>
> (c) Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.
>
> (d) Research misconduct does not include honest error or differences of opinion.

Even with the evolution of a legal definition of research misconduct, consistent incidence and prevalence statistics are not documented in the literature. Statistics reported in the literature are no more than estimates. In a 1987 Editorial in *Science*, the then editor D.E. Koshland, wrote that misconduct is "rare" (Koshland, 1987). This judgment appeared early in the evolution of the misconduct issue, before the current, common definition of misconduct had been adopted and before attempts to quantify misconduct proved relevant. Over a decade later, Steneck (2000) summarized the historical and on-going deliberations about incidence and prevalence for ORI, offering both "direct" and "indirect evidence" from the literature to conclude that prevalence has not been accurately measured. He stops short of providing an estimate, but clearly suggests it is greater than 1%. Others have suggested differing ranges or estimates, such as 32% (Tangney, 1988), 1.5% (Pincus, 1989), and 7% (Glick, 1989). Claxton (2005) estimates the frequency of scientific misconduct for 2000-2002 at less than 0.02%; however, his calculation uses the annual number of published scientific papers as the denominator in his estimate.

The variation in these estimates obscures the fact that there is no documented formula for calculating either incidence or prevalence of research misconduct. In an incidence statistic, the number of new cases of research misconduct could most reasonably be defined as the number of findings of misconduct among researchers. However, not even the term "researchers" is defined in the literature. Is a "researcher" one who conducts research, e.g., a technician? Is a "researcher" an individual who receives federal funding to support the conduct of research, e.g., a scientist who receives a percent of funded effort through a grant? Is a "researcher" a scientist who directs a specific research project, i.e., the principal investigator (PI)? Additionally, the size of the at-risk population has not been described. Steneck (2000), touching on the 1% estimate of research misconduct, briefly considers this critical issue in determining incidence and prevalence - whether misconduct should be measured based on total researchers or active researchers.

Surveys of scientists regarding attitudes on misconduct and experience with peers support the view that even estimates of incidence are attenuated. Hamilton (1994) observes that 27% of respondents of a random survey of 1,500 American Association for the Advancement of Science respondents report observing fabricated, falsified or plagiarized research in the last 10 years of the survey. Martinson, Anderson and de Vries (2000) surveyed, 3,247 NIH funded scientists to find that 12.5% reported "overlooking others use of flawed data or questionable interpretation of data". In 2005, ORI's Intramural Research Program announced sponsorship of a survey approach to determine the frequency of suspected research misconduct in both biomedical and behavioral research (ORI, 2005). The survey was designed to estimate incidence of suspected misconduct as measured by

observations of principal investigators of NIH funded investigator-initiated research grants (R01 grants). Results in the final report published on the ORI website and summarized in a commentary in the journal *Nature* showed a 3% incidence rate based on a 51% survey response rate (Wells, 2008; Titus, Wells & Rhoades, 2008). Table 2 summarizes the differing estimates of incidence and prevalence of research misconduct and the basis of the estimate.

Estimates of incidence and prevalence suffer from basic methodological problems. In calculating incidence and prevalence, both the numerator and denominator must be measureable and well-defined. Only studies of research misconduct based on survey populations, already referenced in the preceding paragraph, document a mathematical approach akin to a reliable incidence/prevalence calculation. Additionally, both Steneck (2000) and Pincus (1989) emphasize that allegations and findings of research misconduct measure only detected cases. Further, Pincus (1989) categorizes fraud as falling into one of three categories: known fraud in the public record, detected fraud not in the public record, and undetected fraud. Formal findings of research misconduct are documented in both the *Federal Register* and the ORI Annual Reports, providing one measure of known "fraud" or research misconduct. Survey findings of suspected or observed but unreported research misconduct documented by Tangney (1987), Hamilton (1994), Martinson et al (2000) and Titus et al. (2008) referenced in Table 2 offer a range of 3% - 32% for detected research misconduct not a matter of public record. And, of course, an estimate of undetected fraud is only conjecture. LaFollette (1992), in *Stealing into Print*, believes that even with the ORI

efforts, questions about incidence and prevalence will remain "unanswered, if not intrinsically unanswerable".

Table 2. Estimates of the Incidence of Research Misconduct

Source	Basis of Estimate	Estimate
Stewart & Feder, 1987	Judgment of authors	Under 1%
Tangney, 1987	Survey of 1,100 scientists at major universities reported suspecting colleague of research misconduct; 22% response rate	32%
Bick, 1988	Scientific fraud-related complaints to NIH and Alcohol, Drug Abuse, and Mental Health Administration	0.03 – 0.1%
Glick, 1989	Authors estimate based on estimated scientific fraud incidents/scientific fraud allegations	0.02% - 0.07%
Pincus, 1989	Estimate of "possible scientific misconduct" extrapolated from FDA audits	6%
Hamilton, 1994	Survey respondents (31% response rate to 1500 random surveys of American Association for the Advancement of Science) encountering research misconduct within past 10 years	27%
Martinson et al, 2000	Survey respondents (N=3,247 NIH funded scientists) reported "overlooking others use of flawed data or questionable interpretation of data"	12.5%
Claxton, 2005	Review article considering frequency of published fraud and plagiarism	< 0.02%
Titus et al., 2008	Random sample. Survey respondents (N=2,212 NIH R01 PI's) reported observing research misconduct meeting federal definition.	3%

Estimating the Burden of Research Misconduct

While measuring the incidence and prevalence or research misconduct has proven difficult, economic considerations have been largely unexplored. The financial burden of policing research misconduct has been acknowledged in discussions of the costs of regulation, scientific audits and case law financial settlements (Steneck, 1994; Shapiro & Charrow, 1989; Anderson, 1993; Pascal, 2000; Lacetera & Zirulia, 2007). Economists have provided theoretical underpinning to understand behavioral incentives to commit research misconduct. For example, Wible (1992) developed an economic framework to characterize scientific fraud and differentiate it from what he labels replication failure, basically the process of sloppy record keeping which does not permit another scientist to validate published work. Wible builds on the work of two separate theorists to adapt an economic model of crime and decision making under uncertainty to the research environment where a scientist knowingly produces research that involves fabrication and/or falsification of data. Wible's model seeks to explain the utility for the scientist engaging in scientific misconduct and concludes by observing, "An economic approach suggests that misconduct will always be part of the landscape of science" (Wible, 1992). Lacetera and Zinulia (2007), working from a behavioral economics perspective, utilize a game-theoretic model to predict levels of fraud given varying levels of scientist type (regarded as "star scientists" and "average scientists"), research area, and level of control for misconduct. The results of this model "imply that there may be a good deal of frauds (sic) the scientific community is not aware of…"(Lacetera & Zirulia, 2007).

General statements of concern about financial implications have appeared infrequently in the literature on research misconduct after 2000. LaFollette (2000) approaches the subject tangentially in his historical overview of the issue of scientific misconduct:

> A vigorous scientific research enterprise is considered essential to the U.S. domestic economy and to American competition in foreign markets. Integrity on the part of scientists has simply been assumed as part of the formula for research support. The reliance on academic institutions to manage billions of dollars of research support is testimony to that political trust.

In the peer-reviewed literature a categorization of several of the major cost components of research misconduct appeared recently:

> The costs of acts of scientific misconduct are carried by the involved individuals and institutions as well as by the society as a whole in the form of ruined careers, lost reputation, long and expensive investigations, useless or even harmful diagnostic and therapeutic procedures, and the loss of public trust in science (Mojon-Azzi & Mojon, 2004).

But measures of the cost of research misconduct have not been addressed in the research integrity/misconduct literature. Gardner (2006), in an unpublished paper funded by an ORI R01 grant and presented at a biennial ORI conference, attempted to quantify the social cost of scientific misconduct and "questionable research" practices. His method blended a thought experiment, an a priori imagining of the impact on health outcomes, with a quasi-economic assessment to postulate a kind of opportunity cost estimate for preventable cardiovascular disease. Gardner estimates social cost of "$B", roughly billions of dollars, would have been avoided if research on the unhealthy effects of smoking had not been manipulated and suppressed by the tobacco industry. He acknowledges in the closing remarks that his analysis does little to measure the economic burden of scientific misconduct. In fact, his example of the well documented response of the tobacco industry to effects of

smoking on health fits into the questionable research practices definition and falls outside the federal definition of research misconduct.

Estimating the cost of research misconduct to measure the burden it places on publicly funded medical research is appropriate both from an economic and public policy perspective. The ORI funding of an attempt at cost measurement as vague as that of Gardner's signals a willingness to broaden the discussion of research misconduct to acknowledge the burden misconduct places on public funding. Further, authors of the ORI Intramural Research Program's study of incidence of suspected misconduct postulate that under reporting might be a function of high investigation costs (Titus et al., 2008). Yet no exploration of investigation costs has been documented.

Study Aims

For this study, the author adopts a descriptive approach utilizing case studies to estimate the burden of research misconduct in publicly funded medical research. This study examines all cases of research misconduct comprised of findings of misconduct attributed to faculty (instructor rank and above) and recorded by ORI and reported in ORI Annual Reports 2000-2005. The definition of research misconduct for the cases in this study is defined by 42 CFR Subpart A: fabrication, defined as "making up data or results and recording or reporting them", falsification, defined as "manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record", and/or plagiarism, "appropriation of another person's ideas, processes, results, or words without giving appropriate credit" (ORI, 2000). The study objectives are: (1) to survey Research Integrity Officers (RIO) responsible for handling

findings of research misconduct among faculty reported during 2000-2005 regarding cost issues; (2) to develop a model to estimate economic costs of research misconduct in publicly funded medical research; and (3) to use the model to estimate economic costs in known findings of research misconduct among faculty engaging in publicly funded medical research during the study period.

STUDY METHODS

This study used a sequential mixed method design to examine cases of research misconduct and develop a model to estimate the economic costs of research misconduct among faculty engaging in publicly funded medical research. Qualitative interviews were conducted to gather background information regarding existing practices and opinions about cost measurement in research misconduct. For the quantitative approach, a model was developed to describe economic costs of a finding of research misconduct and to estimate those costs in selected cases. Costs estimated were economic costs for the research misconduct investigation, grant award referenced in a misconduct finding, costs of imposed administrative actions on a faculty member, and retraction costs for articles. Economic costs were adjusted to 2007 levels using the consumer price index (CPI). Economic costs were from the perspective of NIH but included institutional costs. Institutional costs for research administration are assumed to be economic costs funded through NIH indirect cost dollars awarded to the respective institution.

Study Period

The study period was 2000-2005. During this five year period, regulations for handling scientific/research misconduct were codified in 42 CFR Part 50, Subpart A - Responsibility of PHS Awardee and Applicant Institutions for Dealing With and Reporting Possible Misconduct in Science and policy changes communicated in the *Federal Register* (65 FR 76260) clarifying the definitions for fabrication, falsification and plagiarism, referred to as research misconduct. On June 17, 2005, 42 CFR Part 50, Subpart A was removed and replaced by 42 CFR Parts 50 and 93. Among other changes, the new administrative law (1)

elaborated on the definition of "research misconduct", confirming the move away from the phrase scientific misconduct, (2) expanded applicability of the law to include PHS intramural research programs and contracts, and (3) included PHS supported journal peer review in the definition of plagiarism.

Case findings in the five year study period have two variables that permit economic cost comparisons. Beginning in December, 1999, a 480 day target timeline for completion of investigations of allegations of scientific misconduct was adopted by ORI in response to a recommendation of a HHS Review Group on Research Misconduct and Research Integrity (ORI, 1999). This target timeline, not in place prior to 2000, allows for an assumption of a standard measure of time input for each case finding. Secondly, during this five year period, a common legal definition of research misconduct was employed by the ORI and institutions to investigate allegations of scientific/research misconduct.

Sample Selection

Findings of scientific/research misconduct were taken from the ORI Annual Report for each year in the study period. The ORI Annual Report records and reports findings of research misconduct in the year in which the case is closed. Section I of each Annual Report, "Responding to Research Misconduct Allegations", provides an activity report and descriptive statistics of allegations of research misconduct closed with a finding of research misconduct during the year. Appendix A of each Annual Report, "Summaries of Closed Investigations Resulting in Findings of Scientific/Research Misconduct or Administrative Actions", reproduces the *Federal Register* notice of each allegation closed as a case finding during the year. ORI Annual Reports, Section I and Appendix A, from 2000-2005 were

reviewed to identify each case finding for falsification, fabrication and/or plagiarism. As a matter of clarification, the *Federal Register* notice of the finding is titled "Findings of Scientific Misconduct"; however, the nomenclature "research" misconduct is used following the terminology precedent established in PHS federal policies and administrative law beginning in the 2001 ORI Annual Report.

Sample Inclusion and Exclusion Criteria

Model development was based on a study population drawn from ORI published findings of scientific/research misconduct reported in the 2000-2005 ORI Annual Reports. Table 3 summarizes the findings of scientific/research misconduct by type by year and separates the case respondents into faculty, instructor rank or above, and other groups.

Table 3. Types of Allegations Involved in Closed Inquiries and Investigations Resulting in Findings of Research Misconduct for Faculty and Others, 2000-2005.

Misconduct Type	2000	2001	2002	2003	2004	2005	Total	Faculty	Others
Fabrication	1	2	1			2	6	1	5
Falsification	4	4	3	5	2	3	21	4	17
Plagiarism		1				1	2	1	1
Falsif./Fabric.	1	4	9	5	4	2	25	7	18
Falsif./Plag.	1	2		1	1		5	3	2
Fabric./Plag.		1					1	1	
Falsif./Fabric./Plag.				1	1		2		2
Total	7	14	13	12	8	8	62	17	45

For this time period, ORI reports a total of 62 findings of scientific/research misconduct. Of these total findings, findings for falsification/fabrication represent 40% of cases and findings for falsification alone represent 33.9%. Faculty research misconduct constitutes 27.4% of the total findings of misconduct during 2000-2005. Of faculty research misconduct, findings for falsification/fabrication represent 41% of cases and findings for

falsification alone represent 24%. ORI annual reports of research misconduct distinguish between the three types of research misconduct and four combinations of these separate categories as reflected in Table 3. This study does not attempt to stratify costs by allegation/finding type due to sample size limitations.

The study sample included cases of research misconduct for any person employed at a research institution and at a faculty rank of instructor and above. Research misconduct includes findings for reasons of fabrication, falsification, plagiarism or any combination of the three. Cases where the respondent was not an instructor or above or was employed at a non-research institution were categorized as "other" and excluded from the study sample. "Other" respondent cases included graduate students, research technicians, project coordinators, research nurses, interviewers, and research fellows. The rationale in excluding this group was two-fold and based on an assumption of financial impact. First, the faculty member is often the principal investigator (PI) and, as such, is the recipient of awarded funds. Receipt of the award carries explicit and implicit fiduciary responsibility for safeguard of public funds. The impact of research misconduct committed by a faculty member who as PI or co-investigator is the direct recipient of public funding can be far reaching. Second, faculty cases can be assumed to have a longer timeline for detection than in these other employee groups and, thus, a longer timeline for accumulation of economic impact. Non-faculty grant supported research activities are reviewed routinely, sometimes daily, by the PI and can be assumed to be detected by the faculty mentor/employer sufficiently early in the research process to minimize financial impact. The study sample selected for costing consists of closed cases of research misconduct for instructors and above for the period 2000-

2005 employed at higher education research institutions. There are seventeen cases as displayed in Tables 3 and 4. Appendix C provides descriptive data for the population of all findings of Research Misconduct 2000-2005, both faculty and non-faculty. Appendix D provides Summaries of Closed Investigations resulting in Findings of Scientific Misconduct or Administrative Actions for Faculty at the Instructor Rank and Above, 2000-2005 for each case included in the study sample.

Table 4. Cases of Research Misconduct by Investigator by Rank, 2000-2005.

Rank	**Funding Agency[1]**	**Investigator (Case)**	**MD/PhD**	**Year**	**Misconduct Type**
Professor (N= 4)	NIAMS,NIAD	Kammer	MD	2005	Fabrication/Falsification
	NIA,NIDDK,NCRR	Poehlman	PhD	2005	Fabrication/Falsification
	NIAID	Radolf	MD	2003	Fabrication/Falsification
	NINDS	Prasad	PhD	2002	Fabrication/Falsification
Associate Professor (N=5)	NHLBI	Gelband	PhD	2003	Falsification
	NHLBI	Yao	MD/PhD	2002	Falsification
	NIDCD	Dreyer	MD/PhD	2000	Fabrication/Falsification
	NEI	Hartzer	PhD	2000	Falsification
	NIDDK	Ganz	MD	2002	Fabrication/Falsification
Assistant Professor (N=7)	GM	Xiong	PhD	2001	Fabrication/Plagiarism
	MH	Ruggiero	PhD	2001	Fabrication
	NHLBI	Pandurangi	PhD	2001	Falsification/Plagiarism
	NIAID	Sultan	MD/PhD	2004	Falsification/Plagiarism
	NIAID	Duan	MD	2000	Falsification
	NIDDK	Arnold	PhD	2001	Fabrication/Falsification
	NIA	Padgett	PhD	2001	Plagiarism
Instructor (N=1)	NINDS	Jacoby	MD/PhD	2001	Falsification/Plagiarism

[1]See Appendix E for abbreviations for funding agencies.

Qualitative Interviews

Qualitative interviews were conducted using open-ended and probe questions to query key informants about the experience of each in dealing with findings of misconduct. Additionally, the interviews sought to capture perceptions, knowledge and opinions

regarding specific economic cost measurement issues in research misconduct. Purposeful sampling (Patton, 2002) of the RIOs at each institution with a finding of misconduct among faculty was employed.

Short, single observation interviews described below with administrators responsible for oversight of research misconduct were conducted for background information. The primary aims were (1) to elicit general information on economic cost aspects of research misconduct and on the investigation process mandated by the PHS and (2) to pilot questions for the standardized open-ended interviews planned with institutional RIOs. Five face-to-face or telephone interviews using an informal conversational approach with probe questions were conducted with a small, selected group of research administrators. This purposive sample of research administrators included a former Research Integrity Officer (RIO) who performed that function for over ten years at M.D. Anderson Cancer Center. While he oversaw investigations which resulted in research misconduct findings, none of those cases falls into the study sample. He was regarded as an objective and experienced expert in dealing with research misconduct in publicly funded medical research. Three officials at ORI were included in the background interviews. The current Director and Deputy Director, Division of Investigative Oversight, ORI, were interviewed as well as the Director during the 2000-2005 study period. Additionally, the author interviewed Richard Theriault, M.D., a member of an international team of medical researchers who investigated the Bezwoda case, a well known finding of medical research misconduct not included in the sample, for this study to gain insight into the complexity of an inquiry and investigation of a suspected case of scientific misconduct.

A second set of interviews using a standard open-ended interview approach was directed at RIOs employed at each institution where a finding of research misconduct was included in the study sample. The institution is identified in each published finding. The RIO, an institutional official, usually a scientist and former researcher, responsible for handling research regulatory administrative issues including allegations of research misconduct in any research funded by PHS was identified via internet search. The RIO received an introductory email (1) identifying the author as a doctoral student completing dissertation research, (2) stating the author's research aims, and (3) requesting a telephone interview to collect background information on costs of research misconduct at an institution where a finding of research misconduct among faculty has been recorded in the ORI Annual Report from 2000-2005. The letter of introduction stated that the RIO would not be requested to disclose confidential information. A general qualitative survey instrument, the Research Misconduct Questionnaire (RMQ), was developed as a part of the research design to administer via telephone to each institutional RIO who agreed to a telephone interview. The RMQ approach posed a series of open ended questions to gather information on the (1) RIO time in the RIO position, (2) RIO attitude on importance of estimating costs of scientific/research misconduct, (3) existence of institutional cost data on scientific/research misconduct, and (4) historical cost data on the specific case in the sample at the respective institution (see Appendix B for complete RMQ). Through probe questions, individuals in this group were queried about salient components of economic costs of scientific/research misconduct and pitfalls to constructing an economic model estimating the burden of research misconduct. Interview notes were transcribed and reviewed to identify themes, key

illustrative quotes were extracted, and the final economic cost model development integrated cost considerations discovered during key informant and RIO interviews.

Construction of the Model and Data Collection

Constructing the model to estimate the burden of research misconduct in publicly funded medical research defines distinct types of economic costs in a finding of research misconduct and estimates economic costs associated with each type of economic cost. Figure 2 displays the model of types of the economic costs in a finding of research misconduct.

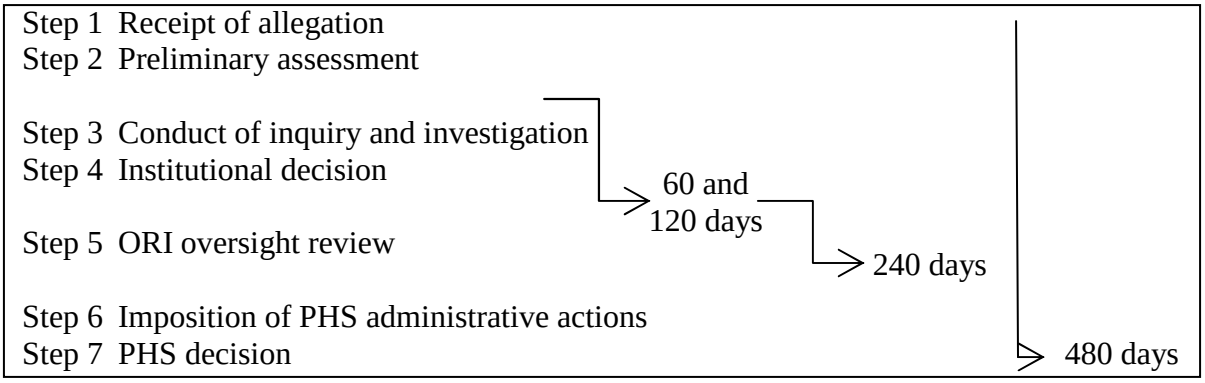
Figure 2. Types of Economic Costs in a Finding of Research Misconduct.

Type 1		Type 2		Type 3		Type 4		
Investigative Costs	+	Grant Award(s)	+	Voluntary Exclusion Agreement	+	Retraction Costs	=	Total Cost

Type 1 – Investigative Costs

Type 1 investigative costs subsume economic costs of the federally mandated investigation process concluding in a finding of scientific misconduct. ORI's "Sample Policy and Procedures for Responding to Allegations of Research Misconduct" details the procedures comprising the investigative process (ORI, 2005). Figure 3 summarizes the categories of Type 1 investigative costs, the seven steps established for handling misconduct allegations that end in case findings, and time requirements specified by PHS to the ORI (ORI, 1999).

Figure 3. Total Time Requirement for Completing Misconduct Cases – Investigative Costs



Steps 1-4 are conducted at the respective institution where the faculty member is appointed. In Step 1, the allegation is received by the RIO, who must determine whether grounds exist to move forward with an inquiry in Step 2. These first two steps, accomplished in 60 days under the mandated timeline, involve primarily the RIO, limited institutional legal staff and, occasionally, institutional police personnel to sequester evidence. Steps 3 and 4 reflect continued time input for the RIO and incorporate the intensive use of faculty in the inquiry and investigation. Both an Inquiry Panel and, subsequently, an Investigation Panel are convened. Panel membership for each of the two panels is estimated at 3-5 full tenured professors with expert knowledge of the subject matter area of the alleged research misconduct. Step 4, institutional decision, reflects continued RIO time input as well as institutional legal counsel and senior administration time inputs for review and approval.

Estimates of the Allegation, Inquiry and Investigation phases, steps 1-4, a major component of Type 1 costs, were arrived at by a combination of three methods. The author requested historical cost and time in puts for each case via interview with the respective institutional RIO using the RMQ. For cases lacking qualitative response data, actual time inputs per case were requested from ORI using the Freedom of Information Act (FOIA)

mechanism and were applied against the assumed RIO wage rate (see below). In the absence of FOIA provided information, investigative costs were estimated by the author. Estimations were calculated by multiplying (1) assumed number of institutional hours spent per case by (2) an assumed institutional wage rate.

Assumptions for institutional hours per case were based on time estimates for the RIO and for additional institutional personnel. 42 CFR Parts 50 and 93, Final Rule documents an estimated Annual Average Burden per Response for Steps 1-4 of the mandated process for institutional receipt of allegation, conduct of inquiry and investigation and institutional decision (70 FR 28370). These estimates, published in 2005 with the new administrative law governing research misconduct, reflected assessments for the 1999 mandated 480 day timeline for completing the inquiry and investigation phases of an allegation of research misconduct ending in a case finding. These time estimates appear to describe the RIO oversight of processes encompassed by Steps 1-4. RIO time estimates per the *Federal Register* were augmented by assumptions of time spent in added institutional oversight by the Inquiry Panel and the Investigation Panel and by institutional legal staff.

For Type 1 Investigative Costs, steps 1-4, an assumed institutional wage rate was calculated as an hourly cost including both a mean compensation component and a benefits component. The mean total annual compensation, excluding benefits, for full professor, basic science ($187,500) or clinical science ($268,800), at public medical schools as documented by the 2007 Report on Medical School Faculty Salaries (AAMC, 2007) was divided by 1920 (48 weeks x 40 hours/week) hours to arrive at a base compensation hourly wage for (1) full professor basic science (Ph.D.) of $98 and (2) full professor clinical science

(M.D.) of $140. A 21% benefits rate was applied to the base compensation hourly wage rate to arrive at the assumed institutional wage rate of $119 for a full professor basic science and $169 for a full professor clinical science. RIO wage rate hours were assumed at the basic science full professor level of $119 per hour unless the case RIO was identified as a clinical scientist or the current RIO was an M.D. For three cases, Duan, Dreyer and Jacoby, the RIO wage rate hours were assumed at the full professor clinical science wage rate. Inquiry Panel estimates assumed a three person full professor faculty member group with a $144 per hour wage rate (1.5 basic science faculty @ $119/hour x 1.5 clinical science faculty @ $169/hour). This same set of assumptions was made for Investigation Panel membership and wage rate. In cases where the respondent's institution had a publicly available document outlining a different panel membership or in cases where the institutional RIO reported a different panel membership, that panel membership number was multiplied by the $144 per hour wage rate. Other institutional hours were assumed to be at the basic science full professor level regardless if the respondent was a Ph.D. or M.D. Time inputs for non faculty specialist, such as institutional lawyers, were assumed at the full professor basic science wage rate of $119 per hour. Economic costs for an institution to complete an inquiry and investigation leading to a finding of scientific misconduct for a faculty member in this study sample were estimated to be $102,115 in cases where a full professor basic science RIO presided and $141,090 where a full professor clinical science RIO presided. Cases were assumed to be completed within the mandated timeline. For cases where the RIO reported an ORI approved exception from the mandated timeline, economic costs for the Investigation Phase ($64,781 for PhD RIO and $89,531 for M.D. RIO) were doubled. In these cases,

economic costs for an institution to complete an inquiry and investigation leading to a finding of scientific misconduct for a faculty member in this study sample were estimated to be $166,896 in cases where a full professor basic science RIO presided and $230,621 where a full professor clinical science RIO presided. Table 5 details model estimations for institutional inputs for Type 1 investigative costs, steps 1-4.

Time estimates and costs were also calculated for Type 1 Investigative Costs, Steps 5-7. Actual time inputs per case were requested from ORI using the FOIA mechanism. In the absence of FOIA provided information, calculations were based on an estimation of a per case ORI cost in the year of the case finding. ORI is charged to oversee and administer research misconduct activities on behalf of PHS (Step 5). The scope of these duties includes recommending administrative actions (Step 6 and 7) to the PHS for approval. Therefore, for purposes of this study, time costs for Steps 5-7 were collapsed into the ORI per case cost assumption. Cost per case estimates were derived from Division of Investigative Oversight (DIO), ORI annual budget figures. DIO 2006 budget figures ($3.5-$4.0 million) were provided by email correspondence from ORI (Dahlberg, 2007) with instructions regarding extrapolating to arrive at historical DIO annual budget amounts applicable to each year of the study period. Following those instructions and assuming a $3.5 million as the budget for 2006, 2000-2005 annual budgets were calculated using the historical percent increase/decrease reflected in the NIH budget (NIH, 2008). Once calculated, those Annual Budget amounts were divided by the number of annual allegations for the respective year as documented by the ORI Annual Report to arrive at a per case cost. Table 6 displays estimated economic costs per case for Type 1 – investigative costs, steps 5-7.

Table 5. Estimated Economic Costs for Institutional Inputs for Type 1 Investigative Costs, Steps 1-4.

Process Step	Mandated Timeline (Days)	Time Input: *Federal Register* Average RIO Process(Hours)	Time Input: Estimated Institutional Added Process (Hours)	Cost Input: PhD ($119/ hour)	Cost Input: MD ($169/ hour)
Receipt of allegation					
Inventory and sequester evidence		35		$4,165	$5,915
Supervise respondent access to record		5		595	845
Subtotal		40		$4,760	$6,760
Inquiry					
RIO administrative oversight (50% effort)[1]			221	$26,299	$37,349
Notify presumed respondent		1		119	169
Respondent review & comment on report		1		119	169
Notice to respondent of investigation		0.5		60	85
Conduct of inquiry					
Receipt and recording of allegation			1	119	169
Inquiry Panel assembly			1	119	169
Inquiry Panel time[2]					
3 Full Professors @ 2 hrs x 3 mtgs			18	2,592	2,592
Panel Preparation Time (3x.5x3 mtgs)			4.5	648	648
RIO support for Panel Inquiry			3	357	507
Legal support			2	238	238
ORI notice of warranted investigation		16		1,904	2,704
Subtotal	60	18.5	250.5	$32,574	$44,799
Investigation					
RIO administrative oversight (50% effort)1			394	$46,886	$66,586
Notify presumed respondent		1		119	169
Conduct of investigation					
Selection of investigation panel			1	119	169
Charge to panel			1	119	169
Administration support for panel					
Investigation Panel time2					
3 Full Professors @ 2 hrs x 5 mtgs			30	4,320	4,320
Panel Preparation Time (3x.5x 5 mtgs)			7.5	1,080	1,080
RIO support for panel investigation			3	357	507
Legal support			4	476	476
Record and transcribe witness interviews		15		1,785	2,535
Required documentation submitted to ORI		80		9,520	13,520
Subtotal	120	96		$64,781	$89,531
Total institutional inputs per case	180	154.5	941.5	$102,115	$141,090

[1]Assumptions for RIO administrative support:
(1) 100% RIO time = Estimated annual burden for ORI defined tasks + institutional tasks
(2) RIO expends 50% of each day during an investigation overseeing the investigation.
(3) Timeline in days
(4) RIO administrative support time = (#days x 8 hrs./ day x .5) - ORI estimated annual burden in hours

[2]Assumption for mixed faculty rank hourly wage rate $144/hr

Table 6. Estimated Per Case Economic Costs for Type 1 – Investigative Costs, Steps 5-7

Year	Allegations Per Year	DIO Annual Budget (Estimated $)	Per Case Cost (Estimated $)
2000	173	4,237,617	24,495
2001	196	3,625,466	18,497
2002	191	3,457,131	18,100
2003	179	3,733,975	20,860
2004	268	3,764,075	14,045
2005	265	3,739,259	14,110

Type 2 –Grant Award(s)

Proven research misconduct in a grant application is sufficient grounds for a finding of scientific/research misconduct. No measure of economic cost for the grant application process was attempted. Rather, grant award costs in the model were measured as the total dollar award of any grant application that resulted in an NIH funded grant. Because the ORI does not differentiate between a grant application and a funded grant, each grant application in the study sample was validated for award approval and then verified for approved NIH funding level. In order to verify total grant award, a four step process was associated with the determination of grant award cost: confirm PI name; verify a funded grant existed; identify year of funding; and determine the state in which the PI was employed when the grant was funded. The ORI Annual Report, Appendix A, summarizing each closed case finding of research misconduct details the granting agency and the unique grant identifier associated with each application for public funds. However, the Findings of Scientific Misconduct provide no information on award status or funding amount. While awards of public funds are technically, a matter of public record, retrieval of that information proved tedious. Grant application identifiers associated with the case respondent were queried via

the Computer Retrieval of Information on Scientific Projects (CRISP) database, a searchable database of publicly funded medical research. The unique grant identifier and case respondent's name were entered into CRISP to attempt to validate award funding and year of award. In instances where the case respondent was PI of a funded grant, CRISP provided the year and PI institution, allowing for state to be determined. In instances where the case respondent was not the PI on the grant application, no verification of grant award was available. In these cases, additional investigative techniques, such as literature searches by case respondent name combined with review of articles and funding support disclosures, on-line queries by respondent's name, FOIA requests to granting agencies, and/or direct request of the respondent's institution for disclosure were employed. Once the PI, year of the award, and state in which the grant was awarded were ascertained, the grant award in dollars could be determined by accessing NIH Awards by State and Foreign Site, an on-line NIH reporting tool which further segregates awarded grant information by state by year. Grant award dollars reflect the total grant award, both direct and indirect costs.

Type 3 – Voluntary Exclusion Agreement Cost

When a finding of scientific/research misconduct is concluded, the respondent is subject to a penalty or penalties described and levied through a Voluntary Exclusion Agreement (VEA). The VEA is a type of contractual agreement between a respondent and a federal agency and the penalties which it describes are synonymous with administrative action actions linked to findings of research misconduct. The determination of the penalty and its review by ORI occur in Steps 5-7 of the Investigative process (see Investigative Costs). The VEA is designed using a variety of administrative actions with a variable time

period (1 year to lifetime) assigned for each administrative action. Imposition of the VEA has a remedial goal (except in cases of lifetime debarment) and is meant to reflect the significance and impact of the misconduct, as well as signal whether the finding is a unique event for the particular researcher. The ORI website provides the following list of administrative actions with the caveat that unspecified actions can also be imposed:

- debarment from eligibility to receive Federal funds for grants and contracts,
- prohibition from service on PHS advisory committees, peer review committees, or as consultants,
- certification of information sources by respondent that is forwarded by institution,
- certification of data by institution,
- imposition of supervision on the respondent by the institution,
- submission of a correction of a published article by respondent, and
- submission of a retraction of a published article(s) by respondent (ORI, 2008).

While the VEA is designed, approved and reviewed during the investigative phase, the VEA is implemented after the case finding has occurred and the *Federal Register* scientific misconduct notice is published. Thus, VEA costs are incurred after the conclusion of the investigative phase and represent a distinct type of economic cost in this model. These costs are incurred by the NIH and the respective research institution to monitor a researcher who remains in the publicly funded research setting subsequent to being found guilty of scientific misconduct. Costs for institutional monitoring were assumed as chargeable as an NIH supported indirect cost administrative expense.

In estimating VEA costs, it was assumed that VEA costs were incurred if the case respondent remained at the institution where the finding was recorded or was employed by any other publicly funded U.S. institution. The author verified 2005 employment for each faculty in the study sample by a variety of techniques. During the telephone interview RIOs were asked to confirm faculty member employment status after the finding of research

misconduct. In cases where no RIO interview was conducted, an internet search using the faculty member's name and degrees was used to verify the employment after the finding of research misconduct For those faculty determined to still employed in 2005 in a university setting, VEA penalties for each of the respondents were inventoried. Debarment and prohibition of PHS service were assumed to have zero cost to the NIH or institution. These actions result in a cost saving of public funds. During the VEA period of debarment and prohibition of PHS service, the case respondent cannot be paid for these specific activities with publicly awarded grant funds. However, the case respondent may continue to be paid for a percent of effort on another PI's grant during the VEA period. If this is the case, certification and supervision actions to review the case respondent's research activities represented additional public funds costs. RIO time estimates for certification and supervision were relied on when available from the interview results. In the absence of a RIO estimate, a time input measure was assumed for each administrative action and the assumed case RIO hourly wage rate was applied to arrive at an estimate of economic cost per VEA certification and supervision action. For all case respondents, retraction costs were considered as separate from VEA cost.

Table 7. VEA Time Period by Investigator by Rank.

Rank	Investigator Case	MD/PhD	Year	Misconduct Type	VEA Period
Professor (N=4)	Radolf	MD	2003	Fabrication/Falsification	5 years
	Kammer	MD	2005	Fabrication/Falsification	3 years
	Prasad	PhD	2002	Fabrication/Falsification	3 years
	Poehlman	PhD	2005	Fabrication/Falsification	Lifetime
Associate Professor (N=5)	Ganz	MD	2002	Fabrication/Falsification	5 years
	Hartzer	PhD	2000	Falsification	3 years
	Dreyer	MD/PhD	2000	Fabrication/Falsification	10 years
	Yao	MD/PhD	2002	Falsification	5 years
	Gelband	PhD	2003	Falsification	10 years
Assistant Professor (N=7)	Sultan	MD/PhD	2004	Falsification/Plagiarism	3 years
	Pandurangi	PhD	2001	Falsification/Plagiarism	4 years
	Arnold	PhD	2001	Fabrication/Falsification	5 years
	Padget	PhD	2001	Plagiarism	3 years
	Xiong	PhD	2001	Fabrication/Plagiarism	3 years
	Ruggiero	PhD	2001	Fabrication	5 years
	Duan	MD	2000	Falsification	3 years
Instructor (N=1)	Jacoby	MD/PhD	2001	Falsification/Plagiarism	5 years

Type 4 – Retraction Costs

Retraction costs are those costs associated with required retraction of a scientific publication included in the published *Federal Register* scientific misconduct notice and the ORI Annual Report. The scientific community supports correcting the scientific literature and the PHS/HHS administrative actions require retraction of an article cited in a misconduct finding. Two categories of retraction costs were identified in this study. One category is linked to the *Federal Register* notice of a finding of scientific misconduct and ORI Annual Report, both of which identify for retraction a specific article title and journal of publication. ORI takes responsibility to notify journal editors of required article retractions for this category of retractions (ORI, 2000). However, the second category of retraction costs

encompasses time costs to validate all published articles by the respondent. These costs required to correct the scientific literature lies with the respondent's institution (Sox & Rennie, 2006). A Med-line search of the cost to retract a journal article and an internet search yielded no references for a cost to retract a journal article. RMQ interview information was used when possible to measure the time cost to retract articles, as RIOs frequently mentioned they also spent administrative time in the retraction process. When there was no specific RIO-provided measure for retraction efforts, the author assumed a two hour effort by the respondent's institution per retraction at the RIO hourly wage rate to estimate the cost to retract a research article identified in the NIH Findings.

Total Cost

A per case cost for each case finding of scientific misconduct attributable to a faculty respondent in the study population was calculated using the model. These were summed and a total cost for findings of scientific misconduct among faculty respondents for 2000-2005 was calculated. Total costs for each of the four cost types were also calculated.

RESULTS

Qualitative Interviews

Each of the five key informants agreed to be interviewed. Of the four queried regarding specific economic cost considerations in research misconduct, one consistent view emerged. Economic costs were not considered nor measured. In conducting the inquiry and investigation leading to a finding of research misconduct, the emphasis was on adhering to the mandated administrative law process while being sensitive to the 480 day completion timeline. The author finalized the RMQ for use in RIO interviews at the conclusion of the key informant interviews.

RIO interviews were conducted after key informant interviews. The 17 findings of research misconduct in the study sample came from 16 different publicly funded institutions with 16 distinct RIOs (see Tables 8 and 9). One institution, Harvard University Medical School, had two cases in the study sample. Tenure in the RIO position varied from a maximum of 26 years to four months.

Table 8. RIO Response to Telephone Interview Request and Status as Case RIO

RIO Interview Participation	Total (n)	Sample %
Total RIOs in sample	16	100
Consented to telephone interview	12	75
Case RIO	6	37.5
Assumed RIO position after case finding	6	37.5
Declined telephone interview	2	12.5
No response to interview request	2	12.5

Each RIO was interviewed using the six questions comprising the RMQ. RIO time in position ranged from less than six months to over twenty years. All RIOs interviewed expressed a positive belief about the importance of estimating costs of research misconduct. RIO attitudes about estimating costs did not differentiate between economic costs, measured using the four types of costs defined in this study, or societal costs. However, none of the RIOs reported collecting cost data. One RIO indicated that their office employed a chargeback scheme for allocating annual department costs. The method appeared to employ a straight forward cost accounting model whereby the 30% of annual departmental costs attributable to research misconduct issues was allocated to users based on the number of cases generated by the user work unit. The RIO referred to this approach as a "forensic" model. Ten RIOs reported that the most costly institutional aspect of a finding of misconduct was "faculty involvement" in the inquiry and investigation phases. RIOs (10) described the faculty committee structure of from three to five tenured full professors participating in the inquiry phase and a different faculty committee structure of from three to five tenured full professors participating in the investigative phase. RIOs emphasized the intensity of their administrative oversight of all phases of the process. One case RIO indicated he spent 100% of his time on the case, a case which surface shortly after he assumed the RIO position. Other case RIOs (5) felt the intensity waxed and waned depending on the phase of the inquiry or investigative process. Two case RIOs were able to recall that the case had exceeded the mandated timeline for institutional inquiry and investigation, but were not able to recall the excess time spent. When probed about time spent by faculty or themselves, the issue of confidentiality was the most mentioned constraint on providing information beyond

publicly available records for each case. In only once case, Eric Poehlman, was a public record of the institution's investigation report available to estimate institutional resource inputs for Type 1 model costs.

Table 9. Summary by Faculty Case - RIO Interview Participation.

Investigator (Case)	Year	Institution	Interview Status	Case RIO
Hartzer	2000	Oakland University	Decline	No
Duan	2000	Thomas Jefferson	Decline	No
Dreyer	2000	Harvard University Medical School	Accept	No
Xiong	2001	University of Texas Health Science Center - School of Public Health	Accept	No
Padget	2001	Ohio State University	Accept	No
Ruggiero	2001	Harvard University	No Response	
Pandurangi	2001	U Missouri - Columbia	Accept	Yes
Arnold	2001	Tulane University	Accept	No
Jacoby	2001	Harvard University Medical School	Accept	No
Prasad	2002	University of Kentucky School of Medicine	Accept	No
Yao	2002	University of North Carolina - Chapel Hill	Accept	Yes
Ganz	2003	Case Western Reserve University	Accept	Yes
Radolf	2003	University of Connecticut - Health Center	Accept	Yes
Gelband	2003	University of Florida School of Medicine	Accept	Yes
Sultan	2004	Harvard University School of Public Health	No Response	
Kammer	2005	Wake Forest University	Accept	No
Poehlman	2005	University of Vermont	Accept	Yes

One case RIO interviewed oversaw a VEA and was able to describe the process and estimate the institutional hours involved for the VEA. For Type 4 retraction costs, only one case RIO (Poehlman case) described the institutional process and estimated costs. It is important to note that both of these RIOs indicated that they had not estimated the time inputs until before they accepted the author's request for an interview. Several RIOs emphasized the undetermined cost of the lost time in research direction and the inestimable societal cost of scientific misconduct. One RIO discussed the harm to the community trust when the case

finding (Poehlman case) was disclosed and recounted phone calls from angry clinical trials participants from the community. Both he and another institutional official interviewed described the resultant added challenge institutional researchers continue to encounter when recruiting clinical trial participants from the community.

Economic Costs of Research Misconduct

Case findings of scientific/research misconduct by a faculty, instructor rank or above, in closed cases reported in the ORI Annual Report 2000-2005 were estimated for the economic cost of misconduct. The model used to estimate economic costs was developed as a product of this research effort. For the model, economic costs were categorized as one of four types: Investigative Costs, Grant Award(s), VEA Costs, or Retraction Costs. Cost types were summed to arrive at a Total Cost per case finding. All cases were found to have measureable costs based on the model's assumptions. Based on model assumptions, no cases were found to have all types of cost. Table 10 summarizes the cost elements and the number of cases with each cost type.

Table 10. Types of Economic Impact of Research Misconduct and Cases.

Type 1 Investigative Costs	Type 2 Grant Award(s)	Type 3 VEA	Type 4 Retraction Cost	Total Cost
17 cases	9 cases	3 cases	7 cases	17 cases

Type 1 – Investigative Costs

All cases in the study sample had calculated economic costs for Type 1 investigative costs. Based on model assumptions, Type 1 investigative costs for the cases in the sample totaled $2,526,458 (see Table 14). The per case Type 1 economic cost ranged from a low of $116,160 (Sultan case) to a high of $320,860 (Gelband case). In the Gelband case, the case

RIO reported during the telephone interview that while he had not estimated "internal" costs at the time of the investigation, he was able to use time records for faculty and general counsel and, using 2007 dollars, conclude that the year long process consumed $300,000 in time costs for Investigative Costs, Steps 1-4. This historical economic cost was combined with the estimated Steps 5-7, attributable to the ORI costs economic costs, to arrive at the Type 1 cost. For the remaining 16 cases, economic costs were estimated by the methodology described above in the Methods section. Type 1 Investigative costs for Steps 1-4 for two cases, Radolf and Poehlman, were doubled based on the RIO interview report that each of these cases had exceeded the 120 day timeline for inquiry and investigation and ORI had approved a time extension. Thus variation in investigative costs for these 16 cases is dependent on (1) RIO terminal degree (Ph.D. vs. M.D.), (2) DIO ORI annual budget and annual investigative caseload, and (3) completion of the process exceeding the mandated timeline (Radolf, Gelband and Poehlman cases).

Type 2 – Grant Award(s)

A total of fifty-four grant applications were referenced in the 17 case findings (see Table 11). Grant applications were slotted into one of three categories for costing by the model. Grant applications with no evidence of funding were assigned a zero dollar value. Thirty-one grant applications fell into this category or 57.4% of grant applications referenced in research misconduct findings. Grant applications funded for an investigator PI who was found guilty of scientific misconduct during the study period were estimated at the total dollar award adjusted by the CPI to 2007 dollars. Nineteen grant applications with a total award funding of $5,390,961 comprised this category, or 35.2% of grant applications. The

third category consisted of grant applications for another investigator who was not the PI was cited for scientific misconduct. This category accounted for 7.4% of grant applications with four funded grant applications totaling $5,644,062. Three investigators in the study sample, Duan, Jacoby and Gelband, were found guilty of falsifying and/or fabricating data included in a grant application for another investigator's funded grant. Costs for this category were excluded from the per case cost estimations.

In two instances, legal proceedings provide the basis for grant awards cost estimates. *US ex rel Yong Wu* v. *Thomas Jefferson University* (1997) required a payment of $544,836 (2007 dollars) in the whistleblower case associated with the Duan research misconduct finding for falsification. In the Poehlman case, *US v. Eric Poehlman* (2005) cites that NIH paid Poehlman grant awards totaling $1.7 million, assuming 2005 dollars. This figure was adjusted to 2007 dollars and then reduced by identified fund grant applications to arrive at the unidentified grant applications' cost of $1,073,963 (see Table 11 – Poehlman).

Table 11 displays, by investigator, the grant applications cited in the respective finding of research misconduct and provides grant award costs in 2007 dollars.

Table 11. Grant Applications Cited in Findings of Research Misconduct and Grant Award(s) by Case Finding.

Investigator	Year	Institution	Grant Application	Amount Awarded($)[1]
Hartzer	2000	Oakland University	-	
Duan	2000	Thomas Jefferson	RO1 AI36552-01[2]	-
			RO1 AI36552-02[2]	-
			Unidentified grant applications	544,836
Dreyer	2000	Harvard	KO8 DC0013 1-01A1	-
Xiong	2001	UTHSC	RO1 GM64353-01	-
Padget	2001	Ohio State Univ.	1RO1 AG20102-01[3]	-
Ruggiero	2001	Harvard	1RO3 MH58586-01	48,662
			F32 MH12868-01	-
			F32 MH12868-01A1	-
			1R01HL065220-01	-
Pandurangi	2001	U Missouri - Columbia	1RO1 HL62517-01A2	-
Arnold	2001	Tulane	1 R29 DK52420-01	-
Jacoby	2001	Harvard	1 PO1 NS37409-01A1[4]	-
			5K08NS01887-03	139,326
			5K08NS01887-05	143,006
Prasad	2002	U of Kentucky	RO1 NS34264-01A1	249,125
			5R01034264-02	244,153
			5R01034264-03	248,211
			5R01034264-04	254,073
			5R01034264-05	258,548
			RO1 NS41918-01	-
Yao	2002	UNC - Chapel Hill	1R01HL067416-01[3]	-
			1R01HL068250-01[3]	-
			1R01HL066230-01A1	-
			1K08HL03881-01	106,652
Ganz	2002	Case Western Reserve	RO1 DK058674-01A2	-
Radolf	2003	U of Conn - Health Center	R01 AI29735-11	447,190
Gelband	2003	U of Florida	R29HL52189-01A2	-
			R01HL56921[5]	-
			F32HD08496	-
			R01/R37HL49254	-
			F32HL08531	42,270
			5 F32HL008531-02	42,393
			5 F32HL008531-02	43,029
			P01DK41315	-
			R01HL69034-01	-
			R01HL52189-05	415,525
Sultan	2004	Harvard	1 PO1 AI060332-01[3]	-
Kammer	2005	Wake Forest Univ	2R01AR39501-12A1	448,904
			1R01AR46526-01A2	296,442
Poehlman	2005	University of Vermont	1R01AG17906-01	-
			1R01AG17906-01A1	-
			R01AG13978-01	-
			R01AG13978-01A1	354,171
			P01AG16782-01	-
			1R01AG18238-01	219,266
			1R01AG18238	-
			P01AG16782-01A1	-
			1R01AG19800-01	-
			2M01RR00109-33	-
			2R01DK052752-05[3]	-
			2R01AG07857-06	244,003
			7R01AG07857-07	-
			5R01AG07857-09	-
			5R01AG07857-08	-
			Unidentified grant applications	1,073,963

[1] Award is Total Cost adjusted to 2007 dollars.
[2] Case respondent is not PI on funded grant. Funded grant award for R01 AI036552-01 is $223,773. Funded grant award for R01 AI036552-02 is $297,980.
[3] Grant application identified as "withdrawn". Withdrawn grant may have been funded, however, if funded, the amount is protected by federal privacy laws applying to both grant applications and "withdrawn" approved and/funded grants.
[4] Case respondent is not PI on funded grant. Funded grant award for 1 P01 NS37409-1-01A1 is $1,242,049.00
[5] Case respondent is not PI on funded grant. Funded grant award for R01HL56921, a multi-year funded award, is $3,880,260.

Grant award(s) cost per case ranged from $48,662 (Ruggiero case) to $1,963,453 (Poehlman case). The magnitude of the grant award cost was driven by the grant award type, which specifies allowable costs, and the number of funded grant applications. R03, investigator-initiated small grant awards (Ruggiero case), and F32, post-doctoral stipends during research training (Gelband case), have estimated costs between $42,270 and $48,662. K08 awards, mentored clinical scientist research career development awards (Jacoby and Yao cases), have estimated costs $106,652 and $143,006 to support salary, benefits and research development support. R01, research program awards, have estimated costs that range from $219,266 (Poehlman case) to $448,904 (Kammer case).

Type 3 – Voluntary Exclusion Agreement

VEA costs totaled $98,358. Of the seventeen cases, three were estimated for VEA cost based on model assumptions. These respondents were the study sample case respondents found to be employed during and after the VEA period at the institution where the finding was recorded. RIO interviews confirmed that an untenured faculty member often elected to resign at some time contemporaneous with the institutional finding. Exact details of timing of resignation and severance package were protected by privacy disclosure agreements. Therefore, no estimates of these economic costs were made.

VEA costs were a function of the type of administrative action imposed and the duration of the action. VEA costs for Xiong and Padgett were calculated using the approach described in the Methods section. General certification of research activities was estimated at 2 hours per month for each month of the certification period at the RIO hourly wage rate. Both Xiong and Padgett were subject to a 36 month certification period. For Xiong,

additional administrative actions were reviewed against his current curriculum vitae (CV) to identify (1) funded and unfunded grants and (2) publications which were subject to institutional certification for the 36 month period. The CV was available from an internet search. Economic costs were estimated assuming a one hour time input by the institutional official (RIO basic science wage rate $119/hour). Other required administrative actions were assumed at one hour time put per action. For Padgett, details of his VEA published in the misconduct finding were reviewed. He was subject to two administrative actions for a 36 month period. No CV was found using the internet search approach or by accessing the faculty site at the university where he is employed. However, an OVID search identified a first author publication falling into the certification period which acknowledged research support from five NIH grants. A CRISP search identified him as PI on two R29 grant awards during the certification period. Table 12 displays the VEA administrative actions, time input assumptions, and wage rate used to arrive at VEA cost for these two cases. VEA costs for the five year certification period in the Radolf case were estimated by the case RIO during the interview. The case RIO reported that for the five year certification period two full professors with annual salaries and benefits expense of $200,000 (2007 adjusted salary level) each spent four to eight hours per certification on 60 certifications. VEA costs for the Radolf case totaled $74,880 (60 hours x 6 hours x 2 faculty at $104/hr.) assuming an average of 6 hours per certification per faculty member.

Table 12. Calculated VEA Cost for Cases without Historical Data

Case		Administrative Action	Time Input	Total Hours	RIO Hourly Wage Rate	Estimated VEA Cost
Xiong						
	1	General certification of research activities for 36 months	2 hours/ month for 36 months	72	$ 119	$ 8,538
	2	Formal written apology	1 hour	1	$ 119	119
	3	Certify publications for 36 months(2002-2004 publication date)	28 publications @ 1 hour/publication	10	$ 119	1,186
	4	Certify grant applications for 36 months	33 grant aplications @ 1 hour/application	33	$ 119	3,913
	5	Review of formal essay of publication quality on plagiarism	1 hour	1	$ 119	119
						$ 13,874
Padgett						
	1	General certification of research attribution for 36 months	2 hours/ month for 36 months	72	$ 119	$ 8,538
	2	Certify grant reports and applications for 36 months				
		PI on two R29	2 grants @ 2 reports/ grant @ 1 hour/report	4	$ 119	474
		PHS funding credit on publication with 2003 publication date	5 grant reports @ 1 hour/report	5	$ 119	593
						$ 9,605

Type 4 – Retraction Costs

Retraction costs for the study sample totaled $31,776. A total of 27 articles published by seven investigators were identified for retraction in the study sample. The range of retraction cost was $237 (Arnold, Prasad and Yao cases with 1 retraction per case) to $28,252 (Poehlman case, >10 retractions). The model calculated $7,386 Type 4 retraction costs in the seven cases where retractions were mandated by the Finding of Scientific/Research Misconduct. In all cases except the Poehlman case, retraction costs was driven by the number of retractions and the RIO hourly wage rate (assuming two hours per retraction).

The Poehlman case included additional costs in the retraction costs category based on RIO interview results. The model calculated retraction costs of $3,388 for the 10 articles mandated for retraction in the misconduct finding. The RIO indicated that the University of Vermont (UoV) determined a review of all Poehlman's peer reviewed published articles would be appropriate given the scope and length of his misconduct. Faced with the daunting task, a UoV faculty committee decided to restrict the review to all of Poehlman's articles

published during his employment at UoV. The faculty committee convened and agreed upon a strategy to validate all articles published during Poehlman's UoV employment. A total of 110 articles met this criteria and were evaluated for falsification and fabrication and categorized as valid, questionable or fraudulent. The RIO estimates of number of personnel, salaries and fringe, and time inputs were used to calculate an additional $24,153 to supplement the $3,388 calculated from model assumptions (see Note 1 in Table 13). Thus retraction costs for Poehlman total $27,541(model calculated costs of $3,388 + $24,153 expanded review costs).

Table 13 displays by case the number of mandated retractions, RIO case wage rate, and calculated cost per case assuming a 2 hour time input .

Table 13. Retraction Costs by Investigator.

Case	# Articles Retracted	RIO Hourly Wage	Retraction Cost
Duan	2	$ 169	$ 678
Ruggiero	4	$ 119	$ 949
Arnold	1	$ 119	$ 237
Prasad	1	$ 119	$ 237
Yao	1	$ 119	$ 237
Gelband	8	$ 119	$ 1,897
Poehlman[1]	10	$ 169	$ 3,388

[1] Additional costs to review 110 publications for retraction per RIO:

Committee chair: 2% x $226,875 x 24 months	$ 9,075
1 support staff: 5% x $50,820 x 24 months	5,082
7 faculty @ 1 hr x 12 months	9,996
	$ 24,153

Total Cost

Total economic cost of research misconduct for the seventeen cases in the sample using model assumptions was calculated to be $8,592,390. Table 14 displays the total

economic costs for the seventeen cases examined as well as the per case cost by investigator in oreder of year of case finding. Investigative costs for the study period were $2,526,458 or 29% of total economic costs. Grant award costs of $5,935,797 represented 69% of total economic costs. VEA costs and Retraction Costs were 1% and less than 1%, respectively, of total economic costs. Using the model, the per case economic cost for a finding of scientific misconduct among faculty ranges from $116,160 to $2,192,620, with a median cost of $170,223. The minimum cost of $116,160, as estimated in the Sultan case, represents a "floor" for economic costs of research misconduct predicted by the model. In the Sultan case no grant award, VEA or retraction costs were estimated. A total of six cases, including the Sultan case, had only investigative costs predicted by model assumptions. The range for these cases was $116,160 - $165,585. The median economic cost was $170,223 in the Ruggeiro case, which included investigative, grant award and retraction costs. The maximum economic cost predicted by the model is $2,192,620, estimated in the Poehlman case. Poehlman's case cost represents the "ceiling" and does not include VEA cost because he was debarred for life from receiving public funds.

Table 14. Estimated Economic Costs of Research Misconduct by Investigator by Year of Case Finding.

	Type 1 Investigative Costs	Type 2 Grant Award	Type 3 Voluntary Exclusion Agreement Cost	Type 4 Retraction Cost	Total Cost
Hartzer	$ 126,610	$ -	$ -	$ -	$ 126,610
Duan	$ 165,585	$ 544,836	$ -	$ 678	$ 711,099
Dreyer	$ 165,585	$ -	$ -	$ -	$ 165,585
Xiong	$ 120,612	$ -	$ 13,874	$ -	$ 134,486
Padgett	$ 120,612	$ -	$ 9,604	$ -	$ 130,216
Ruggiero	$ 120,612	$ 48,662	$ -	$ 949	$ 170,223
Pandurangi	$ 120,612	$ -	$ -	$ -	$ 120,612
Arnold	$ 120,612	$ -	$ -	$ 237	$ 120,849
Jacoby	$ 159,587	$ 282,332	$ -	$ -	$ 441,919
Prasad	$ 120,215	$1,254,109	$ -	$ 237	$1,374,561
Yao	$ 120,215	$ 106,652	$ -	$ 237	$ 227,104
Ganz	$ 122,975	$ -	$ -	$ -	$ 122,975
Radolf	$ 187,756	$ 447,190	$ 74,880	$ -	$ 709,826
Gelband	$ 320,860	$ 543,217	$ -	$ 1,897	$ 865,974
Sultan	$ 116,160	$ -	$ -	$ -	$ 116,160
Kammer	$ 116,225	$ 745,346	$ -	$ -	$ 861,571
Poehlman	$ 201,626	$1,963,453	$ -	$ 27,541	$2,192,620
Total	$ 2,526,458	$5,935,797	$ 98,358	$ 31,776	$8,592,390

DISCUSSION

This study relied on a sequential mixed methods design to estimate the economic costs of research misconduct in faculty found to have committed misconduct as reported by the *Federal Register* and ORI Annual Reports from 2000-2005. Estimating the economic costs of research misconduct is a complex measurement task which begins by defining distinct cost components of research misconduct and proceeds to a per case estimate of costs. This study proposed and tested an economic cost model based on the federal administrative law policies and procedures for investigating and arriving at a determination of research misconduct. The model identified and included economic costs borne by publicly funded institutions carrying out the required steps ending in a finding of research misconduct for a faculty member. Results of this research study have revealed that the neither ORI, the federal agency responsible for oversight of research misconduct, nor individual institutions in the study sample record economic costs or employ a measurement scheme to accumulate economic costs of research misconduct. The cost model and the resulting estimated per case economic costs provide a first time estimate of the economic costs of a finding of scientific/research misconduct for a faculty member engaging in publicly funded medical research. Table 15 summarizes by investigator by rank the type of misconduct finding and the associated per case cost.

Table 15. Per Case Economic Cost of Research Misconduct by Investigator Rank.

Rank	Investigator Case	MD/PhD	Year	Misconduct Type	Total Cost
Professor (N=4)	Radolf	MD	2003	Fabrication/Falsification	$ 709,826
	Kammer	MD	2005	Fabrication/Falsification	$ 861,571
	Prasad	PhD	2002	Fabrication/Falsification	$ 1,374,561
	Poehlman	PhD	2005	Fabrication/Falsification	$ 2,192,620
Associate Professor (N=5)	Ganz	MD	2002	Fabrication/Falsification	$ 122,975
	Hartzer	PhD	2000	Falsification	$ 126,610
	Dreyer	MD/PhD	2000	Fabrication/Falsification	$ 165,585
	Yao	MD/PhD	2002	Falsification	$ 277,104
	Gelband	PhD	2003	Falsification	$ 865,974
Assistant Professor (N=7)	Sultan	MD/PhD	2004	Falsification/Plagiarism	$ 116,160
	Pandurangi	PhD	2001	Falsification/Plagiarism	$ 120,612
	Arnold	PhD	2001	Fabrication/Falsification	$ 120,849
	Padget	PhD	2001	Plagiarism	$ 130,216
	Xiong	PhD	2001	Fabrication/Plagiarism	$ 134,486
	Ruggiero	PhD	2001	Fabrication	$ 170,223
	Duan	MD	2000	Falsification	$ 711,099
Instructor (N=1)	Jacoby	MD/PhD	2001	Falsification/Plagiarism	$ 441,919

Interview results provided a rich set of background information underpinning the complexities of cost modeling for a finding of research misconduct. The total 4.5 hours of purposive sampling informal conversational interviews confirmed the challenges of determining costs of research misconduct and identified potential limitations in the research methodology. These interviews were conducted in Fall, 2007. The interview with the former M.D. Anderson Cancer Center RIO provided a first person account of conducting inquiries and investigations as outlined by the ORI policies and procedures in place during the study period. From this interview, the author began to outline the general structure of the standard open-ended interview approach reflected in the final RMQ used during the RIO interviews that followed the preliminary key informant interviews. The interviews with the ORI DIO officials, current director and deputy director and the retired director, were

designed to provide expert perspectives from the NIH perspective. Individuals in this group have overseen every investigation and finding of scientific/research misconduct conducted since the creation of the ORI in 1992, which includes all cases in the study sample. Interviews with these administrators revealed that ORI records no cost information during any phase of an investigation, including the dollars awarded for publicly funded grant awards tainted by a finding of scientific/research misconduct. The issue of the economic costing of the grant award was explored at length during these interviews. When queried about the impact of a finding of scientific/research misconduct on the validity of the publicly funded research effort embodied by an NIH grant, these experts discussed the uncertainty involved in concluding which portion of that grant is invalidated by the fact of misconduct. Because a grant application proposes multiple study aims, the nature of misconduct may impact one aim or overlap many or all of the aims. It seemed to be their view that determining economic cost impact of a funded grant would require a separate deliberation by scientific experts in the research discipline to determine the economic cost component of misconduct study aim by study aim. In other words, the nature of the public good produced by any particular grant is sufficiently complex that while misconduct was involved, that misconduct might invalidate only a portion of the publicly funded research product. Further, the current DIO officials reflected on whether the type of misconduct, plagiarism vs. fabrication/falsification, might differ in invalidating the research effort and outcome. In contrast, the DOJ, in prosecuting Eric Poehlman in U.S. District Court, took the view that the economic cost of a funded grant award is the total dollar award (ORI-Press Release, 2005).

The RMQ used in RIO interviews was developed and refined during the key informant interviews. As a data gathering technique the telephone administered questionnaire offered a cost effective approach to elicit RIO responses. The overall intention in questionnaire design was to craft key neutral and open ended questions that would support probe questions during a telephone interview. The initial question, "Tell me about your experience handling allegations of research misconduct", allowed the RIO to begin talking freely about a non-threatening subject. The second question quickly narrowed the focus of the interview and introduced the issue of the cost of research misconduct, offering the RIO an opportunity to share both a subjective and objective assessment of economic costs. The range of answers from "no cost" to "inestimable" costs and the interest of the RIO in discussing cost with the author suggest that a dialogue is ripe. Rather than asking the open ended question, "how would you measure economic costs", the author had intentionally scripted the third question to suggest a cost methodology based on the ORI process steps for inquiry and investigation. One interesting finding was the willingness of a few RIOs to prepare for the interview by reviewing the case file or having the case file at hand during the interview. Generally, RIO willingness to cooperate was gratifying even though the results regarding collection of cost data were disappointing. The most provocative outcome during the interview process was the discovery that in the Radolf case a whistleblower call to ORI had resulted in the case being reopened by the institution. In retrospect, the general, brief nature of the RMQ may have had a positive factor in the 75% compliance rate with the interview request.

RIOs interviews utilizing the RMQ followed the conclusion of preliminary key informant interviews. Interview results provided overwhelming evidence that no economic costs are measured by institutions during investigations of research misconduct. The author had hypothesized that at least some institutions would have a financial incentive to record associated time and expenses, given typical annual budget justification processes and resource constraints. One RIO stated that "there are no costs of misconduct except to the faculty member whose career is over". The attitude regarding cost represented by this RIO offers an outlier perspective. The remainder of the RIOs interviewed remarked that faculty, legal, staff, and their own time carried a substantial opportunity cost for their respective institutions. Cost for court reporters was mentioned by RIOs who oversaw cases closed toward the end of the study period. Apparently, during the study period ORI had initiated the recommendation that a court reporter be utilized for transcribing testimony. When pressed by the author several of the RIOs interviewed appeared to be able to informally estimate time spent by different actors for each case. Nevertheless, actual opportunity costs were consistently unmeasured.

The literature on research misconduct does not include a study of the RIO role or experience. Therefore, the author had no way to anticipate the willingness of RIOs to be interviewed or to disclose information about their role in general or in regard to the specific case in the study sample. The 75% response rate for RIO interviews was of interest given the absence of this data. Of the two RIOs who declined to be interviewed (Hartzer and Duan cases), one RIO spoke with the author about the general topic of the interview request, remarking that he had never thought about cost considerations and believed it was an issue

that should be explored. After speaking with his institutional legal counsel, he subsequently declined to be interviewed. Of the 12 RIOs consenting to the telephone interview, 11 were open and comfortable discussing their experience as a RIO, regardless of their status as case RIO. In only one interview did the RIO appear uncomfortable with the process and express hesitance in responding to the questionnaire. When asked whether the RIO's institution collected cost information in investigation research misconduct, the RIO answered that cost information was not collected and then demurred that the she had not gotten institutional approval to disclose that information. Because of her markedly brief responses, the interview was concluded in less than 30 minutes. One RIO asked the author, as a condition of the interview, to provide a specifically worded email that any information gleaned from the interview would be used only for research and publication in peer reviewed journals. After receiving the written assurance, this RIO was generous with his time and freely responded to the RMQ. While the author had a confirmed scheduled telephone interview slot of one hour, over a third of RIO interviews exceeded the time. In those cases, the RIOs had been in the role for greater than 10 years or had overseen a particularly complex investigation.

The model developed in this study to measure economic costs of findings of research misconduct defines categories of economic costs and estimates economic cost types. In the absence of historical economic cost data, the guiding principle for model development was to err on the side of conservative cost estimation for each of the four cost types in the model. This is not perceived by the author as a limitation of the study, but rather as an intentional device to mitigate inflating the impact of economic costs of research misconduct.

Investigative costs were estimated by the author in all but one case in the study sample. The model estimated total RIO effort per case at 778 hours per case. Given the meticulous nature of the process required of a RIO, it is possible that he/she could spend 100% effort for the mandated 120 days and incur $104,640 (120 days x 8 hours x $109/hr for PhD RIO). Interviews with RIOs confirmed that each case was a "unicorn" and the potential for efficiencies from a learning curve effect are minimal. Faculty time in inquiry fact-finding and investigative committee hearings have been estimated assuming a three person committee membership (usually the respondent's department chair, a full professor with research expertise similar to that of the case respondent, and a full professor from a different discipline) in each case in the study sample. This three person full professor committee membership model represents the minimum size for both the inquiry and the investigative committees. Most RIOs reported that committee size flexed up to as large as five members if the nature of the allegation required technical research knowledge (such as biostatistics or genetics) or involved a multidisciplinary research program. Use of each additional faculty member for an inquiry panel or an investigation panel would add $1,080 and $1,800 respectively to the investigative costs per case for a case concluded within the 120 timeline. Staff time, court reporter fees, and legal counsel time in excess of 2 hours per investigation were not estimated for investigative costs. The process of closing a research unit and accommodating staff reassignments while an investigation is on-going was not been estimated in this research study. Cases for associate and full professors should be evaluated for economic cost of research unit closure. For investigations of egregious cases and those exceeding the 480 day timeline, such unmeasured costs will be significant. Economic costs

associated with administrative time to manage whistle blower issues were not considered. Two case RIOs mentioned the challenge of protecting the whistle blower's identity and insuring their continued employment in the institution. Estimation of the investigative costs depends on the accuracy of time inputs taken from the Final Rule estimates for Annual Average Burden per Response for time inputs for the RIO described in the Methods section and the assumed added institutional process time inputs. Neither category of time input assumptions has been validated. RIO interview responses suggest to the author that both categories are likely underestimated.

The assumption for Type 2 grant award(s) economic cost considered 100% of the grant award in total dollars as funding the scientific/research misconduct of the faculty respondent. This appears justified given the fact that the grant application identifier which correlates to a funded grant is identified and published in the *Federal Register* notice and included in the ORI Annual Report as evidence of proven research misconduct. This view attributes 100% of the grant award in direct dollars as a product of scientific/research misconduct. To make an allocation of the total awarded dollars according to validity of specific research aims which would require significant resources and increase the economic cost of each finding (Parrish, 2004). Type 2 Grant award(s) costs are also underestimated in this study. The model included total dollar awards to PIs in the study sample. Several types of grant application costs were not estimated by the model. Economic costs for withdrawn grants and grants awarded to a non study sample PI were not included in model estimation as no accurate economic cost measure exists or could be obtained through FOIA. Economic costs of NIH study section evaluation of the 54 grant applications in the study sample were

not estimated. Study section review costs, conducted by a committee of 10-15 scientific advisors, would have reasonably been expected as incurred in the 19 cases where a funded grant application was identified in the finding of misconduct. Five instances of "withdrawn" grants, grants submitted for funding but subsequently retracted, were confirmed among the 54 grant applications. In two specific Findings of Scientific Misconduct for two faculty in the study sample (one application in the Sultan case and two applications in the Yao case) language specifying "funded grant application" or "research funded by" communicated that a grant award was made. In two other cases (Padgett and Poehlman) conversations with NIH FOIA contacts confirmed that the grant application was withdrawn. However, the author was unable to secure grant dollars for the five grant applications funded and withdrawn. Verifying statistics on the withdrawn status is protected under the FOIA process. FOIA states that unfunded new and competing grant applications will "generally be withheld in response to an FOIA request" (NIH Grants Policy Statement, 2003). Thus grant award costs can be underestimated due to these withdrawn grant applications. A final category of grant costs was estimated but not included in the model. There were four funded grants, totaling $5,644,062, identified in findings of research misconduct attributable to a PI not included in the study sample. In other words, the faculty member in the study sample had funded effort on another PI's grant. The author was not able to access information on these specific grants to determine the impact of misconduct on the grant and, therefore, excluded these grant costs from the model.

VEA cost modeling was based on assumptions estimating costs of the administrative penalties assessed to the faculty member in the finding of research misconduct. While each

of the 17 misconduct findings carried with it a set of assessed penalties, only three cases were modeled for this economic cost. As discussed in the Results section, several RIOs reported that non tenured faculty members resigned at a time near to the formal finding. Exact details of timing of resignations and severance packages were protected by privacy disclosure agreements. Even if known, costs for severance packages would most likely be excluded from the cost model developed here because the economic costs modeled are from the perspective of the NIH. Severance packages would, presumably, not be paid with public funds. Estimating costs for remediation for three of 17 investigators guilty of research misconduct is a provocative finding in the study. Several of the RIOs interviewed commented that the fact of proven misconduct marks the end of a faculty member's career. Even though the numbers in the study sample are small, they confirm that being found guilty of misconduct does not always abort a publicly funded researcher's career.

Estimated retraction costs represent a floor to this cost type. In the cost model employed in this study, the author designed the notion of retraction cost as a place holder for future research on the societal cost of research misconduct. The economic costs reflected in the study sample, $31,776, are minimal at less than 1% of total economic costs. However, the issue of retraction is central to maintaining the integrity of the scientific literature (Smith, 2005; Sox & Rennie, 2006). In the Duan case, the two retracted articles were cited by a total of 13 publications. Citation maps (Figures 4 and 5) for each of these retracted articles visualize the web of influence for misconduct in this case. In these 13 publications, authors acknowledged sources of public funding totaling $7,314,689. It would be irresponsible to suggest that the 13 articles and the $7.3 million in publicly funded medical research are

invalid. But it would be equally irresponsible to claim that harm of the Duan misconduct magically disappeared when the case finding was published in the *Federal Register*. Retraction cost, as demonstrating by these selected citation maps, barely begins to measure the impact of a retracted article. While the ORI's effort to improve the efficiency of misconduct investigations by introducing the mandated timeline, the lag between discovery of misconduct and associated article retraction has an economic impact not measured by this model. For instance, the Prasad article mandated for retraction in the 2002 finding of misconduct was published in 1999 and retracted in 2002. A SCOPUS search shows that the article has been cited 4 times, two instances of which are in articles published after the published retraction. Issues regarding the Poehlman retractions have been mentioned

Figure 4. Duan Citation Map for Retracted *PNAS* Article.

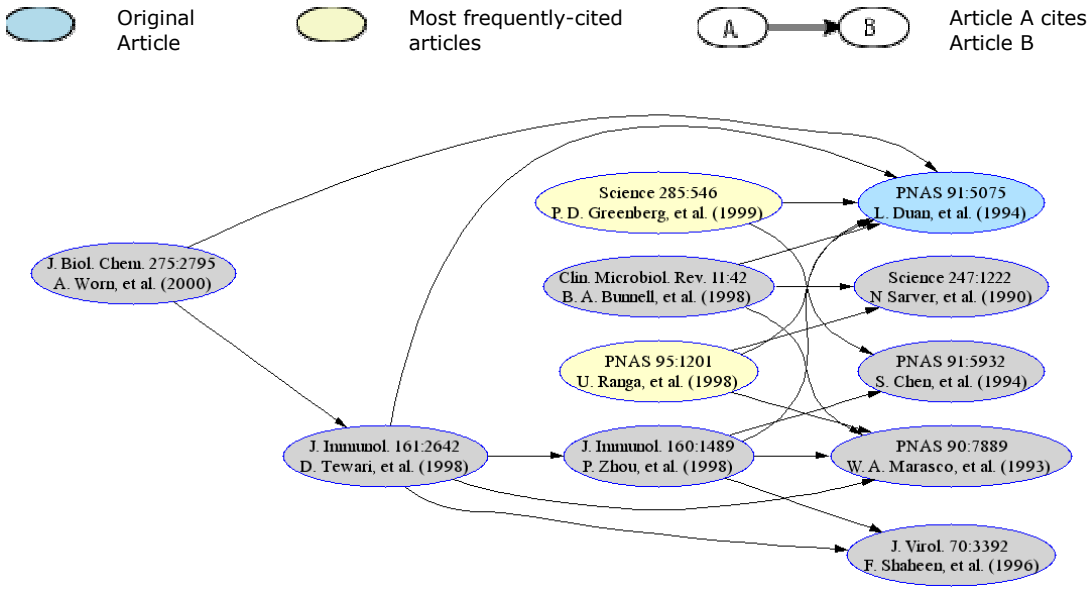
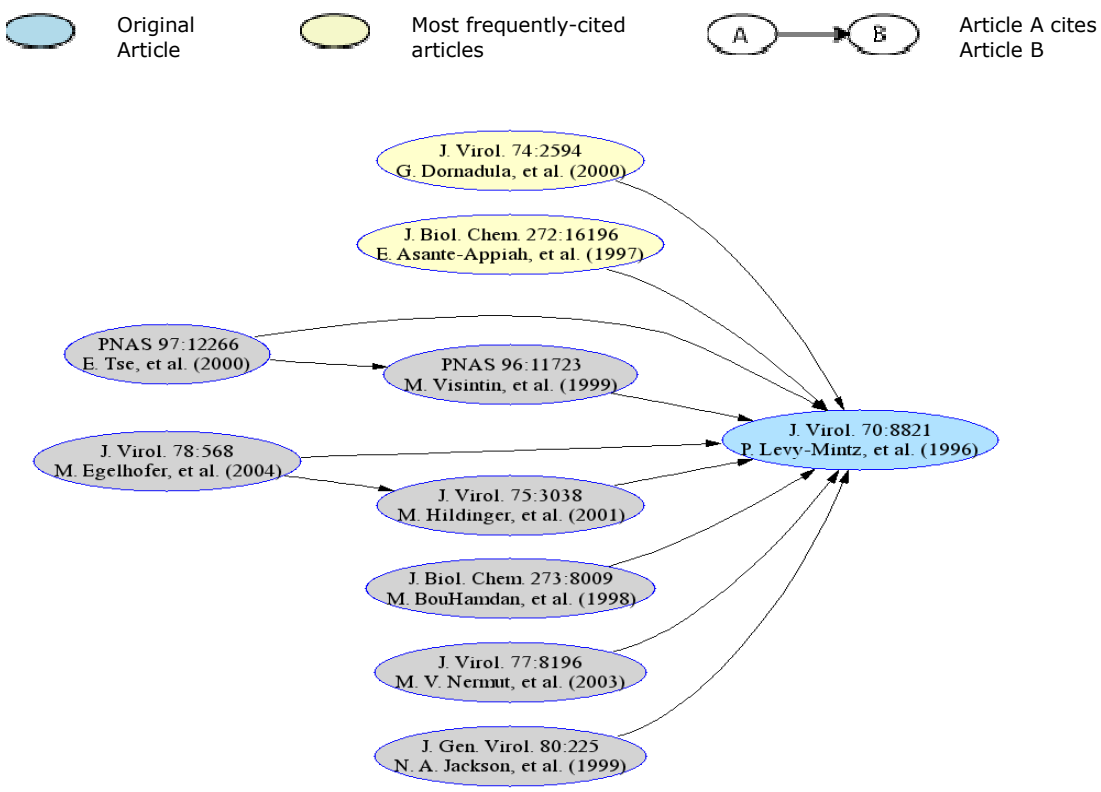


Figure 5. Duan Citation Map for Retracted *J Virol* Article.



previously. Sox & Rennie (2006) suggest that retraction efforts should extend beyond the specific articles cited in a finding of misconduct, "Experience strongly suggests that authors who have committed scientific fraud hardly ever acknowledge every fraudulent article…Treat every article as suspect until proven otherwise." Scrutinizing every article of each of the published articles of faculty in the study sample would substantially increase retraction costs, but would provide added assurance that the scientific literature was thoroughly corrected.

While sample size limitations preclude statistical analysis, variability of economic costs in findings of research misconduct appears straight forward. Predicting cost fluctuation in findings of misconduct relies on the two major components of the economic cost –

investigative cost and grant award(s). Model estimation for investigative cost identified two dependent variables: (1) RIO rank and resulting wage rate and (2) completion of finding within 480 timeline. Repeated misconduct and complexity of grant specific aims for a funded grant both impact completion of the finding within the mandated timeline. These factors expand the scope of the inquiry and investigation potentially increasing the cost for completion with the timeline. If the timeline is exceeded, investigative costs increase. Model estimation for grant award(s) cost depended on the funding status and number of funded grant awards. Cases where an investigator is guilty of repeated misconduct, such as in the Poehlman case, will result in increased economic costs from multiple grant awards. Additionally, timing of the discovery of the misconduct can influence the grant award cost. As reported in the Results section, 57.4% of grant applications cited in findings of research misconduct were either unfunded or withdrawn resulting in no grant award cost for the per case cost. Presumably, the misconduct in these instances was discovered sufficiently early in the pre-award process to avoid economic cost impact. Misconduct discovered during or after grant funded research has begun triggers economic costs. As noted, in the Results section, grant award type is associated with the funding level. Because award type is linked to the investigator's rank, the higher the rank of the investigator, the greater the economic cost of the grant award in the per case cost. Table 16 displays these factors underlying the four cost types defined by the model in this study. Repeated misconduct is the most significant factor impacting economic costs in the study sample. If the investigator is suspected of repeated misconduct, the scope of the inquiry and investigation expands to a broader time period and

to multiple grant applications and funded awards, potentially increasing Investigative Costs, Grant Award(s) and Retraction Cost.

Table 16. Factors Underlying Economic Costs of Research Misconduct.

Investigative Costs	Grant Award	VEA	Retraction Costs
Repeated misconduct	Repeated misconduct	Admisson of Misconduct	Repeated misconduct
Complexity of grant specific aims	Discovery date of misconduct Concurrent with grant application process Pre-award Concurrent with active grant period Post grant project period expiration	Tenure status	
	NIH Award Type Career development awards (K series) Research training/fellowships (T/F series) Research grants (R series) Program project and center grants (P series)		

Approaches to estimating economic costs of publicly funded research misconduct can devolve into a discussion of the nature of science and the definition of truth and, consequently, the value of truth. A research program, whether basic, applied or clinical research, ideally represents an additive progress toward an endpoint discovery. Individual research efforts have multiple aims and represent discrete steps toward "truth". Along the way, replication should serve to exclude poor quality experimental results and reposition research direction toward "truth". Replication failure of the myriad of the discrete steps, according to Wible (1998), is a necessary component of the economics of science. Proving that previously accepted and published research results are reliable through the replication process is a basic tenet of the scientific method and a legitimate economic cost of searching for "truth". But scientific misconduct intentionally introduces deception into the search for "truth". As previously mentioned, for any specific case of research misconduct supported by

public funds (the direct cost grant award) DIO ORI officials I interviewed were reluctant to assess what portion of the public funds could be allocated to the misconduct and what portion would remain as legitimate public funding of research. Rather than a reluctance to admit public funds were squandered, their reticence was due to the complexity of truth finding in science. The economic value of the opportunity costs of research misconduct and the economic costs of grant awards estimated in this study sample represent opportunities lost to fund legitimate science. Assuming an average total award of $300,000 per PI, the $8,592,390 of economic costs of research misconduct would have funded 26 researchers for 1 year.

This study tested whether economic costs of research misconduct were measureable. Results indicate a model can be described and a per case economic cost measure estimated for a case finding of research misconduct. Given that economic costs of research misconduct can be estimated, the next step is to consider why no costs have been measured to date. Qualitative results from this study suggest that investigative costs were frequently considered as administrative overhead funded through indirect cost recovery on grants. This logic implies that costs of rooting out bad actors in publicly funded medical research are built into indirect cost recovery by NIH. Faculty, exclusively tenured full professors, who serve on inquiry and investigation committees were reported by RIOs to participate without hesitation and without regard for the length of time commitment or how time might be assigned in annual Time and Effort reports. If faculty believed their time was supported by NIH indirect cost recovery dollars, it is reasonable to assume they would assign time spent in scientific misconduct findings to “administration” in mandated Time and Effort reporting. However,

RIOs most frequently indicated that they believed faculty assigned time spent to a "service" category. If faculty and RIO time is categorized as funded through indirect cost recovery, estimating cost is irrelevant because indirect cost recovery is capped by NIH at a negotiated rate.

Another viewpoint balances the indirect cost argument with the issue of unfunded mandates. Mandated federal and institutional policies should serve as incentives to encourage institutional oversight of research integrity and quell concerns about wasted public funds. However, 42 CFR Part 50, Subpart A was an unfunded mandate. The Unfunded Mandates Reform Act of 1995 (UMRA), Sections 202 and 205, sets a cap of $100 million or more annual expenditure in one year by the States for enforcement costs. But the implications of UMRA have not been tested as cost data have not been collected and most scientists agree that scientific misconduct is underreported. This poses an exquisite contradiction to the expert culture of the research medical community. On the one hand, researchers are motivated to preserve public trust in their activities to insure continued public funding of their research agenda. A low incidence rate and unestimated economic cost creates a false sense of trust. However, faculty time committed to investigating scientific misconduct is motivated by self-interest (job security, professional advancement, and continued public funding). One hypothesis from this thread is that institutions might be able to recover costs of investigation from the federal government if ORI predicted levels of research misconduct were actually reported and associated costs measured. First, assume that extrapolated incidence findings from Titus et al. (2008) resulted in investigations ending in research misconduct. An incidence rate of 3% for 155,000 PIs and other research

personnel funded by NIH in 2007 would yield 4,650 findings. Applying the $133,431 average per case economic cost for investigative cost of estimated findings for 2007 ($133,431 x 4,650) to those case findings yields an estimated annual cost of approximately $625.4 million and would exceed the $100 million unfunded mandate threshold triggering federal funding to safeguard scientific integrity. If this seems too provocative an estimate, assuming a fifty percent reduction in both the incidence and economic cost (2,325 findings x $66,716 investigative cost/case finding) predicts an estimated annual cost of $155 million, still exceeding the unfunded mandate cap.

What has emerged as a result of this research is that a jumble of misaligned incentives is to blame for the failure of the scientific community to assess the economic costs of research misconduct. Investigations are done "in house", albeit with reviews by ORI, and detection costs, estimated as investigative costs in the model, are borne by the institution. These facts might constitute a negative incentive for robust, thorough investigations. The RIO function is assigned to a senior research administrator also responsible for broad research administration duties such as IRB, Animal Welfare, and sponsored projects administration. The beleaguered RIO must interdigitate misconduct investigations with an already full work agenda. Interviews with RIOs disclosed that misspent grant funds are not recovered. Only one instance of the 17 cases examined, the Duan case, resulted in a return of grant funds required by the research institution. Further, interview results revealed one occurrence where, after the case investigator was terminated as a result of the misconduct finding, the institution was allowed to retain the grant award and assign it to another investigator. Institutions have little risk of reduced grant funds or financial penalty.

Regulation of research misconduct has a goal of reducing and, ideally, eliminating scientific fraud in publicly funded medical research. Criminal deterrence theory and situational crime prevention literature posit four strategies effective in crime deterrence: increasing the difficulty of committing a crime, increasing the risk of committing a crime, decreasing rewards, and increasing the guilt of committing a crime (Siegel, 2006). Given that a majority of misconduct appears to have been detected between grant application and grant award (57.4%), additional efforts in the study section review directed at discovery of research misconduct might increase the likelihood of detecting scientific fraud. The creation of the ORI seems to have made modest, if any, progress in reducing incidence of research misconduct. While all institutions receiving federal funds are required to have a RIO and to provide responsible conduct of research training to investigators and staff, rates of findings of research misconduct have not changed significant since ORI inception. And examining the proportion of faculty to non-faculty research misconduct findings might suggest that detection of misconduct in faculty lags behind detection in non-faculty. This study has revealed that little substantial risk exists for the investigator or his/her institution when misconduct is discovered. Not all faculty found guilty of misconduct are terminated. Only one investigator, Poehlman, in the sample was incarcerated and this was the only investigator debarred for life from receiving public funding for medical research. Otherwise, penalties prohibiting investigators from receiving public funds support for medical research ranged from 3 to 10 years, with a 3 year penalty being the most frequently assessed. Only Thomas Jefferson Medical School was required to return grant funds, and that amount represented less than half of the funded grant cited in the misconduct finding. Physicians who left

university employ were found to be in a private practice setting – ironically a situation which predicts a higher income post misconduct finding than salary in a university setting. The NIH Guide: FINDINGS OF MISCONDUCT banner which appears with an internet search on the study sample investigator names clearly functions as a "guilt" deterrent. Certain punishment can also act as a deterrent. But survey results from Martinson (2005) and, more recently, Titus (2008) on incidence of observed misconduct overwhelms the annual findings of misconduct reported by ORI. From 2000-2005, the 2001 ORI Annual Report reflected the greatest number of faculty guilty of research misconduct. Comparing the 6 faculty findings in 2001cases to the more than 4,000 annual cases predicted by Titus for 2002-2005 confirms that research misconduct is under reported.

Estimating the economic costs of research misconduct is a missing crucial component of public policy debate on research integrity. It is an additional missing element of regulatory reform which produced misaligned incentives and lax deterrence in minimizing loss of public funds to scientific fraud. Effects of the 1980 Bayh-Dole Act on research incentives have already prompted questions of the negative impact on scientific communication and data sharing on the traditional scientific method (Cohen & Siegel, 2008). The stage is set for an expanding arena of publicly funded medical research and increased competition for resources with the move toward state funding of medical research. Two states have led the way -Texas with Proposition 15 ($3 billion over ten years in support of cancer research) and California with Proposition 71 ($300 million over ten years in support of stem cell research). And it is not clear how these state initiatives intend to address issues

of research misconduct. The scrutiny of research misconduct and public policy deliberations begun in the 1990's have failed to aggressively curtail research misconduct.

LIMITATIONS AND DIRECTIONS FOR FUTURE RESEARCH

This study uses case studies to estimate the burden of research misconduct by faculty members in publicly funded medical research. It employs a sequential mixed methods design to develop a descriptive model of the economic costs of research misconduct. In the absence of empirical data on the costs of research misconduct, the descriptive approach seems reasonable. However, in the absence of record keeping of the true economic costs, constructing the cost of seventeen case findings of research misconduct over the period 2000-2005 requires estimates, reliance on averages, and use of proxy costs. The gap between actual and estimated economic costs is an obvious limitation, although the author sought to mitigate the impact by taking a conservation approach to estimations.

The sequential mixed methods approach appears to be an appropriate design given the paucity of empirical data on economic costs in research misconduct. In planning the sequential approach, the research plan assumed the use qualitative results, collection of historical economic cost by case from the RIO, as the foundation for the quantitative phase, model input and cost calculation (Tashakkori & Teddlie, 1998; Tashakkori & Teddlie, 2002). As the qualitative phase developed, it was obvious that little historical cost data could be collected for model input. The RIO interviews, however, did define additional activities for estimation within Investigative, VEA and Retraction Costs type. Given the lack of historical cost records, the author then revised the research plan to estimate economic costs. The advantage of complementarity that can be gained using a mixed methods approach was not fully realized since little economic cost data is recorded either at the federal level or individual research institution level.

FOIA delays presented a consistent challenge in data gathering. In the absence of detailed objective descriptions of individual cases, inputs for inquiry and investigation phases were assumed to be identical for each case unless RIO interviews provided alternative information.

Overall, the model sought to provide a conservative estimate of economic costs, but a variety of costs related to research misconduct were not quantified in this study. Model estimated costs were from the perspective of NIH and the funded institution. Model grant costs were restricted to funded grants awarded to PIs in the study sample. Grant award costs, such as a K08 and F32 award, for career development for a person later found guilty of research misconduct could be included in a sensitivity analysis. No attempt was made to estimate the value of the damaged or ruined career of the faculty member found guilty of research misconduct. Respondent research program closure costs, either during the investigation or in response to investigation outcome, were not estimated. These costs vary by the size of the research program directed by the scientist and the rank of the faculty member, assistant, associate, or full professor. Non faculty research misconduct cases, where respondents are study coordinators or research nurses, have been excluded from the model development.

Lag time opportunity costs, costs incurred because of subsequent funded research and/or clinical care based on unreliable research, were not measured in the study. These costs bridge the lesser economic cost of a research misconduct finding and the substantial societal costs that misconduct in medical research represents Pozzi and David (2007) have estimated “misconduct correction lag”, the time from allegation to ORI finding for

falsification, as a median 3.00 years in all ORI allegations closed with a misconduct finding. While this correction lag includes cases closed before the 1999 imposed 480 day timeline, the underlying issue and impact of correction lag has an unknown multiplier effect on the economic costs of research misconduct. During the correction lag period, the NIH funded national research agenda is infected by fabrication, falsification and plagiarism. One approach to examine lag time opportunity costs is to measure the impact of retracted publications.

As this study estimated economic costs in known cases of research misconduct of public record, findings are admittedly a conservative estimate. One limiting factor is the lack of incidence or prevalence statistics. The economic consequences of detected research misconduct not of public record and undetected research misconduct represent the more concerning burden of misconduct in an era of increased competition for scarce resources. Further, it could be argued that costs for federally mandated Responsible Conduct of Research programs at all institutions receiving PHS funds are a cost of research misconduct, albeit a cost of prevention. Most importantly, this study did not address costs to patients, whether it be in time lost to a cure or actual harm done in a clinical research setting.

As a starting point, future studies on cost aspects of research misconduct might begin with a prospective cost finding study design. The study could test the model developed here for its ability to accurately estimate costs of scientific misconduct among faculty. Once tested, the model could be used to determine per case cost differences between a faculty and non-faculty respondent. Parrish (2004) has noted that the investigative process steps are identical regardless of faculty/non-faculty status. However, it is not known whether inquiry

and investigation panel membership is drawn from tenured full professor ranks for non-faculty. The impact on grant award costs, VEA and retraction cost may vary depending on faculty/non-faculty status. In light of the Texas and California initiatives for state funding of medical research, state laws governing research misconduct could be compared to federal law for regulatory and deterrent aspects. Issues around recovery of grant funding are largely unexplored. The timing of the discovery of research misconduct determines whether grant funds are expended. One RIO disclosed that the institution elected to retain the grant award and assign it to another researcher rather than return the funds to NIH. An empirical study of disincentives to engage in scientific misconduct could be designed based on the theoretical work done by Wible (1998) and Lacetera and Zirulia (2007) in faculty incentives for misconduct. Future directions in examining and measuring costs of research misconduct are virtually uncharted. Empirical questions of cost estimation in research misconduct intersect theoretical literature of traditional economics and cost finding, behavioral economics and incentives, the public policy debate on regulation, and the sociology of medicine and expert culture discussions.

CONCLUSIONS

Implications of research misconduct alarm scientists, policy makers, participants in medical research, and the public. The lack of research on the cost of research misconduct seems paradoxical given the focus on and the investment in the responsible conduct of research programs made by the scientific community. This study has demonstrated that economic costs of research misconduct are measurable. It is the author's conclusion that the absence of misconduct cost estimation is part of a larger problem of misaligned incentives and lax deterrence of research misconduct in publicly funded medical research.

This study represents the first effort to measure the economic cost of research misconduct. It focuses on economic costs of a finding of research misconduct. Societal costs of detected and undetected scientific misconduct remain unmeasured. In a seminal article on Crime and punishment: An economic Approach, Becker (1968) observed, "The more that is spent on policemen, court personnel, and specialized equipment, the easier it is to discover the offenses and convict offenders". The medical research community has taken it upon itself to self-police research misconduct offenses. If Becker is correct, until the medical research community invests more aggressively in misconduct detection, it is possible that it minimizes the discovery of research misconduct. In proposing a model to estimate per case economic cost of a finding of research misconduct, this research points the way toward measuring the societal costs of research misconduct in the hope that such misconduct will be detected and eliminated more aggressively.

APPENDICES

Appendix A Public Health Service Policies on Research Misconduct – 42 CFR Part 50, Subpart A

42 C.F.R. Part 50--Policies of General Applicability

Subpart A--Responsibility of PHS Awardee and Applicant Institutions for Dealing With and Reporting Possible Misconduct in Science

Subpart A--Responsibility of PHS Awardee and Applicant Institutions for Dealing With and Reporting Possible Misconduct in Science

Authority: Sec. 493, Public Health Service Act, as amended, 99 Stat. 874-875 (42 U.S.C. 289b); Sec. 501(f), Public Health Service Act, as amended, 102 Stat. 4213 (42 U.S.C. 290aa(f)).

Source: 54 FR 32449, Aug. 8, 1989, unless otherwise noted.

§ 50.101 Applicability.

This subpart applies to each entity which applies for a research, research-training, or research-related grant or cooperative agreement under the Public Health Service (PHS) Act. It requires each such entity to establish uniform policies and procedures for investigating and reporting instances of alleged or apparent misconduct involving research or research training, applications for support of research or research training, or related research activities that are supported with funds made available under the PHS Act. This subpart does not supersede and is not intended to set up an alternative to established procedures for resolving fiscal improprieties, issues concerning the ethical treatment of human or animal subjects, or criminal matters.

§ 50.102 Definitions.

As used in this subpart:

Act means the Public Health Service Act, as amended, (42 U.S.C. 201, et seq.).

Inquiry means information gathering and initial factfinding to determine whether an allegation or apparent instance of misconduct warrants an investigation.

Institution means the public or private entity or organization (including federal, state, and other agencies) that is applying for financial assistance from the PHS, e.g., grant or cooperative agreements, including continuation awards, whether competing or noncompeting. The organization assumes legal and financial accountability for the awarded funds and for the performance of the supported activities.

Investigation means the formal examination and evaluation of all relevant facts to determine if misconduct has occurred.

Misconduct or Misconduct in Science means fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research. It does not include honest error or honest differences in interpretations or judgments of data.

OSI means the Office of Scientific Integrity, a component of the Office of the Director of the National Institutes for Health (NIH), which oversees the implementation of all PHS policies and procedures related to research misconduct; monitors the individual investigations into alleged or suspected research misconduct conducted by institutions that receive PHS funds for biomedical or behavioral research projects or programs; and conducts investigations as necessary.

OSIR means the Office of Scientific Integrity Review, a component of the Office of the Assistant Secretary for Health, which is responsible for establishing overall PHS policies and procedures for dealing with misconduct in science, overseeing the activities of PHS research agencies to ensure that these policies and procedures are implemented, and reviewing all final reports of investigations to assure that any findings and recommendations are sufficiently documented. The OSIR also makes final recommendations to the Assistant Secretary for Health on whether any sanctions should be imposed and, if so, what they should be in any case where research misconduct has been established.

PHS means the Public Health Service, an operating division of the Department of Health and Human Services (HHS). References to PHS include organizational units within the PHS that have delegated authority to award financial assistance to support scientific activities, e.g., Bureaus, Institutes, Divisions, Centers or Offices.

Secretary means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom the authority involved may be delegated.

§ 50.103 Assurance - Responsibilities of PHS awardee and applicant institutions.

(a) Assurances. Each institution that applies for or receives assistance under the Act for any project or program which involves the conduct of biomedical or behavioral research must have an assurance satisfactory to the Secretary that the applicant:
(1) Has established an administrative process, that meets the requirements of this Subpart, for reviewing, investigating, and reporting allegations of misconduct in science in connection with PHS-sponsored biomedical and behavioral research conducted at the applicant institution or sponsored by the applicant; and

(2) Will comply with its own administrative process and the requirements of this Subpart.

(b) Annual Submission. An applicant or recipient institution shall make an annual submission to the OSI as follows:

(1) The institution's assurance shall be submitted to the OSI, on a form prescribed by the Secretary, as soon as possible after November 8, 1989, but no later than January 1, 1990, and updated annually thereafter on a date specified by OSI. Copies of the form may be requested through the Director, OSI.

(2) An institution shall submit, along with its annual assurance, such aggregate information on allegations, inquiries, and investigations as the Secretary may prescribe.

(c) General Criteria. In general, an applicant institution will be considered to be in compliance with its assurance if it:
(1) Establishes, keeps current, and upon request provides the OSIR, the OSI, and other authorized Departmental officials the policies and procedures required by this subpart.

(2) Informs its scientific and administrative staff of the policies and procedures and the importance of compliance with those policies and procedures.

(3) Takes immediate and appropriate action as soon as misconduct on the part of employees or persons within the organization's control is suspected or alleged.

(4) Informs, in accordance with this subpart, and cooperates with the OSI with regard to each investigation of possible misconduct.

(d) Inquiries, Investigations, and Reporting--Specific Requirements. Each applicant's policies and procedures must provide for:

(1) Inquiring immediately into an allegation or other evidence of possible misconduct. An inquiry must be completed within 60 calendar days of its initiation unless circumstances clearly warrant a longer period. A written report shall be prepared that states what evidence was reviewed, summarizes relevant interviews, and includes the conclusions of the inquiry. The individual(s) against whom the allegation was made shall be given a copy of the report of inquiry. If they comment on that report, their comments may be made part of the record. If the inquiry takes longer than 60 days to complete, the record of the inquiry shall include documentation of the reasons for exceeding the 60-day period.

(2) Protecting, to the maximum extent possible, the privacy of those who in good faith report apparent misconduct.

(3) Affording the affected individual(s) confidential treatment to the maximum extent possible, a prompt and thorough investigation, and an opportunity to comment on allegations and findings of the inquiry and/or the investigation.

(4) Notifying the Director, OSI, in accordance with § 50.104(a) when, on the basis of the initial inquiry, the institution determines that an investigation is warranted, or prior to the decision to initiate an investigation if the conditions listed in § 50.104(b) exist.

(5) Notifying the OSI within 24 hours of obtaining any reasonable indication of possible criminal violations, so that the OSI may then immediately notify the Department's Office of Inspector General.

(6) Maintaining sufficiently detailed documentation of inquiries to permit a later assessment of the reasons for determining that an investigation was not warranted, if necessary. Such records shall be maintained in a secure manner for a period of at least three years after the termination of the inquiry, and shall, upon request, be provided to authorized HHS personnel.

(7) Undertaking an investigation within 30 days of the completion of the inquiry, if findings from that inquiry provide sufficient basis for conducting an investigation. The investigation normally will include examination of all documentation, including but not necessarily limited to relevant research data and proposals, publications, correspondence, and memoranda of telephone calls. Whenever possible, interviews should be conducted of all individuals involved either in making the allegation or against whom the allegation is made, as well as other individuals who might have information regarding key aspects of the allegations; complete summaries of these interviews should be prepared, provided to the interviewed party for comment or revision, and included as part of the investigatory file.

(8) Securing necessary and appropriate expertise to carry out a thorough and authoritative evaluation of the relevant evidence in any inquiry or investigation.

(9) Taking precautions against real or apparent conflicts of interest on the part of those involved in the inquiry or investigation.

(10) Preparing and maintaining the documentation to substantiate the investigation's findings. This documentation is to be made available to the Director, OSI, who will decide whether that Office will either proceed with its own investigation or will act on the institution's findings.

(11) Taking interim administrative actions, as appropriate, to protect Federal funds and insure that the purpose of the Federal financial assistance are carried out.

(12) Keeping the OSI apprised of any developments during the course of the investigation which disclose facts that may affect current or potential Department of Health and Human Services funding for the individual(s) under investigation or that the PHS needs to know to ensure appropriate use of Federal funds and otherwise protect the public interest.

(13) Undertaking diligent efforts, as appropriate, to restore the reputations of persons alleged to have engaged in misconduct when allegations are not confirmed, and also undertaking diligent efforts to protect the positions and reputations of those persons who, in good faith, make allegations.

(14) Imposing appropriate sanctions on individuals when the allegation of misconduct has been substantiated.

(15) Notifying the OSI of the final outcome of the investigation.

§ 50.104 Reporting to the OSI.

(a)

(1) An institution's decision to initiate an investigation must be reported in writing to the Director, OSI, on or before the date the investigation begins. At a minimum, the notification should include the name of the person(s) against whom the allegations have been made, the general nature of the allegation, and the PHS application or grant number(s) involved. Information provided through the notification will be held in confidence to the extent permitted by law, will not be disclosed as part of the peer review and Advisory Committee review processes, but may be used by the Secretary in making decisions about the award or continuation of funding.

(2) An investigation should ordinarily be completed within 120 days of its initiation. This includes conducting the investigation, preparing the report of findings, making that report available for comment by the subjects of the investigation, and submitting the report to the OSI. If they can be identified, the person(s) who raised the allegation should be provided with those portions of the report that address their role and opinions in the investigation.

(3) Institutions are expected to carry their investigations through to completion, and to pursue diligently all significant issues. If an institution plans to terminate an inquiry or investigation for any reason without completing all relevant requirements under 50.103(d), a report of such planned termination, including a description of the reasons for such termination, shall be made to OSI, which will then decide whether further investigation should be undertaken.

(4) The final report submitted to the OSI must describe the policies and procedures under which the investigation was conducted, how and from whom information was obtained relevant to the investigation, the findings, and the basis for the findings, and include the actual text or an accurate summary of the views of any individual(s) found to have engaged in misconduct, as well as a description of any sanctions taken by the institution.

(5) If the institution determines that it will not be able to complete the investigation in 120 days, it must submit to the OSI a written request for an extension and an explanation for the delay that includes an interim report on the progress to date and an estimate for the date of completion of the report and other necessary steps. Any consideration for an extension must balance the need for a thorough and rigorous examination of the facts versus the interests of the subject(s) of the investigation and the PHS in a timely resolution of the matter. If the request is granted, the institution must file periodic progress reports as requested by the OSI. If satisfactory progress is not made in the institution's investigation, the OSI may undertake an investigation of its own.

(6) Upon receipt of the final report of investigation and supporting materials, the OSI will review the information in order to determine whether the investigation has been performed in a timely manner and with sufficient objectivity, thoroughness and competence. The OSI may then request clarification or additional information and, if necessary, perform its own investigation. While primary responsibility for the conduct of investigations and inquiries lies with the institution, the Department reserves the right to perform its own investigation at any time prior to, during, or following an institution's investigation.

(7) In addition to sanctions that the institution may decide to impose, the Department also may impose sanctions of its own upon investigators or institutions based upon authorities it possesses or may possess, if such action seem appropriate.

(b) The institution is responsible for notifying the OSI if it ascertains at any stage of the inquiry or investigation, that any of the following conditions exist:
(1) There is an immediate health hazard involved;

(2) There is an immediate need to protect Federal funds or equipment;

(3) There is an immediate need to protect the interests of the person(s) making the allegations or of the individual(s) who is the subject of the allegations as well as his/her co-investigators and associates, if any;

(4) It is probable that the alleged incident is going to be reported publicly.

(5) There is a reasonable indication of possible criminal violation. In that instance, the institution must inform OSI within 24 hours of obtaining that information. OSI will immediately notify the Office of the Inspector General.

§50.105 Institutional compliance.
Institutions shall foster a research environment that discourages misconduct in all research and that deals forthrightly with possible misconduct associated with research for which PHS funds have been provided or requested. An institution's failure to comply with its assurance and the requirements of this subpart may result in enforcement action against the institution, including loss of funding, and may lead to the OSI's conducting its own investigation

Appendix B Research Misconduct Questionnaire

Research Misconduct Questionnaire

_____	_____
RIO Name	Date
_____	_____
Institution	Case (Last Name)

1. Tell me about your experience handling allegations of research misconduct.

   - How long have you been in this position?

2. Do you believe it is appropriate to ask the question, "how much does research misconduct in publicly funded medical research cost?"

3. Do you or your institution estimate of the costs of investigation research misconduct using the steps defined by ORI? (Receipt of allegation; Preliminary assessment; Conduct of inquiry and investigation; Institutional decision; ORI oversight review; PHS decision; Imposition of PHS administrative actions)

4. What is the most costly element of the process in your opinion?

5. Regarding the specific case (if appropriate):

   a. Duration of investigation from state to finish
   b. Was cost information collected or estimated
   c. Institutional policy for faculty salary support (% external funding)
   d. Salary level of faculty member at time of Voluntary Exclusion Agreement (if appropriate)
   e. Of the steps outlined in #3 above, which were conducted

6. Other

Appendix C: ORI Closed Investigations Resulting in Findings of Research Misconduct, 2000-2005, Descriptive Data

Year	Funding Agency	Rank	MD/PhD	Name	Gender
Faculty in an Academic Setting					
2005	AR	Prof	MD	Kammer	M
2005	NIA + various	Prof	PhD	Poehlman	M
2003	NIAID	Prof	MD	Radolf	M
2002	NINDS	Res Professor	PhD	Prasad	M
2003	HL	Assoc P	PhD	Gelband	M
2002	HL	Assoc P	MD/PhD	Yao	M
2000	NIDCD	Assoc P	MD/PhD	Dreyer	M
2000	NEI	Assoc P	PhD	Hartzer	M
2002	NIDDK	Assoc P	MD	Ganz	M
2001	GM	Asst Prof	PhD	Xiong	M
2001	NIA	Asst Prof	PhD	Padget	M
2001	MH	Asst Prof	PhD	Ruggiero	F
2001	NHLBI	Asst Prof	PhD	Pandurangi	M
2004	NIAID	Asst Prof	MD/PhD	Sultan	M
2000	NIAID	Asst Prof	MD	Duan	M
2001	NIDDK	Asst Prof	PhD	Arnold	M
2001	NINDS	Inst	MD/PhD	Jacoby	M

Year	Funding Agency	Rank	MD/PhD	Name	Gender
Physicians in a Hospital Setting					
2005	NCI	Staff Physician	MD	Geisler	M
Non Faculty					
2001	AI	Counselor	-	Valentin	F
2002	AI	Post Doc	PhD	Tracy	M
2002	AI	Study Coor	-	deSales	M
2001	CDC	Res Asst	-	Elster	M
2001	CDC	Res Asst	-	Sanchez	M
2005	DE	Post Doc	MD/PhD	Li	M
2003	DE	Res Sci	PhD	Karunakaran	M
2002	DK	Grad Stu	-	Pennington	M
2002	DK	Res Fellow	MS	Munjee	F
2002	GM	Grad Stu	BS	Morrow	M
2003	GM	Lab Tech	-	Eagan	M
2003	GM	Post Doc	PhD	Koltover	M
2005	GM	Post Doc	-	Lilly	M
2004	GM	Post Doc	PhD	Hoffman	M
2003	GM	Post Doc	PhD	Smith	M
2004	MH	Ast Res Sci	-	Palmer	F
2004	NCI	Clin Res Assoc	RN	Hanneken	F
2005	NCI	Fellow	MD	Highshaw	M
2000	NCI	Post Doc	PhD	French	M
2002	NCI	Visiting Fellow	PhD	Arichi	M
2002	NHBL/NIH	Visiting Fellow	MD/PhD	Handa	M
2003	NHLBI	Grad Stu	Lin	Lin	M

Year	Funding Agency	Rank	MD/PhD	Name	Gender
2001	NHLBI	Grad Stu	DVM	Lin	M
2001	NHLBI	Res Tech	-	Smith	M
2003	NHLBI	Tech	MS	Xu	M
2004	NIAID	Post Doc	PhD	Ramalingam	M
2004	NICHD	Post Doc	PhD	Horvat	F
2001	NIDDK	Res Fellow	MS	Munjee	F
2001	NIH	Post Doc	PhD	Saleh	M
2002	NIH T32	Post Doc	PhD	Muenchen	F
2001	NIH-FIC	Post Doc	MBBS	Sarker	F
2003	NIMH	Interviewer	-	Blackwell	F
2003	NIMH	Interviewer	-	Creek	F
2003	NIMH	Interviewer	-	Woodard	F
2000	NINDS	Doc Stu	-	Garey	F
2004	NINDS	Grad Stu	-	Rudick	M
2000	NINDS	Exec Mgr	-	Qian	M
2005	NINDS	Proj Coor	-	Grol	F
2005	RIA	Res Tech	-	Luce	M
2002	RR	Lab Tech	MD	Shishov	M
2004	SAMHSA	Interviewer	PhD	Strout	F
2002	SBIR	Res Coor	-	Lipski	M
2000	Various/NCI	Doc	PhD	Simmons	M
2003	Various/NCI	Post Doc	PhD	Rooney	M

Appendix D: Summaries of Closed Investigations resulting in Findings of Scientific Misconduct or Administrative Actions for Faculty at the Instructor Rank and Above, 2000-2005

PROFESSOR RANK

2005 Gary M. Kammer, M.D., Wake Forest University: Based on the Wake Forest University (WFU) Investigation Report, the respondent's admission, and additional analysis conducted by ORI in its oversight review, the U.S. Public Health Service (PHS) found that Gary M. Kammer, M.D., former Professor, Division of Rheumatology, Department of Internal Medicine, and Department of Microbiology and Immunology at the WFU School of Medicine, engaged in scientific misconduct by falsification and fabrication of research in grant application 2 R01 AR39501- 12A1, "T Lymphocyte Dysfunction in Lupus Erythematosus," submitted to the National Institute of Arthritis and Musculoskeletal Skin Diseases (NIAMS), National Institutes of Health (NIH), and in 1 R01 AI46526-01A2, "Protein Kinase A-II in the Pathogenesis of Lupus," submitted to the National Institute of Allergy and Infectious Diseases (NIAID), NIH. Specifically, PHS found that:

- the respondent fabricated Families 2 and 3 in Figure 6 and related text in application 2 R01 AR39501-12A1 (pp. 29-30), entitled "T Lymphocyte Dysfunction in Lupus Erythematosus") by:

  a. making up both of the pedigrees,
  b. fabricating 13 PKA-I and 13 PKA-II values for these non-existent affected and unaffected family members, and
  c. composing the false text describing these two fabricated families.

- the respondent falsified the text describing the results in Figure 20 ("Inhibition of c-fos luciferase activity in S49 T cells transiently transfected with pIRES2-RIIb-EGFP and treated with 8-Cl-cAMP") in application 1R01 AI46526-01A2 (p. 27), by falsely reporting N = 4, P less than 0.002, when the experiment had been performed only one time at the time that the application was submitted.

PHS also concluded that the respondent further demonstrated a lack of present responsibility as a Principal Investigator by submitting NIH grant proposals with additional unsupported experimental results:

- The pedigree and data for the family reported in grant application 2 R01 AR39501-12 and for Family 1 in grant application 2 R01 AR39501-12A1 are incorrect, and the data pertaining to this family that Dr. Kammer subsequently provided to WFU after the inquiry were not the data reported in the applications. Dr. Kammer stated that he did not recall who in his laboratory gave him this pedigree. ORI noted that the actual PKA data for the "proof-of-principle" family, while suggesting that low PKA values may be hereditary (the presence of low PKA-I values in three generations), do not

support the claims of the fabricated and mixed-up pedigree and data that show that low PKA-I values were associated with Systematic Lupus Erythematosus (SLE) (application 2R01 AR39501-12).

- In application, R01 AI39501-12A1, the following unsupported statement was also included: “In both normal and disease controls, all T cells express CD59+ and there is no significant difference in its cell surface expression on CD4+,CD45RA+, CD4+,CD45RO+, CD8+,CD45RA+, CD8+,CD45RO+ subsets (n=4 each control group; data not shown).” No data could be produced to support the information in the grant application about these control experiments.

Dr. Kammer has entered into a Voluntary Exclusion Agreement (Agreement) in which he has voluntarily agreed for a period of three (3) years, beginning on February 15, 2005: (1) to exclude himself from serving in any advisory capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant; and (2) to exclude himself from any contracting or subcontracting with any agency of the U.S. government and from eligibility or involvement in non-procurement programs of the U.S. government referred to as “covered transactions” as defined in the debarment regulations at 45 C.F.R. Part 76. This voluntary exclusion precludes the respondent from receiving federal research, research training, or other research-related funds from the federal government for three (3) years, but shall not apply to the respondent’s participation in a federal health care program as defined in section 1128B(f) of the Social Security Act and shall not apply to federal funds used solely for purposes of teaching or training medical students, residents, or fellows in clinical medical matters

2005 Eric T. Poehlman, Ph.D., University of Vermont: Based on the report of an investigation conducted by the University of Vermont (Report), admissions made by the respondent, and additional analysis conducted by ORI in its oversight review, the U.S. Public Health Service (PHS) found that Eric T. Poehlman, Ph.D., former Professor, Department of Medicine at the University of Vermont College of Medicine, engaged in scientific misconduct in research. The research was supported by National Institutes of Health (NIH) grants from the National Institute of Aging (NIA), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and the National Center for Research Resources (NCRR). Specifically, PHS found that the respondent is responsible for scientific misconduct by engaging in the misleading and deceptive practices set forth herein below. The report is available on the ORI web site under Case Summaries.

Group 1: Longitudinal study of aging; Protocol 678 and associated Excel Spreadsheets

Proposing Research (Report, pp. 22-25)

1. That the respondent falsified preliminary data purportedly obtained in a longitudinal study of aging in NIH grant application 1 R01 AG17906-01, submitted May 27, 1999; specifically, the claim of 130 subjects at visit one (T1) and 70 subjects at visit two (T2), mean values for total energy expenditure (TEE) obtained with a doubly-labeled water technique were falsified; additional parameters such as physical activity energy expenditure (PAEE), resting metabolic rate (RMR), fat-free mass, appendicular skeletal muscle mass, and percent body fat were falsified to show significant trends during the aging process that were not reflective of the actual data (Abstract and pp. 19, 21, 22, 23, 27, 29, 34, 41, 42).

2. That the respondent falsified preliminary data purportedly obtained in a longitudinal study of aging in NIH grant application 1 R01 AG17906-01A1, submitted February 2000, specifically, the claim of 130 subjects at visit one (T1) and 70 subjects at visit two (T2), mean values for total energy expenditure (TEE) obtained with a doubly-labeled water technique were falsified; additional parameters such as physical activity energy expenditure (PAEE), resting metabolic rate (RMR), fat-free mass, appendicular skeletal muscle mass, and percent body fat were falsified to show significant trends during the aging process that were not reflective of the actual data (Abstract and pp. 32, 34, 38, 39, 45, 46).

Conducting Research

3. That the respondent systematically falsified a number of metabolic and physical measures of subjects in the longitudinal study of aging; these falsifications of specific types of data in the Protocol 678 spreadsheet commenced immediately after he assigned responsibility for maintenance of the data to a young technician and simultaneously arranged to have personal access to the data; his widespread alteration of data in specific fields has been detected in a number of different versions, often

with cumulative effect, and several were transmitted to different co-workers for specific reasons, as detailed in the following sub issues:

a. That in the spreadsheet labeled "678data3.xls," produced during the late spring/early summer of 2000, the respondent falsified and fabricated numerous values in the fields called underwater fat mass (UWFM), underwater fat-free mass (UWFFM), leisure time activity (LTA), and maximum oxygen consumption (VO2 Max);

b. That on July 16, 2000, the respondent transmitted a subset of the Protocol 678 spreadsheet to a witness (TB) entitled "RevisedTEE_ s.xls," which had 135 values each for T1 and T2 for TEE; many values were fabricated and most of the remaining values had been falsified by reversing the original T1 and T2 values (Report, pp. 6-8);

c. That the respondent falsified additional data fields in the version of the 678 data set called "ExcelLongitudinal2.xls," on or about August 17, 2000; specifically, values for total cholesterol, insulin, resting metabolic rate (RMR), and glucose values of the subjects with names in the second half of the alphabet were falsified (often by reversing T1 and T2) or fabricated (Report, p. 10);

d. That the respondent gave falsified data to another witness (MT) in August 2000 to provide him with data for a presentation to be given in September 2000 to UVM staff (initially postponed until February 2001); the spreadsheet given to MT contained the falsified and fabricated TEE and underwater body composition values of RevisedTEE_s.xls; the spreadsheet, when subsequently obtained by ORI, was labeled "LongitudinalBodyCompMT.xls";

e. That the respondent falsified additional data in another version of ExcelLongitudinal2.xls" that he sent to another witness (AT) on or about August 22, 2000; specifically, this version contained the falsifications already described above (Issues 3a through 3c) and, in addition, the remainder of the glucose values, and individual lipid components (triglycerides, HDL, and LDL) were extensively falsified and fabricated; this spreadsheet was transmitted to AT with the expectation that he would write a paper describing the effect of aging on lipid metabolism (Report, pp. 8-10);

f. That the respondent provided a falsified version of the Protocol 678 spreadsheet to a witness (ER) in the fall of 2000 so that ER could write a review article;

g. That the respondent, in late September/early October 2000, extensively

falsified body composition data (a number of parameters including, but not limited to, fat mass and fat-free mass) obtained with the DEXA method in a spreadsheet transmitted to a witness (CG) so that CG could write a paper using the DEXA method to demonstrate body composition changes with age (Report, pp. 5 and 39);

Reporting Research

h. That the respondent reported falsified data from the longitudinal study of aging at the annual North American Association for the Study of Obesity (NAASO) meeting in October 2000, and to the Vermont community; the falsifications on his slides included falsified values for both the number of subjects tested at T1 and T2 for TEE and the claim of a significant difference between the means for TEE at T1 versus T2; values for RMR, PAEE, and body composition (fat mass and fat-free mass) were also falsely reported (Report, p. 34);

i. From the falsified data set that the respondent provided him, ER developed a review article: Rawson, E., and Poehlman, E.T. "Resting metabolic rate and aging." *Recent Research Developments in Nutrition* 4, 2001, coauthored by the respondent, which included falsified yet unpublished results about the decline in RMR upon aging (p. R1792). These results, ORI determined, are very similar to the falsified results that the respondent presented at NAASO, based on the falsified Protocol 678 data set;

Conducting Research

j. That on October 16, 2000, the respondent provided a witness (WD) a version of the Protocol 678 data set entitled "ExcelLongitudinal4 xls" that included falsified cholesterol and individual lipid component data (as well as falsified parameters such as insulin, glucose [all subjects], TEE, RMR, PAEE, and underwater body composition data) so that WD could write a paper on the effect of aging on lipid composition (Report, pp. 8-10); and

Other

k. That the respondent falsely testified to the University of Vermont Investigation Committee that he had never used data from the longitudinal study of aging in grant applications or in public presentations (Report, pp. 34 and 36).

Group 2: Muscle biopsy results

Proposing Research

4. That the respondent reported fabricated muscle biopsy data in NIH grant application 1 R01 AG17906-01A1 (p. 27), submitted in February 2000; specifically, he falsely claimed to have successfully tested five individuals on two occasions (1994 and 1999) when he had not (Report, pp. 25-26).

Group 3: Protocol 467, including the "longitudinal menopause study" and other falsifications/fabrications

Reporting Research

5. That the respondent published falsified thyroid hormone results for women entered in a cross-sectional study (Protocol 467) (Figures 3A and 3B and related text and the portion of Table 2 related to T3 and free T3) in the following paper: Poehlman, E.T., Goran, M.I. Gardner, A.W., Ades, P.A., Arciero, P.J., Katzman-Rooks, S.M., Montgomery, S.M., Toth, M.J., and Sutherland, P.T. "Determinants of decline in resting metabolic rate in aging females." *American Journal of Physiology 264(Endocrinol Metab*. 27):E450-E455, March 1993 (correction required).

6. That the respondent published in November 1995 falsified and fabricated data from a longitudinal study of menopause in women in the following paper: Poehlman, E.T., Toth, M.J., and Gardner, A.W. "Changes in energy balance and body composition at menopause: A controlled longitudinal study." *Annals of Internal Medicine* 123(9):673-675, November 1, 1995; the respondent has admitted that this longitudinal study was never conducted (the number of women seen at T1 was falsified, and there were at most 3, rather than 35, women seen at T2) (Report, pp. 27-32) (retracted by the editor; letter from the respondent required).

Proposing Research

7. That the respondent repeatedly reported this non-existent longitudinal menopause study and cited the 1995 *Annals of Internal Medicine* paper in NIH grant applications as proof that the respondent could conduct such longitudinal studies, and the falsified and fabricated data supported his proposed hypotheses:

    a. The respondent provided for the annual report for the University of Vermont General Clinical Research Center (GCRC) grant (M01 RR00109) for the period December 1, 1994-November 30, 1995, information about the falsified longitudinal menopause study, and the *Annals of Internal Medicine* paper was cited as having used the

University of Vermont GCRC facilities;

b. In application 5 K04 AG00564-05, submitted July 18, 1995, the respondent reported the results of a seven (7) year1 followup study of pre- and post-menopausal women, noting an article was in press in the *Annals of Internal Medicine* 1995 (unnumbered p. 3);

c. In application R01 AG13978-01, submitted in September 1995, the respondent reported falsified and fabricated data on menopause-related changes in metabolism, body composition, and other variables in Preliminary Data (pp. 35, 41, and 42), and cited the published *Annals of Internal Medicine* 1995 paper;

d. In application R01 AG13978-01A1, submitted in July 1996, the respondent reported falsified and fabricated data on menopause-related changes in metabolism, body composition, and other variables in Preliminary Data (p. 33), and cited the published 1995 paper in the *Annals of Internal Medicine* and a submitted manuscript on the same topic (pp. 25, 29, 33, 40, 44, and 49);

e. In Project 1 of application P01 AG16782-01, submitted in June 1998, the respondent reported (p. 233) fabricated data showing that menopause led to significant changes in body composition (pp. 229 233, 246, and 256) (Report, p. 32);

f. In application 1 R01 AG 18238-01, submitted in April 1999, the respondent reported falsified and fabricated data from his longitudinal menopause study (RMR, leisure time physical activity, fat-free mass, fat mass, waist-to-hip ratio, and insulin, pp. 9, 18-20, 22, 23, 33, 37, and 44);

g. In application 1 R01 AG17906-01, submitted in May 1999, the respondent reported falsified and fabricated data in the description of his longitudinal menopause study (RMR, leisure time physical activity, and fat-free mass, p. 25);

h. In Project 1 of application P01 AG16782-01A1, submitted in January 2000, the respondent reported the falsified and fabricated longitudinal menopause study (pp. 214, 220, 221, 228, and 250) (Report, p. 32);
i. In application 1 R01 AG17906-01A1, submitted in February 2000, the respondent reported the falsified and fabricated longitudinal menopause study (pp. 31 and 59); and

j. In application 1 R01 AG19800-01, submitted in September 2000, the

respondent reported the falsified and fabricated longitudinal menopause study (pp. 18 and 43).

Reporting Research

8. That the respondent continued to publish papers on the fictitious longitudinal menopause study, referring to the same cohort of 35 women, 18 of whom purportedly went through the menopause transition during the 6-year followup period; all or parts of the following additional papers2 reported this non-existent study and require correction or retraction:

   a. Poehlman, E.T., Toth, M.J., Ades, P.A., and Rosen, C.J. "Menopause associated changes in plasma lipids, insulin-like growth factor I and blood pressure: A longitudinal study." *European Journal of Clinical Investigation* 27(4):322-326, April 1997 (Report, p. 30) (retraction required);

   b. Tchernof, A., and Poehlman, E.T. "Effects of the menopause transition on body fatness and body fat distribution." *Obesity Research* 6(3): 246-254, May 1998 (pp. 249-251) (correction required);

   c. Tchernof, A., Poehlman, E.T., and Despres, J.P. "Body fat distribution, the menopause transition, and hormone replacement therapy." *Diabetes and Metabolism* 26(1):12-20, February 2000 (Report, p. 31) (p. 17 correction required);

   d. Rawson, E., and Poehlman, E.T. "Resting metabolic rate and aging." *Recent Research Developments in Nutrition* 4, 2001 (correction required);

   e. Poehlman, E.T. "Menopause, energy expenditure, and body composition." *Acta Obstetricia et Gynecologica Scandinavica*. 81(7):603-611, July 2002 (retraction required); and

   f. Poehlman, E.T., and Tchernof, A. "Traversing the menopause: Changes in energy expenditure and body composition." *Coronary Artery Disease* 9(12):799-803, 1998 (correction/retraction required).

9. That the respondent reported falsified and fabricated longitudinal menopause data in a talk presented in October 2000 at the annual NAASO meeting and to the Vermont community; specifically, he reported to NAASO falsified RMR and fat mass data on 40 women followed over 6 years (17 premenopausal, 18 post-menopausal, and 5 peri-menopausal) and RMR, FM, F-FM, PAEE, WHR, and insulin (Vermont Community) (Report, pp. 33-34).

Other

10. That the respondent falsely wrote to the University of Vermont Investigation Committee that the subjects in the longitudinal menopause study had not stayed overnight in the GCRC for the second visit. In fact, no women were seen a second time at the GCRC on an in patient or outpatient basis (Report, p. 29).

Group 4: Protocol 646 - Hormone replacement therapy and visceral fat and weight loss; the genetics of an obesity gene.

Proposing Research

11. That the respondent included Protocol 646 in grant application 2 M01 RR00109-33 (funding for the University of Vermont, GCRC), submitted in February-March 1996, in which he provided falsified and fabricated data on 40 women with and without the variant gene Trp64Arg; falsified parameters included body weight, body mass index, and percent body fat that were falsely claimed to be significantly different between the two groups.

12. That the respondent reported falsified and fabricated preliminary data and results in application 1 R01 AG18238 on HRT and its preferential effect on abdominal fat content:

    a. The respondent, in grant application 1 R01 AG18238-01 (p. 24), submitted in April 1999, presented falsified data in Table 1, on a study of women who had reported to be on, or not on, hormone replacement therapy (HRT); specifically, he claimed that women on HRT had significantly lower intra-abdominal fat than non-users and that there was a significant difference in PAEE between the two groups;

    b. The respondent also falsely claimed to have evaluated the effect of HRT on intra-abdominal fat loss in a double blind placebo controlled study of 27 weeks' duration (Figure 4); the actual study was not unblinded until 2002;

    c. The respondent also falsely claimed (pp. 36-37) to have completed a 6-month pilot study on the effect of exercise weight loss on postmenopausal women administered HRT, compared to women not on HRT.

13. That the respondent, in grant application 1 P01 AG16782-01A1, submitted in January 2000, presented (p. 230) falsified data:

a. On a study of women reported to be on, or not on, HRT; specifically, the number of subjects in Table 4 was 25 for HRT users and 23 for non-users, while seven of eight values for PAEE and intra abdominal fat (3 means and 4 standard deviations) were unchanged from Table 1 of Application 1 R01 AG18328-01, where the number of subjects was 13 for each group;

b. The respondent repeated the false claim in the April 1999 application to have evaluated the effect of HRT on intra-abdominal fat in a double blind placebo controlled study of 27 weeks' duration; the actual study was not unblinded until 2002; the respondent admitted to falsifying the figure in this application relative to the version in the 1 R01 AG18328-01 application; and

c. The respondent falsely claimed (p. 231) to have studied eight post menopausal women on HRT and seven women not on HRT in a 6 month weight loss program, when the average ages, standard deviations, and certain mean values were unchanged from the smaller, and purportedly different, groups described in the April 1999 application (see PHS Issue 12 c. above).

14. That the respondent, in grant application 2 R01 DK052752-05, submitted in June 2000:

a. Falsified the number of subjects carrying or not carrying the Trp64Arg genotype in Tables 4, 5, and 6 (pp. 30-31); specifically in the application, he falsely claimed to have tested 40 in each group; the respondent admitted that the actual number tested varied from 8 13, depending on the group and parameter being measured;

b. The respondent also falsely claimed that the number of women recruited to his funded grant on the menopause transition was 85 (p. 49).

15. That the respondent, in grant application 1 R01 AG19800-01, submitted in September 2000:

a-c. Made the same three false claims with respect to HRT as in application 1 P01 AG16782-01A1 (Findings 13 a-c); in addition, the respondent falsely claimed in Table 5 that the number of subjects with and without HRT participating in the 6-month weight loss program (see PHS Issue 13 c. above) was now 10 in each group rather than the group sizes of 8 and 7 claimed in Table 5 of the 1 P01 AG16782-01A1 application;

many of the means and standard deviations in these two tables match the values obtained in a 6-month weight loss pilot study described on pp. 36-37 of application 1 R01 AG18238-01, where the two groups consisted of 3 and 4 individuals (pp. 13, 15, 17, 20, and 21; Tables 4 and 5; and Figure 6);

d. Falsely claimed (Table 3, p. 19) to have weight-reduced 70 obese women in the genetic study.

Reporting Research

16. That in public presentations or material prepared for these fora, the respondent falsified or fabricated data and results of the effects of HRT and of the effects of the Trp64Arg genotype:

a. That the respondent, at talks given at the annual NAASO meeting in October 2000, and to the Vermont Community (October 17, 2000), presented false information on the effects of HRT on visceral fat loss and glucose disposal when the HRT users and non-users were on a 6 month weight loss program; and

b. That the respondent, in both NAASO and Vermont Community talks, falsely claimed that Trp64Arg carriers have significantly lower rates of glucose disposal than non-carriers.

Other

17. That the respondent falsely testified to the University of Vermont Investigation Committee that the slide shown at NAASO regarding the loss of visceral fat in women on, or not on, HRT during a 6-month weight loss program (Issue 16a) had been labeled "hypothesized." The respondent falsely labeled the NAASO slide "hypothesized" and submitted it to the University of Vermont Investigation Committee with the intention of misleading the committee (Report, pp. 34, 37).

Group 5: Alzheimer's disease

18. That the respondent, in applications 2 R01 AG07857-06 and 7 R01 AG07857-07, submitted June 26, 1992, and March 28, 1994, respectively, falsified certain preliminary data (average ages, height, and fat-free weight values) to show that the Alzheimer's and control patients were more closely matched for age than shown in the original data;

19. That the respondent, in application 5 R01 AG07857-09, submitted May 18, 1995, falsified preliminary data; specifically, compared to data in the

preceding 5 R01 AG07857-08 application, where the number of Alzheimer's and control subjects was 7 and 13, respectively, the number of Alzheimer's and control subjects was doubled to 14 and 26, respectively, while many of the data values and standard deviations remained unchanged; in the latter application, however, the respondent claimed that Alzheimer's patients had significantly lower fat-free mass and significantly higher fat mass than control patients, while no claim of significant differences had been made in the earlier application.

Group 6: Effect of endurance training on metabolism

20. The respondent admitted to falsifying norepinephrine data (a measure of sympathetic nervous system activity) in two papers published in 1992 and 1994 and agreed to retraction of the papers.3 Specifically:

    a. The respondent falsified norepinephrine data in Table 2 and Figure 4 of Poehlman, E.T., Gardner, A.W., and Goran, M.I. "Influence of endurance training on energy intake, norepinephrine kinetics, and metabolic rate in older individuals." *Metabolism* 41(9):941-948, September 1992, in order to strengthen the relationship between endurance training and increased norepinephrine levels and rate of appearance (paper to be retracted);

    b. The respondent falsified norepinephrine data in Table 2 and associated text of Poehlman E.T., Gardner, A.W., Arciero, P.J., Goran, M.I., and Calles-Escandon, J. "Effects of endurance training on total fat oxidation in elderly persons." *Journal of Applied Physiology* 76(6):2281-2287, June 1994, in order to make the claims that norepinephrine concentration and norepinephrine appearance were significantly enhanced following endurance training (paper to be retracted).

Dr. Poehlman has entered into a Voluntary Exclusion Agreement (Agreement) in which he has voluntarily agreed, beginning on March 9, 2005:

(1) to exclude himself permanently from serving in any advisory capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant;

(2) to exclude himself permanently from any contracting or subcontracting with any agency of the U.S. government and from eligibility or involvement in non-procurement programs of the U.S. government referred to as "covered transactions" as defined in the debarment regulations at 45 C.F.R. Part 76; the respondent agrees that he will not petition HHS to reverse or reduce the

scope of the permanent voluntary exclusion or administrative actions that are the subject of this Agreement; and

(3) to execute and deliver letters requesting retraction or correction to the editors of the journals that published the 10 papers named in the Agreement and cited above, and to sign the letters requesting the retraction or correction prepared for his signature by ORI without alteration or modification in any way.

2003 Justin Radolf, M.D., University of Connecticut Health Center: Based on *the* report of an investigation conducted by the University of Connecticut Health Center (UCHC Report), Dr. Radolf's admissions, and additional analysis conducted by ORI in its oversight review, the U.S. Public Health Service (PHS) found that Dr.Radolf, Professor at UCHC's Center of Microbial Pathogenesis, engaged in scientific misconduct in research supported by National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), grant R01 AI29735-11 and incorporated false claims into a grant application entitled "Tick Inhibitors of Hemostatis: Novel Therapeutic Agents and an Anti-Tick Vaccine" to the United States Department of Agriculture (USDA). Dr. Radolf falsified and fabricated preliminary research data to falsely claim that the genes that he proposed to characterize were specifically expressed in the tick salivary gland. Dr. Radolf represented the products of control samples as positive tests for mRNA expression from different genes and presented data as positive for genes that had not been tested. Specifically, PHS finds that Dr. Radolf falsified and fabricated data in January 2000 by altering the labeling of a figure included in a USDA grant application and by falsifying the text in both the USDA application and in an overlapping application to a state-sponsored program. This incident of falsification and fabrication is significant because the data was the first direct evidence that the isolated clones represented genes expressed in the tick salivary gland, and therefore represented proteins that could be targets of vaccine development to protect the hosts from tick-transmitted microbial diseases. The misinformation of the extent of the progress in this project had the potential to mislead grant reviewers and the scientific community about an area of research that could have led to the prevention of Rocky Mountain Spotted Fever and other ticktransmitted diseases. The Respondent submitted the following admission to ORI:

> In January of 2000, I engaged in scientific misconduct involving research supported by the National Institutes of Health. The misconduct occurred during the preparation of grant proposals submitted to the United States Department of Agriculture and Connecticut Innovations, Inc. More specifically, I falsified and fabricated preliminary data by intentionally altering the labeling of an ethidium bromide-stained agarose gel purporting to demonstrate the expression of genes in the salivary glands of feeding *Dermacentor andersoni* ticks. In so doing, I misrepresented the products of control samples as positive tests for the presence of mRNAs derived from unrelated genes, and I fabricated data to show the expression of genes that, in fact, were not tested. The texts of the two proposals also contained inaccurate statements relating to these falsified and fabricated data. By inaccurately portraying the extent of our progress in characterizing salivary gland proteins that might interfere with tick feeding, my actions would have misled the reviewers of the

> proposals into thinking that we were closer to the development of an anti-tick vaccine than we actually were.
>
> Truthfulness in the recording, presentation, and reporting of data–the accuracy and reliability of the research record–is the foundation of all scientific research. By intentionally misrepresenting preliminary findings in the two grant proposals, my actions violated this basic precept, compromised my scientific integrity and placed my 20-year career as a biomedical researcher in jeopardy. My actions also could have compromised the integrity and careers of individuals with whom I work, individuals who place their trust in me and who look to me for scientific leadership. I take full and complete responsibility for this misconduct. I committed this wrongful act without prompting by other individuals and without the consent or knowledge of others. I am deeply remorseful for my behavior and offer my strongest assurance to the Office of Research Integrity that it will never recur.

Dr. Radolf has entered into a Voluntary Exclusion Agreement in which he has voluntarily agreed for a period of five (5) years, beginning on March 10, 2003: (1) to exclude himself from serving in any advisory capacity to PHS including but not limited to service on any PHS advisory committee, board, and/or peer review committee, or as a consultant; (2) that any institution which submits an application for PHS support for a research project on which Dr. Radolf's participation is proposed or which uses Dr. Radolf in any capacity on PHS-supported research, or that submits a report of PHS-funded research in which Dr. Radolf is involved, must concurrently submit a plan for supervision of Dr. Radolf's duties to the funding agency for approval; the supervisory plan must be designed to ensure the scientific integrity of Dr. Radolf's research contribution; a copy of the supervisory plan must also be submitted to ORI by the institution; Dr. Radolf agrees that he will not participate in any PHS-supported research until such a supervision plan is submitted to ORI; and (3) to ensure that any institution employing him submits, in conjunction with each application for PHS funds or report, manuscript, or abstract of PHS-funded research in which Dr. Radolf is involved, a certification that the data provided by Dr. Radolf are based on actual experiments or are otherwise legitimately derived, and that the data, procedures, and methodology are accurately reported in the application or report. Dr. Radolf must ensure that the institution sends the certification to ORI.

2002 M. Renuka Prasad, Ph.D., University of Kentucky School of Medicine (UK): Based on the UK investigation report and additional analysis conducted by ORI in its oversight review, PHS found that Dr. Prasad, a former Research Professor of Surgery, UK, engaged in scientific misconduct by fabricating and falsifying data. The research was supported by the National Institute of Neurological Disorders and Stroke (NINDS), NIH grant R01 NS34264, "Phospholipases in traumatic brain injury." This researchis important to understanding the mechanism of breakdown of the bloodbrain barrier and swelling from edema that occurs after traumatic injury of the brain. Specifically, PHS found that Dr. Prasad: (1) fabricated data to calculate a standard error of the mean for Bcl-2 mRNA intensity values for the sham group: 16 values (4 percentages for each of the 4 brain regions assayed), when only a single sham value of 100 percent was actually available, for the error bars shown in Figures 2 and 3 of a manuscript, "Regional expression of Bcl-2 MRNA and mitochondrial cytochromec release after experimental brain injury in the rat," submitted to *Brain Research,* and included in Figures 11 and 12 of NINDS grant application R01 NS41918-01, "Neurochemical mechanisms in traumatic brain injury;" and (2) knowingly reported falsified data in Figures 1 and 3 and in the text of Dhillon, H.S. & Prasad, M.R. "Kynurenate attenuates the accumulation of diacylglycerol and free fatty acids after experimental brain injury in the rat." *Brain Research* 832:7-12, 1999.

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 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.

ASSOCIATE PROFESSOR RANK

2003 Craig H. Gelband, Ph.D., University of Florida: Based on the reports of two investigations conducted by the University of Florida (UF) (UF Reports) and additional analysis conducted by ORI in its oversight review, the U.S. Public Health Service (PHS) found that Craig H. Gelband, Ph.D., Associate Professor, Department of Physiology, College of Medicine at UF, engaged in scientific misconduct in research. Publications and manuscripts containing the falsified data cited support from National Institutes of Health (NIH) grants, or falsified data was included in NIH grant applications, as follows: R29 HL52189-01A2 (then R01 HL52189-05), R01 HL56921, F32 HD08496, R01/R37 HL49254, F32 HL08531, P01 DK41315, and R01 HL69034-01. Specifically, PHS found that:

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

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

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

C. by falsifying EC50 values in Table 1 in NIH grant application HL52189-05; the EC50 values had been interpolated from the falsified mean and SEM data shown in Figures 5 and 6 in the *Hypertension* 2000 paper #1.

II. Dr. Gelband falsified data in the reporting of research, misrepresenting

current/voltage (I/V) data to be results from totally different experimental models or preparations in six publications (including one manuscript "In-Press") and in NIH grant application HL52189-05, specifically:

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

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

C. as Figure 4A, in Gelband, C.H. "Protein kinase C regulation of renal vascular K*v* and Ca++ channels in hypertension." *Hypertension Online* paper, withdrawn (subsequently referred to as the "*Hypertension Online* paper").

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

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

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

1. Dr. Gelband also falsified data in the proposing of research

by submitting the above data as Figures 3, 14A, 14B, and 15 in NIH grant application HL52189-05.

2002 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 flourescent 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 cytomegalovirusbased 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 myocardiocyte cultures treated with an opiate antagonist (staurosporine).

However, this histogram had been published by Liu, H., McPherson, B.C., & Yao, Z. "Preconditioning Attentuates Apoptosis and Necrosis: Role of Protein Kinase Ç and -̣ 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 ̣1 Receptors, Mitochondrial KATP Channels, and Protein Kinase C during Cardiocyte Apoptosis. *J. Mol. Cell. Cardio.* 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 (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.gal and subjected to ischemia-reperfusion and that panel d represented a tissue section from a rat transfected with Ad.PKC-FL.

Panel c is a horizontally compressed copy of panel b, purported to be a nontransfected 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 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 electophoresis 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, that Dr. Yao falsified the stated size of the fragments in the DNA marker ladder by altering the positionof 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 □M NE and by 15 nM TNF-.

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.

2002 Michael B. Ganz, M.D., Case Western Reserve University (CWRU): Based on the CWRU investigation report and additional ORI analysis, PHS found that Dr. Ganz, Associate Professor of Medicine, CWRU, engaged in scientific misconduct by falsification and fabrication of research in grant application R01 DK058674-01A2, "The role of protein kinase C and shuttling proteins in diabetic kidney disease," submitted to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), NIH. Specifically, PHS found that Dr. Ganz engaged in scientific misconduct by: (1) falsifying Figure 16 in NIH grant application R01 DK058674-01A2 by claiming that photomicrographs of glomeruli were from a streptozotocin model of induced diabetes in rat, while the photomicrographs were actually from tissue of human or other primate origin; (2) falsifying Figure 16 of this NIH grant application by claiming that six photomicrographs all represented glomeruli from different animals, whereas they actually were from only three different glomeruli, with each glomerulus being shown in two images with different orientations and/or magnifications; and (3) falsifying and fabricating documents, purportedly showing the source of the falsified Figure 16 in the NIH grant application, which Dr. Ganz provided to the CWRU inquiry committee. The research was significant because it was designed to develop a therapy to prevent the progressive glomerular hypertrophy and matrix deposition that occur with the renal disease associated with diabetes in animals and humans.

Dr. Ganz entered into a Voluntary Exclusion Agreement in which he voluntarily agreed for 5 years, beginning December 18, 2002: (1) to exclude himself from procurement and non-procurement transactions, including but not limited to contracts, subcontracts, grants and cooperative agreements with the U.S. Government; and (2) to exclude himself from serving in any advisory capacity to PHS.

2000 **Evan B. Dreyer, M.D., Ph.D**., Massachusetts Eye and Ear Infirmary (MEEI) and Harvard Medical School (HMS): Based on the findings and evidence documented in a report, dated November 17, 1997, by a joint inquiry panel and additional information obtained by the Office of Research Integrity (ORI) during its oversight review, the PHS issued its findings on April 14, 2000, that Dr. Dreyer, former HMS Associate Professor of Ophthalmology at MEEI, engaged in scientific misconduct by falsifying or fabricating experimental results. These results were included in National Institute on Deafness and Other Communication Disorders (NIDCD), NIH, grant application K08 DC00131-01A1. Specifically, Dr. Dreyer falsified or fabricated experimental results to support the hypothesis that elevated levels of the amino acid glutamate play a role in Meniere's disease and reported these falsified or fabricated results in six documents:

1. an NIH grant application, K08 DC0013 l-0lA1, "Glutamate toxicity in endolymphatic hydrops," submitted to NIH for a Mentored Clinical Scientist Development Award in July 1996. PHS found that the experimental results for 19 amino acids reported in Table 2 and the text (pp. 58-59) were falsified or fabricated.

2. an abstract, Cliff A. Megerian, M.D., Michael J. McKenna, M.D., Joseph B. Nadol, Jr., M.D., and Evan B. Dreyer, M.D., Ph.D. "Elevated Perilymphatic Glutamate and Type-1 Spiral Ganglion Cell Loss in the Hydropic Ear," submitted on August 1, 1996, for the Triological Society Eastern Division Meeting scheduled for early February 1997. PHS found that the text reports the same falsified or fabricated experimental results for the amino acid glutamate that were reported in the K08 DC00131-OlA1 grant application to support the conclusion that elevated levels of glutamate may play a role in Meniere's disease.

3. a manuscript, Cliff A. Megerian, M.D., Michael J. McKenna, M.D., Joseph B. Nadol, Jr., M..D., Barbara J. Burgess, B.A., David Zurakowski, Ph.D., and Evan B. Dreyer, M.D., Ph.D. "Elevated Perilymphatic Glutamate and Type-1 Spiral Ganglion Cell Loss in the Hydropic Ear." PHS found that Table 1 and the text (pp. 2 and 8) contained the same falsified or fabricated experimental results that were reported in the K08 DC00131-OlA1 grant application.

4. a draft NIH grant application, listing Dr. Dreyer as Principal Investigator, in which Table 2 and the text of the draft NIH grant application contained the same experimental results that the PHS found were falsified or fabricated in K08 DC00131-OlA1. 5. two computer spreadsheets, which contained the same results that the PHS found were falsified or fabricated in the K08 DC00131-OlA1.

6. magneto-optical computer disk, which contained files with 21 fabricated chromatograms of amino acid elution patterns. On January 21, 1997, Dr. Dreyer provided the computer disk to MEEI officials in response to requests for the primary data and laboratory notebooks supporting the amino acid results reported in the documents described above. On April 7 and May 21, 1997, Dr. Dreyer admitted that he fabricated each of the 21 chromatograms.

On May 10, 2000, Dr. Dreyer appealed the proposed PHS findings and administrative actions to the HHS Departmental Appeals Board ("DAB"), DAB Docket No. A-2000-72, "which commenced a *de novo* hearing to consider the charges of scientific misconduct." Although the hearing was scheduled to run 3 weeks, on November 13, 2000, Dr. Dreyer entered into a Voluntary Exclusion Agreement (Agreement) with PHS in which he agreed to withdraw his appeal of the PHS findings of scientific misconduct against him. On November 17, 2000, the DAB dismissed the case.

Under the terms of the Agreement, Dr. Dreyer did not admit that he falsified or fabricated the results at issue, but he recognized that if the DAB case proceeded to conclusion, there was sufficient evidence upon which the DAB may make a finding of scientific misconduct. However, with respect to material identified in item 6 above, Dr. Dreyer admitted that he fabricated the 21 chromatograms contained in the magneto-optical computer disk that he provided to institutional officials after questions were raised about his research. He further admitted that the fabrication of the data on the disk amounts to scientific misconduct.

Dr. Dreyer voluntarily agreed for a period of 10 years beginning November 15, 2000, to exclude himself from: (1) any contracting, subcontracting, or involvement in grants and cooperative agreements with the U.S. Government; (2) serving as a mentor to any graduate student, fellow, or other individual who applies for or receives Federal funding; and (3) serving in any advisory capacity to PHS. The Agreement, however, does not apply to Dr. Dreyer's practice of clinical medicine as a licensed practitioner or to Federal funds used for purposes of teaching or training medical students, residents, or fellows, in clinical medical matters.

2000 **Michael K. Hartzer, Ph.D**., Oakland University (OU): Based on the report of an investigation conducted by OU and additional analysis conducted by ORI during its oversight review, PHS found that Dr. Hartzer, former Associate Professor of Biomedical Sciences, Eye Institute, OU, engaged in scientific misconduct by falsifying the status of support materials in eight National Eye Institute (NEI), NIH, grant applications. Specifically, Dr. Hartzer falsified the status of 11 manuscripts in 8 grant applications by listing them as "accepted" or "in press" when the papers had either not been subsequently published or had been rejected. The repetition of these actions over several years indicates a pattern of knowingly misrepresenting the research record. Dr. Hartzer accepted the PHS finding and entered into a Voluntary Exclusion Agreement with the PHS in which voluntarily agreed for a period of 3 years beginning November 20, 2000: (1) to submit with each PHS research application, continuing application, or report, a statement of certification, endorsed by an institutional official, that all manuscripts or publications are properly and accurately cited in the application; the institution must also submit a copy of the certification to ORI; and (2) to exclude himself from serving in any advisory capacity to PHS.

ASSISTANT PROFESSOR RANK

2004 **Ali Sultan, M.D., Ph.D**., Harvard School of Public Health: On October 19, 2004, the U.S. Public Health Service (PHS) entered into a Voluntary Exclusion Agreement with the President and Fellows of Harvard College (Harvard) and Ali Sultan, M.D., Ph.D., former Assistant Professor of Immunology and Infectious Diseases at the Harvard School of Public Health (HSPH). Based on HSPH's inquiry report, the respondent's admission, and additional analysis conducted by ORI in its oversight review, PHS found that Dr. Sultan engaged in scientific misconduct in research funded by National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), grant 1 P01 AI060332-01, "Chemical genetics and malaria drug development," Subproject 2, "Screening of target-rich environment." Specifically, PHS and Harvard found that: (1) Dr. Ali Sultan plagiarized text, plagiarized three figures showing results of an immunofluorescence assay, a phosphorimage, and Northern blot analysis (Figures 3, 4, and 5, respectively), and falsified the data as results of experiments on *Plasmodium bergheii*, instead of *P. falciparum* as reported in a subproject of the PHS grant application 1 P01 AI060332- 01, "Chemical genetics and malaria drug development;" and (2) Dr. Ali Sultan fabricated portions of an e-mail from his postdoctoral student that he presented to the HSPH inquiry committee purportedly to falsely implicate the student in the submission of the plagiarized materials for the grant application.

The Voluntary Exclusion Agreement states that for a period of three (3) years, beginning on October 19, 2004: (1) Dr. Sultan agreed to exclude himself from any contracting or subcontracting with any agency of the U.S. Government and from eligibility or involvement in nonprocurement programs of the U.S. Government as defined in the debarment regulations at 45 CFR Part 76; and (2) Dr. Sultan agreed to exclude himself from serving in any advisory capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant.

2001 **Momiao Xiong, Ph.D., The University of Texas Health Science Center at Houston (UTHSCH)**: Based on the UTHSCH inquiry report, and any related actions and findings by UTHSCH, as well as additional analysis conducted by ORI in its oversight review, PHS found that Dr. Xiong engaged in scientific misconduct by plagiarizing and fabricating data in National Institute of General Medical Sciences, NIH, grant application R01 GM64353-01, "Genetics of Human Pigmentation and Skin Response" (Pigmentation Application), on which he was a co-investigator. The plagiarized and fabricated data were essential to the scientific validity of the proposed research and were important for NIH's scientific evaluation of the Pigmentation Application. Dr. Xiong admitted his actions. Specifically, PHS and UTHSCH found that Dr. Xiong: (1) plagiarized text from another researcher's grant application, which Dr. Xiong had obtained during the NIH confidential review process and used without appropriate citation in the Pigmentation Application; and (2) falsified research in the Pigmentation Application by (a) falsely claiming that he had performed an extensive series of simulations to evaluate the power to detect genes influencing pigmentation traits by the proposed statistical analysis, and (b) falsely representing estimates from previous work on unrelated individuals as being appropriate for large families in the proposed research.

The Agreement states that beginning November 26, 2001, Dr. Xiong: (1) will not serve as a principal investigator on PHS grants for 1 year; (2) will exclude himself from serving in any advisory capacity to PHS for 3 years; and (3) agrees that for 3 years, he and any institution employing him are required to certify, in every PHS application or report in which Dr. Xiong is involved: (a) that all persons who contribute original sources of ideas, data, or research results to the applications or reports are properly cited or otherwise acknowledged; and (b) that the applications or reports do not contain any falsified, fabricated, or misleading information. This requires Dr. Xiong and the institution, with respect to Dr. Xiong's contributions to the application or report, to certify that all individuals (both within and outside the institution) who contributed to the application or report are acknowledged. The institution must also send a copy of the certification to ORI; and (4) accepts the following UTHSCH administrative actions: (a) Dr. Xiong must send a formal, written apology to the principal and co-investigators explicitly acknowledging his plagiarism from their grant application; (b) for a 1-year period starting October 11, 2001, Dr. Xiong may not: (i) submit, as a principal investigator, any new grant applications, including applications to any Federal, State, or local government agencies, as well as any private foundations or agencies; or (ii) submit any publications without providing certification, co-signed by his immediate supervisor, that any manuscript for publication does not contain any plagiarized information or any falsified, fabricated, or misleading information; (c) for an additional 2 years, Dr. Xiong must similarly certify any grant application or publication; (d) for the next 3 years, to submit any grant application or publication, Dr. Xiong must have a signed statement from his immediate supervisor stating that the supervisor reviewed the materials and finds no indication of plagiarism, falsification or fabrication of data, nor any other form of scientific misconduct; (e) for the next academic year, Dr. Xiong is required to participate in a course in the responsible conduct of research, and in the year after completing the course, serve as a co-instructor in a small discussion group for all breakout sessions of the course; and (f)

within 2 years, Dr. Xiong must write a formal essay, of publication quality, in English and Chinese, on plagiarism for submission to the Executive Vice President for Research, UTHSCH, and for publication.

2001 **David A. Padgett, Ph.D., Ohio State University (OSU)**: Based on the OSU investigation report, Dr. Padgett's admissions, and additional analysis conducted by ORI in its oversight review, PHS found that Dr. Padgett, an Assistant Professor at the OSU College of Dentistry, engaged in scientific misconduct in grant application 1 R01 AG20102-01 submitted to the National Institute of Aging, NIH. Specifically, PHS found that Dr. Padgett plagiarized and misrepresented as his own research data for Figures 1 and 2 of this NIH grant application, data which represented unpublished experiments originally conducted by a researcher at another institution for a private company. The plagiarism was a significant misrepresentation because the data appeared in the preliminary results section of the NIH grant application. Dr. Padgett used these experiments, which were relevant to the proposed research, to support the request for funding.

Dr. Padgett entered into an Agreement in which he voluntarily agreed for 3 years, beginning, October 4, 2001, to exclude himself from serving in any advisory capacity to the PHS, and that any institution that submits an application for PHS support for a research project on which his participation is proposed or that uses him in any capacity on PHS-supported research, must
concurrently submit a plan for supervision of his duties to the funding agency for approval. The supervisory plan must be designed to ensure the scientific integrity of Dr. Padgett's research contribution. The institution must also submit a copy of the supervisory plan to ORI.

2001 **Karen M. Ruggiero, Ph.D., Harvard University (HU)**: Based on the HU report, and related actions and findings by HU, as well as additional analysis conducted by ORI in its oversight review, PHS found that Dr. Ruggiero engaged in scientific misconduct by fabricating data in research supported by the NIH. Specifically, PHS and HU found that: (1) Dr. Ruggiero fabricated three experiments, including data reported as having been obtained from a total of 240 participants, published in the following paper: Ruggiero, K.M. & Marx, D.M. "Less pain and more to gain: Why high-status group members blame their failure on discrimination." *Journal of Personality and Social Psychology*, 77(4):774-784, 1999 (the "*JPSP* paper"). These experiments were also proposed in the "Research Plan" of an application submitted to the National Institute of Mental Health, NIH, by Dr. Ruggiero in September 1997 for grant 1 R03 MH58586-01, which was acknowledged as a source of support in the *JPSP* paper. Dr. Ruggiero admitted that she fabricated the data on the 240 participants in the *JPSP* paper. At her request, a notice of retraction of this paper appeared in the *Journal of Personality and Social Psychology* 81(2):178, 2001. (2) Dr. Ruggiero fabricated two experiments, including data reported as having been obtained from a total of 360 participants, published in the following paper: Ruggiero, K.M., Steele, J., Hwang, A., & Marx, D.M. "Why did I get a 'D'? The effects of social comparisons on women's attributions to discrimination." *Personality and Social Bulletin* 26(10):1271-1283, 2000 (the "*PSPB* paper"). These experiments were also proposed in the "Research Plan" of the application submitted by Dr. Ruggiero in September 1997 for grant 1 R03 MH58586-01, which was acknowledged as a source of support in the *PSPB* paper. Dr. Ruggiero admitted that she fabricated the data on the 360 participants in the *PSPB* paper. At her request, a notice of retraction of this paper appeared in the *Personality and Social Psychology Bulletin* 27(9):1237, 2001. (3) Dr. Ruggiero's admittedly fabricated research from the *JPSP* and *PSPB* papers was cited in and served as the basis for an NIH Individual National Service Award application, F32 MH12868-01 and -01A1, formerly F32 HD41874, "Status effects in perceptions of preferential treatment," submitted in August 2000 by one of Dr. Ruggiero's post-doctoral fellows, with Dr. Ruggiero listed as the sponsor. (4) In connection with a Harvard School of Public Health grant application to NIH, 1 R01 HL065220- 01, "Measuring racial discrimination for health research," Dr. Ruggiero submitted a subcontract in September 2000 citing the admittedly fabricated research from the *JPSP* and *PSPB* papers in support of her qualifications to serve as a subcontractor. (5) In July 1999 and July 2000, Dr. Ruggiero cited and included as "Preliminary Studies" her admittedly fabricated, PHS-supported research from the *JPSP* and *PSPB* papers in applications, "The ironic status effect," that she submitted to the National Science Foundation.

Dr. Ruggiero agreed to exclude herself from any contracting, subcontracting, or involvement in grants and cooperative agreements with the U.S. Government for a period of 5 years beginning November 26, 2001, and to exclude herself from serving in any advisory capacity to PHS. She agreed to submit a letter, with a copy to ORI and HU, to the *Personality and Social Psychology Bulletin* requesting retraction of the following paper: Ruggiero, K.M. & Major, B.N. "Group status and attributions to discrimination: Are low- or high-status group members more likely to blame their failure on discrimination?" *Personality and Social Psychology Bulletin* 24:821-838, 1998. Dr. Ruggiero further agreed that the letter would state

that the retraction is warranted “because serious questions exist concerning the validity of the data which relate solely to my own work and which do not implicate my coauthor in any way.” She submitted a copy to ORI. (4) Dr. Ruggiero agreed to submit a letter, with a copy to ORI and Harvard, to *Psychological Science* requesting a retraction of the following paper: Ruggiero, K.M., Mitchell, J.P., Krieger, N., Marx, D.M., & Lorenzo, M.L. “Now you see it, now you don’t: Explicit versus implicit measures of the personal/group discrimination discrepancy.” *Psychological Science* 22:57-67, 2000. Dr. Ruggiero further agreed that the letter submitted would state that the retraction is warranted “because I improperly excluded some participants who should have been included in the analyses and that this exclusion affected the reported results. Moreover, the improper exclusion of data was solely my doing and was not contributed to or known by my coauthors.” She submitted a copy to ORI.

2001 **Raghoottama S. Pandurangi, Ph.D., University of Missouri—Columbia (UM-C)**: Based on the UM-C investigation report and additional analysis conducted by ORI in its oversight review, PHS found that Dr. Pandurangi, a former Research Assistant Professor at UM-C, engaged in scientific misconduct by plagiarizing and falsifying research data taken from journal article published by other scientists for use in supplementary materials of an NIH research grant application. Specifically, PHS found that Dr. Pandurangi plagiarized the images of data in Figures 2A and 2B and related text in supplemental material he submitted in connection with NHLBI, NIH, grant application 1 R01 HL62517-01A2, "Myocardial Viability by AII Receptor-99mTc Conjugates," in which he was the principal investigator. Specifically, Figures 2A and 2B and related text were plagiarized from Figures 7C and 7D of the following journal publication: Gibson, R., Beauchamp, H., Fioravanti, C., Brenner, N., and Burns, H.D. "Receptor Binding Radiotracers for the Angiotensin II Receptor: Radioiodinated [Sar_1, Ile_8]Angiotensin II." *Nuclear Medicine and Biology* 21:593-600, 1994. In addition, Dr. Pandurangi falsified the text in the supplement to his NIH grant application by claiming that Figures 2A and 2B represented a compound he had developed. Namely, He claimed that Figure 2A represented radioionated compound ^{123}I-2C and Figure 2B represented radioionated compound ^{123}I-2C with nonradioactive compound 2C added as a competitor. However, Figures 2A and 2B were plagiarized from the figures in the above *Nuclear Medicine and Biology* article, which in reality represented radiolabeled [Sar_1, Ile_8]Angiotensin II, with compound L-158,809 as a blocker/competitor. Dr. Pandurangi entered into an Agreement with PHS in which he voluntarily agreed beginning July 17, 2001, to exclude himself from any contracting, subcontracting, or involvement in grants and cooperative agreements with the U.S. Government for 1 year, his participation in any PHS-funded research is subject to supervision requirements for 3 years, to exclude himself from serving in any advisory capacity to PHS for 4 years.

2001 **Steven F. Arnold, Ph.D., Tulane University (TU)**: Based on the TU investigation report dated July 16, 1999, and additional analysis conducted by ORI in its oversight review, the U.S. Public Health Service (PHS) found that Dr. Arnold, former Research Assistant Professor at the Center for Bioenvironmental Research at Tulane University Medical Center, engaged in scientific misconduct. Dr. Arnold committed scientific misconduct by intentionally falsifying the research results reported in Table 3 of a paper published in the journal *Science*[1] and by providing falsified and fabricated materials to investigating officials at Tulane University in response to a request for original data to support the research results and conclusions reported in the *Science* paper. In addition, PHS finds that there is no original data or other corroborating evidence to support the research results and conclusions reported in the *Science* paper as a whole. Specifically, PHS found that Dr. Arnold's research reported in the *Science* paper involved a finding that environmental chemicals, such as certain insecticides and hydroxylated polychlorinated biphenyls (PCBs), which have a weak estrogenic activity when acting alone, were up to 1,000 times more potent in mimicking estrogen when tested in combination. These research results and conclusions were important to the public health because they suggested that the Environmental Protection Agency (EPA) may need to adjust its guidelines on exposure limits to such chemicals. The *Science* paper was withdrawn July 25, 1997. See *Science* 277:462 (July 25, 1997). This research formed the basis of National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), grant application 1 R29 DK52420-01, "Two Estrogen Binding Sites on the Estrogen Receptor."

Dr. Arnold entered into a Voluntary Exclusion Agreement (Agreement) with PHS in which he voluntarily agreed for 5 years beginning September 20, 2001, 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. Dr. Arnold was cooperative with ORI and accepted responsibility for his actions, admitted to scientific misconduct, and conceded that there were no original data or other corroborating evidence to support the conclusions reported in the *Science* paper.

[1] Steven F. Arnold, Diane M. Klotz, Bridgette M. Collins, Peter M. Vonier, Louis J. Guillette, Jr., John A. McLachlan. "Synergistic Activation of Estrogen Receptor with Combinations of Environmental Chemicals." *Science* 272:1489-1492 (June 7, 1996) (hereafter referred to as the "*Science* paper").

2000 **Lingxun Duan, M.D., Thomas Jefferson University (TJU)**: In a case related to a Global Settlement Agreement n a *qui tam* suit between the United States and TJU, and based on an oversight review conducted by the Office of Research Integrity (ORI), the U.S. Public Health Service (PHS) entered into a Voluntary Exclusion Agreement (Agreement) with Dr. Duan, former Research Assistant Professor of Medicine, Division of Infectious Diseases, Department of Medicine, TJU. The PHS alleged that Dr. Duan engaged in scientific misconduct by reporting research that was inconsistent with original data or could not be supported because original data were not retained. Dr. Duan denied all allegations of scientific misconduct and contended that some of his original data is missing. The research in question was supported by a National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), grant, R01 AI36552, entitled "Intracellular antibodies and HIV 1." Specifically, the research in question was reported in an NIAID, NIH, grant application; in an FDA-approved phase I gene therapy investigational new drug (IND) application entitled "Intracellular immunization against HIV-1 infection using an anti-rev single chain variable fragment (SFV);" and in two publications: (1) Duan, L., Bagasra, O., Laughlin, M.A., Oakes, J.W., & Pomerantz, R.J., "Potent inhibition of human immunodeficiency virus type I replication by an intracellular anti- Rev single chain antibody," *Proc. Natl. Acad. Sci*. USA 91:5075-5079, 1994; and (2) Levy-Mintz, P., Duan, L., Zhang, H., Hu, B., Dornadula, G., Zhu, M., Kulkosky, J., Bizub-Bender, D., Skalka, A.M., and Pomerantz, R.J., "Intracellular expression of single-chain variable fragments to inhibit early stages of the viral life cycle by targeting human immunodeficiency virus type 1 integrase," *J. Virol*. 70:8821-8823, 1996.

Under the terms of the Agreement, Dr. Duan voluntarily agreed, beginning June 7, 2000: (1) to exclude himself from any contracting, subcontracting, or involvement in grants and cooperative agreements with the U.S. Government for a period of 2 years; (2) that for 1 year after the conclusion of the voluntary exclusion period, his participation in any PHS-funded research is subject to supervision requirements; and (3) to exclude himself from serving in any advisory capacity to PHS, for a period of 2 years. Dr. Duan also agreed that he will not oppose the submission to journals of a statement summarizing the current state of the science with respect to the scientific matters at issue relating to grant R01 AI36552, which was jointly agreed to by TJU and the United States in the Global Settlement Agreement.

INSTRUCTOR RANK

2001 David R. Jacoby, M.D., Ph.D., Harvard Medical School (HMS) and Massachusetts General Hospital (MGH): Based on the HMS and MGH report and additional analysis conducted by ORI in its oversight review, PHS found that Dr. Jacoby, instructor, Department of Neurology, MGH, engaged in 15 acts of scientific misconduct by plagiarizing and falsifying research data taken from another scientist's different experiment in a published journal article for use in an grant application that was subsequently funded. Specifically, Dr. Jacoby plagiarized an image of a Southern blot analysis of genomic DNA that appeared as Figure 3A in Balagu , C., Kalla, M., & Zhang, W.-W. "Adeno-associated virus rep78 protein and terminal repeats enhance integration of DNA sequences into the cellular genome." *J. Virology* 71:3299-3306, 1997. Dr. Jacoby first falsified the image by adding molecular weight markers and lane labels that misrepresented the image as his own experimental data. He further falsified the image using computer software to intensify a band he claimed was a site-specific integration and to remove identifiable background spots present in the original image. The effect of Dr. Jacoby's falsifications was to misrepresent the image as data from his own experimental analysis of clonal cell lines derived from the infection of a human cell line with a recombinant hybrid virus incorporating two transgenes and adeno-associated virus genes into a herpes simplex virus amplicon. Dr. Jacoby's falsified image was material to his research because it supported his claim that the transgene DNA had integrated into the cell genome at a specific site. These plagiarized results were reported in (1) appendix material supporting an application for a Program Project Grant, Molecular Etiology of Early Onset Torsion Dystonia, 1 P01 NS37409-01A1, submitted by Dr. Jacoby's supervisor; Dr. Jacoby's supervisor relied upon falsified written and oral information provided to her by Dr. Jacoby in her description of his recent research progress; (2) three presentations by Dr. Jacoby's supervisor to colleagues at MGH in May 1998 regarding the status of the research in her laboratory; Dr. Jacoby's supervisor relied upon falsified written and oral information provided to her by Dr. Jacoby in her description of his recent research progress; and (3) a grant application to NIH for continuation of Dr. Jacoby's Clinical Investigator Award grant, 5 K08 NS01887-03. In addition, Dr. Jacoby subsequently altered the falsified image described above further by changing the location of the molecular weight markers to make it appear more consistent with the expected experimental results. Dr. Jacoby then submitted the plagiarized and falsified results to a MGH colleague, who included them in a presentation at the First Annual Meeting of the American Society of Gene Therapy, held in Seattle, Washington, May 30, 1998. During the institutional investigation in 1998, Dr. Jacoby presented another falsified image as data from his own experiment. Specifically, he used computer software to scan Figure 3A in Balagu et al., and then alter the locations of three major bands in an effort to conceal the origin of the falsified image (i.e., Figure 3A) and to deceive investigating officials into believing that the results were from an independent experiment. Dr. Jacoby then used the different band locations as "evidence" of the differences between Figure 3A by Balagu et al. and the data purportedly from his own experiment by presenting the falsified image: (1) to the Chief of MGH's Neurology Service; (2) to a scientist assisting the Inquiry Committee by attempting to reproduce Dr. Jacoby's experiments; and (3) to the Inquiry Committee as data from his own independent experiment.

After the institution concluded that Dr. Jacoby had engaged in scientific misconduct, Dr. Jacoby forged the signature of the institutional official for the MGH Grants and Contracts Office and knowingly included false and material information on his NIH non-competing renewal application for a Clinical Investigator Award, 5 K08 NS01887-05. Specifically, after ceasing to work in his supervisor's laboratory and after being told by his supervisor that she would no longer serve as his mentor on the Clinical Investigator Award, Dr. Jacoby (1) listed his former supervisor as his mentor on his 5 K08 NS 01887-05 application; (2) claimed that he was continuing to conduct grant-funded research in her laboratory; (3) forged the signature of the MGH institutional official to avoid detection by MGH; and the (4) submitted the completed application directly to NIH on or about August 1, 2000. Dr. Jacoby's actions amount to significant and serious falsifications in the proposing and reporting of research. His falsifications gave NIH reviewers inaccurate information for their evaluation of the progress made by the research group at MGH in its PHS-supported research. His falsifications also substantially hindered the progress of the PHS-funded research project. Finally, his falsifications induced NIH to award research funds for Dr. Jacoby's 5 K08 NS01887-05 grant at a time when he was no longer conducting research. Accordingly, PHS further found that Dr. Jacoby engaged in a pattern of dishonest conduct through the commission of 15 acts of data falsification and plagiarism, including additional steps taken to conceal the true nature and origin of the research data, that further demonstrated a lack of present responsibility to be a steward of Federal funds. Dr. Jacoby entered into an Agreement with PHS in which he voluntarily agreed for 5 years beginning June 12, 2001, 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.

Appendix E: Abbreviations for Federal Funding Agencies

CDC	Centers for Disease Control and Prevention
DE	National Institute of Dental and Craniofacial Research
GM	National Institute of General Medical Sciences
MH	National Institute of Mental Health
NCI	National Cancer Institute
NCRR	National Center for Research Resources
NEI	National Eye Institute
NIA	National Institute on Aging
NIAMS	National Institute of Arthritis and Musculoskeletal Skin Diseases
NIAID	National Institute of Allergy and Infectious Diseases
NIDCD	National Institute on Deafness and Other Communication Disorders
NIDDK	National Institute of Diabetes and Digestive and Kidney Disease
NINDS	National Institute of Neurological Disorders and Stroke
NHLBI	National Heart, Lung and Blood Institute

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VITA

Elizabeth Gammon was born in Brenham, Texas, the daughter of Mamie Karcher and D.W. Gammon. She received her Bachelor of Arts in English from Texas A&M University in 1971 and her Master of Arts in English from the University of Houston in 1977. She is a Certified Public Accountant in the State of Texas.

Elizabeth's early professional experience was in accounting and finance. She was employed during her C.P.A. residency by an international accounting firm. Following completion of that residency, she spent three years at a Fortune 500 company specializing in insurance and financial services.

Her career focus, however, has been health care administration. She was employed by M.D. Anderson Cancer Center for over 16 years. Included in the positions she held was Director of Financial Resources Assessment and Planning for the Cancer Center for five years. For the last ten years of her tenure at the Cancer Center she was Division Administrator for the Division of Cancer Prevention and Population Sciences. In this position, she received the Rogers Award for Excellence in Administration.

Concurrently, from 1994 through 2002, Elizabeth was a faculty member of the Texas Woman's University, Master of Health Care Administration program. She taught courses in management of health services organizations, financial management, advanced financial management, financial accounting and cost accounting for healthcare.

She began her doctoral studies in management and policy science at the University of Texas School of Public Health in 2005.