
PART 6

The Regulatory Environment for Science

In 1986, the Office of Technology Assessment produced a report entitled “The Regulatory Environment for Science—A Technical Memorandum” (OTA-TM-SET-34) which examined the social and legal forces that act to restrict or regulate scientific and engineering research. At the time, controversies over the use of animals in experimentation, national security controls on scientific communication, and the impact of regulations on research had become the focus of Congresses attention. Fifteen years later, these issues are still salient and continue to engender serious discussion within the scientific community. Part 6 offers four chapters on the current regulatory environment for science and touches on old concerns as well as newer ones such as financial conflicts of interest, rules regarding the accountability and availability of data, and the protection of human subjects in both biomedical and social science research.

Rutgers’ David Guston begins this part with a chapter on the integration of societally mandated regulations and their impact upon scientific integrity and responsibility. He informs readers that political context for the relationship between the federal government and the scientific community has changed. The old version was simple and contractual, while the new vision is “more like a complex social realm where the full range of human motivations and the attendant opportunities to influence them are at play.” This new vision has created complex relationships and regulations concerning issues such as financial conflicts of interest, and rules regarding the accountability and availability of data. Guston believes however that these new rules are not necessarily a threat or impediment to science, writing: “The study of regulation indicates that it often provides a service to the regulated industry or community.”

In Chapter 20, Greg Koski of the Office for Human Research Protections at HHS offers his insights on the protection of human subjects in research. He says that protection is not an administrative process or a burden, but part of science. “It is part of what we do when we experiment on human beings, because we have a responsibility to put their interests first.” He cites the deaths of Nicole Wan and Jesse Gelsinger

as examples of why regulations are needed, pointing out that scientists and physicians have failed to do what is necessary and appropriate to protect their research subjects. Koski recommends that we build a system that promotes the protection of subjects and has true accountability in human research. He suggests that we strive for “a public-private partnership that establishes clear standards of excellence and clear expectations.”

Philip E. Rubin of the National Science Foundation (NSF) outlines the NSF’s activities concerning human subjects protection in Chapter 21. He reminds readers that research involving human participants is not limited to biology and medicine but includes a wide variety of other areas such as cognition, learning, memory, language, perception, and social and economic behavior. Rubin says that the majority of NSF-supported research involving human participants is in fact performed in the behavioral and social sciences, and includes work in the areas of computer science, education, engineering, and mathematics. He provides a “Top Ten List,” which provides his personal perspective on critical issues in non-medical research, and points to consider as new guidance and policies are developed. Rubin concludes his paper with an extensive list of Web sites and other resources concerning protecting human research participants.

Howard K. Schachman of the University of California at Berkeley concludes Part 6 with a paper on the impact of regulation on biomedical research. In Chapter 22, he highlights a number of regulatory burdens in areas in which “regulations are needed and widely accepted as well as those that are of little benefit to society, redundant and the subject of much controversy.” According to Schachman, these areas include the treatment of human subjects, the humane care and use of laboratory animals, restrictions on the use of research funds, conflict of interest, public access to data, and whistleblower protection. He suggests that an effective regulatory environment depends both upon the justification of the regulations as well as their fair implementation.

19 The Regulatory Environment for Science: Does Democracy Trump Science?

David H. Guston

Issues of integrity and responsibility in science generate headlines, but rarely are they connected with questions of democracy in science. This paper offers some first steps toward a more democratically integrated vision of the regulation of scientific integrity and responsibility. It contrasts an old, contractual model of the relationship between science and society, which addressed only a narrow scope of issues in integrity and responsibility in but a constrained way, with a new model that manages a wider scope of issues through more democratic processes. These issues include research misconduct, data availability, conflicts of interest, human subjects of research, and cultural limits to knowledge.

This chapter presents six points. The first point is, very simply, “that was then, this is now”—meaning that the political context for research and the relationship between the federal government and the scientific community have fundamentally changed, and that members of both communities have to come to terms with it.

The old division of the relationship between science and society was something of a contractual one, as if two autonomous groups had agreed on certain principles of exchange to achieve independent but mutually beneficial aims. In the new vision, however, society views science as a little less like a simple input-output device and a little more like a complex social realm where the full range of human motivations and the attendant opportunities to influence them are at play.

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We can quibble about the time of this transition between “then” and “now.” The year I favor as pivotal is 1980, when Congress passed the Bayh-Dole Act and some important changes in the administration of scientific misconduct cases took place (Guston 2000).

The second point is that in the old vision of the relationship between politics and science, there were fewer rationales and opportunities for the regulation of science, broadly speaking. There was financial accountability (to be sure), the beginnings of formal protection for human and animal research subjects, and some questions about what were called the limits of scientific inquiry, with, for example, the creation of the Recombinant DNA Advisory Committee (RAC) (Holton and Morison 1979).

These arrangements were not entirely without controversy when they occurred, but now they seem almost like second nature. Certainly research should be held to the same principles of financial accountability as all other recipients of public funds. Research must respect the autonomy of human subjects, and must ensure that animal subjects (especially primates, dogs, and cats) are not treated cruelly. As long as scientists themselves were doing the regulation, institutions like the RAC were acceptable.

Regulatory issues in the new vision of the relationship between science and government are more varied and more complicated. Some issues extend earlier concerns. They include: the extension of financial accountability with the Government Performance and Results Act; research misconduct, which in some of its aspects is another extension of financial accountability; the variety of questions about human subjects (see Koski, Chapter 20 of this volume); and the extension of the protection of animal subjects, potentially from the large and easily anthropomorphized animals covered in the original Animal Welfare Act to more frequently used birds and rodents.

New issues have arisen in this new, more complex relationship. They include: financial conflicts of interest that exacerbate issues concerning human subjects and research misconduct, not to mention more traditional regulatory issues; rules about the accountability and availability of data under the Freedom of Information Act, and the publicity of science advice under the Federal Advisory Committee Act; and what might be called “the cultural limits to knowledge” in such laws as the Native American Graves Protection and Repatriation Act. In summary, there were fewer opportunities in the past for the regulation of science, but we now have a much more complex environment.

The third point is about the stake of these regulations for scientific inquiry. I will elaborate on a couple of these issues in order to develop what I mean by “stake.” In essence, the discussion of the regulation of science as I have framed it, and I believe as others have framed it too, is about values. It is about what values get to compete seriously with scientific inquiry, and, in some cases, what values get to trump the value of pursuing scientific inquiry. In other words, what values get to supersede the value of scientific inquiry, if any, and under what circumstances? In regulating the use of human subjects, for example, most people have concluded that the value of human autonomy, at least in some circumstances, trumps, or supersedes, the pursuit of scientific knowledge. That is, we as a society and the scientific community itself so value the ability of a single human being to conceive of and pursue his or her own path, that we have preemptively agreed that experiments will not be conducted, or may be halted, should a human subject not provide informed consent. That is a rather extreme way of saying it. An analogy for that extremity is saying that this is the scientific equivalent of that individual civilian standing in front of a tank and halting its progress.

I certainly do not want to cast researchers in the same position as that of corrupt Communist dictators. Informed consent rarely gets to that stage of confrontation. But by accepting the principle of informed consent, we also accept the principle that a lone individual, at least at some point in time, can halt scientific inquiry. I think we accept informed consent at that level of commitment because we understand the brutality of a system that does not accept it, because the concepts of information and consent are so central to our broader conception of what good government is, and because actual harm, to the extent that criminal law recognizes some failures of informed consent as assault, can come in not accepting it.

These factors are not as much at issue in a new category that I have labeled “the cultural limits to inquiry.” For example, under the Native American Graves Protection and Repatriation Act, native tribes can lay claim to what are known as “culturally affiliated artifacts and human remains,” whether or not they have been studied scientifically. The Act became rose to prominence in the controversy over what became known as Kennewick Man, which was a set of well-preserved human remains found on the banks of the Columbia River in Washington State in 1996. Five tribes claimed the remains and desired them repatriated without scientific study. Some research ended up occurring on the remains, which were dated to about 7,000 B.C.E., and questions about their biological

and genealogical connections to the tribes that claimed them were raised in these early scientific inquiries. An article in *The New Yorker* displayed a computer-reconstructed face that researchers put on the skull of Kennewick Man. According to some of the researchers Kennewick Man was possibly not affiliated with the groups that we traditionally think of as genealogically associated with Native Americans. At one point, a researcher claimed that Kennewick Man looked more like Patrick Stewart, the actor who played Jean Luc Picard on one of the *Star Trek* series. He did not have the sort of features typical of the ancestors of Native Americans.

It is possible that further scientific scrutiny could have settled the matter, at least as far as scientists were concerned. But Native Americans thought otherwise, and then-Secretary of the Interior Bruce Babbitt concluded that the remains had been studied thoroughly enough, and that geographic and oral history provided enough evidence to repatriate them. A federal court ordered the Interior Department to reconsider, and the case now sits in the courts.

The story of Kennewick Man shows the difference between the Graves Protection and Repatriation Act and human subjects protection. In the Act, scientific inquiry is trumped, not by issues of individual autonomy and safety, but by a set of values ranging from the distribution questions about who benefits from culturally and economically important artifacts to religious questions about the sacredness of human remains.

Native Americans and researchers have had more productive interactions over this Act. Museum curators will often tell you that these interactions have been very helpful. But Congress has essentially granted a community the ability to halt a small number of scientific inquiries because of values situated in that community. The same kind of problem appears in conflicts in stem cell research and human cloning.

The fourth point elaborates on the comparison between human subjects and the cultural limits to inquiry. It is essentially this: Whereas informed consent gives an individual the right to trump an experiment, the Graves Act gives a group the right to trump a whole line of inquiry. Does democratic society more broadly and appropriately possess this trump card? Over what scale or level of organization of science might democratic society possess this trump card?

Consider, for example, that we ask social scientists to follow the requirements for informed consent because of possible emotional and mental risks to their subjects. And consider that federal requirements protect the families of human research subjects. In a recent case, re-

searchers in Virginia were sanctioned because they failed to gain informed consent from family members of survey participants who were asked sensitive questions about those family members. And yet we do not protect non-subjects in the general population from similar or even more profound risks from research. Instead of extending informed consent requirements to those who are affected but are not subjects of scientific research, we labor under two assumptions: 1) there is broad consensus in society for scientific research, regardless of the risks to safety or culture; and 2) the extant mechanisms for funding, priority setting, and conducting research are themselves sufficiently consensual. Yes, there is great public support for research in most or all of its manifestations. And yes, research and development (R&D) policy is part of a generalized democratic system. But I believe that neither of these are truly sufficient to support these assumptions.

The fifth point is that we need to talk more about how to make democratic decisions about R&D policy and the regulation of science, particularly because the word “democratic” means so many different things to so many different people. Meanings range from participatory town meetings to the application of high constitutional principles.

In a 2001 editorial in *Science*, Irving Weissman and David Baltimore argue against limits on stem cell research. They write, “Scientists alone should not make the decisions about the ethical conduct of their work or about its social implications.” That is a clear and valuable statement. They continue, “It is appropriate that governments, with appropriate public input, define the societal interest, in particular, lines of research.” This statement is also valuable, but notice how much work that word “appropriate” modifying “public input” is doing. We need to have a lot of discussion about what that word “appropriate” means in this context.

Weissman and Baltimore conclude, “But in making those policies, the state should minimize purely political considerations and be mindful of the separation of church and state.” Here, I think, is a major difficulty. “Purely political considerations” could mean the disparate values that motivate politics, and the concerns of elected officials for outcomes like reelection and power, rather than outcomes that are simply good public policy. I will be very explicit here: In my view of democracy, minimizing these considerations eviscerates democracy itself.

Weissman and Baltimore also ask us to be mindful of the separation of church and state, and here there is some critical common ground. We have in the United States an agreement that when the daily politics of legislative and executive institutions fail, we return to constitutional

principles. I take Weissman and Baltimore here to mean that they believe arguments with an explicit religious basis—for example, whether a conceptus has a soul or not—should not be considered relevant to public decision making, at least apart from the ability of individuals who might hold that belief to act on that belief.

But we can also take their point more generally and agree, at the very least, that questions about the regulation of science should be made under these same constitutional principles. This agreement would mean, for example, that there is no right to research as such, but that there is a right to speech, a right to association, a right to due process, and so forth, and that even these constitutional rights have defined (but flexibly defined) limits under the law.

The sixth and final point is this: The regulation of science, particularly the democratic regulation of science that is constitutionally grounded, does not need to be conceived of only as a threat to science. The study of regulation indicates that it often provides a service to the regulated industry or community. For example, it can secure a wider market, as in the case of the requirement that prescription drugs be found safe and effective. It can also provide barriers to entry against potential competitors, as in the case of the licensing of professionals or regulating polluting enterprises.

So in an age of worries over the commercialization of research at universities and the proliferation of pseudo-knowledge on the World Wide Web, democratically produced regulations for the responsible conduct of research can provide a service to the scientific community, as well as, in some cases, restrict it.

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20 Protection of Human Research Subjects: From Compliance to Conscience

Greg Koski

How many people should we allow to be killed in human research trials? In 1995, Nicole Wan, a 19-year-old graduate student died at the University of Rochester from an overdose of lidocaine given to make her comfortable during bronchial alveolar lavage. The New York State Department of Health investigated and found that no safeguards were built into the protocol for the appropriate dose of lidocaine. No appropriate monitoring was conducted after the procedure was completed and she was sent out on her own. The Department found gross deficiencies in the entire process, with neglect of responsibilities by the investigators, the internal review board, and the institution.

There are, of course, other cases. We must ask ourselves why we have regulations being imposed on us in the first place. We must think about this when we complain about regulations and the government. When was the last time you saw a regulation to prohibit excessive contributions to valuable charities?

I spent about 30 years at a university as a basic, clinical investigator. I also worked in the research administration area, dealing with exactly the kinds of headaches and problems that these regulators impose on researchers. I have lived with them from both sides. And I know that you have to ask why the regulations are there.

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Why is there an enormous public focus and discussion about conflicts of interest in human research? Why are people demanding that our academic institutions shine lights into dark corners of their institutions where financial relationships exist that could compromise either the objectivity of the science or the well-being of the patients participating in the trials?

People are not talking about conflicts of interest because there is no problem. Consider the case of Jesse Gelsinger, an 18-year-old with a genetic disease who entered a trial in 1999, without full knowledge of what was going to be involved. He was not presented with information that might have been valuable in making a decision in concert with his family about whether or not to participate in the trial. There were gross deficiencies in the conduct of the trial, gross deficiencies in documentation of the data, and gross deficiencies in reporting requirements. And this was at one of our nation's premier academic centers and by one of our country's finest scientists (the acknowledged leader in the field).

Many people look to the death of Jesse Gelsinger as that line that defines where we had been and where we are now. As tragic as it is, and as painful as it is for the University of Pennsylvania and, especially, his family, to hear that story told over and over again, his death has done more to galvanize the necessary energy to address the problems that exist in this area than any other event that has occurred recently.

This case shows why we have to have regulations. Without regulations, we scientists and physicians have failed to make the commitments necessary to do what is appropriate to protect those we depend on to take part in our science, at least as far as human science goes.

Suppose we had a different world where everyone did the right thing all of the time. How would it be different? How could we get there? Wouldn't it be wonderful if the code of ethics described by Howard Schachman in Chapter 22 of this volume was actually followed by all the people who are members of that society?

The American Society of Gene Therapy (ASGT), after the Gelsinger affair, said, "We will not allow anyone in our organization to have an equity interest in a trial in which they are an investigator." I do not know how they are going to police that. I would hate to think that they would have to police that. I would hate to think that anybody who had an equity interest in a trial would have the poor judgment to actually participate as an investigator.

I do not yet know how many members of ASGT have been removed because they did a trial in which they had an equity interest. I would

like to believe that they all follow that guideline, just as I would like to believe that every investigator in this country adheres completely to the principles in the Belmont Report.¹ But they do not. We need to get to that place where they do. We need to get to that place where people truly embrace the notion that if you are going to experiment on your fellow humans, you must put their interests ahead of your own interests, whether financial, academic, or personal.

Protection of human subjects in research is not just an administrative process. It is not just an administrative burden. It is part of the science. It is part of what we do when we experiment on human beings, because we have a responsibility to put their interests first.

Why do we have regulations? In the 1960s, before we had regulations, people had procedures performed on them by the National Institutes of Health and the best academic centers across the country without being told that the procedures were life-threatening. That is why we have regulations. Right now we have a reactive, regulatory-based system, and that is unfortunate. We should move toward a different system, one that is proactive and performance-based.

That is what we are trying to do. We are trying to get scientists who do human research in this country to embrace the notion that the protection of subjects is inherent in what they do, not just an administrative burden. We need to build a system that promotes that, and we are trying to make that shift in the paradigm.

We are trying to do this in a way that achieves many important goals, not the least of which is simplifying the process that we have. I think everyone would endorse that. How can people do the right thing when they cannot figure out what it is? The system now is very complex, with many differences across many agencies and different systems.

We must achieve greater simplicity and uniformity. This is our mantra. We go all over the country saying this. With greater simplicity and uniformity, we can achieve the kinds of efficiencies and effectiveness of process that we need.

Jerry Kassirer recently published an article titled "Pseudoaccountability" in the *Annals of Internal Medicine*.² It reflects on the fact that in medicine in particular (the audience he is addressing) we have continued to develop systems, codes, and ethics that we expect people to adhere to. Sadly, they do not. So we have systems of pseudoaccountability, as he puts it.

We need to move to a system where we have true accountability in human research, because we have seen too many examples of lack of trust for too long. The list is very long.

When the Office for Protection from Research Risks (OPRR) made 20 site visits to our major academic centers, more than half of them had gross deficiencies in the process. A lot of that process is paperwork and compliance-based, but you know you have to do the paperwork. You made a commitment to the government as a recipient of funds that you will do the paperwork correctly. Many places have one half-time equivalent person dedicated to a process that supports over 2,500 ongoing human research protocols. This is not accountability or assurance. This is gross negligence. We have got to find ways to do better.

We are looking at getting rid of every ineffective regulation that we can so we can focus on a process that moves toward a smaller, more effective government. We have not passed a single regulation since I have been in office.

We will soon convene a brainstorming session that will bring together the stakeholders from the research community as well as people from government. We will look at every conceivable way that we can eliminate regulations that don't serve a valuable purpose. I personally, and my office, expect every one of the institutions, and every person involved in this process, to make a commitment similar to ours, that if you are going to do it, you are going to do it right.

In addition, the National Human Research Protections Advisory Committee of the OPRR is the first committee to work on an ongoing basis to bring public dialogue into the development of effective policies for the appropriate and responsible conduct of human research. We are directing all of our efforts toward making it easier for people to make the promise that they will do it right and to make it easier to enter into collaborative relationships to relieve some administrative burdens. We are redirecting the resources in the office toward support, outreach, education, and quality improvement. This is a very different approach from what was done in the past.

If we work together in a public-private partnership that establishes clear standards of excellence and clear expectations, we can get people to rise to this higher level of performance that is directed toward achieving our goals. If we use a minimized kind of government and work in partnership with those public processes such as certification and accreditation, I think we will have a system that is doing what it is supposed to do, a system that adds value rather than becomes a system of paperwork.

Compliance by itself does not do a thing to protect people. That is why you cannot get too worried about having every consent form dated just right. If we thought that dating consent forms properly was going to help protect people, that would be worth doing. But I do not believe that. I think an effective consent process is something that helps protect people. If we could get people to do an effective consent process, we probably would not have to focus so much on dating the consent forms correctly.

We have gotten to where we are through our own actions. We are going to have to work together now to get back to a place where reason prevails, and we are doing things for the right reasons rather than doing them because we have to.

Endnotes

1. *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, April 18, 1979.
2. Kassirer, Jerome P. "Pseudoaccountability." *Annals of Internal Medicine* 134, no. 7 (April 2001): 587-590.

21 The Regulatory Environment for Science: Protecting Participants in Research

Philip E. Rubin

The federal government has had a long-standing interest in research as a means for improving the well-being of our citizens. As a result, it supports a diverse range of research involving people. This research includes nonmedical research such as behavioral and social science research as well as biomedical research.

The federal government also has responsibilities in areas such as social science that the citizens of our country endorse. For example, the National Science Foundation (NSF) supports data collection efforts, such as the Panel Study of Income Dynamics, that enable our elected and other government officials to plan effectively for education, housing, medical care, and concerns in a wide variety of areas. In addition, research on cognition, learning, memory, language, perception, and social and economic behavior helps us understand, among other things, how humans deal with complex tools and environments ranging from computers and the Internet to workplaces and playgrounds. These are just a few examples of the enormous breadth and complexity of research that the National Science Foundation supports. To be effective, systems for human protection in research must understand this complexity and deal with it flexibly. This is an awesome undertaking.

The majority of NSF-supported research that involves human participants is *basic research in the behavioral and social sciences*. However,

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a number of Directorates also fund research involving human participants. Examples include work in the areas of *computer science* (such as in the area of human-machine interface design), *education* (for example, research on the science of learning), *engineering* (such as studying the societal and economic impact of developments in nanotechnology and other technologies), and *mathematics* (including research on the development of math and science literacy). Most of this research is non-biomedical and all of it is nonclinical. NSF also supports a large amount of *international research* (again, this work is mostly non-biomedical).

Those involved in research and its oversight have the dual responsibilities of advancing knowledge and protecting human participants. Approaches to the protection of human participants should be designed so that they include the kinds of expertise that are appropriate for the particular work that will be conducted. These approaches should ensure that the review and oversight is proportional to the risk of harm, in order to avoid expenditure of time and effort with no gain in public safety and a loss in research capacity. Review procedures should be guided by sensitivity to the kind of research, the local conditions in which it will occur, and the actual risk of harm.

Protecting participants in research is a priority at the National Science Foundation. We support research involving human participants when a responsible party determines that the project complies with the federal government's "*Common Rule*" (*Code of Federal Regulations*, Title 45, Part 46). For the sort of research that NSF funds, adherence to the guidance of this rule has proven to be extremely satisfactory both from the perspective of providing adequate protection to research participants and from an internal administrative point of view. At present, we see no need to change this "Common Rule" for the kind of research that we support. Although this seems to be the dominant view across agencies, it is by no means universally agreed upon and remains an active topic of discussion.

It has become clear, however, that universities, institutional review boards (IRBs), researchers, and policymakers are not always aware of the existing institutional flexibility and delegation of authority stipulated in the Common Rule, particularly as it applies to research in the social and behavioral sciences, and to other non-biomedical research. We encourage the National Human Research Protections Advisory Committee (NHRPAC) and the Office of Human Research Protections (OHRP) to craft the solutions that are needed to remedy this confusion. We are working with them and other agencies to improve this situation.

International collaboration is crucial for conducting research in the modern world and is also an important part of the NSF mission. Sensitivity to varying cultural considerations is essential to this enterprise and should be mirrored in the approaches that are adopted as well as their administration. We must take extra care to make sure that we increase opportunities for international collaboration and not introduce new, unnecessary roadblocks. Our dual goals are to protect participants in research and to enhance the strength of our nation by promoting research in science and education. These goals need not be in conflict. We are disappointed that recent changes in the requirements for IRB approval for foreign collaborators have more and more frequently resulted in delays of funding or cancellation of plans for minimal-risk research (such as recording foreign speech for cross-language linguistic analysis).

We are active participants in ongoing efforts to help ensure the protection of participants in research. To do this properly, we must make sure that the approaches being considered are flexible enough to address the concerns of all research communities, including non-biomedical research, particularly in the area of the behavioral and social sciences and international research. To that end we are working cooperatively with OHRP, its director, Dr. Greg Koski, (see Chapter 20 in this volume) and his staff. Our participation includes representation (in the form of a NSF *ex officio* representative) on the National Human Research Protections Advisory Committee. We also participate in the National Science and Technology Council Committee on Science, Humans Subjects Research Subcommittee, and its Behavioral and Social Working Group. We are eager to participate in the improvement of this system, while also bringing to the attention of all relevant decision-makers the particular concerns of NSF, and of the many diverse communities that we support through research funding.

A quick overview of some of the crucial issues relevant to non-medical research is provided in the following “Top Ten List.” This list is not intended to cover all of the important issues that are presently being deliberated. Rather, it represents my personal perspective on some of the points to consider as new guidance and policies are developed.

1. It would be useful to *conduct research and collect data on the human research protection process*. Agencies such as the National Institutes of Health, NSF, and OHRP could help in the process of seeking and providing funding for research on this important topic. An example of a research topic is the issue of informed consent, especially in

nonmedical settings. For example, there is a need to experiment with ways to make informed consent more effective.

2. Ethnographic studies, other field research, survey research, oral history, etc., often involve special concerns related to *informed consent*. We need to develop innovative approaches that emphasize a “process” for obtaining consent, going beyond the single-minded concern with a consent form. Documented informed consent from individuals may not be feasible, but it may be very important to make sure that the community as a whole is aware that the research is going on, what it entails, who is responsible, etc. IRBs need to have informed expertise available to them to evaluate this issue.

3. *Guidelines should be developed* that discuss the potential kinds of harm in behavioral and social science research and that clarifies the differences between low risk and high risk research.

4. It is essential that *IRBs have the expertise that is tailored to the kind of research* they will be considering. If an IRB is going to evaluate behavioral-social science research, it should have a sufficient representation of behavioral-social scientists.

5. The OHRP should take *proactive steps* to counter the increased regulatory burden caused by the recent upheavals in the human research participants enterprise.

6. *The OHRP staff should have a behavioral-social scientist devoted to facilitating the process* for behavioral-social science researchers running into bureaucratic problems because of the misinterpretation or lack of understanding by IRBs, universities, etc., of regulations as they are applied to behavioral-social science. Examples include a lack of understanding of expedited reviews and issues related to informed consent. The behavioral-social facilitator should be readily available and should be seen as *working for this research community*.

7. The new requirements *for foreign IRB approval for minimal-risk research* have created unique, and unfortunate, difficulties that are resulting in long delays in getting research started and, sometimes, the cancellation of research plans. Given that many foreign countries do not recognize behavioral-social science in their IRBs and that much behavioral-social science research occurs outside institutions, the appropriate IRB is often that of the U.S. home institution. Usually, no reduction of risk is obtained by holding up such projects in order to insist on creating new IRB structures in the foreign setting.

8. The issue of *balancing risks* needs to be taken seriously. The purpose of the regulations is to limit the potential of research to harm par-

ticipants. Minimal-risk research should not be given the same degree of oversight as high-risk research. Major resources should be devoted to overseeing higher-risk clinical, biomedical research. This should be coupled with a significant reduction in the oversight of lower-risk research.

9. The solutions crafted in this enterprise need to be flexible and easy to change, and should impose minimal regulatory burden. Wherever possible, those engaged in this process should go beyond a “regulatory” approach to find other ways of promoting ethical behavior.

10. We should *always* remember that *the protection of participants in research should be our highest priority.*

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Readings and Web Sites

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Note: Below are some URLs for further exploration on matters concerning human subjects.

The NSF Human Subjects Web site is at: <http://www.nsf.gov/sbe/bcs/common/humsub.htm>

The official NSF version of the Code of Federal Regulations 45CFR690.101-124 can be found through <http://www.access.gpo.gov/nara/cfr/index.html> by searching on "45CFR690.101". The similar NIH version is at <http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm>

The Office of Human Research Protections (OHRP) (part of the U.S. Department of Health and Human Services) can be found at: <http://ohrp.osophs.dhhs.gov> This office is in charge of IRB registration and assurance filing, and is presently developing a variety of new policies and procedures, including new federal-wide assurance procedures, training requirements, and international considerations. Information on the new federal-wide assurance procedures can be found at: <http://ohrp.osophs.dhhs.gov/irbasur.htm>

The National Human Research Protections Advisory Committee (NHRPAC) provides input to OHRP, and can be found at: <http://ohrp.osophs.dhhs.gov/nhrpac/nhrpac.htm>

The Office of Research Integrity (ORI) created OHRP. Its Web site is at <http://ori.dhhs.gov> It has links to the recent congressional interactions with ORI related to "PHS Policy on Instruction in the Responsible Conduct of Research": <http://ori.dhhs.gov/html/programs/congressionalconcerns.asp>

The National Science and Technology Council (NSTC) Committee on Science, Humans Subjects Research Subcommittee (HSRS), is an interagency group. A roster of the members is at <http://ohrp.osophs.dhhs.gov/references/humansubcomrost.htm>

The National Academies Institute of Medicine (IOM) (<http://www4.nationalacademies.org/iom/iomhome.nsf>) is conducting ongoing studies that include several components, including a fast-track study related to the accreditation of human research review programs, and more long-term studies related to other issues of human subjects protections. A public meeting was held on January 22, 2001, in Washington, DC, to solicit public input on the accredita-

tion issue. The URL related to the ongoing studies of this committee is at <http://www.iom.edu/IOM/IOMHome.nsf/Pages/human+research+protections>

The National Bioethics Advisory Commission (NBAC) was established by President Clinton in 1995 to advise the Administration about bioethics and human subjects protections. It has issued a report, "Ethical and Policy Issues in Research Involving Human Subjects." The NBAC Web site is at: <http://bioethics.gov/>

Researchers conducting behavioral and social sciences research often have questions about the applicability of their research to federal regulations protecting human subjects (research participants). A document from NIH addresses many such issues and is posted at <http://obssr.od.nih.gov/IRB/protect.htm>. It is also available as an Adobe Acrobat file at <http://obssr.od.nih.gov/IRB/protect.pdf>

22 Impact of Regulations on the Conduct of Research

Howard K. Schachman

Introduction

Most scientists acknowledge, respect and support regulations promulgated with the goal of protecting human subjects, animals, and the environment. Regardless of the inconvenience, cost, and burden, they abide by those regulations widely recognized as protecting the interests of society. Nonetheless, it must be recognized that scientists temperamentally and culturally are skeptical about the legitimacy of rules; instinctively they tend to oppose regulations as an unnecessary burden impeding research. Without question, scientists desire freedom to pursue their research devoid of encumbrances. Similarly, regulators want enlarged mandates as implied in the quip “Dogs bark, cows moo, and regulators regulate” attributed¹ to Frank E. Young, former commissioner of the Food and Drug Administration. Public policy is not, and should not be, governed by extremists at either end of the spectrum—those opposing all regulations and those wanting to impose more and more regulations.

Invariably scientists express frustration over those government regulations which are imposed as a result of political pressures, provide very little benefit, appear ill-advised or poorly crafted, are costly and do indeed impede scientific research. In his article,² “Government Regulation of Research: The Good, The Bad, and The Ugly,” Robert Rich praised some regulatory efforts and their outcomes, questioned the value of other regulations, condemned still others, and expressed particular concern about a few impending regulations. Doubtless there are

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legitimate differences of opinion as to whether a given regulation is poorly conceived, inappropriately interpreted, or incorrectly enforced. Various constituencies frequently clash over a specific regulation as to whether its implementation costs too much time, effort, and money without providing additional protection. Such differences in evaluations of existing and proposed regulations are not only inevitable but also valuable. The clash of ideas and viewpoints is likely to lead to regulations that will better serve society and the elimination of those that are not warranted. Scientists, therefore, should be active in the debate over regulations while recognizing the views of other groups in society. In particular, scientists should strive to ensure that newly proposed regulations are consonant with the culture of science and the conduct of research.

The accompanying list of various regulatory burdens affecting biomedical researchers encompasses areas in which regulations are needed and widely accepted as well as those that are of little benefit to society, redundant and the subject of much controversy.

Regulatory Burdens

- Treatment of Human Subjects
- Humane Care and Use of Laboratory Animals
- Disposal of Hazardous Material
- Restrictions on Use of Funds Awarded for Research
- Conflict of Interest
- Public Access to Raw Data
- Training in Responsible Conduct of Research
- Whistleblower Protection
- Rats, Mice and Birds—Animal Welfare Act

Compiling this list was based on my experience as a working scientist for more than a half century and as chair of the Department of Molecular Biology and director of the Virus Laboratory at the University of California, Berkeley. More recently, in my role as special advisor to the director of the National Institutes of Health (NIH) and as NIH ombudsman in the basic sciences, I visited almost 50 major research institutions throughout the country. This activity afforded me an opportunity to meet virtually all the constituencies in universities from graduate students to deans of medical schools and university presidents. A two- or three-day visit at each of these institutions provided much praise about NIH and government funding of scientific research. But the recipients of that largesse were not at all shy about communicating innumerable complaints about requirements, rules and restrictions. Much of the irritation was attributed to the NIH bureaucracy, whereas often the burdens stemmed from regulations imposed by other government agencies. The broad list of regulatory burdens presented here encompasses areas in which my experience is limited; hence detailed discussions of those subjects will be left to others with more expertise. My remarks will be focused mainly on those policies and regulations that are particularly burdensome without recognizable compensatory benefits.

Treatment of Human Subjects

In the community of working scientists, there are virtually no complaints about the need to protect human subjects. Regulations aimed at providing such protection are clearly justified. There are objections, of course, when such regulations are poorly formulated or applied by over zealous administrators to encompass research on cells, tissues, protein molecules or DNA taken from a living person. Privacy, confidentiality of information and intellectual property rights are to be expected; but there is little justification for a requirement that technicians take a course on dealing with human subjects when they and the living persons are not likely ever to be in contact with one another. Biophysicists studying abnormal hemoglobins should not be impeded by overly expansive regulations dealing with clinical care. Specimens may be identifiable, and therefore biophysicists working with human materials need some appreciation of issues dealing with human subjects. But they should not be held to the same requirements as clinician-scientists. The

principal issue raised in visits to medical schools dealt with requirements for approval of proposed grant applications by numerous committees on campuses before the applications were submitted to NIH. There was enormous waste and little justification for every grant proposal emanating from a university campus being examined by a host of committees when only one third, or less, of the proposals was likely to be funded. Hence researchers and university administrators were enthusiastic about reducing the burdens by postponing some internal reviews and certifications until a decision was made at NIH about the likelihood of funding a specific proposal. The institution of the "Just-in-Time" process was a magnificent mechanism for reducing regulatory burden without sacrificing the necessary review by IRB's or committees responsible for supervising the disposal of hazardous materials.

There is agreement that instances of abuses and mistakes in the treatment of human subjects, though rare, are too frequent. The remedies proposed to address legitimate concerns must be based on a clear understanding of the enterprise. Infallibility, unfortunately, can not be expected. How the goals for which we all strive are to be achieved is now a highly contentious issue. The recent tragic deaths in clinical research settings understandably have led to clamors for new regulations. But first the scientific community, universities, medical schools, hospitals, drug companies, and government should see to it that existing rules are implemented effectively. Only then should the imposition of new regulations be considered.

Humane Care and Use of Laboratory Animals

Until recently working scientists had few complaints about regulations dealing with the humane care and treatment of laboratory animals. Indeed, members of the Federation of the American Societies for Experimental Biology (FASEB) have long been ardent advocates for responsible care and use of animals in research.³ Scientists recognize that knowledge resulting from their research will be of value to both animals and human beings, and they support policies that benefit animals despite the burden of regulations and the administrative costs. What has happened to disrupt the excellent working relationships between those concerned with proper implementation of the Animal Welfare Act and the researchers who use animals in biomedical research? The recently proposed action⁴ of the Animal and Plant Health Inspection Service

(APHIS) of the United States Department of Agriculture (USDA) dealing with “Animal Welfare: Definitions for and Reporting of Pain and Distress” has become a controversial issue leading to vigorous responses from FASEB, the American College of Laboratory Animal Medicine (ACLAM) and other groups. Many biomedical researchers have serious concerns about the proposed definition of distress referring to

a state in which an animal cannot escape from, or adapt to, the internal or external stressors or conditions it experiences, resulting in negative effects on its well-being.

This language, which causes distress for those merely reading it, is vague and could lead to widely varying, highly subjective interpretations. It is worth noting that stress responses are integral to life and often help animals adapt. As pointed out by Hendrix⁵ in commenting on behalf of FASEB, “*There are no simple physiological or behavioral criteria to mark the point when an animal that experiences stress becomes distressed.*” Distress is manifested in different ways not only between species but also among different individuals within the same species.

In their editorial “In the Battle Over Animal Welfare, Truth is not Always What it Seems,” Joseph Haywood and Molly Greene⁶ point out the role of the animal rights groups in initiating this type of action. It seems that local Institutional Animal Care and Use Committees (IACUC’s) are the likely source of wisdom on this controversial issue, and the ongoing dialog may lead to a solution satisfactory to most constituencies. However, those in society who vehemently oppose all use of animals in biomedical research will certainly not be satisfied. Nor is it likely that biomedical scientists can find suitable alternatives to the use of animals in certain types of invaluable research.

Disposal of Hazardous Material

This is an area where recently there has been significant progress. For years, scientists in academia have been dismayed by being subjected to policies and rules devised principally for disposal of industrial level wastes. Why is a regulation designed for a factory disposing of hundreds of gallons of a toxic solvent being applied to a university laboratory that may discard a few milliliters of that solvent? The conflicts resulted from poorly crafted and inappropriately implemented regulations coupled with overzealous inspectors on university campuses. Through the collaborative project sponsored by the Howard Hughes

Medical Institute,⁷ many of the sources of irritation over managing hazardous waste in academic research institutions are likely to be remedied. The development of consensus best practices conveying purpose and intent rather than specificity should lead to responsibility and accountability along with policies and procedures yielding protection with a minimum of interference in research activity. There was a loud outcry in Berkeley some years ago when faculty members were informed that, according to the Environmental Protection Agency (EPA) and Occupational Safety and Health Administration (OSHA) rules, they could not label a test tube containing toxic material with the chemical symbol. Instead they had to write "carbon tetrachloride" on the label. Such absurd practices serve no useful role.

Restrictions on Use of Funds for Research

Although administrators in granting agencies such as NIH and National Science Foundation (NSF) are most cooperative in allowing changes in budgetary allotments on awarded grants, their hands are tied by regulations from the Office of Management and Budget (OMB). There have been innumerable complaints over the inability of scientists to use their grant funds for the support of secretaries. Restrictions on the use of funds for computers and books were another source of irritation. By and large, however, this type of regulation is not too burdensome and most of the difficulties stem from overzealous administrators on university campuses rather than from government itself. It was astonishing to learn how administrators on campuses differ in their interpretations of the policies promulgated by government agencies. As a result, complaints at one institution do not exist at another. Relatively benign regulations from OMB can be over interpreted with the result that scientific research is impeded. The struggles over indirect costs and charges levied by some universities against individual grants continue unabated. On many campuses the charges for disposal of hazardous material are levied against individual grants (as a direct cost), whereas principal investigators argue that they should be classified as indirect costs. In the implementation of regulations covering this and other areas, researchers and university administrations continue to do battle. Scientists maintain that indirect costs should be used to aid and abet the research for which the funds were awarded. University administrators want more freedom in the use of the funds while maintaining they do not receive "full cost

recovery.” The Office of Management and Budget has yet to formulate clear policies and regulations that satisfy all constituencies. Indirect costs for the support of research are clearly necessary, but it must be recognized that research is a responsibility of universities and that “full cost recovery” from the government should not be expected.

Conflict of Interest

By far, the most complicated problem facing scientists, university administrators, government officials, and the for-profit, private sector is “conflict of interest.” Self-interests are pervasive, and conflicts are inevitable because of the disparate goals of the various participants in the research enterprise. The remarkable success of biomedical research has led to extensive intermingling of academia and commerce. As a result, the culture of universities (and especially medical schools) has changed so dramatically that one can summarize the present situation by the quip of H. L. Mencken, “*If they say it's not about money, it's about money.*”

Discussions of conflict of interest frequently deal with clinical trials, treatment of human subjects and informed consent. In each of these areas there are numerous regulations from different agencies of government. Despite these existing rules and policies, there are unfortunately abuses of human subjects and lapses in the application of informed consent. But, as indicated above, proper implementation of existing regulations must be achieved before new regulations are considered and imposed. In addition to these concerns, there are major problems over financial issues and bias in the research record resulting from academic-industrial ties.⁸⁻¹² Many proposals have been made in attempts to deal with these potential conflicts of interest.¹³⁻¹⁵ As yet there is no consensus.

Joint funding of academic research by government and industry has led and will continue to lead to major conflicts over proprietary rights and ownership of intellectual property. Confidentiality agreements with restrictions on the right to publish research findings are intolerable.¹⁶⁻¹⁸ Unfortunately on too many occasions, university administrators have been remiss by accepting agreements with for-profit companies that limit the freedom of investigators to communicate their findings. This type of restraint, imposed by a company and sanctioned by high university officials, was used in an attempt to prevent Dr. David G. Kern, director of the Brown University Program in Occupational Medicine, from communicating information that he deemed of importance to the health of

workers in a factory.¹⁹ In response to that action, the American Thoracic Society released the following statement.¹⁹

Barriers to the open communication of scientific information must be resisted. In particular, the threat of litigation and/or elimination of financial support to prevent the open communication of scientific information is abhorrent.

It is appalling that the operations of medical schools and universities, on the one hand, and private industry, on the other, have become so intermingled that the openness of academic institutions has been compromised. In commenting on the restraint imposed on Dr. Nancy Olivieri by an industrial firm and sanctioned by the Hospital for Sick Children, Professor John Polanyi of the University of Toronto wrote²⁰

Even in an age of commerce, we need enclaves in our society where the views that are expressed have not been purchased.

Despite articles such as “Is Academic Medicine for Sale?” by Marcia Angell²¹ and “What’s For Sale These Days in Higher Education: Two Stories” by Robert M. Rosenzweig,²² medical schools and universities have done little to devise effective remedies for potential conflicts of interest. Most of the focus justifiably has been on individual researchers and their ties to industry. But there is little likelihood that appropriate measures will be implemented to reduce these conflicts because the institutions themselves have extensive financial ties to the commercial sector. According to Angell,²¹ “research institutions need to have more stringent regulations.” Unfortunately and paradoxically the phenomenal progress in biomedical research is likely to lead to even more conflicts of interest. The availability of the structure of the human genome and the ability to work with human embryo stem cells almost certainly will exacerbate disputes over patents and distort the openness essential to a university. Conflicts will persist, and probably increase, unless and until there is a resolution of the contrasting goals of the Public Health Service (PHS) and the Bayh-Dole Act. Individual scientists and institutions are finding that freely making available the results of PHS funded research will often be in conflict with the privatization now so frequently pursued. The recently proposed model for biomedical research,²³ in the article “Academic Relationships with Industry,” will probably not satisfy either those advocating more openness or those stressing the need for commercialization of discoveries. Formulating policies to reduce

conflicts of interest are dependent upon a resolution of these partially inconsistent goals.

Journals devoted to the publication of scientific research are also targets of criticism because of the lack of requirements about their authors' ties to commerce.²⁴⁻²⁵ For years it has been taken for granted that conflicts of interest are readily avoided if there is disclosure of the relationship between the academic researcher and the for-profit company. The recent action of many journals,²⁶⁻²⁷ aimed at assuring the freedom of authors to publish their findings without restrictions from the companies supporting the research, is a step in the right direction. But, as pointed out in a recent editorial²⁸ by Thomas R. Cech and Joan S. Leonard, "*Disclosure of already signed agreements, which currently provides the basis for managing conflicts of interest at medical schools and research universities, is a bit like bolting the barn door after the horse has fled.*" As those authors indicated, it is time to move beyond disclosure.

Public Access to Raw Data

Nearly everyone in the scientific community enthusiastically voices their support for freedom of information and the free exchange of results of their research. But, like other members of society, not all of them practice what they preach. As a consequence, conflicts arise and inappropriate remedies proposed. None was more foreboding than the response of Senator Richard Shelby (R-AL)²⁹ to what he, and others, considered unreasonable withholding of data by from a federally funded investigation at the Harvard School of Public Health which provided justification for some proposed EPA air pollution regulations. The amendment proposed by Senator Shelby, and attached to the FY 1999 Omnibus Spending Bill (Public Law 105-277), was designed to correct what was perceived to be a serious transgression. This action by Congress required OMB to revise Circular A-110 so that all data produced through Federal funding be made available under the Freedom of Information Act (FOIA). Just imagine the reaction of an investigator who receives the following note³⁰ from a manufacturer who used FOIA to request

...all records relating to study design and methodology, study protocol(s), individual data for all study results and data, data sets, statistical calculations, methodologies, and analyses; correspondence, meeting minutes, notes and other documentation of Dr. X and any other University researchers, any departmental staff or other research committees; meeting minutes, reports and other documentation by Institutional Review Board and/or any other oversight committees within or outside the University.

Fortunately, in revising Circular 110-A, the OMB recognized the threat to scientific investigations and responded by formulating a reasonable modification to an unreasonable mandate. Regrettably this issue is not settled because of court challenges to the actions of the OMB. Depending on the ultimate outcome of this potential litigation, FOIA may be used for the harassment of scientists whose research leads to government policies such as air pollution standards. Unfortunately we are now confronted with a new potentially burdensome regulation. As a result of action analogous to that leading to the Shelby Amendment, the Congress included in the Treasury and General Government Appropriation Act for Fiscal Year 2001 (Public Law 106-554) a section which directs the OMB to issue government-wide guidelines that

provide policy and procedural guidance to Federal agencies for ensuring and maximizing the quality, objectivity, utility, and integrity of information (including statistical information) disseminated by Federal agencies.

The guidelines proposed by OMB in response to this congressional action were published in the *Federal Register* of June 28, 2001 with a deadline for comments of August 13, 2001. How this issue will be resolved is not at all clear. But it seems like an almost insuperable burden to place on a government institution like NIH the responsibility to “ensure and maximize the quality, objectivity, utility and integrity” of the research published by the scientific staff. The proposal illustrates the pitfalls encountered when regulations affecting research are drafted without an understanding of the culture and practice of scientific investigations. Peer review is the hallmark of research, and “quality” is assessed through the long-term evaluation of competing points of view. Individual scientists are not impartial, objective and unbiased in conducting their research. It is through the clash of individual, passionate positions of independent practitioners that “objectivity” is achieved in

science as a collective activity. It is that very bias leading scientists to challenge accepted dogma that results in important discoveries. Guidelines or regulations threatening that independence must not be imposed. Research of poor “quality” or lacking in “integrity” or of little “utility” is generally recognized through the process of continual peer review, and those responsible for shoddy research suffer the consequences. A regulation requiring that scientific data be “substantially reproducible upon independent analysis of the underlying data” is virtually an invitation leading to harassment of scientists by requests for “underlying data.” Will implementation of the resulting set of guidelines condone “non-peer” review by individuals displeased with the results of a scientific investigation? What constitutes “underlying data?” How OMB will cope with the numerous criticisms from scientists, professional societies, and representatives of universities remains to be seen. In its present form, the proposal represents an unacceptable regulatory burden without compensatory benefits.

Training in Responsible Conduct of Research

On December 1, 2000, the Office of Research Integrity (ORI) released the newly proposed Public Health Service Policy on Instruction in the Responsible Conduct of Research.³¹ Although issued as a *policy*, the version released by the ORI seemed to many research workers and university administrators to be, in effect, a new *regulation*. The so-called Policy contained precise stipulations about compliance along with requirements for assurances from institutions receiving federal funding. Much of the justification in the ORI statement describing the need for training stems from one of the many recommendations made by the Commission on Research Integrity in a long and largely discredited report³² in 1995. A reading of this new PHS Policy gives the impression that scientists and institutions cannot be trusted. Based on this reasoning, the government must require special, rigorous training in the responsible conduct of research. Such training, presumably, would prevent the research scandals that were so widely depicted in the press about a decade ago.

Critics who now hold this dim view of scientists think that imposition of more rules and policies will correct the perceived deficiencies in the conduct of research. There is no doubt that some (others would say many) scientists, like others in our society are self-serving and selfish,

competitive and contentious, as well as opportunistic, ambitious, aggressive and arrogant. Dealing with them occasionally seems “impossible.” But that does not mean that they are crooks and can not be trusted. Nor does it warrant the imposition of mandatory government regulations aimed at making us “nicer.” This policy is doomed to fail. A look at a little history may be of interest. On September 27, 1885, *The New York Times* published the following commentary on scientists.³³

Like other men they are self-seeking, ambitious, and have their personal ends to gain. Can we assume that morally they are any better than their neighbors; or that, if they get possession of place and power, they will not use and pervert them to the promotion of their selfish objects? It is to be hoped that in the future science will become so developed as to react upon character and give us men morally as well as intellectually superior; but we are far from any such happy result as yet.

It is now 116 years later. We are still “far from any such happy result as yet.” Officials at the ORI must recognize that new regulations may not lead to the desired improvements in behavior. Regulations are not likely to be the most efficient and effective way to achieve the desired outcomes. There also must be some recognition of the cost in terms of what is likely to be an illusory benefit. In this regard, the following statement³⁴ by Professor Harold Edgar in an article on “Criminal Law Perspectives on Science Fraud” is of particular relevance.

Criminal law experience teaches one to be realistic about human nature. There is nothing surprising about the fact that frauds will occur in settings where millions of dollars are paid out with scant supervision. And criminal law theory would predict that the incidence of fraud would be highest in settings where perpetrators believe they are not likely to be caught, or that if caught they can explain away the charges. These circumstances point to social sciences and biomedical and behavioral sciences as opposed to physical sciences as the likely loci of abuse. Experience to date tends to support these expectations.

The issue is not whether we should countenance science fraud. Of course, we should not, anymore than we should countenance burglary. But a criminal law perspective teaches that it's not worth the resources—both economic and ideological—to try to prevent *all* burglaries. The issue is how many burglaries are tolerable giv-

en the alternatives. By contrast, leading scientists discussing science fraud at times sound as though collective guilt is justly imposed every time someone is caught cheating.

In the statement for training in responsible conduct, the ORI lists nine core areas for instruction. They include data acquisition, management, sharing, and ownership; mentor/ trainee relationships; publication practices and responsible authorship; peer review; collaborative science; human subjects; research involving animals; research misconduct; and conflict of interest and commitment. According to the Policy, the description of these core areas was intended for guidance only, and requirements for demonstration of competency rests with the institution. This seeming flexibility is then countered in another section in which it is made clear that all research staff “*shall have received a program of instruction*” in responsible conduct of research. The statement then continues, “*In the event that a newly-hired individual has previously completed timely instruction in any of the core instructional areas described in the policy, that person may receive credit for that portion of the program of instruction that was completed.*” Coping with that section of the Policy would require substantial changes in the operations of academic institutions. Much federally supported research in universities is performed by post-doctoral fellows who are recruited on the basis of their prior work and recommendations of previous mentors. In most instances, there is no knowledge of courses taken by the individuals and credit for graduate courses is rarely given. Does the ORI propose that academic institutions change their ways according to some government edict? An examination of the Assurances section indicates clearly that the intent of the Policy is to regulate the activity of institutions.

A. Each institution that applies for or receives PHS funds for research or research training must assure by October 1, 2001, that:

1. The institution has a program of instruction that complies with this policy and has a written description documenting the program. The written description must address the provisions of this policy, its applicability to all research staff at the institution, and how the institution plans to document completion of RCR [Responsible Conduct of Research] instruction by its research staff. The institution may include in its written plan a description of the role it expects the principal investigator to play in assisting the institution to imple-

ment the policy. Defined roles of principal investigators in this context will augment, but not supplant, the responsibility of the institution to provide RCR instruction as required. ORI may ask an institution to submit the written description of its RCR program of instruction at any time.

2. The institution will publish, or otherwise make accessible, the written description of the program of instruction to research staff at the institution and to others who work on the PHS-supported research project.

3. The institution will carry out its program of instruction.

4. Implementation of the institution's program of instruction for existing staff will be completed by October 1, 2003.

B. The RCR instruction assurance will be provided in conjunction with the Assurances/Certifications on the grant application, Form PHS 398, and in conjunction with the submission of the Annual Report on Possible Research Misconduct (Form 6349) by institutions, to the Office of Research Integrity. Compliance for work conducted under contracts will be assured under a different mechanism.

Not only is the proposed Policy an unfunded mandate amounting to a *regulation*, but it involves unwarranted government intrusion into academic institutions and it constitutes an unjustifiable burden not likely to yield compensatory benefits. Officials in the ORI have indicated that a three-hour course available on the web can be used to satisfy the requirements for training in Responsible Conduct of Research. How can anyone seriously believe that such a program would be effective in conveying ethical principles in mentoring, authorship practices, peer review, sharing of data, and resolving conflicts of interest? These are complex issues requiring continuous debate, changing standards and examination of notable past cases of ethical violations. Trivializing them by indicating that an investigator can satisfy the requirements of the training program with a few "sound-bytes" obtained by sitting at a computer is a disservice to the cause of promoting scientific integrity. Scientists in universities are subjected to a lifetime of peer review. All of their published work is reviewed, criticized and praised by others. Many successful scientists serve on editorial boards of journals that have ethical standards dealing with fairness and confidentiality. What can a web-

Figure 1



I have to fake my data... with all these ethics seminars I don't have time to do the experiments!

site contribute to instruction in “peer review” that is not already common experience of established research workers? The accompanying cartoon (Figure 1) provides a humorous and not altogether inappropriate reaction to the proposed requirement for instruction in responsible conduct of research.

Can officials in one university, in filing an assurance of compliance with the Policy, require that a collaborator at another institution has had the appropriate training? Which of the collaborating groups will decide what is “appropriate?” If one of the groups is a private company that is interested primarily in proprietary rights with a focus on secrecy, how will the university ascertain that the collaborator had the required training? Collaborative research is now commonplace in the biomedical field, and there are significant problems arising daily because of the diverse goals and customs in academia and the commercial sector. Is it appropriate for a university to infringe on the autonomy of a for-profit company because a faculty member at the university receives support from an NIH grant and, therefore, is subjected to this Policy? The proposed Policy is replete with flaws. Although the drafters maintained that it was only a Policy, it is clear that it attempts to *regulate* activities at grantee institutions. It is not surprising, therefore, that the ORI was the target of stinging criticism in a letter³⁵ from Representative W. J. “Billy”

Tauzin (R-LA), chairman of the House of Representatives Committee on Energy and Commerce. In that letter of February 5, 2001, chairman Tauzin wrote,

While we strongly support federal efforts to encourage responsible and ethical scientific research practices, we are troubled by ORI's process in implementing such efforts. Based on the Committee staff's review, we are concerned that a policy aimed at improving the ethics of those outside government may have been issued by a government agency in apparent disregard of federal law.

Subsequently the ORI announced the suspension of implementation of the PHS Policy on Instruction in the Responsible Conduct of Research *"to permit review both of the substance of the policy and the process for adoption."*

Now there is an opportunity to revisit this issue. ORI can resolve the discrepancy between a policy, on the one hand, and a regulation, on the other, by completely redrafting the statement. Prescriptive language should be removed. Directives that essentially instruct universities whom to educate must be eliminated. The scope of the recommended instruction should be reduced drastically. Overlap with other policies and regulations, such as treatment of human subjects, should be minimized. Intrusion of government into the policies and operations of academic institutions should be avoided. With such changes and through the support of voluntary programs by providing resource material of educational merit, the ORI could develop a real policy that would receive widespread acceptance by the scientific community and university administrations. Then these groups could work collectively with government toward the common goal of fostering responsible conduct of research.

Appropriate Responses to Policy Issues about Responsible Conduct in Research

Responsible conduct in research and scientific integrity are dependent upon contributions from all the constituencies in the scientific enterprise. This includes not only research workers but also university administrations, funding agencies both public and private, journals that publish the results of research, and professional societies. For investigators to earn the trust of the public and government agencies, certain obligations must be fulfilled. The freedom essential to the pursuit of science is de-

pendent on the integrity of research workers and the responsible conduct of research. Increasingly professional societies have devoted efforts to this ongoing problem of maintaining the confidence of the public in scientific research through education and the development of codes of ethics. One such code adopted several years ago by the American Society for Biochemistry and Molecular Biology (ASBMB)³⁶ is presented here to illustrate the contribution of professional societies.

American Society for Biochemistry and Molecular Biology

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 experimental details;

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 their 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.

There is no mechanism for responding to allegations that a specific individual's behavior was not consistent with the code. Nor was one intended by the ASBMB. Most professional societies operate on the basis of trust and are ill equipped to conduct investigations of alleged wrongdoing. Their codes of ethics are generally proposed as educational and inspirational tools. Similarly journals published by professional societies have no means for adjudicating charges of plagiarism and fabrication or falsification of data. When such allegations arise, the societies must rely on the institutions in which the research is performed to conduct the investigations and impose sanctions when appropriate. This limited role for professional societies and scientific journals may not satisfy those who want to impose government regulations; but it should be recognized that such regulations are unlikely to be any more effective in achieving the common goal of responsible conduct of research. Despite existing policies for investigating allegations of plagiarism, fabrication and falsification followed by the imposition of sanctions as severe as debarment from receiving federal funds, there continue to be such cases. Fortunately they are rare, but regrettably they do exist. Imposing severe penalties on those who commit these acts is appropriate, leading almost inevitably to the termination of the scientific career of the individual. Coupling the imposition of sanctions with disclosure of the actions would serve as a deterrent for recidivism. Such a course is far more preferable to subjecting the entire scientific community to regulatory burdens that are ineffective.

Whistleblower Protection

Over the course of the past two decades, discussions of misconduct in science (formerly termed fraud) dealt with a vast array of issues including the role of universities in responding to allegations of misconduct. There was widespread recognition of the responsibility for government oversight. Procedures were adopted for investigating charges and adjudicating cases in such a way as to provide due process. These extensive deliberations and actions also included the imposition of sanctions when warranted, disclosure of actions, and protection of the whistleblowers responsible for the initial allegations. Despite the inclusion of "protection of whistleblowers" in virtually all discussions of research integrity, the ORI continues to refer to a section in the report³² of the Commission on Research Integrity entitled "Responsible Whistle-

blowing: A Whistleblower's Bill of Rights." This mockery of the Bill of Rights was followed by a notice of proposed rulemaking in the Federal Register of November 28, 2001 entitled "Public Health Service Standards for the Protection of Research Misconduct Whistleblowers" [42 CFR Part 94]. The proposal is a classic example of "overkill" by government officials interested in regulating. Although entitled "standards", the notice of proposed rulemaking in fact mandates the creation of a complex, burdensome and redundant system with requirements which, in the opinion of many, exceeds the agency's statutory authority. There is widespread acceptance in academia of the sentiment "Institutions have a duty not to tolerate or engage in retaliation against good faith whistleblowers." Nonetheless, the proposal extends that desirable goal (not tolerating or engaging in retaliation) to the impossible one of "preventing." It has been demonstrated throughout history that educational institutions, religious bodies and government agencies cannot "prevent" misconduct. Nonetheless, the ORI persists in using the phrase "prevent" in communications dealing with misconduct or unethical behavior.

The notice points out that the proposed regulation does not apply to Federal agencies which are already covered under the Federal Whistleblower Protection Act of 1989. It also recognizes that there are state and local whistleblower protection statutes that are clearly applicable to public universities. Many research institutions already have established local policies and rules providing for the protection of whistleblowers. Despite this abundance of existing measures, the notice of proposed rulemaking would require additional burdensome and costly requirements which may indeed conflict with existing state laws and employment contracts. The proposed regulation would establish an elaborate structure with unrealistic time frames for adjudicating cases. As presently written, the proposed regulation constitutes an invitation to individuals for the filing of grievances, and it provides them with a road map for proceeding. It seriously under estimates the burden and cost to research institutions. In summary, there is no need for this overlapping, redundant and highly prescriptive regulation. A set of standards that could be implemented by institutions in accord with local requirements would be far more preferable and effective.

Rats, Mice and Birds—Animal Welfare Act

For many years following the 1972 action of the United States Department of Agriculture (USDA), mice, rats and birds were exempted from the list of laboratory animals regulated under the Animal Welfare Act of 1966. The Animal Welfare Act was designed for large animals and was concerned with the protection of family pets. Standards and regulations established for cats and dogs did not seem appropriate for rodents bred for research purposes. Nonetheless rats, mice and birds are protected by other rules and regulations, with oversight by the Public Health Service and the Association for the Assessment and Accreditation for Laboratory Animal Care, International. The decision of the USDA, which affects more than 95 percent of all research animals, clearly did not sit well with animal-rightist activists who have been trying incessantly to reverse the policy. In a lawsuit filed by a coalition led by the Alternatives Research and Development Foundation (ARDF), an undergraduate psychology student at Beaver College claimed that she had suffered an “aesthetic injury” from observing laboratory rats who had allegedly received “inadequate housing, water, food, and veterinary care.”³⁷ Rather than responding in the courts where there was a risk of a potential adverse judgment by the U.S. District Court, the USDA entered into a settlement agreement with ARDF. This capitulation to the demands of the plaintiffs’ petition prevented a host of professional societies and universities from participating in either the court proceedings or the settlement negotiations.³⁸ The unfortunate outcome was an agreement by which the USDA proposed rulemaking to amend the regulation excluding rats, mice and birds from coverage under the Animal Welfare Act.

Fortunately this out-of-court settlement on the part of the USDA in response to the potential litigation was thwarted by a last minute addendum to the USDA appropriations bill precluding them from using funds to draft rules for care of rats, mice and birds. This respite was for only one year, and the issue is now before the Congress once again. It should be noted that the Public Health Service Policy on Humane Care and use of Laboratory Animals covers rats, mice and birds and requires the filing of an Animal Welfare Assurance committing research institutions to responsible animal care. In a devastating critique³⁸ of this action of the USDA, Estelle A Fishbein points out

Imposing the absurd documentation requirements of the USDA on mice, rats, and birds, regulations that are ill-suited to these species, may serve the ends of animal rights advocates, but they most certainly do not serve the needs of patients or the public health.

This potential inclusion of rats, mice and birds under the Animal Welfare Act represents a prime example of an inappropriate response to a vociferous group of non-scientists with a political agenda that is in conflict with the culture and practices of biomedical research. Clearly this group is entitled to advocate its point of view, but government officials should have recognized that the imposition of this regulation would constitute an unacceptable, costly burden “without redeeming features.” An extension of the one-year ban on implementing the USDA plan on rulemaking is now being considered by the Congress and seems to be in the offing. Nonetheless efforts must be directed toward a permanent solution based on local control and oversight by Institutional Animal Care and Use Committees followed by on-site evaluations conducted by the Association for the Assessment and Accreditation of Laboratory Animal Care International. These mechanisms coupled with the policy of the Public Health Service requiring institutions to file an Animal Welfare Assurance already suffice to ensure humane care and use of rats, mice and birds.

Summary

An effective regulatory environment depends not only on the justification of the regulations but also on their fair and judicious implementation. Much of the difficulty in the various areas described above derives from legislative action leading frequently to a multiplicity of agencies proposing and mandating vague, overlapping and inconsistent regulatory policies. Researchers recognize that the protection of human subjects, animals and the environment requires regulations. But it is in precisely these areas where multiple and often conflicting regulations are so prevalent. The efforts of researchers must not be directed reflexively toward opposition to all regulations. Rather they must be involved in opposing those regulations which impede research of value to society and which provide no redeeming benefit. The regulatory burden stemming from agencies unfamiliar with the culture and practice of scientific research must be the focus of attention of the research community. Attention of agencies propounding additional regulations must be redirected toward formulating policies which foster “best practices” as a

more plausible remedy to existing deficiencies. Results should be the goal. Voluntary programs based on carefully formulated “best practices” are much more likely to be effective than overly broad, prescriptive regulations that defy the culture and practice of scientific research.

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