

[Charles Peirce](#), the 19th century American philosopher, wrote in 1868: "The real [truth] is that which, sooner or later, information and reasoning would finally result in, and which is therefore independent of the vagaries of me and you. Thus, the conception of reality essentially involves the notion of a COMMUNITY, without definite limits, and capable of an indefinite increase of knowledge."

Anyone who is engaged in scientific inquiry recognizes their dependency on the prior work of others, the methods that others have validated, and the results from others that form the background section of any successful grant. Research misconduct and conflict of interest strikes at the heart of scientific objectivity, raising doubts about the integrity of the scientific enterprise and the extent to which we can trust in the work of others. It is for this reason that assuring the integrity of the scientific quest is an obligation each one of us assumes the moment we claim to be a scientist; that is, a member of the community that pledges itself to furthering our knowledge of "the real."

This third module examines the concept of scientific misconduct, reviews the policy and procedures regarding misconduct in research at CHOP, discusses the importance of eliminating conflicts of interest within the research enterprise, and briefly reviews the conflict of interest policies at CHOP. CHOP staff who have a University of Pennsylvania appointment are also subject to the conflict of interest policies of the University of Pennsylvania. Our collective goal should be to assure the objectivity of our research and to maintain the public trust by moving beyond a simple compliance with institutional policies to create and sustain a culture of integrity and responsibility.

Every institution that receives funds from any organizational unit located within the Public Health Service of the Department of Health and Human Services (for example, NIH) is required "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" ([42 CFR 50.101](#)). The federal definition of research misconduct is currently being revised, although the new definition has not yet been officially accepted ([Status Report](#)). The current definition for Misconduct or Misconduct in Science is "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" ([42 CFR 50.102](#)). The proposed definition is similar but adds more specification about the nature of fabrication, falsification and plagiarism.

According to the [proposed new definition](#) "research misconduct is defined as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results." The phrase "reviewing research" has been added to deal with a number of high-profile cases involving plagiarism that occurred during the pre-publication peer review process. Fabrication is defined as "making up results and recording or reporting them." Falsification is 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." Note here that the simple failure to report all results could be considered falsification. Plagiarism is defined as "the appropriation of another person's ideas, processes, results, or words without getting appropriate credit, including those obtained through confidential review of others' research proposals and manuscripts" ([64 FR 55722-55725](#)). Both the current and the proposed new definition recognize that there may be "honest error or honest differences" that should not be considered

research misconduct; however, the current definition refers to "interpretations or judgments of data," while the new definition talks of simply "opinion."

The CHOP Policy and Procedures regarding Misconduct in Research is based on the current, not proposed, policy ([45 CFR 50, Subpart A](#)). The process of investigating an accusation of research misconduct is similar between the current and proposed federal policy. The initial step taken by CHOP is to appoint an independent committee to make an "inquiry" to determine whether the allegation warrants an investigation. During this phase, the identity of the complainant remains confidential. If a formal investigation is warranted, a new independent committee is formed. It is during this phase that the respondent learns the source of the complaint. The proposed federal policy adds a third phase called "adjudication" during which actions are taken which "are appropriate to the seriousness of the offense."

The proposed federal policy also adds three conditions that are required for a finding of research misconduct. These three conditions are: "there be a significant departure from accepted practices of the scientific community for maintaining the integrity of the research record; the misconduct be committed intentionally, or knowingly, or in reckless disregard of accepted practices; and the allegation be proven by a preponderance of evidence." ([64 FR 55723](#)). The proposed policy also provides further specification for evaluating the "seriousness of the misconduct." Factors to consider include "whether the misconduct was intentional or reckless; was an isolated event or part of a pattern; had significant impact on the research record; and had significant impact on other researchers or institutions" ([64 FR 55724](#)).

There are two additional sections of the [CHOP Policy and Procedures regarding Misconduct in Research](#) that should be highlighted. First, the paragraph that defines research misconduct includes the statement: "Some forms of misconduct, such as failure to adhere to requirements for the protection of human subjects or to ensure the welfare of laboratory animals, are governed by specific federal regulations and are subject to the oversight of established Hospital committees. However, violations involving failure to meet these requirements also may be covered through the procedures discussed here governing misconduct in research." In effect, failure to adhere to the requirements for human subject protection may be considered research misconduct. Second, the range of actions that could be taken in response to a finding of research misconduct "include, but are not limited to, termination, suspension, loss of Hospital privileges, removal from a particular project, a letter of reprimand, special monitoring of future work, probation, or below average salary increases, including a zero salary increases, for one or more years." Although our stated ideal is that researchers should "establish and maintain the highest standards of ethical practices in their research," failure to abide by these practices is a "serious breach" of our research community.

Financial conflicts of interest and their impact on research has been a major national issue over the past year. This past August, a [conference was held at NIH](#) which specifically focused on the impact of an investigator's financial interests on the objectivity and findings of the research. It is likely that there will be new guidance or perhaps regulations from the federal government concerning this issue. The existing [Conflict of Interest policy at CHOP](#) can be divided into two main areas: conflicts of interest between an investigator and CHOP, and conflicts of interest which undercut the objectivity of the investigator's research. All investigators should be sure that they are familiar with the CHOP Conflict of Interest policy as well as [Attachment A](#), which deals with Conflicts of Interest in the Research Setting. The details of

the policy will not be presented as part of this module. Instead, some more general remarks and observations on the policy will be highlighted.

First, the conflict of interest policy applies to potential, perceived and actual conflicts of interest. Although a given situation may not create an actual conflict, one should avoid even a perception of potential conflict. Second, conflict of interest extends to include the investigator's family and/or persons with whom the investigator "maintains living arrangements approximating a family relationship." Third, specific guidance is given concerning gifts (do not accept any gift of more than nominal value from anyone who may do business with the Hospital), inside information, and outside interests and activities (including equity holdings). The CHOP policy defines as a conflict of interest any "ownership or management interest in any company that does, or seeks to do, business with the Hospital" to less than \$10,000 or no more than five percent ownership interest. In some case, even a lesser amount may create a conflict of interest. This threshold is also used in Attachment A concerning research conflict of interest to find a "significant financial interest." Fourth, the investigator is required to disclose at least annually all potential conflicts of interest.

The CHOP policy recognizes that there are special conflicts of interest that can arise in the research setting (Attachment A). Among other issues, the institution is interested in protecting "intellectual property rights" as well as any inappropriate restriction on publication or other research that an investigator would be permitted to pursue outside of any contractual agreement. However, the issue of conflict of interest in the research setting raises the question about the objectivity and integrity of the research. Research that is funded by either the [National Science Foundation](#) and/or the [Public Health Service](#) (including the [National Institutes Of Health](#)) requires the "disclosure and consideration of the financial interests of individuals involved in the design, conduct and reporting of such research" (Attachment A).

This concern about the impact of financial interests on the objectivity of scientific research is illustrated by the FDA regulations concerning financial disclosure by clinical investigators (21 CFR 54 and [63 FR 5233-5254](#)). The sponsor is required when submitting a marketing application for a drug, a device or biological product to submit a financial conflict of interest statement for each clinical investigator who participates in studies demonstrating either efficacy and/or safety (using [Form FDA 3454](#)). The concern on the part of the FDA is for the "reliability of the data." "FDA may consider clinical studies inadequate and the data inadequate if, among other things, appropriate steps have not been taken in the design, conduct, reporting, and analysis of the studies to minimize bias. One potential source of bias in clinical studies is a financial interest of the clinical investigator in the outcome of the study because of the way payment is arranged (e.g., a royalty) or because the investigator has a proprietary interest in the product (e.g., a patent) or because the investigator has an equity interest in the sponsor of the covered study" ([21 CFR 54.1](#)). It should be emphasized again that the FDA focus is on the integrity of the study data, not on the impact of financial conflict of interest on recruitment, disclosure to potential research participants, or other concerns that focus on the investigator/participant relationship. The FDA will accept a study design that "may adequately protect against any bias created by a disclosable financial interest" such as multi-institutional studies, "blinding, objective endpoints, or measurement of endpoints by someone other than the investigator" ([21 CFR 54.5](#)).

Only recently has the question of financial conflict of interest been raised in the context of the safety of individual research participants. At the recent NIH conference on conflict of interest, Dr. Jane Henney of the FDA observed: "If a crisis in confidence develops, if research subjects no longer feel safe, then medical research will grind to halt" (The Philadelphia Inquirer, August 16, 2000). Here, the question is not the integrity of the research, but the safety of the research participant.

The [American Society of Gene Therapy](#) (ASGT) recognized that the current policy of disclosure did not address the question of public confidence in the judgment of researchers. Accordingly, in April 2000, the ASGT adopted the following policy: "In gene therapy trials, as in all other clinical trials, the best interest of the patients must be always primary. International, national and institutional guidelines on standards of care must be rigorously followed, approved protocols strictly adhered to, serious adverse events promptly reported to all appropriate regulatory and review bodies. Relevant federally and institutionally established regulations in financial conflicts must also be abided by. In addition, all investigators and team members directly responsible for patient selection, the informed consent process and/or clinical management in a trial must not have equity, stock options or comparable arrangements in companies sponsoring the trial. The American Society of Gene Therapy requests its members to abstain from or to discontinue any arrangement that is not consonant with this policy" (Policy of the American Society of Gene Therapy on Financial Conflict of Interest in Clinical Research, Adopted April 5th, 2000).

Guidance and policy in the area of the impact of financial interests on the trust and protection of research participants is evolving. The policy of the ASGT may well be a harbinger of the future.