Ambiguity, Trust, and the Responsible Conduct of Research

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ABSTRACT: *Ambiguity associated with everyday practice of science has made it difficult to reach a consensus on how to define misconduct in science. This essay outlines some of the important ambiguities of practice such as distinguishing data from noise, deciding whether results falsify a hypothesis, and converting research into research publications. The problem of ambiguity is further compounded by the prior intellectual commitments inherent in choosing problems and in dealing with the skepticism of one's colleagues. In preparing a draft code of ethics for the American Society of Biochemistry and Molecular Biology (ASBMB), an attempt was made to take into account the ambiguities of practice. Also, the draft code adopted trust as its leading principle, specifically the importance of trust as a condition necessary for there to be science. During revision of the code, the focus on trust was changed. The new orientation was on trust as a consequence of carrying out science responsibly. By addressing the obligations necessary to engender trust, the ASBMB ethics code not only sets professional standards, but also makes a clear statement of public accountability.*

INTRODUCTION

Discussions concerning responsible conduct of science often accept science as an objective, linear, methodological process, and fail to adequately take into consideration what doing science actually entails. In particular, there has been insufficient recognition of the ambiguity inherent in carrying out and reporting research and of the necessity for trust between investigators. This essay begins by outlining some important aspects of ambiguity and trust with reference to the problem of defining misconduct in science; then explains how I attempted to incorporate these ideas into

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the 1997 draft code of ethics written for the American Society of Biochemistry and Molecular Biology; and finally describes how and why the focus on trust was changed in the final version of the code adopted in 1998.

THE NORMATIVE STRUCTURE OF SCIENCE AND THE PROBLEM OF DEFINING MISCONDUCT

More than 50 years ago, Robert Merton described what he called "the normative structure of science".[1] Merton identified the institutional imperatives that comprise the ethos of science, namely, universalism, communism, disinterestedness, and organized skepticism. These imperatives were meant to describe "patterns of institution control" over the behavior of scientists, patterns to which scientists were expected to conform. Rather than personal moral integrity, Merton attributed "the virtual absence of fraud in the annals of science" to this institutional control. That is "the activities of scientists are subject to rigorous policing, to a degree perhaps unparalleled in any other field of activity".[1 (p. 276)]

The effectiveness of this policing came under scrutiny, however, beginning in the late 1970's as a result of several well-publicized cases of fraud in science. Beginning with Congressional Hearings in 1981, a deluge of workshops, commissions, and reports attempted to understand and respond to misconduct. It quickly became evident that there were few effective, external mechanisms to deal with fraud when the "rigorous policing" embodied in the institution of science itself failed.

As new mechanisms for dealing with fraud evolved, the scientific community found itself unable to reach consensus on how to define misconduct in science. While there was general agreement that fabrication, falsification, and plagiarism (FF&P) should be included, the legal definitions of misconduct established in 1989 by Health and Human Services and in 1991 by the National Science Foundation also contained a clause about "other practices that seriously deviate from those that are commonly accepted in the scientific community".[2, 3] The serious deviation clause was opposed by the Federation of American Societies for Experimental Biology and the Committee on Science, Engineering, and Public Policy (COSEPUP) of the National Academies.[4] Those who opposed the clause argued that misconduct should be limited specifically to FF&P.[5] Those in favor, believed that fabrication, falsification, and plagiarism were not meant to stand alone, but were examples of serious deviations.[6]

Subsequently, the Congressionally-mandated Commission on Research Integrity (CRI) attempted to correct deficiencies in the previous definition and proposed a new and expanded version based on *misappropriation, interference, and misrepresentation.*[7] The CRI definition failed to win broad support, however, and at the time of writing of this essay, a Government-wide definition of misconduct is being developed (see Francis, pp. 261-272, this volume).

AMBIGUITY IN THE PRACTICE OF SCIENCE

One explanation for the difficulty encountered by the scientific community in reaching a consensus on how to define misconduct is the ambiguity inherent in the practice of science. This essay outlines some of the important parameters of ambiguity. Readers who wish a more detailed introduction to these ideas should consult previous works.[8,9]

The problem that ambiguity poses is implied in COSEPUP's report on responsible conduct of science when it states: "The selective use of research data is another area where the *boundary between fabrication and creative insight may not be obvious*" (my italics).[4 (p.29)] The idea that one might be unable to distinguish fabrication from creative insight suggests a picture of science in which ambiguity can confound the logical, clearly defined process emphasized in the traditional view. The traditional view, however, is hypothetical rather than actual practice. As outlined below, ambiguity is important in all aspects of research.

Distinguishing data from noise: In research at the edge of discovery, the difference between data and noise often is not obvious. Discovery at the forefront of knowledge requires learning to recognize something when one doesn't know beforehand what it looks like. Choosing what counts for data will depend on an investigator's experience and intuition—in short, his/her creative insight. By way of contrast, in a pre-approved clinical trial, researchers agree in advance what will count for data, and what a positive or negative result should look like. The pre-approved clinical trial provides a closer fit to the traditional view of science than does research at the edge of discovery.

Deciding whether results falsify a hypothesis: Carrying out an experiment requires one to anticipate what the results will be like and to choose methods suitable to observe them. Stated in another way, the choice of methods limits the results that can be obtained. Results that appear to contradict expectations might indicate either that the hypothesis was wrong or that the choice of methods was inadequate. These alternatives have led to the commonplace adage not to give up a good hypothesis just because the data do not support it.

Converting research into published science: Research projects evolve though a series of heuristic experiments (learning something new—often how not to do the experiment) and demonstrative experiments (suitable for presentation to the scientific community). In publications, only a small proportion of the experiments are selected, and these are woven into a coherent story often completely unlike the actual historical process, a story whose plot is none other than *the scientific method*. Nobel Laureate Sir Peter Medawar objected to this distortion of the adventure of science when he asked the question: *Is the scientific paper a fraud?*[10] Medawar's question emphasizes the problem that outsiders to the scientific community may have when they try to evaluate the "truthfulness" of scientific publications.

The above examples focus on the ambiguity inherent in carrying out and reporting the results of research. Related to this ambiguity are the inherent intellectual commitments that make problematic the common attribution of objectivity to individual researchers, as outlined below.

Choosing problems: Choosing a problem means committing oneself to the belief that there is a question unanswered; that answering the question would be worthwhile; and that it would be possible to successfully answer the question. Making wrong choices results in using up one's limited resources (e.g., time, money, and personnel), losing one's opportunity to contribute to science, and possibly losing one's career in science. At the very outset of a research study, therefore, investigator objectivity is challenged by initial commitments.

Dealing with the skepticism of one's colleagues: To succeed, researchers often must become advocates for their work, attempting to persuade their colleagues of its validity. The same features that make a hypothesis important and exciting -- novelty and unexpectedness—often lead the community to resist the idea because it contradicts prevailing beliefs. Success in overcoming this resistance requires commitment in the face of skepticism and rejection (for instance of research papers and grants). The need to become an advocate for one's work further undermines investigator objectivity. Thus, while individuals may aim to be objective, the true source of objectivity is embedded in the social structure of science.

In summary, rather than a clearly defined, always logical process, the everyday practice of science is typically characterized by ambiguity and inherent intellectual commitments that affect every aspect of doing experiments and publishing results. The pervasiveness of this ambiguity explains why sometimes "the boundary between fabrication and creative insight may not be obvious". Also, it makes it evident why truthfulness and fairness, which CRI attempted to adopt as leading principles in its treatment of misconduct,[7] cannot be applied to the practice of science in any simplistic way. In recognition of the ambiguity inherent in science, the ASBMB's code of ethics (Appendix B, p. 214) attempts to avoid oversimplifications. For instance, it states that "investigators will represent their best understanding of their work in their descriptions and analyses of it."

THE PRELIMINARY DRAFT OF THE ASBMB CODE OF ETHICS

In the fall of 1996, Howard Schachman decided that the ASBMB Public Policy Committee should develop a code of ethics for possible adoption by the society and asked me to prepare a preliminary draft. At that time (and now) Schachman was chair of the committee, and I was one of the committee members. Adopting a code of ethics is an important way in which professional societies can promote responsible research practices, and the process of developing a code requires members to focus their attention in an explicit manner on matters that often remain implicit. The challenge was to develop a code that would provide a moral standard against which researchers would be able to judge their own behavior and that of their peers, and at the same time a code that would be consistent with everyday practice of science.

As described by Frankel,[11] a code of ethics can be aspirational, educational, or regulatory. Aspirational codes present ideals towards which one should strive. Educational codes add explicit guidelines for achieving these ideals. Regulatory codes present detailed and (presumably) enforceable rules of behavior along with sanctions for non-compliance.

Schachman and I agreed that the ASBMB code of ethics should aim primarily to be aspirational and definitely not regulatory. We believed that an aspirational code was more likely to achieve a broad consensus than a regulatory code, and achieving consensus was a concern given the problems that the scientific community had with defining misconduct. An aspirational code also would advance educational opportunities by promoting discussion both within the society, and within the diverse institutions where society members carry out their research.

A regulatory code, on the other hand, was likely to generate controversy not only because of disagreements over regulatory details, but also by opening the society to receipt of allegations regarding questionable conduct by its members. Both by custom and Federal policy, investigation and legal resolution of alleged misconduct cases, at least initially, take place in the research institutions where the events occur. Even with the legal capacity to investigate charges and impose sanctions when appropriate, research institutions have found dealing with allegations of misconduct a formidable task. By avoiding a regulatory code, we would avoid putting the society in the potential position of itself becoming an investigatory body.

Before beginning to draft the ASBMB code, I consulted several other ethics codes: American College of Neuropsychopharmacology, American Federation for Clinical Research, American Physical Society, American Society of Microbiology, Ecological Society of America, and the Chemist's Creed (all brought to my attention by Mark Frankel, Director of The Scientific Freedom, Responsibility and Law Program at the American Association for the Advancement of Science). Some of these codes begin with a preamble stating the mission of the society followed by a commitment to leading ethical principles. I decided to use a similar format.

TRUST BETWEEN INVESTIGATORS AS AN ASSUMPTION NECESSARY FOR DOING SCIENCE

The preliminary draft code (Appendix A, p. 213) began with a preamble that focused attention on trust as the fundamental principle of science. Subsequent sections of the proposed code specified elements of trust between the public and researchers, between researchers, and between trainees and researchers.

Analysis of the importance of trust in science often focuses on the question of what makes research trustworthy.[12] I had something else in mind. Selecting trust as a fundamental principle of science reflected my belief that trust between investigators is *a prior commitment necessary before there can be science*. At first sight, this notion might seem unusual given the institutional imperative of organized skepticism as described by Merton.[1] Such skepticism is reflected in the motto of the Royal Society, *Nullius in verba*, which Sir Peter Medawar translated: “Don’t take anybody’s word for it;”[13] or as inspired by Jean Shepherd,[14] *In God We Trust, All Others Bring Data*.

“Don't take anybody's word for it,” however, refers only to questioning the quality and importance of experimental work. Even if one believes that the data in published papers or in submitted manuscripts are wrong (e.g., artifactual), one begins by accepting it on faith that the data come from experiments that actually were carried out and results that actually were obtained.[8] As Michael Ruse puts it:

> (I)n science, you have got to have trust. You simply cannot spend your time checking everybody’s experiments and calculations. When you submit a paper to a journal, you have no choice but to accept that the editor and the referees will not use your work to their own ends . . . The editor in turn must assume as a norm that a paper submitted is by the person or persons on the title page—that there has been no plagiarism, for example—and also that the results are not simply a function of creative imagination. . .
> (*Evolution Biology and the Question of Trust*, unpublished)

The assumption that peer-reviewers will not use others’ submitted work to advance their own ends deserves further comment. Peer-reviewers in science typically are experts in the same field as is the work under review. While they are in the best position to offer an informed opinion about the quality of the work, they also are in the best position to take advantage of advance knowledge. Consequently, the level of trust in the peer-review process is unparalleled in any other field of activity (to use Merton’s standard).

Translated into the game of poker, peer-review is like showing your competitors your cards—possibly even asking their advice—with the expectation that they will continue to play their own cards as if they had never seen yours. Carrying the poker analogy further, one might question whether players would indeed still be able to play their cards the same once they had seen those of their competitors. Clearly, this is highly unlikely if not impossible. When investigators act as peer-reviewers they are bound to be affected by what they learn.

CHANGES IN THE CODE OF ETHICS DURING THE REVISION PROCESS

The preliminary draft of the code of ethics was completed in January 1997 and distributed to other members of the ASBMB public policy committee. Subsequent meetings and communications between members of the committee as well as the ASBMB council occurred during 1997, and the final version of the code (Appendix B) was adopted by consensus in early 1998, made public and available on the society’s web page,[15] and distributed through the society’s newsletter.[16]

During the revision process, the major points in the preliminary draft stayed intact, but many were clarified, and negative statements were reworded as much as possible into a positive format. Also, an explicit commitment was added to promote cultural diversity in the laboratory. The most substantial change, however, was the complete reorientation of the notion of trust in relationship to responsible conduct. Unlike the preliminary draft, in which trust was presented as a prior assumption necessary for science, the final version of the code understands trust as a consequence of carrying out science responsibly. This is made explicit in the preamble where the ASBMB "encourages its members to engage in the responsible practice of research *required for such trust by fulfilling the following obligations*" (my italics). The remainder of the code then details the obligations of investigators to the public, to other investigators, and to trainees.

By placing the focus on obligations necessary to engender trust, the ethics code not only sets professional standards against which individual researchers can judge their own behavior and that of their peers, but also presents a clear statement of public accountability. In this way, professionalism and public accountability are brought together, a combination that advances public trust.[11]

Orienting the code of ethics towards public trust was important given the history of the scientific community's response to allegations of misconduct, which often has been criticized. Members of the community have argued, for instance, that the occurrence of fraud does not undermine progress in science, pointing to peer-review and the self-correcting nature of science as protection against not only error, but also fraud, the former occurring much more frequently than the latter. This limited perspective, however, misses the point of view of those most concerned with guarding the public trust, a point made clear when (then) Congressman Albert Gore opened the 1981 Congressional Hearings on *Fraud in Biomedical Research*:

> At the base of our investment in research lies the trust of the American people and the integrity of the scientific enterprise. If that trust is threatened ... then not only are the people placed at potential risk, but the welfare of science itself is undermined.[17 (p. 1)]

CONCLUSIONS

Promoting responsible conduct of science requires a clear description of what doing science entails. Science traditionally is presented as a linear, methodological process carried out by objective observers, a view that fails to adequately take into consideration the ambiguity inherent in carrying out and reporting research and the intellectual commitments of investigators necessary for carrying out these activities. The presence of this ambiguity has confounded attempts to reach consensus on how to define misconduct in science.

Doing science also depends on trust between investigators. Trust is a prior condition necessary for there to be science, and events that destroy this trust undermine the operations of the scientific enterprise. In this regard, financial conflicts-of-interest may potentially be even more harmful to continued trust than misconduct. When, for instance, researchers' intellectual "property rights"[1] become financial rights under the influence of patents and equity holdings, then the communal ownership of science disappears, secrecy replaces openness, and sharing research materials becomes a problem rather than an expectation.[18]

Finally, trust has broad implications for the relationship between science and society. The final version of the ASBMB code of ethics focuses on this relationship by recognizing public trust as the consequence of responsible conduct of science.

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APPENDIX A
PRELIMINARY DRAFT CODE OF ETHICS
American Society for Biochemistry and Molecular Biology
January, 1997

Members of the ASBMB are engaged in the quest for knowledge in biochemical and molecular biological sciences with the ultimate goal of advancing human welfare. Underlying this quest is the fundamental principle of trust. The ASBMB encourages its members to adhere to the fundamental principle of trust as described below and engage in the responsible practice of science that fulfills this trust. Trust and responsible practice are essential to the ongoing pursuit of science in the service of human welfare.

The public (and its representatives) trust:

> that researchers will seek to avoid and discourage practices that might harm the public interest or well-being.
>
> that researchers will use public funds appropriately for the purposes granted or contracted;
>
> that researchers will follow government and institutional requirements regulating research such as those insuring the safety of human and animal subjects and the environment;
>
> that research findings made possible by public funding will be reported openly in the scientific community and not kept secret;
>
> and that unique materials developed through publicly-funded research will be shared with other researchers in a reasonable fashion;

Researchers trust:

> that experiments reported by others will actually have been carried out;
>
> that the description and analysis of research will represent an investigator's best understanding of his/her work;
>
> that experimental details provided will accurately reflect methods used;
>
> that researchers will not report the work of others as if it were their own;
>
> that in their publications, researchers will acknowledge relevant previous work by others;
>
> that submitted manuscripts and grants will be treated by referees as personal and confidential and not used inappropriately or communicated to others;
>
> that financial and other interests will be disclosed that might present a conflict-of-interest in the various activities in which researchers engage such as reporting research results, serving as referees, and mentoring trainees.

Finally, trainees trust

> that the researchers in whose laboratories they work will act as mentors;
>
> that they will receive training and experience to advance their scientific skills and knowledge of ethical research practice as well as appropriate help in advancing their careers;
>
> that their research contributions will be recognized;
>
> and that the results of their research will not be subject to hidden limitations regarding publication.

APPENDIX B

CODE OF ETHICS
American Society for Biochemistry and Molecular Biology
January, 1998

Members of the ASBMB are engaged in the quest for knowledge in biochemical and molecular biological sciences with the ultimate goal of advancing human welfare. Underlying this quest is the fundamental principle of trust. The ASBMB encourages its members to engage in the responsible practice of research required for such trust by fulfilling the following obligations.

In fulfilling OBLIGATIONS TO THE PUBLIC, it is EXPECTED that:

investigators will promote and follow practices that enhance the public interest or well-being;

investigators will use funds appropriately in the pursuit of their research;

investigators will follow government and institutional requirements regulating research such as those ensuring the welfare of human subjects, the comfort and humane treatment of animal subjects and the protection of the environment;

investigators will report research findings resulting from public funding in a full, open, and timely fashion to the scientific community;

and investigators will share unique propagative materials developed through publicly-funded research with other scientists in a reasonable fashion.

In fulfilling OBLIGATIONS TO OTHER investigators, it is EXPECTED that:

investigators will have actually carried out experiments as reported;

investigators will represent their best understanding of their work in their descriptions and analyses of it;

investigators will accurately describe methods used in experiments;

investigators will not report the work of others as if it were their own;

investigators in their publications will adequately summarize previous relevant work;

investigators acting as reviewers will treat submitted manuscripts and grant applications confidentially and avoid inappropriate use;

and investigators will disclose financial and other interests that might present a conflict-of-interest in their various activities such as reporting research results, serving as reviewers, and mentoring students.

In fulfilling OBLIGATIONS TO TRAINEES, it is EXPECTED that:

investigators serving as mentors will provide training and experience to advance the trainees' scientific skills and knowledge of ethical research practices;

investigators will provide appropriate help in advancing the careers of the trainees;

investigators will recognize research contributions of the trainees appropriately;

investigators will encourage and support the publication of results of trainees' research in a timely fashion without undisclosed limitations;

and investigators will create and maintain a working environment that encourages cultural diversity.