
Research Misconduct — An Indictment and Possible Solution

by Hans Uffelmann

The core problems of scientific misconduct are systemic to the infrastructure of the conduct of scientific research itself, and therefore are probably immune to any short-term solutions. Renaming federal agencies, reorganizing monitoring activities, appointing new personnel, and other similar proposed remedies are necessary but insufficient measures. Indeed, the etiological factors in misconduct include an erosion of trust that stands in the way of the ethical integrity flowing from the major ethical principles identified in the Belmont Report. To make those principles applicable and useful to meet the challenges of current research activities, especially those involving human subjects, depends on our ability to foster an unprecedented cooperation of community resources.

Reports of research misconduct are not new or unique phenomena in the history of science. Indeed, serious deviations in the conduct of scientific investigation constitute important landmarks along the chronological evolution on the path of science and technology. Frequently, violations of established practices and precepts have elicited scorn, disapprobation, and sometimes ostracism from the scientific community of researchers who will eventually be celebrated as pioneers and founders of new ways in "doing science." Such achievements comprise significant turning points in the evolution of many scientific disciplines. The literature is replete with such instances, which serve frequently as reminders of the presence and role of creativity necessary to real scientific progress.

It is doubtful, however, that such explanation counts as a major factor in the recent and current proliferation of cases of scientific misconduct such as that involving seventeen-year-old Jesse Gelsinger, who suffered from a congenital liver disease that prevented him from metabolizing ammonia, a by-product of protein digestion. Jesse was

recruited on September 9, 1999, and enrolled in a nontherapeutic (Phase I) gene therapy trial conducted by the University of Pennsylvania. In September 1999, he experienced severe complications,

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allegedly related to the use of adenovirus particles used as vectors (i.e., gene transfer agents) in the experiment. Effects of the alleged adverse event quickly accelerated from nausea and pain, to coma, to multisystems failure, to respiration failure, and death. The family sued the University and its research team, including an internationally renowned biomedical ethicist.

The charges filed in court included among the cause of action wrongful death, strict products liability, intentional assault and battery, and an inadequate informed consent procedure. The case specifically cited the enrollment of a minor in a nontherapeutic study, the use of questionable procedures (e.g., the four-month shelving of material, which significantly reduced vector effectiveness), omission of over 100 adverse effects experienced in previous animal trials as well as in humans, a violation of the protocol's exclusion criterion, and

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a failure on the part of the principal investigator to disclose a conflict-of-interest (e.g., a possible financial gain worth about \$13.5 million from the sale of stocks invested in the sponsoring company, Genovo). The case alleged common-law fraud and was settled out-of-court in fall 2000. Terms of the settlement were not disclosed but the university discontinued genome transfer research and therapy.

The Gelsinger case serves as a vivid, albeit extreme, example of the nature of scientific misconduct that threatens to destroy the necessary collegial and public trust that furnishes the ethical moorings of science both as a professional pursuit and as a social institution. The incident also serves as a reference point to the discussion of ethical principles in research.

This essay will establish that the core problems of scientific misconduct are systemic to the infrastructure of the conduct of scientific research itself, and therefore are probably immune to any

short-term solutions. Renaming federal agencies, reorganizing monitoring activities, appointing new personnel, and other similar proposed remedies are necessary but insufficient measures. The etiological factors include an erosion of trust that stands in the way of the ethical integrity flowing from the major ethical principles identified and elucidated in the Belmont Report. Whether or not those foundational principles are applicable and useful to meet the challenges of current research activities, especially those involving the protection of human subjects, in an environment that requires the collaboration of academic, corporate, government and community entities, will depend on our ability to foster an unprecedented cooperation of community resources.

The author's methodological approach is the result of more than twenty-two years' experience as member and chair of several institutional review boards (IRBs), and acquaintance with the relevant literature and arguments in biomedical ethics during the past thirty-seven years.

What Is Scientific Misconduct?

The definition of scientific misconduct is open to much disagreement. Legal definitions are often too narrow and arbitrary, although they provide a safe haven to protocol-type decision making and are therefore preferred by administrators and bureaucrats. Beyond providing a short-lived psychological refuge, however, they lack cognitive value and their efficacy is limited to arbitrarily established taxonomic tasks.

On the other hand, so-called perfect definitions, whether stipulative or analytic, are also of questionable use primarily because they are noncognitive and arbitrary, or because their inherent redundancy renders them circular. Thus, to define scientific misconduct in terms of committing a breach of any number of specified sections enumerated in a code of professional or organizational prohibitions is not informative or helpful in the determination of the borderline cases that provide the most frequent and perplexing dilemmas.

Frequently, the characteristic features of scientific misconduct are described in terms of their op-

erational or functional manifestations. They are not perfect definitions in the sense of being exhaustive and final, and they carry with them a potential for change if sufficient evidence is presented. Therefore, the fear voiced by some scientists that any definition of scientific misconduct would inhibit, in fact eliminate, the element of creativity necessary for the conduct of scientific investigation is unfounded.

Before one capitulates in the face of seemingly complex and prohibitive definitional problems and obstacles, one should be mindful of the primary function of all definitions, namely, to reduce ambiguity in the language. Definitions are task-specific and contextual; they serve as a means to a more important end or goal, but they are not ends in themselves.

The current revised definition of scientific misconduct, which is used by federal agencies and established by means of soliciting suggestions and recommendations from scientists and laypersons, is sufficiently adequate for our present purposes. It states that

Misconduct in science is defined . . . as 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 judgment of data (CFR 56, 1993).

This definition avoids charges of "essentialism" and is sufficiently flexible to accommodate a variety of scientific misconduct while preserving an exercise of creativity on the part of scientists. For example, instances of misappropriation, misrepresentation, and interference as well as practices involving authorship and ethically questionable conflicts of interest are included while unavoidable potential errors inherent in all research activities are excluded. It is important to remember that the identification and assessment of scientific misconduct is primarily an epistemic and only secondarily a methodological problem and is always case-specific and contextual.

Instances of scientific misconduct are relatively rare, and the recent wave of disclosure is bound to exert a repressive, even paranoid, effect on scientists, especially during the present climate of historically unheard of activity and success. One might suggest, therefore, that focusing on occasional trespasses is counterproductive and damaging to the scientific effort as such. The relatively low incidence rate, combined with the admittedly wide-ranging degree of offenses, greatly diminishes detection, and certainly fails to end such behavior.

Such criticisms and concerns miss the point. It is unlikely that the exact incidence rate of scientific misconduct can be established with certainty.

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The nature of science precludes such determination. Other barriers to obtaining an exact estimate of the extent and severity of this problem include a reliance on largely anecdotal evidence, a continuing "conspiracy of silence" within the scientific community and its corporate and sponsoring institutions and interested stakeholders, denial on the part of perpetrators, and the often inadequate protection of whistleblowers.

The fact that such conduct is extremely personal and professionally sensitive, and morally and legally consequential conspires against disclosures. Finally, since the identification and validation of scientific misconduct requires establishing intent, the bar for meeting the criteria is raised considerably and further mitigates against the likelihood of success.

Whether or not we can establish the precise number of offenses, we know that there are fundamental dangers to the scientific enterprise inherent in

nefarious research practices. They threaten the collapse of the necessary ethical base on which science is built. The available reports in the literature and on the Internet provide sufficient cause for alarm and action.

Ethical Foundations of Scientific Research

The authority of science, as distinguished from other approaches taken in the pursuit of truth, relies heavily on a claim to objectivity. This attribute of science includes the achievement of methodological vigor, in the form of a standard methodology, an achievement of precision, the application of universal tools of verification, and the dissociation of personal bias on the part of the practitioner/investigator. As a matter of epistemic import, claims in favor of unbiased objectivity omit the presence and function of intuition, such as in "playing hunches," reliance on the indisputable and self-authenticating veracity of observation, even when controlled/or by empirical methods and other so-called venues to truth.

More important, however, is the realization that the very basis of scientific investigation requires a fundamental belief in the truth-value of scientific data which manifests itself throughout the course of scientific investigation and expresses itself in the need for intersubjective verification and validation, the replicability of results, the dissemination, and the general sharing of scientific conclusions with professional and public communities. Thus good science and good ethics are not only complementary, they exist in a symbiotic relationship. Science, like other human activities, is a social activity. It therefore requires a community to exist, strive, and survive. It cannot succeed in a social and communal vacuum.

The Aristotelian insight on which the bond between the individual and society rests, a realization of the limits of self-sufficiency and a reciprocity of needs, pervade the conduct of scientific research from the time of the investigator's education and training, through the selection of research topics all the way to dissemination and application of the fruits of the work. All these stages of the

work rely on the community's financial support and its creative nurturing. Without community, science and technology are barren and pointless activities. Mutual trust is the fabric constituting the core of this activity. Thus, the necessity of an ethical foundation for the responsible conduct of scientific research. Scientific misconduct is a breach of this ethical bond and cannibalizes the moral moorings of science and society.

Yet, the community's trust cannot be blind, unilateral, and passive — that is, undeserved. It manifests itself as integrity, which is a function of

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the necessary, though not always sufficient, ethical principles that constitute the moral core of responsible scientific research.

We acknowledge a long history of biomedical ethics in the form of prayers, credos, oaths, codes, and other guidelines and procedures designed to assure moral behavior, from the time at least as early as Hammurabi (ca. 2400 BCE), Hippocrates, Maimonides, and Percival, to the precursor of the "Current Opinions" issued by the American Medical Association over 150 years ago. Still, the elucidation of research ethics principles has only entered its sixth decade. It began originally as a result, a backlash, to the horrific atrocities committed in the name of science and by scientists under the Nazi regime. The Nuremberg Code is the first of a number of efforts to address the ethical problems pertaining specifically to research.

Research violations in the United States during the 1960s and 1970s further inflamed public sentiment and exerted sufficient political pressure on Congress to pass the National Research Act of 1974. Among other accomplishments, the National Research Act established the National Commission for the Protection of Human Subjects of Bio-

medical and Behavioral Research. The Belmont Report of 1978 is frequently regarded as the “Bill of Rights” of human research subjects and was strongly influenced by the World Medical Assembly’s 1964 Helsinki Declaration, which explicitly linked scientific research and ethics. The President’s Commission was also instrumental to the creation of a formal monitoring process which

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resulted in federally mandated regulatory agencies, including Institutional Review Boards (IRBs) subject to state and federal guidelines as well as institutional rules.

The principle of research integrity, based on the ethical value of trust, consists of a wisely conceived and executed balancing of the frequently conflicting and competing principles contained in the Belmont Report. They include respect for persons, beneficence, and justice (fairness). A similarity to the ethical principles elucidated by the Kennedy Institute at Georgetown University in the 1970s and referred to as the “Georgetown Mantra” is neither surprising nor accidental. The principles of autonomy, beneficence, nonmaleficence, and justice are grounded in the metaphysical concept of dignity or respect for persons. They comprise the basis of principlism as distinct from virtue ethics in contemporary biomedical ethics.

In the Belmont Report, respect for persons focuses on the characteristics of choice, together with its correlate, the assumption of responsibility for one’s choices and the implications attending this relative freedom of choice and accountability. Within the context of research ethics, it refers to the inherent value of “being human,” not for instrumental, pragmatic, or utilitarian reasons but on grounds of unconditional self-worth.

Thus, using a human research participant as a means to the achievement of an external goal such as the pursuit of individual or social goods, or because it is particularly suitable or convenient for specific research purposes, is contrary to the Kantian proscription: never use a human being as a means but only as an end-in-itself. Examples of this violation include, for example, the practice of fee splitting, which treats human beings as commodities. Other examples of respect violations include a failure to obtain adequate informed consent, incursions of privacy and breaches of confidentiality, and refusing to allow a subject to discontinue participation in a protocol at his or her request.

This enumeration of common research infractions is incomplete and only denotes instances of violations of the dignity or respect for persons principle. These failures, including failure to tell the truth, deprive participants of the knowledge and understanding they need to make informed choices. Collectively, they constitute irresponsible research behavior. Breaches of confidentiality and privacy constitute an invasion of one’s moral space. Therefore, the principles of respect for persons and autonomy are vulnerable to assaults and provide many opportunities for irresponsible scientific research. The burden of justification for overriding this principle rests with the perpetrator and may be defended in terms of beneficence or justice. In short, this principle requires information, comprehension, and voluntarism to fulfill the intent of the Belmont Report.

The etymological root of beneficence connotes “good” or “goodness,” and this principle focuses on the assurance that one’s ministrations, including one’s objectives, methodology, and study results will contribute to the well-being of participants in some way. Engagement in research with a maleficent intent is likewise a sign of irresponsible conduct. To conduct research while lacking expertise and skills endangers the well-being of the subject as clearly as if we were to use disproved or unprovable substances, procedures, or devices. Such reckless behavior is not in the best interest of the subject.

The intent to enhance the well-being of the subject raises the issue about whose well-being is to be served. Given the ubiquitous nature of this phenomenon, conflict-of-interest issues often arise. Beneficence is an important principle that establishes a favorable risk/benefit ratio and assures confidence in the investigator and the research project. This principle may be waived in some cases, mostly involving single or double-blinded studies and participation in controlled, placebo, and other experiments involving deception.

Ordinarily, the informed consent process and form include permission for participation in those phases of the study involving deception, and debriefing opportunities must be provided. Vulnerable populations, including but not limited to children and adolescents, must derive a demonstrable benefit from the study as at least one necessary condition for admission to the protocol. This requirement is one among many controversial topics of current discussion.

The principle of justice, in a wider sense, requires equitable distribution of risks and benefits in all places of scientific research, beginning with solicitation recruitment, observance of inclusion and exclusion criteria, consistent and fair determination of risk/benefit ratios, and informed consent procedures. Investigators must attend carefully to the worth of the participants' contribution, including the expenses one incurs and appropriate compensation. Compensatory considerations may extend beyond financial reward and may include therapeutic and emotional benefits even in the event that a therapeutic benefit had been excluded or declared unlikely.

The therapeutic misconception may entice subjects to enroll in studies for which they are not appropriate subjects. This practice raises serious questions about equity in the conduct of research. Such issues are especially relevant to studies involving vulnerable populations in experimental trials. Discriminatory recruitment and reward practices introduce a bias that threatens the application of the principle of distributive justice: the equal sharing of benefits and risks involved in scientific research activities.

Thus, selection and admission of particular persons, populations, or groups using extrinsic criteria or scientifically unjustifiable criteria invite discriminatory practices that are not only unethical but also constitute bad science by skewing the results. An obvious example is the traditional categorical exclusion of females of reproductive potential and other similarly unwarranted exclusions based on convenience, gender, race, age, lifestyle, or social and economic status. Prejudicial practices that are harmful or that cannot be justified scientifically violate the principle of justice. Vulnerable populations often represent the majority

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of victims. It is also noteworthy to observe that an uncritical and complacent attitude toward the prevailing mores of society perpetuates the status quo and thereby continues to validate such ethically reprehensible behavior.

Admitting the Primary Causes

A necessary first step toward preventing misconduct and rehabilitating the research community is to admit that the primary causes of the malady are endemic and systemic to the institution of science

itself and cannot be relieved by individuals and organizations working in relative isolation.

The problem is systemic because the etiological and presenting elements of the disease rest within the very organizational environment that provides, allows, supports, and expects to benefit from research activities — personally — and as individuals and members of the community. The symptoms of this moral corruption are manifest at every level throughout the structural maze, ranging from the immediate physical and psychological dangers presented by irresponsible scientists and the increased hazards of their work to the well-being of the subject/participant/patient, to the financial risks and perils that can damage the reputation of participating and sponsoring academic and corporate institutions.

Without this admission, the focus on the sources, practices, and consequences of irresponsible behavior is misdirected to an almost exclusive emphasis on individual perpetrators. Consistent with the usual administrative, regulatory, and bureaucratic mind-set, this investigative approach is appealing because it is simple and efficient; it thrives, moreover, on the powerlessness of individual agents while protecting the actual decision makers who direct and distribute research funding and activities. The continuing practice of shifting the administration, names, and titles of governmental agencies charged with the important fiduciary responsibilities relating to research involving human subjects signifies little more than political posturing. The revolving doors of administrative governmental regulatory agencies and institutional review boards attest to an extraordinary rate of turnover, and to cyclical reorganizational exercises in Washington, D.C., and among IRBs throughout the country.

The latest trend on the part of governmental regulatory and oversight agencies and ad hoc focus and task force groups appears to consist in the recruitment and appointment of past offenders and conspirators involved in research misconduct, somewhat analogous to rehabilitative methods employed by the criminal system and by some addiction counseling service agencies. Credentialed

as expert in the field mainly by virtue (no pun intended) of their past improprieties, their recruitment for educational and leadership purposes appears deceptively credible but raises serious concerns about propriety, role modeling, and quality in the realm of moral education.

Academic institutions and research centers are facing critical and increasingly severe decision-making dilemmas within a context of unprecedented change in the environment in which research must be conducted. Attributes that formerly served traditional scholarship well, such as a relative freedom from encumbrances from extra-institutional

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pressures (e.g., political, social, economic), and other pragmatic and increasingly utilitarian demands, have been eliminated. The ethos of intellectual and scholarly purity of motivation and action that once provided the academician with a relative degree of safety and impunity has also disappeared.

We are a society in the midst of a valuational crisis, one that makes instant multimillionaires of teenagers who have not even completed their high school education, and whose sole claim to fame rests on one-dimensional performances on the stage or athletic field. When otherwise ordinary individuals can receive \$47,000 each time they step up to hit a ball with a stick, and when political, religious, and in many cases, civic leaders engage in immoral conduct, it should come as no surprise that a similar state of affairs exists within institu-

tions of higher education and research. Intellectual and moral leadership is seldom in view, and we are losing sight of our proper goals — the arousal of curiosity, wonder, and doubt, the acquaintance with and the application of the basic rules of evidence, and being engaged in the pursuit of truth regardless of the consequences. In order to achieve those objectives, teachers and researchers who are duly credentialed experts must initiate, elicit, guide, nourish, and assess the individual and social processes of learning.

The principal “products” are persons who are appreciative, skilled, and competent to function both as responsible practitioners in their chosen

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field, and as educated citizens. The conduct of research in academic institutions has been a necessary critical process for both students and teachers. Thus, there is a high correlation and symbiotic relationship between teaching and research for the good of the individual and society. This special relationship distinguishes an academic research center from a corporate and industrial research institution. The primary product of the latter may be more tangible and more directly applicable to the immediate use of consumers, but it does not allow for “basic research.”

Administrators, in order to be optimally effective, must possess an expertise that educates and otherwise qualifies and credentials them to facilitate and care for the educational process and its members. In addition to a familiarity with the unique requirements of particular disciplines, administrators need strong systems and managerial

expertise and skills. The securing, distribution, and stewardship of adequate funding resources of personnel, equipment, and other necessary operational activities are among the primary responsibilities of particular administrators, especially the chief executive officer of the department, division, school, college, campus, or system in a typical academic institution.

The ultimate executive power and responsibility is, of course, vested in the governing board. Qualifications for membership to the governing board are rarely based on academic or professional credentials and experience in the field of education, particularly teaching and research. Social and economic status, and, at least in the case of public-supported institutions, political influence as well as name-recognition are the leading criteria. In some cases, the candidate will also have a history in the philanthropic community, membership in the correct religious group (in the case of theologically oriented institutions) and business acumen.

Conclusion

I offered this admittedly sketchy outline of the typical infrastructure of academic teaching and research institutions to establish the following points relevant to the present topic. Whenever faculty members, especially research scientists neglect, and thereby abdicate, their professional and institutional responsibilities or fail to report research misconduct, they violate the trust invested in them by their patient/subjects and the society that supports and relies on their work. Ethical insensitivity and breach of trust undermines the integrity of all research and constitutes a threat to unsuspecting subjects who placed their confidence in the investigator, institution, and process.

Whenever administrators fail to adequately support the conduct of responsible and safe research, they commit the ethical equivalent to aiding and abetting in research misconduct. Failing to provide adequate monitoring activities, sufficient support staff, and faculty participation on IRBs represents a disservice to the research community. And finally, failure to support IRB decisions and unresponsiveness to, or mishandling of, whistleblowers

are actions that make administrators coconspirators of those who engage in research misconduct. Both set a bad example to all those involved in research involving human subjects. Irresponsible faculty and administrators do not sufficiently realize the threat to themselves and to their institutions that can be incurred by a single case or even by the accusation of misconduct.

Whenever members of the governing board of an academic institution intervene in the conduct of research on behalf of special interest groups or by means of allowing administrators, staff, and faculty to provide an ethos of mutual distrust, they also become coconspirators to dangerous conduct,

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thereby undermining the ethical integrity of research conducted in and by the institution, a reputation that transcends particular investigators and research projects and sends a message to other academic institutions, corporate entities, and present as well as prospective private and governmental sponsors.

In an environment in which competitiveness and grantsmanship increasingly determine individual and institutional survival, many academic institutions force faculty members to become entrepreneurs, a role for which they are neither trained nor rewarded. Conflicts-of-interest that might otherwise be avoided result from this lack of training and experience.

Decreasing funding sources and the competitive nature of the research race greatly exacerbate the complexity of research opportunities and conduct, and spawn unthinkable alliances on a local, national, and international scale among competing institutions and research centers. Each one intends to maintain the research integrity needed to protect individual participants and the social good. However, none of them can, on their own, provide reasonable assurance that all of them will pursue ethically safe and responsible conduct.

The endeavor to provide integrative and cooperative oversight and integrity of purpose — precisely because it cannot be responsibly handled by institutions that are self-involved in research — reverts to the community. The expertise and proven accomplishments of nonprofit, interdisciplinary, and community-based organizations, such as Midwest Bioethics Center, have the integrity and, we hope, the detachment to help others solve the ethical dilemmas posed by the scientific and technological crises inherent in biomedical research and practice.

The Kansas City Initiative to Promote Integrity in Biomedical Research is a model for helping communities secure the ethical moorings of their research activities. Midwest Bioethics Center has picked up the challenge, but the outcome of the experiment depends on all of us and is not guaranteed.

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