JOURNAL OF CLINICAL RESEARCH BEST PRACTICES

Vol. 6, No. 11, November 2010 "Can You Handle the Truth?"

Dealing with Misconduct in Biomedical Research: A Review of the Problems and the Proposed Methods for Improvement

By Malhar N. Kumar

Abstract

The increasing complexity of scientific research has been followed by increasing varieties of research misconduct. Dealing with misconduct involves the processes of detecting, reporting and investigating misconduct. Each of these steps is associated with numerous problems that need to be addressed. Misconduct investigation should not stop with inquiries and disciplinary actions in specific episodes of misconduct. It is necessary to decrease the personal price paid by those who expose misconduct and to protect the personal and professional interests of honest researchers accused of misconduct unfairly or mistakenly. There is no dearth of suggestions to improve the objectivity and fairness of investigations. What is needed is the willingness to test the various options and implement the most suitable ones.

Introduction

Biomedical research has gained leadership status in scientific research. The total funding for biomedical research in the United States doubled to $94.3 billion from 1994 to 2003. The number of principal investigators (PIs) holding grants from the National Institutes of Health (NIH) of the United States has increased from 9,492 in 1972 to 21,643 in 2002, and the postdoctoral researchers have increased in number from 7,097 in 1972 to 30,677 during the same period (Moses et al., 2006). The increased competition resulting from this increase in money and manpower has also led to changes in research practice. Publication pressures, careerism and thirst for fame and fortune have induced misconduct on many occasions (Woolf, 1986; Petersdorf, 1986; Mishkin, 1988; Dingell, 1993; Kassirer, 1993; Silverman, 1994). The impression of the general public as well as the scientific community itself is that scientists consider their vocation to be a calling and not just a profession (Martinson et al., 2006). The former director of National Science Foundation, Walter Massey, said that "it is a paradox of research that the reliance on truth is both the source of modern science and engineering's enduring resilience and its intrinsic fragility" (Swazey et al., 1993). Minimization of misconduct is important to increase the resilience and decrease the fragility.

It is naïve to wish that misconduct would go away on its own, given the "tournament model" (few winners and large number of losers) of operation of current scientific research

(Freeman et al., 2001). People who fund and control research are busy pointing their fingers at the researchers, without realizing that they are also a big part of the problem. In the United States, the number of junior biomedical researchers has been continuously increasing, but the proportion of grants by the NIH to junior researchers has declined drastically over the last 25 years. Robert Merton observed long ago the "Matthew effect" of credit going to the well-known researchers at the expense of lesser-known researchers who actually did the job (Merton, 1968). Methods of detection and investigation of research misconduct should keep pace with the changes in research practice. If this does not happen, it is possible that the definitions, rules and methods of dealing with misconduct will become irrelevant to the current research scenario. This review summarizes the current problems of dealing with research misconduct and the methods suggested by contemporary experts to improve the state of affairs.

Modes of Discovery of Scientific Misconduct

Detection of scientific misconduct at present is almost entirely dependent on what has been called "personally motivated reporting" of misconduct (Shamoo and Dunigan, 2000). Most cases of research misconduct are anecdotal reports attributable to accidental discoveries. Personally motivated reporting of research misconduct has been undertaken by four different groups of people: peer groups, investigative journalists, special interest groups, and bystanders.

Scientific misconduct is most often exposed by peer group evaluation either before or after publication of a fraudulent article. Peer review occurs through institutional review boards, fellow researchers and collaborators, graduate students in the project, grant peer reviewers, publication peer reviewers, editors of scientific journals, and readers (postpublication peer review). Hwang Woo Suk's claim of having cloned human embryonic stem cells was later shown to be fraudulent through the process of postpublication peer review by the readers of the article, and the article was later retracted from "Science" (Hwang et al., 2005; Kennedy, 2006). Responsible editors have pointed out instances of misconduct that have catalyzed investigations later on. Richard Smith, during his tenure as the editor of the British Medical Journal (BMJ), played an active role in bringing to the attention of the scientific community the research misconduct of Dr. Ranjit Chandra of Canada (Smith, 2006).

Investigative journalists working for newspapers also can expose research misconduct. Brian Deer, a journalist with the Sunday Times (U.K.) exposed the fallacious research of Andrew Wakefield and co-authors concerning the Mumps-Measles-Rubella (MMR) vaccine and autism (Wakefield et al., 1998; Deer, 2004). The article was eventually retracted in 2004 (Murch et al., 2004). Journalist David Willman's award-winning investigative report in 2003 in the Los Angeles Times drew widespread attention to the fact that many National Institutes of Health (NIH) scientists on federal payroll had simultaneous consulting agreements with private pharmaceutical companies (Willman, 2003).

Special interest groups may be instrumental in drawing attention of professionals as well as the lay public regarding fraudulent research. Kathleen Seidel spared no effort in exposing all the inaccuracies in the article by David and Mark Geier in the journal Hormone Research in May 2006 (Geier and Geier, 2006; Neurodiversity Weblog, 2006). The Geiers had claimed a link between autism and the thimerosal in vaccines based on pseudoscientific research, and they were busy providing expert testimony in many legal cases brought against vaccine manufacturers by the misguided parents of autistic children. Lawyers and judges may be involved in questioning the integrity of certain scientific research data that have been used in the courtroom. They have acted as indirect peer reviewers of researchers and scientific research that enters the courtroom. The criticism of the work of David and Mark Geier by the legal professionals is an example (Office of Special Masters, 2003).

Bystanders are not usually part of either the conduct or evaluation of research but sometimes sense something unethical occurring in their vicinity and feel compelled by conscience to expose it. Whistle-blowing by a hospital employee exposed the fabricated research of Malcolm Pearce, who was the first author of two fraudulent articles in the British Journal of Obstetrics and Gynaecology in 1994 (Dyer, 1995). Jon Sudb's fabricated research on the role of nonsteroidal anti-inflammatory drugs in prevention of oral cancer was detected accidentally when Camilla Stoltenberg, an epidemiologist at the Norwegian Institute of Public Health, noticed the discrepancies in the article after she read about the research in a newspaper report (Couzin and Schirber, 2006; Zeus Reports, 2006).

Difficulty in Detection of Misconduct

Even if motivation is there, detection of misconduct may not be possible in all cases. It is estimated that for every one case of scientific fraud that becomes public, there are many more cases that go undetected (Shamoo and Resnik, 2003). Some of the reasons for difficulty in detection are as follows:

1. Perception of misconduct: There are differences in the definitions of misconduct between countries and between the national bodies dealing with research misconduct within each country. In the United States, the narrow federal FFP (fabrication, falsification and plagiarism) definition has evolved, allegedly, as a result of lobbying by vested interest groups (Culliton, 1991; Maisonneuve, 2004). In the United Kingdom, there are at least five definitions proposed by various national bodies. There is a need for an internationally accepted definition and classification of research misconduct (Resnik, 2009). Consensus is also needed as to the gravity and the quantum of censure called for by different types of misconduct. Resnik proposed a more comprehensive definition, which states that "misconduct is a serious and intentional violation of accepted scientific practices, commonsense ethical norms, or research regulations in proposing, designing, conducting, reviewing or reporting research" (Resnik, 2003). In the scientific community, there is a mixed response to the misconduct issue. In one survey, 40% of researchers felt that certain deviations (such as honorary authorship) could be accepted in some circumstances (Abbott and Graf, 2003). It was advocated that the definition restricted to FFP could be used for the purposes of disciplinary actions, while a broader definition could be used for the purpose of prevention (Resnik, 2003; Nylenna and Simonsen 2006). Classifications of research misdemeanours by The National Academy of Sciences (Council of Science Editors, 2006) and the Global Science Forum of the OECD (Organization for Economic Cooperation and Development) are useful in this regard (OECD, 2007). Swazey et al. (1993) suggested a quantum of punishment for each type of misconduct, based on the classification of the National Academy of Sciences.
2. Peer review drawbacks: Editorial peer review, considered sacrosanct by most readers of scientific journals, often cannot detect fraud in research because the peer reviewers cannot be expected to visit the laboratory or hospital where the research was done. They have to judge what is given to them, and that is usually an anonymous manuscript. Peer review is said to assess the clarity, validity, transparency, accuracy and utility of manuscripts (Campbell, 2007; Jefferson et al., 2002). The fact is that even a faked study can be made to appear entirely clear, transparent, accurate and very useful. Occasionally, peer reviewers themselves may engage in fraud, instead of detecting and eliminating it (NIH Guide, 1993).
3. Lack of reproducibility: Even the most ingenious fraudulent experiment will be detected when fellow researchers cannot reproduce the experiment. This is easier done in branches of science like physics and mathematics, where it is easier to conduct precise and repeatable experiments. Biologists find it easier to cheat, using the umbrella of

biologic variability to explain the lack of repeatability of experiments (Goodstein, 2002). This is one reason fraudulent research is more common in biomedical research compared to other branches of science. A German survey found that misconduct is considered a major problem in clinical research (80%) and life sciences (59%), and only 4% felt that misconduct was a serious problem in physics or chemistry (Abbott and Graf, 2003). Clinical research involving long-term follow-up can be nearly impossible to replicate. Even science sociologist Harriet Zuckermann, who held reproducibility of scientific experiment as the foundation of social control of science, accepted that it is a difficult goal to achieve in practice all the time (Shamoo and Dunigan, 2000).

4. Complexity of research networks: Publications from international collaborations doubled during 1999-2000, accounting for nearly 16% of all scientific publications indexed in the ISI Web of Knowledge (Wagner and Leydesdorff, 2005). The increasing number of scientists and their support staff makes monitoring difficult and expensive. Team research, national and international collaborations between scientists, complexities of university and industry relations and governmental regulations have made the process daunting for administrators (Boesz and Lloyd, 2008). Group research has reduced the personal touch of the mentors over their projects and has diluted their supervisory responsibilities (Sovacool, 2005). Investigating allegations of malpractice in international collaborative research is difficult due to the different philosophies and yardsticks in each of the participating countries. Coordination between investigating agencies of different countries is also difficult (Boesz and Lloyd, 2008).

Problems in Reporting Misconduct

A recent survey by the Office of Research Integrity (ORI) estimated that around 1,000 cases of "likely misconduct" went unreported over a three-year period between 2002 and 2005. Only around 24 cases of scientific misconduct were reported to the ORI per year (Titus et al., 2008). It is obvious that the reported instances of misconduct are only the tip of the iceberg. Whistle-blowing is a well-known medium of exposing scientific misconduct. One definition states that a whistle-blower is one who acts to prevent harm to others, not him- or herself, while possessing evidence that would convince a reasonable person (Glazer and Glazer, 1989). Whistle-blowers are a part of the "informal social control" of research conduct. Informal social control is considered the "unofficial activity that is collectively practiced to increase and maintain conformity with the organization's unwritten rules" (Adams and Pimple, 2005). Its advantage is its ability to detect misconduct that cannot be detected by formal administrative processes. Because of its presence everywhere, informal social control is difficult to evade.

Fear of retribution by the accused, shame of being identified as a traitor, and inculcated obedience to the chain of command are some of the reasons that are thought to decrease a whistle-blower's motivation (Bolsin, 2003). Wilmhurst says that editors of medical journals "are more worried about being sued for libel than about ensuring research is valid." He claims that his articles to journals exposing research fraud were scrutinized by an "army" of libel lawyers and frequently rejected (Wilmhurst, 2004; Ferriman, 2003). Whistle-blowing has both desirable and undesirable aspects. Accurate whistle-blowing done in good faith falls in the good zone of whistle-blowing; noisy whistle-blowing and bad-faith whistle-blowing fall in the bad zone; and mercenary whistle-blowing falls in the grey zone, with ongoing debate on its ethical basis.

Good-Faith Whistle-Blowing

Good-faith whistle-blowers are driven by a higher-than-average sense of personal ethics and think of whistle-blowing as their sacred duty. Three main negative consequences faced by "good faith" whistle-blowers are suppression, retribution and apathy. Martin says that

suppression of dissent can occur in many ways, from formal reprimands through forced transfer or dismissal to mental and physical torture (Martin, 1999). The "smoke screen syndrome" is a typical method of retribution against whistle-blowers, where the accused person or company tries to discredit the whistle-blower, rather than trying to provide objective evidence in their own defence (Lenzer, 2004). Exposure of fraudulent research from a particular university has a negative impact on the prestige of the university, and cover-up attempts by the university may follow. Whistle-blowers are often forced to fight a lone battle, and the universities support big industries rather than their own employees due to the lure of funding that the industry brings to them. At least two-thirds of whistle-blowers go through adverse experiences because of their actions (Lubalin and Matheson, 1999). Negative impact on the health of the whistle-blowers has also been reported (Lennaec, 1993).

Even if whistle-blowers do not face retaliatory action, officials may be apathetic towards their reports. The "deaf effect" describes the reluctance of the authorities and policy makers to hear bad news (Cuellar et al., 2006). This allows malpractice to escalate to the point of crisis, when action becomes inevitable. The "inner circle phenomenon" is another reason for apathy, and it has been described by James Fanto as a "powerful psychosocial reality." Whistle-blowers usually are not part of the inner circle, and their reports are treated by the inner circle with resistance, hostility or denial (Fanto, 2004).

The community's perception of the scientists is threatened by the whistle-blower's breach of trust, leading to the whistle-blower being ostracized by the community (Silverman, 1994). During 2005-2006, graduate students at the University of Wisconsin blew the whistle on deliberate falsification by their professor in research grant applications for nearly $1.8 million of federal funds (Couzin, 2006; Ruhlen, 2006). It was a moral victory for the whistle-blowers when investigations confirmed their allegations. Grants were cancelled and the professor resigned. In the days that followed, the students had to change laboratories, restart their theses with loss of years of effort, or altogether quit scientific research. The university played by the rules and did support them during the investigation, but left them high and dry later on.

Public Health Service (PHS) regulations require institutions to protect "good faith" whistle-blowers from retaliation and to sanction retaliators (Commission on Research Integrity, 1995). Even though official guidelines exist on protection of whistle-blowers from retaliatory action, such protection may not exist or may be woefully inadequate. In fact, whistle-blowers have been advised to ask for official or governmental help with caution (DeMaria and Cyrelle, 1996). Media coverage and contact with other whistle-blowers have been found to be more helpful than official and governmental resources.

The committee of the National Academy of Sciences of the United States declared in 1995 that "someone who has witnessed misconduct has an unmistakable obligation to act" (National Academy Press, 1995). There are also arguments to the contrary, which state that society has no right to make whistle-blowing a morally obligatory act because whistle-blowing is a fiendishly complicated task. It is best left for the individual to decide (Bouville, 2008). There is plenty of free advice for whistle-blowers, but none can assure them a trouble-free existence. Whistle-blowers have been advised to exercise tremendous patience through their ordeal and be mentally prepared for the eventuality of things going wrong (Gunsalus, 1998). A cynic would question the need for a whistle-blower to go through this grind to help the same society that has made the process so tiresome and affords no protection should things go awry.

Noisy Whistle-Blowing

Occasionally, whistle-blowers may have blown the whistle wrongly based on their own subjective impressions (heuristical errors) and not on facts. Experts in cognitive psychology

have coined the term "heuristics" to refer to intuitive methods of decision-making that people employ when making judgments under conditions of uncertainty (without having access to all the facts). This type of decision-making is often subject to errors caused by psychological biases (Tversky and Kahneman, 1974). Nancy Levitt gives examples of heuristical errors such as recall bias, alarmist bias, stereotyping bias (race and gender bias), overconfidence and overoptimism bias, egocentric bias, framing effect (a person's response to an event depends on the way in which it is presented to him or her), and anchoring effect (originally held beliefs do not alter even when challenging new facts are available). Potential whistle-blowers should be alert to the presence of these heuristic errors in their allegations (Levit, 2006).

Bad-Faith Whistle-Blowing

Investigating authorities in certain universities were said to have received 20 to 40 complaints each year, out of which only three to five were worthy of further investigation. The rest turned out to be due to personal grievances or personality conflicts between researchers (Taubes, 1993). Special interest groups may discredit even a good researcher whose philosophy is opposed to that of the group. The Traditional Values Coalition, a conservative advocacy group in the United States, blew the whistle on many scientists who were conducting research on AIDS and human sexuality. The whistle-blowers, who were ideologically opposed to any kind of research into human sexuality, managed to convince a few senators that such research was a wasteful use of taxpayers' money (Russell, 2003).

Another possible motive for malicious whistle-blowing is the ambition of the whistle-blower to enhance his or her own standing in the scientific community quickly. Junior researchers who blow the whistle on leaders in their fields may be motivated by a sense of opportunity to further their own reputation, rather than moral compulsion. Silverman has called this "gun fighter syndrome" after the Wild West model of the 19th century United States when "a young man with a gun could hope to establish his own reputation quickly by challenging the leading gun fighter in the hope of gunning him down, thus showing his superiority" (Silverman, 1994).

Mercenary Whistle-Blowing

The ethics and morality of private whistle-blowers (qui tam relators) in the United States reporting financial fraud in federally funded institutions is being debated. Qui tam relators can file confidential complaints that a university has defrauded the United States government and their complaints will be investigated under the False Claims Act (FCA). The Department of Justice can investigate such cases on behalf of the whistle-blower or, if it does not, the whistle-blower can file a legal suit on his or her own (Kalb, 1999). Qui tam relators are entitled to 15 to 25% of the money recovered by the courts from the erring universities. The 1986 amendment to the FCA allowed for increased financial rewards and protection for whistle-blowers. Mercenary whistle-blowing for personal profit cannot be considered a noble example of altruism. Innocent researchers can be harassed by malicious whistle-blowers who could be disgruntled former employees, competitors or personal enemies, wanting to satisfy their thirst for revenge as well as money in one go (Weinberg, 2005).

Grant stated that whistle-blowers are "saints of secular culture" and any issue of reward pollutes the ethical quality of the act itself (Grant, 2002). However, others have argued that there is no moral objection to the qui tam legislation, because even if the motivation for the whistle-blowing is morally wrong, the act (to blow the whistle) itself is morally right, and its social benefits override moral objections (Carson et al., 2008). Because it removes the anxiety related to loss of job and income, it reduces the number of cases where whistle-blowers do not come forward due to such fears. To reduce the greed motive in whistle-

blowing, they propose that a ceiling should be imposed on the amount paid to whistle-blowers (Carson et al., 2008).

Problems in Investigating Scientific Misconduct

It is said that less than 10 countries in the world have a national body for investigating misconduct and fraud in science (Council of Science Editors, 2006). In the United States, the Office of Research Integrity (ORI) was created in 1992 to monitor the integrity of biomedical research and is supported by the U.S. PHS. The ORI documents an assurance from organizations whose research is funded by the PHS that they have the mechanisms in place to investigate allegations of scientific misconduct. It expects such institutions to investigate cases of possible misconduct and to submit a report of the investigation to the ORI. The ORI determines whether the investigation has been conducted thoroughly and objectively and reserves the right to conduct its own investigation at any time if deemed necessary (ORI Handbook, 1995). Only about 5% of cases are said to be investigated by the ORI independently.

The problem with ORI is that it investigates misconduct only in government institutes and institutions that receive federal funding. It has no oversight authority over privately funded research. Secondly, the ORI seems to be confident about the institutional mechanisms and commitments to investigate research misconduct, but many in the scientific community do not share this confidence. Several objections have been raised against institutional investigations:

a. Lack of procedural uniformity. There is lack of uniformity in the procedures of investigation between various universities.

b. Difficulty in establishing "intent." Even if deviation from established norms is detected through painstaking and lengthy investigations, it is often difficult to establish "intent" to defraud. Researchers may get away with attributing the discrepancies to oversight, loss of data, and unintended errors in the experiments.

c. Lack of due process. Process exists in ORI investigations, but it is the lack of "due process" that has been criticized by many. There is growing legal concern about the abuse potential of the ORI policy of investigation, and some have considered it a violation of the Fourth Amendment (Spece Jr. and Marchalonis, 2001). Researchers are not allowed to have any say "during" institutional investigations. Accused scientists have scant procedural safeguards, such as presumption of innocence, high burden of proof for the prosecution, right to legal representation, and the right to examine evidence and confront witnesses (Mello and Brennan, 2003). Even criminals being tried in the courts of law are entitled to better procedural safeguards than scientists undergoing misconduct enquiry. Perhaps the authorities feel that high degrees of safeguards are not essential as the researchers are not given the same punishment as the criminals. However, mere absence of criminal proceedings should not mean that misconduct trials are free of bad effects. Researchers face the prospect of loss of job and income, loss of reputation, and often, destruction of an entire career. Even those who have been investigated and eventually exonerated of misconduct have significant negative impacts, including physical and mental health problems (RTI, 1996).

d. Dependence on institutional leadership. Institutional inquiry depends heavily on the attitudes of the leaders of the institutions. If this attitude is biased or uninterested, justice will not be done. Surveys have identified some universities that have done much better than others in handling misconduct, and the reason for better performance was able and proactive leadership (Taubes, 1993). Gunsalus stated that the "single most

important component in an institutional culture of research integrity is institutional leadership committed to ethical conduct" (Gunsalus, 1993).

e. Conflicts of interest. Resnik has pointed out that members of an institution often have complex professional and financial relationships involving research projects, and conflicts of interests may interfere with institutional inquiries of research misconduct (Resnik, 2008). Conflicts of interests undermine fairness and objectivity in misconduct investigations. The PHS has issued guidelines regarding conflicts of interest in misconduct investigations, but there is lack of data regarding the extent of such conflicts. Further research on the incidence and forms of conflicts of interest is urgently needed (Resnik, 2008).

Improving Investigation of Research Misconduct

If the scientific fraternity does not regulate itself, it will not be long before the government is forced to take up the task of regulation to restore public confidence in science and its methods. Increase in political oversight means a decrease in the autonomy that is treasured by all scientists. It is up to the scientific community to decide between intrusion and autonomy. Methods of improving accountability in research include the following:

1. Protection of good-faith whistle-blowers. Some organizations have been formed to offer guidance and help to whistle-blowers suffering harassment. The Whistle-blowers for Integrity in Science and Education (WISE) society, formed by former whistle-blowers Carolyn Phinney and Robert Sprague, is one such society (Home for scientific whistleblowers 1997; Holden, 1987). The Whistle-Blowers Association of Australia (WBA) is another example of support group for whistle-blowers. Martin (Martin, 1998) and Gunsalus (Gunsalus, 1998) have made useful recommendations for potential whistle-blowers. The "Government Accountability Project" is a public interest group based in Washington, D.C., that offers legal aid to whistle-blowers (G.A.P., 2008). It provided legal help to Dr. David Graham, the FDA executive who testified in 2004 on the issue of cardiovascular risks associated with rofecoxib (Lenzer, 2004). The Whistleblower Protection Act (WPA) was passed by the U.S. Congress in 1989 to protect government employee whistle-blowers, and it was amended in 1994. However, the Department of Justice had a monopoly on judicial review of the act, and the judiciary's view was that whistle-blowers seeking protection under the WPA should be investigated to determine the motives behind whistle-blowing. However, this subjected whistle-blowers to harassment and intimidation. In March, 2007, the U.S. House of Representatives approved the Whistle-Blower Protection Enhancement Act (H.R. 985) to address the earlier loopholes in the WPA (Kintisch, 2007). The Senate approved the bill in December 2007, and it is currently awaiting presidential approval. In the United Kingdom, the Public Interest Disclosure Act (1999) provides legal protection for whistle-blowers. Programs to allow anonymous whistle-blowing (whistle-blowing lines) have been set up by the Government Accountability Project in the U.S. and more recently by the U.K. Financial Services Authority.
2. Optimization of response to whistle-blowing. The quality of response is important because it will influence the behavior of other potential whistle-blowers in the future. The response should encourage the right kind of whistle-blowing and discourage the wrong kind. Heyes and Kapur have recommended a graded response (Heyes and Kapur, 2009). Enforcement agencies should first decide whether the whistle-blowing is noisy or evidence-based. If it is evidence-based, the next step should be to ensure the motivation for whistle-blowing. Heyes and Kapur have discussed three models of whistle-blowing motivation in their recent article: the social welfarist model, the conscience cleansing model, and the punishment model. In the social welfarist model,

whistle-blowing serves some purpose in correcting or preventing harm to the society and does more good than harm. In the conscience cleansing type, whistle-blowers disclose because they dread living with a corrupted self more than they dread the other outcomes. In the punishment model, the whistle-blower is predominantly interested in punishing an individual or an institution. Whistle-blowing without "noise" and based on social welfarist motivation deserves maximal response (every reported case should be pursued and every proven offence should be dealt with using maximal penalties). When the motivation is "conscience cleansing," less than complete responsiveness is justifiable, but maximum penalties should be awarded if wrongdoing is detected. Whistle-blowing with punishment motivation deserves incomplete response and less than maximal penalty.

3. Educating researchers and whistle-blowers. The Triandis theory of social behavior encompasses most of the factors underlying whistle-blowing actions (Kingston et al., 2004). As stated in their article, the Triandis equation is as follows: probability of act = [habit + intention] motivation facilitating conditions. Intention includes social factors (such as beliefs, attitudes and impact of peers); affect (the emotions generated in the person at the thought of the behavior), and perceived consequences (positive and negative). In the hospital setting, they showed that nurses were more receptive to the idea of formal incident reporting than doctors. The difference in the behavior of the two groups is probably due to the different emphasis in the education of nurses and doctors. Whistle-blowing attitudes have been shown to be influenced by factors such as local cultures, socioeconomic status, religiosity, nationality and ethnicity of the whistle-blowers (Alford, 2001; Jackson and Artola 1997; Patel 2003; Barndt et al., 1996). To achieve uniformity of attitude towards whistle-blowing, education about the ethics of research should be introduced right from the junior levels of training in medicine and biology. Some institutions, such as the Australian National University Medical School, have taken this seriously. Medical students are taught the ethical and legal principles behind the act of whistle-blowing (Faunce et al., 2004). It has been reported that education changes attitudes towards whistle-blowing in the students and as few as six weeks are sufficient to detect changes in attitudes among trainees (Goldie et al., 2000). This kind of education is required to counter the "hidden curriculum" in medical schools that creates an impression among students that whistle-blowing is unethical and should be avoided (Hafferty and Franks, 1994; Hundert, 1996). The goal of institutional leaders should be "to educate and rehabilitate, rather than to punish and destroy" (Gunsalus, 1998). Several scholars believe that sustained efforts at educating all researchers regarding misconduct issues are essential (Rhodes, 2002; Eisen and Berry, 2002; Bruhn et al., 2002). Without regular reminders, researchers are likely to forget the ethical obligations expected of them.

4. External oversight. External agencies to carry out random checks are considered necessary in the interest of public safety, as academic institutions and hospitals have repeatedly failed to deal properly with misconduct within their precincts (Wilmhurst, 2004; Faunce and Bolsin, 2004). Fear of loss of industry support for research, loss of prestige, and negative publicity from scandal may reduce an institution's motivation to detect and report misconduct within its own premises. Rhodes and Strain (2004) have provided four excellent examples of biased and inept handling of misconduct allegations by universities. In each of the four cases, the institutional enquiry concluded that there was no fraud. The whistle-blowers received censure, rather than the support of their institutions, and they had to resort to external intervention to address their concerns. Independent investigations done subsequently by external agencies clearly established the occurrence of misconduct in all four cases and vindicated the whistle-blowers. Routine audits of all research similar to the auditing done for accounting purposes has been suggested (Shamoo and Dunigan, 2000). Shamoo suggested in an article in AAA

Observer in 1988 that there is a need for establishing an independent unit of data auditors whose sole function is to monitor the quality and integrity of research data (Shamoo, 1988; Loeb and Shamoo, 1989). These auditors should be independent of academic institutions and government agencies. If researchers were aware that their data would be audited routinely, they would perhaps be careful regarding preservation of data and wary about manipulation of data. Effectiveness of auditing is dependent on recordkeeping. Poor recordkeeping was reportedly observed in around 40% of research misconduct investigations across 90 universities in the United States (Wilson et al., 2007). Schreier et al. have outlined the best practices for contemporary research recordkeeping and suggested that records should be maintained at three levels: individual researchers, research group leaders, and departmental heads (Schreier et al., 2006).

5. Effective mentoring. Setting high standards in ethical research conduct by respected mentors is said to be far more effective than didactic lectures on principles of ethics and studying examples of egregious misconduct in the literature (Pellegrino, 1992; Wocial, 1995). A review of the closed files of research misconduct at the ORI showed that nearly three-fourths of mentors had not reviewed the source data and two-thirds had not set research standards. Nearly 50% of trainees who received punitive measures had confessed to being stressed by the institutional environment. It was suggested that mentors should review source data, set and teach specific research standards, and create a good institutional atmosphere to minimize stress for their protégés (Wright et al., 2008). Anderson et al. (2007) have expressed that mentoring can both increase and decrease the likelihood of misconduct.
6. Institutional liability. Rhodes and Strain (2004) suggest that institutions should be held responsible for the actions of individuals employed by them and serious sanctions should be imposed on the erring institutions. They cite the example of the Institutional Animal Care and Use Committees (IACUC) model in the U.S., which allows sudden, surprise inspections by state or federal authorities regarding the handling of animals in the laboratories. It applies external pressure upon the institutions rather than individuals when misconduct has occurred. In such a case, the institution would look upon whistle-blowers as their allies, rather than trouble-makers. They would also understand that to avoid sanctions they should penalize guilty researchers instead of whistle-blowers. The federal False Claims Act (FCA) is a welcome move in that employers can be held liable for the actions of their employees. Universities have been held liable for misuse of federal funds or false statements made by individual researchers, even when the administrators of the university claim lack of awareness of misconduct (Kalb and Koehler, 2002).
7. International agency for investigating international fraud. Since international research collaborations are increasing, collaboration of research misconduct investigating agencies is also being perceived as a real need. The World Conference on Research Integrity is one such forum attempting to harmonize international ethics and procedures in research misconduct investigations. The first world conference was held in Lisbon, Portugal, in September 2007 through the joint efforts of many agencies, most prominently the European Science Foundation (ESF) and the U.S. ORI. Participants from 47 different countries attended the meeting (First World Conference on Research Integrity, 2007). In December 2007, the Global Science Forum (GSF) of the OECD held the inaugural meeting of the OECD "Co-ordination Committee for Facilitating International Research Misconduct Investigations." Members of 14 countries participated in it (Boesz and Lloyd, 2008). The committee identified a set of general principles in research misconduct investigation that the member countries can use when comparing and contrasting their own national policies. Secondly, the need for a central database of

research misconduct policies in various countries as well as a directory of investigating officials in various countries was identified. This facilitates smoother conduct of cross-border investigations. In tandem with the OECD, The ESF and United Nations Educational, Scientific, and Cultural Organization (UNESCO) are also involved in similar efforts.

Conclusion

The current model of "personally motivated reporting" of research misconduct needs to be improved in terms of efficiency, objectivity and safety for whistle-blowers, as well as the accused researchers. A better option is regular monitoring of research integrity and standardized methods of dealing with transgressions. Instead of waiting for whistle-blowers to come forward and sacrifice their careers by exposing misconduct, universities can implement some of the suggested improvements to minimize research fraud. The system could be improved without excessive personal sacrifice from a few persons who care more than others (Taubes, 1993). Even ORI officials who depend on whistle-blowers to detect misconduct admit that whistle-blowing is not a good career option (Couzin, 2006). Significant intellectual contributions have been made to improve the methods of dealing with research misconduct. Implementing the suggested improvements requires the enhanced collective will of academics and federal agencies.

Acknowledgment

The author appreciates and acknowledges the guidance and support of the peer reviewers in improving the quality of this article.

References

1. Abbott, A. and Graf, P. (2003) Survey reveals mixed feelings over scientific misconduct. Nature 424:6945, p. 117.
2. Adams, D. and Pimple, K. D. (2005) Research misconduct and crime lessons from criminal science on preventing misconduct and promoting integrity. Accountability in Research 12:3, pp. 225-240.
3. Alford, F. C. (2001) Whistleblowers. Cornell University Press, Ithaca, NY
4. Anderson, M. S., Horn, A. S., Risbey, K. R., Ronning, E. A., DeVries, R. and Martinson, B. C. (2007) What do mentoring and training in the responsible conduct of research have to do with scientists' misbehaviour? Findings from a National Survey of NIH-funded scientists. Academic Medicine 82:9, pp. 853-860.
5. Barndt, T., Bass, K. and Brown, G. (1996) Religiosity, ethical ideology and intentions to report a peer's wrong doing. Journal of Business Ethics 15, pp. 1161-1174.
6. Boesz, C. and Lloyd, N. (2008) Collaborations: Investigating international misconduct. Nature 452, pp. 686-687.
7. Bolsin, S. N. C. (2003) Whistle blowing. Medical Education 37, pp. 294-296.
8. Bouville, M. (2008) Whistle blowing and morality. Journal of Business Ethics 81:3, pp. 579-585.
9. Bruhn, J. G., Zajac, G., Al-Kazemi, A. A. and Prescott, L. (2002) Moral positions and academic conduct: Parameters of tolerance for ethics failure. The Journal of Higher Education 73:4, pp. 461-493.
10. Campbell, P. (2007) Misconduct in research: Who is responsible for what? Fraud in Research Conference. London — 8 May 2007
11. Carson, T. L., Verdu, M. E. and Wokutch, R. E. (2008) Whistle blowing for profit: An ethical analysis of federal false claims act. Journal of Business Ethics 77:3, pp. 361-376.

12. http://ori.dhhs.gov/documents/report_commission.pdf — Commission on Research Integrity. (1995). Integrity and Misconduct in Research
13. http://www.councilscienceeditors.org/editorial_policies/whitepaper/3-2_international.cfm — Council of Science Editors. (2006). International models for responding to research misconduct, in "CSE's white paper on promoting integrity in scientific journal publications"
14. Couzin, J. (2006) Scientific misconduct: Truth and consequences. Science 313:5791, pp. 1222-1226.
15. Couzin, J. and Schirber, M. (2006) Fraud upends oral cancer field, casting doubts on prevention trial. Science 311:5760, pp. 448-449.
16. Cuellar, M. J., Keil, M. and Johnson, R. D. (2006) The deaf effect response to bad news reporting in information systems projects. E-Service Journal 5:1, pp. 75-97.
17. Culliton, B. J. (1991) NIH need a clear definition of fraud. Nature 352, p. 563.
18. http://briandeer.com/wakefield/nick-chadwick.htm — Deer, B. (2004). Molecular testing in Wakefield's own lab rebutted the basis for his attack on MMR
19. DeMaria, W. and Cyrelle, J. (1996) Behold the shut-eyed sentry! Whistle blower perspectives on Government failure to correct wrong doing. Crime, Law, and Social Change 24, pp. 151-166.
20. Dingell, J. D. (1993) Shattuck Lecture: misconduct in medical research. New England Journal of Medicine 328, pp. 1610-1615.
21. Dyer, O. (1995) Consultant struck off for fraudulent claims. British Medical Journal 310, p. 1554.
22. Eisen, A. and Berry, R. M. (2002) The absent professor: Why we don't teach research ethics and what to do about it. The American Journal of Bioethics 2, pp. 38-49.
23. Fanto, J. (2004) Whistle blowing and the public director: Countering corporate inner circles. Oregon Law Review 83, pp. 435-539.
24. Faunce, T. and Bolsin, S. N. C. (2004) Three Australian whistle blowing sagas: lessons for internal and external regulation. Medical Journal of Australia 181:1, pp. 44-47.
25. Faunce, T., Bolsin, S. and Chen, W. P. (2004) Supporting whistle blowers in academic medicine: training and respecting the courage of professional conscience. Journal of Medical Ethics 30:1, pp. 40-43.
26. Ferriman, A. (2003) Have editors got their priorities right? British Medical Journal 327, p. 1113.
27. http://www.icsu.org/5_abouticsu/PDF/WC_final_report.pdf — First World Conference on Research Integrity. Fostering Responsible Research, Lisbon, Portugal, 16-19 September 2007
28. Freeman, R., Weinstein, E., Marincola, E., Rosenbaum, J. and Solomon, F. (2001) Competition and careers in biosciences. Science 294:5550, pp. 2293-2294.
29. http://www.whistleblower.org/template/page.cfm?page_id=121 — Government Accountability Project (GAP). (2008). Whistleblower protection act and amendments
30. Geier, M. and Geier, D. (2006) A clinical and laboratory evaluation of methionine cycle — Transsulfuration and androgen pathway markers in children with autistic disorders. Hormone Research 66:1, pp. 33-39.
31. Glazer, M. P. and Glazer, P. (1989) The Whistleblowers Basic Books, New York, N.Y
32. Goldie, J., Schwarz, L. and Morrison, J. (2000) A process evaluation of medical ethics education in the first year of a new medical curriculum. Medical Education 34, pp. 468-473.
33. Goldie, J., Schwartz, L. and McConnachie, A. (2000) Student's attitudes and potential behaviour with regard to whistle blowing as they pass through a modern medical curriculum. Medical Education 37, pp. 568-575.
34. http://www.aaup.org/AAUP/pubsres/academe/2002/JF/Feat/good.htm — Goodstein, D. (2002): Scientific misconduct, Academe, 88(1)

35. Grant, C. (2002) Whistle blowers: Saints of secular culture. Journal of Business Ethics 39, pp. 391-399.
36. Gunsalus, C. K. (1993) Institutional structure to ensure research integrity. Academic Medicine 68(Supplement), pp. S33-S38.
37. Gunsalus, C. K. (1998) Preventing the need for whistle blowing: practical advice for university administrators. Science and Engineering Ethics 4:1, pp. 75-94.
38. Gunsalus, C. K. (1998) How to blow the whistle and still have a career afterwards. Science and Engineering Ethics 4, pp. 51-64.
39. Hansen, T. B. (2006) Academic and social responsibility of scientists. Journal on Science and World Affairs 2:2, pp. 71-92.
40. Hafferty, F. W. and Franks, R. (1994) The hidden curriculum, ethics teaching and restructure of medical education. Academic Medicine 69, pp. 861-871.
41. Heyes, A. and Kapur, S. (2009) An economic model of whistle blower policy. Journal of Law, Economics and Organization 25, pp. 157-182.
42. Holden, C. (1987) NIMH finds a case of serious misconduct. Science 235, pp. 1566-1567.
43. Home for scientific whistleblowers (1997) Random samples. Science 277:5332, p. 1611.
44. Hundert, E. M., Douglas-Steele, D. and Bickel, J. (1996) Context in medical education: the informal ethics curriculum. Medical Education, 30 pp. 353-364.
45. Hwang, W. S., Roh, S. I., Lee, B. C., Kang, S. K., Kwon, D. K., Kim, S., Kim, S. J., Park, S. W., Kwon, H. S., Lee, C. K., Lee, J. B., Kim, J. M., Ahn, C., Paek, S. H., Chang, S. S., Koo, J. J., Yoon, H. S., Hwang, J. H., Hwang, Y. Y., Park, Y. S., Oh, S. K., Kim, H. S., Park, J. H., Moon, S. Y. and Schatten, G. (2005) Patient specific embryonic stem cells derived from human SCNT blastocysts. Science 308, pp. 1777-1783.
46. Jackson, T. and Artola, M. C. (1997) Ethical beliefs and management behaviour: A cross-cultural comparison. Journal of Business Ethics 16, pp. 1163-1173.
47. Jefferson, T., Wager, E. and Davidoff, F. (2002) Measuring the quality of editorial peer review. Journal of American Medical Association 287, pp. 2786-2790.
48. Kalb, P. E. (1999) Health care fraud and abuse. Journal of American Medical Association 282:12, pp. 1163-1168.
49. Kalb, P. E. and Koehler, K. G. (2002) Legal issues in scientific research. Journal of American Medical Association 287, pp. 85-91.
50. Kassirer, J. P. (1993) The frustrations of scientific misconduct. New England Journal of Medicine 328, pp. 1634-1636.
51. Kennedy, D., Austin, J., Urquhart, K. and Taylor, C. (2004) Supply without demand. Science 303:5661, p. 1105.
52. Kennedy, D. (2006) Editorial retraction. Science 20:311 (57-59), p. 335.
53. Kingston, M. J., Evans, S. M., Smith, B. J. and Berry, J. G. (2004) Attitudes of doctors and nurses towards incident reporting: a qualitative analysis. Medical Journal of Australia 181:1, pp. 36-39.
54. Kintisch, E. (2007) Open Government, House OKs whistle blower bill. Science 315:5819, p. 1649.
55. Lennaec, K. J. (1993) 'Whistle blowing': A health issue. British Medical Journal 307, pp. 667-670.
56. Lenzer, J. (2004) Public interest group accuses FDA of trying to discredit whistle blower. British Medical Journal 329, p. 1255.
57. Levit, N. (2006) Confronting conventional thinking: The heuristics problem in feminist legal theory. Cardozo Law Review 28:1, pp. 391-440.
58. Loeb, S. E. and Shamoo, A. E. (1989) Data audit: Its place in auditing. Accountability in Research 1, pp. 23-32.
59. Lubalin, J. S. and Matheson, J. L. (1999) The fall out: What happens to whistle blowers and those accused but exonerated of scientific misconduct? Science and Engineering Ethics 5:2, pp. 229-250.

60. Maisonneuve, H. (2004) Britain is ahead of most countries. British Medical Journal 328, p. 229.
61. Martin, B. (1998) Advice for the dissident scholar. Thought and Action 14:1, pp. 119-130.
62. Martin, B. Freudenberg, W. R. and Youn, T. I. K. (eds) (1999) Suppression of dissent in science. Research in Social Problems and Public Policy 7, pp. 105-135. JAI Press, Stamford, CT
63. Martinson, B. C., Anderson, M. S., Crain, A. L. and DeVries, R. (2006) Scientist's perception of organisational justice and self-reported misbehaviours. Journal of Empirical Research on Human Research Ethics 1:1, pp. 51-66.
64. Mello, M. M. and Brennan, T. A. (2003) Due process in investigations of research misconduct. New England Journal of Medicine 349, pp. 1280-1286.
65. Merton, R. K. (1968) The Matthew effect in science. Science 157:3810, pp. 56-63.
66. Mishkin, L. (1988) Fraud is a symptom of a deeper flaw. Scientist 9, p. 12.
67. Moses III, H., Dorsey, R. E., Matheson, D. H. M. and Thier, S. O. (2006) The financial anatomy of biomedical research. Journal of American Medical Association 295:9, pp. 1000-1001.
68. Murch, S. H., Anthony, A., Casson, D. H., Malik, M., Berelowitz, M., Dhillon, A. P., Thomson, M. A., Valentine, A., Davies, S. E. and Walker-Smith, J. A. (2004) Retraction of an interpretation. The Lancet 363:9411, p. 750.
69. National Academy of Sciences (1995) On being a scientist: Responsible conduct in research. Committee on Science, Engineering and Public policy, National Academy Press p. 18. 2nd,
70. http://neurodiversity.com/weblog/article/97/ — Neurodiversity Weblog. (2006). Significant misrepresentations, Mark Geier, David Geier, and the evolution of the Lupron protocol
71. http://grants.nih.gov/grants/guide/notice-files/not93-177.html — NIH Guide. (1993). Final findings of scientific misconduct
72. Nylenna, M. and Simonsen, S. (2006) Scientific misconduct: A new approach to prevention. The Lancet 367:9526, pp. 1882-1884.
73. http://www.oecd.org/dataoecd/37/17/40188303.pdf — Organisation for Economic Cooperation and Development (OECD), Global Science Forum. (2007). Best practices for ensuring scientific integrity and preventing misconduct
74. http://www.casewatch.org/civil/geier.shtml — Office of Special Masters, In the United States Court of Federal Claims (2003). Jeanine Weiss and Joseph Weiss, parents of Christopher Weiss v. Secretary of the Department of Health and Human Services, NO. 03-190v published, filed October 9, 2003
75. http://ori.dhhs.gov/documents/rio_handbook.pdf — Office of Research Integrity (ORI). (1995). Handbook for Institutional Research Integrity Officers
76. Patel, C. (2003) Some cross cultural evidence on whistle blowing. Journal of International Accounting Research 22, pp. 69-96.
77. Pellegrino, E. D. (1992) Character and the ethical conduct of research. Accountability in Research 2, pp. 1-11.
78. Petersdorf, R. G. (1986) The pathogenesis of fraud in science. Annals of Internal Medicine 104, pp. 252-254.
79. Rajan, T. V. (2005) Biomedical scientists are engaged in a pyramid scheme. Chronicle of Higher Education 51:39, p. 616.
80. Research Triangle Institute (RTI) (1996) Survey of accused but exonerated individuals in research misconduct cases: Final report Washington D.C — June 1996
81. Resnik, D. B. (2003) From Baltimore to Bell labs: Reflections on two decades of debate about scientific misconduct. Accountability in Research 10, pp. 123-135.
82. Resnik, D. B. (2008) COI issues in research misconduct inquiries and investigations. ORI Newsletter 16:4, p. 1.

83. Resnik, D. B. (2009) International standards for research integrity: An idea whose time has come? Accountability in Research 16:4, pp. 218-228.
84. Rhodes, R. (2002) The pressing need for post doctoral research ethics education. American Journal of Bioethics 2:4, pp. 1-3.
85. Rhodes, R. and Strain, J. J. (2004) Whistle blowing in academic medicine. Journal of Medical Ethics 30, pp. 35-39.
86. Ruhlen, R. L. (2006) What happens to whistleblowers? Science 314:5797, pp. 251-252.
87. http://www.commondreams.org/headlines03/1028-05.htm — Russell, S. (2003). AIDS, Sex Scientists in federal list fear their research is in jeopardy
88. Schreier, A. A., Wilson, K. and Resnik, D. (2006) Academic research record-keeping: Best practices for individuals, group leaders and institutions. Academic Medicine 81:1, pp. 42-47.
89. Shamoo, A. E. (Nov 4, p 1998) We need data audit. AAA Observer p. 4.
90. Shamoo, A. E. and Dunigan, C. D. (2000) Ethics in Research. Proceedings of the Society for Experimental Biology and Medicine 224, pp. 205-210.
91. Shamoo, A. A. and Resnik, D. B. (2003) Responsible Conduct of Research 2nd, Oxford University Press, New York
92. Silvermann, S. (1994) Process and detection in fraud and deceit. Ethics Behavior 4:3, pp. 219-228.
93. Smith, R. (2006) Research misconduct: the poisoning of the well. Journal of the Royal Society of Medicine 99, pp. 232-237.
94. Sovacool, B. K. (2005) Using criminalisation and due process to reduce scientific misconduct. American Journal Bioethics 5:5, pp. W1-7.
95. Spece Jr., R. G. and Marchalonis, J. J. (2001) Fourth Amendment restrictions on scientific misconduct proceedings at public universities. Health Matrix Clevel 11:2, pp. 571-626.
96. Swazey, J., Anderson, M. and Louis, K. (1993) Ethical problems in academic research. American Scientist 81, pp. 542-553.
97. Taubes, G. (1993) Misconduct: Views from the trenches. Science 261, pp. 1108-1111.
98. Titus, S. L., Wells, J. A. and Rhoades, L. J. (2008) Repairing research integrity. Nature 453:7198, pp. 980-982.
99. Tversky, A. and Kahneman, D. (1974) Judgment under uncertainty: Heuristics and biases. Science 185, pp. 1124-1131.
100. Wagner, C. S. and Leydesdorff, L. (2005) Network structure, self-organisation and the growth of international collaborations in science. Research Policy 34, pp. 1608-1618.
101. Wakefield, A. J., Murch, S. H., Anthony, A., Linnell, J., Casson, D. M., Berelowitz, M., Dhillon, A. P., Thomson, M. A., Harvey, P., Valentine, A., Davies, S. E. and Walker-Smith, J. A. (1998) Ileal-lymphoid nodular hyperplasia, non specific colitis and pervasive developmental disorder in children. The Lancet 351:9103, pp. 637-641.
102. http://forbes.com/forbes/2005/0314/090_print.html — Weinberg, N. (2005). The dark side of whistle blowing
103. Wilmhurst, P. (2004) External checks must be imposed to protect the public. British Medical Journal 328, p. 230.
104. Wilson, K., Schreier, A., Griffin, A. and Resnik, D. (2007) Research records and the resolution of misconduct allegations at research universities. Accountability in Research 14:1, pp. 57-71.
105. Wocial, L. D. (1995) The role of mentors in promoting integrity and preventing scientific misconduct in nursing research. Journal of Professional Nursing 11:5, pp. 276-280.
106. Woolf, P. K. (1986) Pressure to publish and fraud in science. Annals of Internal Medicine 104, pp. 254-256.

107. Wright, D. E., Titus, S. L. and Cornelison, J. B. (2008) Mentoring and research misconduct: an analysis of research mentoring in closed ORI cases. Science and Engineering Ethics 14:3, pp. 232-236.
108. http://www.zeusinfoservice.com/reports/January23-2006-6.html — Zeus Reports. (2006). Another case of research falsification published by The Lancet

Author

Malhar N. Kumar, MD is a Consultant Orthopedic Surgeon, HOSMAT Hospital in Bangalore, India. Contact him at docmnkumar@gmail.com.

