Book Review

Responsible Conduct of Research

Adil E. Shamoo and David B. Resnik, 345 pages +viii, ISBN 0-19-514846-0, Oxford University Press, New York (2003), $29.50 softcover.

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In an article published in the *New York Times* on November 29, 2006, Nicholas Wade reported on the 2004 and 2005 fabrications of the South Korean stem cell researcher Dr. Hwang Woo-suk that were published in the journal *Science*. Gerald Schatten of the University of Pittsburgh was the first author of one of the publications even though he had conducted none of the experiments described in the publication. Both publications were subsequently retracted. These fraudulent publications were not detected by safeguards in the scientific process, but by a whistle-blower in Dr. Hwang's laboratory who broke the story to the South Korean television station MBC.

One consequence of this egregious aberration of conduct of research was the formation of a panel led by John I. Brauman at Stanford University. The panel recommended four changes in the review policy of *Science*: (1) a risk-assessment method should be developed to flag high-visibility manuscripts for additional review and scrutiny, (2) authors should identify their unique contributions to a manuscript, (3) more raw data in support of the publication should be contained in an online site, and (4) leading science journals including *Science* and *Nature* should develop common standards for review in order to prevent deceitful authors from favoring journals with lower review standards.

Perhaps there is the necessity for another commandment for researchers: Thou shall not deceive or engage in duplicitous behavior. This statement means that scientists must not fabricate, falsify, or misrepresent data or information. A closely related topic is that of bias; scientists should strive to avoid or at least to minimize all forms of bias in their work. In the same ethical category is the failure to acknowledge the relevant work of others.

Another egregious ethical offence is the act of plagiarism in which an individual knowingly or unknowingly claims to be the originator of someone else's words, ideas, or images. Since the ethical problem of plagiarism is so often discussed I present a standard definition. Plagiarism is the representation of someone else's ideas, words, images, or concepts as one's own. Both plagiarism and underserved authorship are examples of violations against the principle of fairness, which is one of the foundations of responsible conduct of research.

Recent advances in biotechnology and biomedicine continually generate new ethical concerns and questions. Historically the patent system was conceived and developed to protect mechanical inventions, processes, machines, manufacturing methods, and the composition of matter. All of these classes are tangible. Patents related to the genome are different: they involve not only molecules, but new information. During an initial period in genomic research and the rapid rise of biotechnology, the United States Patent and Trademark Office (USPTO) granted patents on sequences of bases (information). New and difficult ethical problems emerge when we attempt to patent DNA sequences as well as living organisms. As shown in the recent Supreme Court rulings it is possible to patent a product of human ingenuity, but not a product of nature. Many new contentious cases involve discoveries and inventions in the field of molecular biology that were made in university and government laboratories. In the Clinton administration the USPTO had new and more restrictive rules: the patent must show a "clear, substantial and specific" utility for their application.

The key ethical question for scientists is usually of the form "What should I do?" These questions are in the areas of ethics and affect researchers, clinicians, and our entire society. Why are ethics important or even relevant for scientists? The process of science occurs in a social context; science is a cooperative process that is based on cooperation, collaboration, and trust among its researchers. Trust is also fundamental to the relationship between scientists and the public. Failure to ensure this continuing trust can cause an erosion of public support for science.

Scientists must conduct their research in compliance with numerous applicable statutes, regulations, and guidelines. Scientists are subject to a wide variety of laws, rules, and policies. Research is protected intellectual property, but it is disseminated in international journals, through the World Wide Web, and at international conferences. Science is a truly international endeavor. There are several levels of law that are applicable: international law, national law, state law, local ordinances, rules and policies of scientific organizations, policies of colleges and universities, and rules of corporations and foundations. Are not these statutes, regulations, and guidelines sufficient for researchers to perform ethically the practice of science?

So why is responsible conduct of research (RCR) training necessary? Principles and guidelines can help the researcher to identify what actions are ethically desirable and which actions are ethically incompatible, but researchers still face many difficult decisions in their professional lives. For the individual researcher there are numerous pressures that impinge on their research: economic, political, social, cultural, and religious. Responsible conduct of research is not self-obvious; therefore, it is imperative that everyone involved in research, principal investigators, postdoctoral students, gradu-

ate students, technicians, and staff receive comprehensive education in RCR.

In support of this noble educational objective we are fortunate to have an excellent textbook and guide, *Responsible Conduct of Research*, written by Adil Shamoo and David Resnik. This book provides numerous real-life scenarios that pose the question "What should I do?" to stimulate critical thinking, honest debate, and public discourse. *Responsible Conduct of Research*, a seminal book, shows us through insightful argument and critical discussion how we may avoid scientific misconduct and conduct research in an ethical manner by learning the principles of responsible conduct of research.

Adil Shamoo, PhD, founded and is the editor-in-chief of the journal *Accountability in Research*. In 2000, Dr. Shamoo was appointed to the National Human Research Protections Advisory Committee. He is a member of the graduate faculty of Applied Professional Ethics at the University of Maryland, Baltimore. Dr. Shamoo has been teaching since 1991 a graduate course on "Responsible Conduct of Research." He chaired nine international conferences on ethics in research and human research protections and testified on this issue before congressional committees and the National Bioethics Advisory Commission. He chaired (2004–2006) the Ethics and Regulatory Forum of the Association of Clinical Research Professionals. David Resnik, PhD, is a philosopher and ethicist. He is currently a professor of medical humanities at the Brody School of Medicine at East Carolina University. He is the author of *The Ethics of Science: An Introduction* (1998) and a co-author of *Human Germ-line Gene Therapy: Scientific, Moral, and Political Issues* (1999).

I will pose three questions and then I will attempt to answer them. First, why should the readers of the *Journal of Biomedical Optics* (JBO) be concerned and be interested in the book, *Responsible Conduct of Research*? Second, why is this book useful to the readers of JBO? Third, what features of *Responsible Conduct of Research* support my recommendations in response to the previous two questions?

The answer to the first question is simply that when conduct of research is not responsible it undermines the basic fabric of the scientific process (trust, truth, transparency, open communication of results, and fairness) and destroys public trust in the process of science and therefore the work of scientists. Science occurs in a social context and therefore scientists have an obligation to maintain the support and the trust of the public.

The training of scientists at both the undergraduate and the graduate levels does not typically include explicit instruction on the responsible conduct of research. The lack of such formal training can result in scientific misconduct. The Office of Research Integrity (ORI) provides scientists with its definition of scientific misconduct: "fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted with the scientific community for proposing, conducting, or reporting research, it does not include honest error or honest differences in interpretations or judgments of data." ORI maintains a Web site that contains additional useful guidelines and federal policies (http://ori.dhhs.gov/).

In 2000 the ORI presented a recommendation that mandated education and training in RCR for all individuals involved in research that is funded by the U.S. Public Health Service (USPHS). The recommendations are applied to both grants and contracts, and include the principle investigators, postdoctoral students, graduate students, and technical staff. The ORI report listed nine basic areas for RCR education as well as continuing education and these recommendations are implemented in the *book Responsible Conduct of Research*.

Without uniform, systemic, and comprehensive training, scientists are devoid of the tools to respond to the question "What should I do?" *Responsible Conduct of Research* provides an excellent textbook and guide for university courses as well as individual study and learning about this important topic. Readers as well as contributors of JBO would gain from perusal of this book and their subsequent practice of science that is consistent with the concepts described therein.

Finally, I address the content and the pedagogical features that prove to be so useful, important, and critical for scientists. Shamoo and Resnik have developed an integrated format of guidelines combined with key questions and the presentation of case studies that stimulate thought and promote class discussion. They cover the broad topics of human and animal experimentation, the social responsibility of scientists, and questions of research funding and conflicts of interest in peer review and publications and scientific presentations. While the authors' primary focus is on biomedical research (in line with the topics published in JBO) they also present materials on the ethical aspects of keeping appropriate laboratory records (all entries in laboratory notebooks should be made legibly with permanent, nonerasable ink and signed and dated), the design of experiments, proper citation and attribution in written and oral scientific communication, and the decision of authorship. The authors also provide clear and informative sections on peer review, intellectual property, authorship, and conflict of interest of scientists.

The chapter on intellectual property will appeal to JBO readers who are in the process of filing, or intend to file, patent applications. In addition to presenting a concise but useful discussion of patents, trademarks, the ownership of research, and several intellectual property court cases, the authors present more controversial cases such as those involving patents on biological materials. They also discuss the Bayh-Dole Act that was amended by the Technology Transfer Act of 1986. These laws encourage individuals and companies to commercialize the research that was supported by government funds.

It is of historical interest that intellectual property laws in the United States derive from Article 1, Section 8 of the U.S. Constitution (1787), which states that Congress shall have the power to "promote the progress of science and useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries." In order to obtain a U.S. patent an individual must file an application with the USPTO. Inventors have exclusive rights to their

invention for a period of 20 years from the filing date of the patent application. The criteria to award a patent include: the invention is a product of human ingenuity, the invention is new or innovative, the invention is nonobvious to an individual in the discipline, the invention must have a practical use, and the applications must describe the invention in enough detail so that a person trained in the field could make and use the invention. Note that even when a U.S. patent is granted a court can overturn the patent if it can be shown that it was not correctly granted or that relevant prior art is discovered to demonstrate that the invention is not new. A good example is the invention of the two-photon excitation microscope for which the patents were contested in both Europe and the United States.

Copyrights are another area in which the readers and contributors of JBO are familiar. Copyrights are exclusive rights given by the U.S. government to authors of original works such as books, papers, software, movies, and artistic works. The authors can make copies, perform the work, and sell and distribute copies of the works. Anyone other than the holder of the copyright that performs these acts without the specific permission of the holder of the copyright violates the copyright. For example, when we publish a paper in a scientific journal (JBO) the author signs a form that transfers the copyright to the publisher. There is a very important exception and that is the idea of fair use. This doctrine states that it is permissible to copy the author's work in whole or in part without the author's permission if the copy is to be used for personal, educational, or research purposes.

Science is a cooperative process and occurs in a social environment; therefore, the introductory chapter discusses the historical, philosophical, economic, political, and legal aspects that impact science and scientists. Over one half of the book is devoted to the following topics, which reflects their growing importance in the practice of modern research: conflicts of interest (COI), collaboration between academia and private industry, the use of human subjects in research, the use of animals in research, genetics and human reproduction, and the role of scientists in society.

Recently several major medical journals have made financial disclosure mandatory for publication of papers involving clinical studies. This initiative followed the disclosure that the majority of papers dealing with medical devices or clinical studies were written by individuals with financial ties to the company that produced the device or the drug. I concur with this policy and opine that JBO should follow the financial disclosure policy of such journals as the *New England Journal of Medicine* and the *Journal of the American Medical Association* that require financial disclosure prior to acceptance of papers for publication. The National Institutes of Health require their authors and researchers to disclose conflicts of interest. It is noteworthy that after the Watergate scandal, the U.S. Congress passed the Ethics in Government Act, which also requires financial disclosure.

As more and more universities form contracts and cooperative agreements with private industry there is continuing debate about the resulting ethical issues. The basic goals of colleges and universities and private corporations differ. The goals of the former include the education of students, the advancement of human knowledge, and the provision of public service. The goals of the latter are to produce wealth; however, they can also include the advancement of knowledge and the improvement of the world. A major difference is that private corporations have obligations to their stockholders and they compete with other corporations in the market. *Responsible Conduct of Research* guides the reader through the conundrums of individual COIs, institutional COIs, and institutional review boards (IRBs).

The reader may think that following the Nuremberg Code (1949), the first code of human research ethics with international recognition, and the Declaration of Helsinki (1964) the use of human subjects in research is well controlled to prevent a repetition of the all too numerous egregious examples in the history of human experimentation such as: the Nazi experiments on concentration camp prisoners (prior to and during the Second World War), the Tuskegee syphilis study in Tuskegee, Alabama (1932–1972), the Willowbrook hepatitis experiments at Willowbrook State School in Willowbrook, New York (1956–1980), and the human radiation experiments in the United States that were located in various hospitals and institutions (1944–1974). This is a partial listing of some of the horrible examples that were brought to national attention through the news media.

Unfortunately, unethical examples of human experimentation continue to occur. The Gelsinger case, in which Dr. Wilson at the University of Pennsylvania conducted a gene therapy trial on Jesse Gelsinger that resulted in his death, clearly demonstrates the severity of the consequence when major COIs occur and the patient consent form presents only partial disclosure of the risks and no disclosure of failures of the gene therapy experiments on animals. In spite of the IRB approval, all of the above ethical violations resulted in the death of a patient.

All of us involved in research with human subjects will gain from the detailed presentation of case studies and proposed procedures that serve to limit human harm and ethical violations. I think that this chapter in *Responsible Conduct of Research* will have a chilling effect on the readers; however, on the positive side it will stimulate researchers to press for more stringent human safeguards. For the reader in need of a reference specifically oriented to biotechnology I recommend the following books: *Genetics: Ethics, Law and Policy, Second Edition* (L. B. Andrews, M. J. Mehlman, and M. A. Rothstein, Eds., St. Paul, Minn., Thomson/West, 2006) and *Ethics in Research With Human Participants* (B. D. Sales and S. Folkman, Washington, D. C., American Psychological Association, 2000). Readers can find current U.S. policies and regulations related to all areas of federally funded research at the U.S. Department of Health & Human Services Web site (http://dhhs.gov/policies).

Another useful book that expands the content of *Responsible Conduct of Research* especially on the subject of biomedical ethics is *Principles of Biomedical Ethics, Fifth Edition* (Beauchamp and Childress, New York, Oxford University

Press, 2001). The authors discuss the fundamental moral theories from utilitarianism to Kantianism and provide a foundation for ethical discussions. In particular, they describe and contrast the fundamental concepts of autonomy (respect for the decision-making capabilities of persons), nonmalfeasance (to avoid harm, first do no harm), beneficence (a term that relates to acts of kindness or charity that extend beyond a strict obligation), and justice (to ensure an equitable and impartial distribution of benefits, risks, and costs among individuals) that are integral to all discussions of biomedical ethics.

Many of the readers of JBO are involved in research that requires nonhuman animals. The authors cite a range of the number of animals used in research that varies from 17 to 70 million. Regardless of your personal views on animal research we can agree with the authors that animal research is one of the most controversial topics in research ethics. Do animals suffer and feel pain? What is the moral status of nonhuman animals? The USPHS has issued a Policy on the Humane Care and Use of Laboratory Animals (2000), which applies to all vertebrate animals used in research supported by USPHS funds. The authors present many of the key questions as well as case studies that serve to stimulate debate and discussion on this very important area of research ethics.

In their final chapter the authors open the discussion with this important question: what is the scientist's role in society? Scientists are not only involved in the work of research and teaching; they are engaged in many other roles: peer review of grant applications and manuscripts, policy advisers, expert testimony, and science advocacy. Scientists support and advise the military and many scientists are supported by funding from the Department of Defense. Since the knowledge derived through the process of science has enormous societal impact, scientists have an important social responsibility. As the authors point out, scientists have strong obligations to be honest, open, and objective, to allocate credit fairly, to respect intellectual property, and to obey the law. Scientists face many moral dilemmas in part based on their work obligations that can conflict with their obligations to society. This final chapter is thought-provoking and the discussions and case studies presented by the authors are crucial to framing the debate on these complex and contentious issues.

Responsible Conduct of Research is a current, cogent, thought-provoking book—and that is the aim of the authors. You will not find an answer to the question "What should I do?" However, the reader will be given the tools and the guidelines to formulate their own answer. The reader will be guided to the stimulating questions and arguments, and hopefully this stimulation will lead each researcher to their unique responses and responsible actions. I applaud the scholarship and the didactic presentation of the authors and recommend this book to everyone involved in the process of scientific research.

I end this book review with a quote from the speech that J. Robert Oppenheimer gave to the workers at Los Alamos on November 2, 1945. "It is not possible to be a scientist unless you believe that the knowledge of the world, and the power which this gives, is a thing which is of intrinsic value to humanity, that you are using it to help in the spread of knowledge, and are willing to take the consequences."

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