

22 Impact of Regulations on the Conduct of Research

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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.

Acknowledgement

I am indebted to Dr. Ed Himelblau for permission to use his cartoon, “copyright 2001 Ed Himelblau.” Also, I thank Dr. Howard Garrison for valuable comments and suggestions.

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