Conflicts of Interest

We often find ourselves in situations where two or more competing interests create the perception -- or the reality -- of an increased risk of bias or poor judgment. Such challenging situations come up regularly in both our personal and professional lives. Collectively, we refer to these as conflicts of interest. Such conflicts are not inherently bad. Indeed, they are to be expected. It's how they are handled that can lead to improper, inappropriate, or bad outcomes.

Scientists have professional, fiduciary, and ethical interests in the responsible conduct of research, but these interests may be compromised by personal interest. A common worry is that financial interest in the outcomes of research can result in unethical behavior or even criminal misconduct. However, it is also plausible that interests other than financial interests could compromise the responsible conduct of research. Examples of non-financial interests that might conflict with the integrity of science include career advancement, publishable results, service to patients or students, fame, power, or family and friendships. Another potential conflict can come in the form of conscience. An individual might suffer a conflict of interest if the mission or expectation of, for example, the institution is not compatible with his or her personal values.

Conflicts of interest are not merely a hypothetical problem. Financial conflicts are associated with altered outcomes of research. Stelfox et al. (1998) reviewed the literature in 1995 and 1996 for reports on the safety of calcium channel antagonists. They classified reports as being supportive, neutral, or critical of these drugs. They found that for reports supportive of calcium channel antagonists, virtually all authors had financial relationships with drug companies. However, only 43% of the authors of reports critical of the drugs had such connections with drug companies. Many different hypotheses might explain this trend, but it seems clear that it would be valuable to know if a published study was supported by industry.

A variety of regulations and guidelines govern the disclosure and management of conflict of interest. Although many concerns could be generalized to any form of conflict of interest, the focus of most regulations is financial. The most relevant of these are federal regulations, notably those of the Public Health Service (PHS) and National Science Foundation (NSF).

> PHS and NSF policies are substantially the same regarding conflicts of interest (PHS, 1995; NSF, 1995). Under PHS policy: '...investigators are required to disclose to an official(s) designated by the institution a listing of Significant Financial Interests ... that would reasonably appear to be affected by the research proposed for funding by the PHS.' The institutional official(s) are responsible to review 'those disclosures and determine whether any of the reported financial interests could directly and significantly affect the design, conduct, or reporting of the research and, if so, the institution must, prior to any expenditure of awarded funds, report the existence of such conflicting interests to the PHS Awarding Component and act to protect PHS-funded research from bias due to the conflict of interest.' Significant Financial Interests are defined to be: '...anything of monetary value, including, but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options or other ownership interests); and intellectual property rights (e.g., patents, copyrights and royalties from such rights).'

Federal regulations defer, in part, to institutional definitions of conflicts of interest. Not surprisingly, institutional standards vary greatly. Regarding stock ownership, many use the federally defined threshold of $10,000 or 5% of total shares as a definition of significant financial interest that must be declared. However, some institutions have been somewhat stricter. For example, Harvard scientists are prohibited from working for a company in which they have more than $20,000 in stock (Brainard, 2000).

Professional societies and journals are another important source for guidance on the management of conflicts of interest. These are quite variable in their scope and rarely enforced, but two examples are noteworthy. The first is a policy statement from the American Society of Gene Therapy (ASGT). In a statement adopted in April of 2000, the ASGT concluded that '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 supporting the trial.' (Woo, 2000). The second example is the stated requirements for publication in the New England Journal of Medicine. As early as 1984, the journal requested that 'all authors disclose to [the Editor] any associations they had with businesses that could be affected by their work -- including direct employment and consultancy, stock ownership, and patent-licensing arrangements.' (Angell and Kassirer, 1996). These guidelines and regulations represent a recognition by regulatory and scientific communities that the integrity of science is placed at risk by the presence of unmanaged or substantial conflicts of interest.

Conflicts of interest do not necessarily amount to research misconduct. However, if the potential for personal gain is great, then principles that guide responsible conduct in research may be compromised. The following are some things to consider.

Unavoidable Consequences: It is possible that the adverse consequences of conflicts of interest will eventually be partially mitigated by the structure of science. For example, false or misleading reports will be displaced by attempts to duplicate the flawed work. However, in practice, this strategy does not address the harms to subjects in clinical trials, misinformation entering the literature, and increased cynicism about science.

Unintentional bias: Conflicting interests might result in unintentional bias. For example, because research is expensive, the research interests of individual scientists are likely to drift toward those topics, methods, and approaches for which support is available. In the design of experiments, scientists may be unconsciously biased to choose, or stick with, approaches likely to provide 'marketable' findings, rather than those designed to increase basic understanding of mechanisms. In the collection of data, a researcher with significant financial interests may unwittingly introduce bias into enrollment of subjects for a clinical trial, into evaluation of data dependent on subjective judgments, or even into the reading of objective measurements. Finally, unintentional bias could alter choices about data selection, statistical methods, and presentation of results. Unintentional bias can be a more serious threat than deliberate misconduct, because even those who are biased would be unaware of the ways in which their behavior had been altered.

Misperceptions about scientists and science: When large sums of money are involved, it may be difficult for the public, legislators, the judicial system, and even colleagues to be convinced that results were not biased for personal gain. Perceived impropriety can result in consequences as damaging as if intentional misconduct had been committed. With increased media, governmental, and public scrutiny, a researcher's reputation, research funding, and employment can depend as much on perceptions of integrity as on integrity itself.

Disclosure usually occurs only for financial interests, and such disclosure is not routine in the biomedical literature (Krimsky et al., 1998). In a survey of 789 scientific papers published by Massachusetts scientists in the leading journals of cell and molecular biology, Krimsky and his colleagues contacted the authors and found that 34% of the articles had at least one Massachusetts author with a significant financial interest. Despite this high rate of financial interests, Krimsky et al.

reviewed 62,000 papers and found that only about 0.5% included disclosure statements. Unfortunately, even as financial conflicts and the risks for bias are increasing, the minimal expectation that those conflicts would be disclosed is not being met.

Responsibilities of Researchers

- Comply with regulations
  Researchers should ask about and adhere to institutional and governmental requirements for identifying, disclosing, and managing conflicts of interest.
- Avoid and minimize conflict
  Although it is not possible to avoid all sources of conflict, it is in the best interests of the scientific community and of individual scientists to recognize conflicts of interest and to take steps to nullify or mitigate those conflicts.
- Disclose interests
  If conflicts cannot be avoided, then those conflicts should be disclosed. At minimum, the institution and any other parties with a significant interest should be made aware of the extent and nature of the conflict.
- Manage conflicts
  Disclosure is often not enough. For every step of the research process, attempts should be made to isolate the conflicted individuals from all decision-making functions.
- Keep learning
  Both the potential for conflicts of interest and the strategies for dealing with those conflicts are evolving. Considering the potential for misperceptions of a researcher's motives, it is best to assume that good intentions are not enough. Seek out information so as to comply with the spirit and letter of current regulations.
- Be aware of the potential for conflicting interests to cause bias, or the perception of bias. Acknowledge that conflicts of interest increase the risk of both intentional bias (e.g., research misconduct) and unintentional bias.
- Conflicts of interest aren't inherently bad, but need to be acknowledged so that they can be handled properly

Case Study 1
Dr. Mitchell Conrad has received a grant from an industrial source to do basic research that has long-term implications for commercialization. A new graduate student, Michelle Lawless has just joined his lab following the completion of one semester of graduate coursework. Dr. Conrad outlines several projects that can be pursued by Michelle under this industrially-sponsored research program. Dr. Conrad indicates that there is a proviso listed in the industrial grant agreement which says that all material to be submitted for publication first be reviewed by the company. This review must always be completed within 120 days. Dr. Conrad points out that this presents only a minimal disruption to the normal publication process as compared to the unrestricted publication of material gathered under federal research grants. He also mentions that the positive aspects of working on this proposal include the fact that there is money in the grant for Michelle to travel to at least two meetings per year. Also the

grant application provides money for a personal computer that will be placed at Michelle's lab station while she is working on the project. Dr. Conrad emphasizes that working on the project will likely give Michelle an "inside track" with the company should she want to pursue job possibilities there following graduation. Michelle agrees to work on the project. Comment on the ethical and conflict of interest implications of this scenario.

Case Study 2

Dr. Wilkins has a modest research program supported by a grant from a local foundation. Wilkins brings a personal check for $3,000 into the office of Mr. Cole, the departmental administrator, and says that it is a gift which may be used by the department at the discretion of the chair. When Mr. Cole consults with Dr. Vaughn, he learns that Dr. Vaughn and Dr. Wilkins have already discussed this arrangement. Dr. Vaughn says she has agreed to let Dr. Wilkins spend this money as it will help him strengthen his research program to the point where he'll be able to successfully compete for federal grants. Over the course of the next several months Dr. Wilkins uses some of the money to purchase a new computer and printer which he installs in his home. He uses the remainder of the money to attend a meeting in his research field. At the end of the year Dr. Wilkins donates $5,000 to the department. Over the next several months he uses this money to attend two other meetings, and to pay for several subscriptions to scientific journals, and to an electronic database subscription. Comment on any conflict of interest considerations of this scenario.

Case Study 3

Mr. Asset, a graduate student of Dr. Bond, has been conducting physicochemical studies on the properties of a new polymer. The research is sponsored by Chemical Industries, Inc. and it is understood by Mr. Asset and Dr. Bond that the results are proprietary, confidential, and cannot be used in Mr. Asset's thesis. Mr. Cash, the technical liaison from Chemical Industries, Inc., meets with Mr. Asset and Dr. Bond and expresses his pleasure with the outcome of the recent studies and observes that the new results are the last data required to market a new generation of fire-resistant electrical insulating material. Mr. Cash further comments that this is the product that Chemical Industries, Inc. needed to regain its market share, and the stock of Chemical Industries, Inc. would soar once investors knew of the new product. That evening at dinner with his wife and brother-in-law, an investment banker, Mr. Asset tells them about Mr. Cash's enthusiasm about their recent research results and Mr. Cash's expectations that Chemical Industries' stock would greatly increase in value as soon as the new product was announced. The next day Mr. Cash's brother-in-law advises several of his clients to purchase Chemical Industries' stock. Did Mr. Asset breach his confidentiality agreement by discussing his research results with his wife and brother-in-law? Does Mr. Asset profit by the disclosure of the research results that will increase the value of the stock of Chemical Industries, Inc.? Discuss a scientist's responsibility for maintaining the confidentiality of research results.

Works Cited

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