# 27 New Secrecy in Science: Government-Imposed to Self-Imposed

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During World War II and for some time following the cessation of hostilities, scientists in American institutions of higher learning were deeply involved in widespread secret research. Many universities and research institutions, which traditionally fostered the free exchange of ideas and information, were subjected to curbs from government, which seemed necessary and were readily accepted. Some graduate students were in uniform, and others had draft deferments because of their research activity. Most of the time we did not know what our colleagues were doing. The requirements for secrecy and the safeguards to impose it had a large impact on the culture and ambience of universities, and it was recognized after the war that such research and the attendant restrictions were antithetical to the openness essential in institutions of higher learning.

In using the term, "New Secrecy in Science," I refer to any type of restriction that impedes or limits the freedom to pursue research and to disseminate the results of investigations aimed at understanding natural phenomena and improving the quality of life. Thus, "new secrecy" differs from the secrecy during and after World War II, which prevented, not the actual research, but rather the discussion and release of findings derived from the research. Now we have impediments to openness in scientific investigations, the communication of results and even restrictions on certain types of research. These limitations stem from actions of government, industry, universities and the investigators themselves. Thus the title: New Secrecy: Government-Imposed to Self-Imposed.

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## Research with Human Embryos, Fetal Tissue, and Stem Cells

Although government-imposed secrecy which prevented discussion of the research has been curtailed to a substantial degree and is now largely confined to special laboratories separated from universities, we in the biological field are experiencing restrictions in conducting certain types of research which many consider essential to the goal of understanding basic biological phenomena and developing tools aimed at treating human disease. Much research on human embryos and fetal tissue cannot now be funded by the National Institutes of Health. This prohibition by President Clinton in 1994, came in response to the Report of the National Institutes of Health Human Embryo Research Panel, which recommended limited use of embryos for research.[1, 2] That restriction was followed by an additional ruling by Congress so all-encompassing that NIH, in effect, could not fund any research on human embryos. Following the announcement of the cloning of adult sheep by scientists in Scotland, came another policy edict that "no federal funds shall be allocated for cloning of human beings". The President then asked the National Bioethics Advisory Commission "to review the legal and ethical issues associated with this (cloning) technology and to report back within ninety days with recommendations". In a very thoughtful report the Commission concluded that "it is morally unacceptable for anyone...to attempt to create a child using somatic cell nuclear transfer cloning."[3] This overall conclusion was followed by a series of recommendations including the continuation of "the current moratorium on the use of federal funding in support of any attempt to create a child by somatic cell nuclear transfer." In recommending federal legislation to prohibit such activity, the Commission urged that there be a sunset clause to review the issue after a specified time period (three to five years) to determine whether the prohibition should be extended. In another recommendation, the Commission urged that any regulatory or legislative actions undertaken "should be carefully written so as not to interfere with other important areas of scientific research." Unfortunately, in statements by Members of Congress and in action by some State Legislatures, the language on banning cloning has been so overly broad, imprecise and ambiguous that it can limit or restrict important research.[4]

As a consequence of these administrative and legislative actions, much research in this field, to the extent that it is going on, is confined to laboratories supported by private funds. Not only is there the risk that the research may be of lower quality than would occur with NIH funding,

but ethical guidelines and accompanying regulations are much more inadequate than would be obtained if federal funds were being used. Over the course of the past five years, this struggle in Washington has intensified and expanded to include the use of pluripotent human stem cells, for research. Early in 1999, about 70 members of the House of Representatives and seven Senators went on record in opposing a ruling that would have allowed NIH to support research on the use of human stem cells, and this contentious issue is now being debated. Following that release, many scientists and officials of professional societies dealing with biological research responded, in letters to President Clinton and Members of Congress, with the claim that there is a "moral imperative" to pursue research with human stem cells because of its potential for treating human disease.[5] Some of those who oppose this research do so because of their concern over, and opposition to, cloning human beings. Scientists, to an overwhelming degree, join them in opposing the cloning of human beings, but we stress that those who urge restricting this research fail to differentiate between creating knowledge and applying knowledge. Whereas there could certainly be useful discussions about restricting applications of new biological techniques, it is difficult to understand how one can oppose the acquiring of knowledge. It is important to note that others, and perhaps the majority, who stridently oppose the use of stem cells have another agenda. Their opposition derives from their views on abortion and the source of the human stem cells. Moreover, they condemn the use of stem cells regardless of the source, a position which is probably not acceptable to most scientists.

Today, stem cells constitute a research tool which can be used by biologists to study the growth and differentiation of cells basic to our understanding of human development. Discoveries based on their use could lead to treatment of abnormalities in human development and to a source of differentiated cells and tissues for transplantation therapy. With these possibilities of enormous benefit to society, how could one justify banning the use of federal funds for such research, especially since this type of work does not impinge directly on the morality issues associated with cloning of human beings.[6] Scientists and members of the lay public who support research on human stem cells were pleased by the announcement on January 19, 1999 that "current law permits federal funds to be used for research using human pluripotent stem cells."[7] That statement by Harold Varmus, as Director of NIH, was based on an interpretation of existing law by the general counsel of the Depart-

ment of Health and Human Services. Based on that interpretation of existing rules and clauses in appropriation bills, which differentiated between the development and use of stem cell lines, the NIH published thoughtful and carefully crafted guidelines in the *Federal Register* early in December of 1999 for funding research involving human pluripotent stem cells.[8, 9] The comment period for responses to the announcement expired February 22, 2000, and a final statement of requirements for grantees and regulations for acceptable use of stem cells is expected soon. Despite these announced policies, it should be recognized that this contentious issue is not yet settled and that congressional opposition is likely.

## The Shelby Amendment, OMB, Circular A-110, and FOIA

It is somewhat ironic that at the time we are contending with government imposed restrictions limiting the freedom of research, we are also being confronted with the possibility of regulations, again from government, that will certainly be very burdensome, expensive, and time-consuming. Moreover this seemingly innocuous action could cause a serious violation of privacy rights, prove deleterious to academic-industrial collaboration, and actually lead to the cessation of potentially promising biomedical research. This issue, arising out of an amendment introduced by Senator Shelby (R-AL) to the FY 1999 Omnibus Spending Bill (Public Law 105-277) of the last Congress, required the Office of Management and Budget (OMB) to revise Circular A-110 so that all data produced through federal funding be made available to the public through procedures established under the Freedom of Information Act (FOIA).[10] Circular A-110 describes the "Uniform Administrative Requirements for Grants and Agreements with Institutions of Higher Education, Hospitals, and other Non-Profit Organizations." In response to that amendment in the congressional spending bill, the OMB published some proposed changes in A-110 in the *Federal Register*, and opened discussion of the suggested alterations for public comment.[11] The comment period ended on April 5, 1999. In the early part of the 60-day comment period, the number of criticisms and suggestions for modification of the revision proposed by OMB was very limited. Spurred by the American Society for Biochemistry and Molecular Biology and other professional societies, their members communicated detailed criticisms of the proposed Circular A-110. Indeed over 1,000 critical, constructive letters were sent to the OMB before the end of the comment period. But in the last few days before the deadline about 9000 almost

identical messages were sent to the OMB by members of the NRA and the Chamber of Congress. These messages praised the proposed revisions in Circular A-110. Fortunately, officials in the OMB read the communications, considered the suggestions and criticisms and, in a final revision on September 30, 1999, formulated a reasonable response to an unreasonable mandate.[12] Their revision although reducing the burdens on the scientific community will still permit some potential harassment. It is clear that the use of FOIA is the wrong remedy for the existing problem of making data available. Although Senator Shelby, the author of the amendment to Public Law 105-277, expressed strong criticism of the revised circular, he seemed to accept the OMB formulation and apparently is not challenging OMB's formulation and narrowing of the requirement that "all" data be made available. Others, however, have not given up in the effort to have access to all research data. The United States Chamber of Commerce, in an apparent attempt to provoke a lawsuit over what they termed as OMB decimating Congressional intent, has filed three FOIA requests seeking "key documents, research data and studies that the EPA used or cited in their recent regulations on National Ambient Air Quality Standards, Environmental Justice guidelines, and standards for automobile tailpipe emissions."[13] We can agree with Senator Shelby in his effort to require that data collected at the Harvard School of Public Health under a federally funded grant and used as part of the justification for proposed EPA air pollution regulations be made available to the public. However, the language of the amendment when applied, for example, to clinical studies funded by NIH would virtually cripple such investigations because of the violation of the privacy of patients. Similarly, the violation of proprietary information in academic-industrial collaborations through supplying the data, required by the Shelby amendment, would have a chilling effect on the way that collaborative science is conducted.

Although many of us applaud the purposes of the Freedom of Information Act, and FOIA has been used for good purposes in our society, it behooves us to be aware of the unintended consequences that may result from its implementation. Some groups, displeased with a government regulation or the conclusion of a scientist regarding the efficacy of a drug used in a clinical trial, use FOIA for harassment. Imagine an investigator and a university receiving the following note from a manufacturer who used freedom-of-information provisions 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.[14]

In a letter dealing with the original OMB response to the Shelby Amendment, Bruce Alberts, President of the National Academy of Sciences, wrote:

> The potential implications of applying FOIA to federally funded research are daunting. For example, in a famous FOIA lawsuit from the 1970s involving a large, NIH-funded, long-term clinical study by private federally funded research grantees, the plaintiffs were seeking access rights under FOIA to more than 55 million grantee records! The U.S. Supreme Court ultimately ruled against the plaintiffs in that case; this is why, until the recent action by Congress, other federal research grantees have not faced this type of problem.[15]

We obviously do not know how the Chamber of Commerce legal challenges to the OMB revised Circular 110-A will fare. Regardless of that outcome, we share the views of Congressman Rush Holt (D-NJ) that, despite the good job done by the OMB in implementing a bad law, the Shelby Amendment can hinder the open exchange of information and ideas.[16] The long-range solution to this potentially serious curtailment of the freedom to conduct scientific investigations is the repeal of the law. Such a bill was indeed introduced by the late Congressman George Brown, Jr. (D-CA), and Congressman Holt has now assumed the leading role in sponsoring this repeal. We hope that there will be widespread support in this effort. It is worth noting that a proposal requiring scientists to make public their raw data had surfaced in 1997 when a member of the House of Representatives attached an amendment to the spending bill for the Postal Service and the Treasury. The final language in that proposal would have required recipients of federal research grants to submit to the government a plan for making "the results (including all underlying data and supplementary materials)…available for public use and inspection." Fortunately this amendment was voted down.[17]

## Self-Imposed Secrecy

Let us now turn from beating-up on government and look at ourselves. Many codes of ethics adopted by scientific professional societies and discussions about responsible conduct of science have language dealing with the sharing of research findings or resources. For example, the code of the American Society for Biochemistry and Molecular Biology has the following language:

> 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 timely fashion.[18]

How well are we doing in this regard? About a decade ago, many investigators received a letter from a prominent scientist at a non-profit research institution that offered highly desired material on condition

> …that recipients (1) not share the material or by-products with anyone else, (2) notify the providing institution 60 days in advance of any publication, and (3) yield the providers first rights on any improvement of the vector or products made with it.[19]

Although many scientists signed this unconscionable agreement, others were outraged and vociferous in denouncing the "offer," and some institutions, through their technology licensing offices, objected to the conditions. What is the government policy relating to the distribution of unique resources produced with Public Health Service (PHS) funding? According to the policy statement, unique resources include synthetic compounds, organisms, cell lines, viruses, cell products, and cloned DNA as well as DNA sequences, mapping information, crystallographic coordinates, and spectroscopic data. Now let us look at the policy of the PHS relating to the distribution of unique resources produced with PHS funding:

> It is the policy of PHS to make available to the public the results and accomplishments of the activities that it funds. Restricted availability of unique resources upon which further studies are dependent can impede the advancement of research and the deliv-

> ery of medical care. Therefore, when these resources are developed with PHS funds and the associated research findings have been published or after they have been provided to the agencies under contract, it is important that they be made readily available for research purposes to qualified individuals within the scientific community. This policy applies to grants, cooperative agreements, and contracts.[20]

This policy seems clear, and one wonders how well it is being implemented and whether grantees adhere to it. Investigators conducting biomedical research frequently develop unique resources, such as cloned DNA, DNA sequences, and crystallographic coordinates. Let us look at one field of science where there have been numerous complaints and widespread disagreements over the issue of sharing data.

About 20 years ago, the community of crystallographers was deeply divided over the deposition of atomic coordinates deduced from X-ray diffraction studies. Whereas many agreed that the results of such studies should be made available to biological scientists as part of the publication process, there was a feeling that individual investigators could justify withholding or delaying the deposition of the coordinates in data banks customarily used by the scientific community. This justification was based on the need of the crystallographer for continued refinement of the structure and the recognition that the years of effort required to determine a precise structure should allow the individuals additional time to exploit their findings. After extensive discussions held by the International Union of Crystallography, where the range of the proposed delay in releasing coordinates varied from four years to zero years, a compromise was generally accepted where the maximum hold period would be one year. In the following decade it has become increasingly common for coordinates to be deposited in the Protein Data Bank (PDB) with no hold at all, but the one-year option was frequently used. Because the PDB does not release coordinates without the express authorization of the depositors, there was no assurance that such coordinates will be released in a timely manner. In addition, some investigators do not deposit the coordinates, despite publishing detailed papers containing structures.

As in other branches of science, the field of crystallography has changed dramatically. There are many more laboratories throughout the world doing crystallography, the techniques have improved enormously, the average time required to determine a structure has been re-

duced a great deal, and biological scientists require and use the results of X-ray diffraction studies at an ever increasing pace. It was, therefore, the view of many scientists that coordinates should be deposited in the PDB and be made available to biological scientists at the time the paper is published.[21]

In the view of researchers in very diverse fields, the essential characteristic of a scientific publication is that the results be accessible both for validation of the work and for its extension in new directions. Hence, they maintain that all the necessary information must be made available at the time of publication. If individual crystallographers, academic or industrial, wish to satisfy special concerns by withholding data then they should delay the publication of the work in the scientific journals until such time as all information can be made available.

Stimulated by complaints over delays in obtaining access to important results in published papers, a group of distinguished crystallographers wrote to Dr. Harold Varmus, Director of NIH, in early 1998, expressing the view that coordinates from crystallographic studies be released at the time of publication. Through his intervention, that position was then communicated to the Editors of about ten major scientific journals in which structures of macromolecules are frequently published. As a result of the ensuing discussion, the policies of many of the journals were altered in 1999 so as to require that detailed structural information be made available at the time of publication.[22, 23] It is astonishing that a significant number of reputable journals still do not require as a condition of publication that the relevant evidence be available when the paper is published. In the interim, revisions were announced in NIH policies relating to deposition of atomic coordinates into structural databases.[24] Now purse strings can be used to implement policies requiring sharing of data obtained with federal funds.

## Institutionally-Imposed Secrecy

In my use of the phrase "self-imposed," I refer not only to scientists who withhold data but also to institutions which impose limitations on the dissemination of the results of scientific investigations. In the past few years, there have been several egregious examples of the attempted suppression of research findings that deserve the attention of the scientific community. In response to a major struggle[25-27] involving Dr. David

G. Kern as director of the Brown University Program in Occupational Medicine, the American Thoracic Society released the following:

> 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.[25]

Beginning with a visit of a textile worker referred to him by a pulmonary physician, Dr. Kern at the Memorial Hospital of Rhode Island Occupational and Environmental Health Service became deeply involved in a conflict encompassing scientific integrity, ethical issues in the practice of occupational medicine, and the release of information essential to the health of patients. This initial visit led to the discovery by Dr. Kern, as the director of the Brown University Program in Occupational Medicine, of a cluster of cases of interstitial lung disease among employees of a textile manufacturing plant. According to Kern's account, he and his team met increasing resistance in their efforts to uncover evidence of a work-related cause of the disease and to communicate their findings to the workers and the union. As in most struggles, there are different points of view, and this case is no exception. The company, with some officials of the medical school and the university supporting them, maintains that an Agreement of Secrecy and Confidentiality precluded dissemination of the findings. That Agreement dealt with trade secrets, and one would be hard pressed to conclude that the confidentiality agreement could be construed as preventing the reporting of potential risks to the health of employees. The problems escalated when the plant's management dismissed the occupational medicine team and threatened legal action if it published or presented its scientific findings. Neither the administration of the Medical School or that of Brown University seemed willing to come to Kern's aid in this struggle. This posture is particularly ironic since the Operating Principles and Guidelines of the hospital and university for the program in occupational medicine lists as its second point:

> It is accepted that our primary objective as occupational health consultants is to promote and protect the health and safety of employees.[25]

It is hard to conceive of a confidentiality agreement not being superseded by medical school officials when patient risks are involved. The

issue was stated clearly by the American College of Occupational and Environmental Medicine.

> History is replete with examples where delay or suppression in the reporting and dissemination of health risks led to serious human and financial consequences.[25]

The issues raised by the Kern case are evident as well in the conflict involving Dr. Nancy Olivieri, the Hospital for Sick Children, and the University of Toronto. That two-year struggle[28-31] dealt with informing patients of the potentially harmful effects of a drug being used in treatment of them, the publication of results of clinical trials, and the enforcement of a confidentiality agreement she had signed with a company financing the clinical trials she was supervising. During the trial, Dr. Olivieri discovered that the drug being used to treat patients suffering from thalessemia was actually causing toxic effects rather than benefiting them as originally thought. Despite threats from the company funding the clinical trial, she did publish her results and conclusions, leading to her dismissal as the principal investigator in the study and as director of the hemoglobinopathy program at the Hospital for Sick Children. The furor over this case received widespread publicity throughout Canada and attracted the attention of leading hematologists in the United States and England. Through their intervention, this unfortunate matter has been resolved, validating the actions of Dr. Olivieri in releasing information to patients that a treatment may be deleterious (rather than beneficial).[31] It is difficult to understand how the officials in the drug company and the hospital failed to recognize that informing patients of potential harm from a treatment and communicating such information to the medical community at large must take precedence over any confidentiality agreement. This case provoked John Polanyi, a University of Toronto Nobel Laureate, to remark, "Even in an age of commerce, we need enclaves in our society where the views that are expressed have not been purchased."[28]

## Academia and Industry

Suppose your university or research institute was seeking industrial support for some of its research activities. Can you imagine an agree-

ment containing the following clause?[32]

> Company X would provide Institution Y "general funding" for research of its choice in return for an exclusive worldwide license to all Institution Y inventions related to medical or manufacturing products, excluding existing research agreements with third parties.

Indeed, such a proposal was made and it included the following:

> Company X would be allowed to review invention disclosures stemming from federally funded research at Institution Y before the disclosures are filed with the government.

Although Institution Y seemed willing to accept this proposal, the outcry over this proposed agreement reached Congress and led to its demise, but the issue of "reach through" rights imposed or suggested by many companies has become too common.

I illustrate this issue by a report[33] of the discussion at a meeting a decade ago where

> The Chief Executive Officer of Corporation X shocked a roomful of investors, analysts and even his own scientific board members when he told the group he'd come up with a plan to commercialize the then brand-new technology known as ZZZ. In a crowded conference room, the CEO explained how he planned to offer nonexclusive licenses to all academic researchers as well as anyone else who bought automated ZZZ systems and they could amplify Y to their heart's content in any research lab. But if a product eventually results from this work, he told the room, Corporation X would expect royalties on it.
>
> Many in the room were floored. The company's own scientific advisors engaged the CEO in a heated argument. One suggested it was akin to demanding royalties from a best seller when all you did was sell the author a typewriter. While the ZZZ technology's use in test kits and for specific diagnostics has become a viable, protected business, the idea of following its trail to a marketed product never worked.

The issue of reach-through rights and the implementation of patents

by commercial concerns is illustrated by the following letter received by an academic scientist:

> The animal(s) contained within this shipment are produced and distributed under patent rights licensed from Company X. The recipient of the animal(s) is NOT authorized to breed, cross-breed, reproduce, transfer possession of, or otherwise make ANY use (including use for research purposes) of the animal(s) or biological material derived therefrom (including without limitation cells, eggs, or embryos), without first obtaining a license from Company X. Any making, using, offering to sell, or selling of the animal(s) or any biological material derived therefrom without an appropriate license will be considered an infringement of the patent rights by Company X.[34]

According to a recent news brief in *Science* entitled, "NIH, DuPont Declare Truce in Mouse War," the license agreement sent to investigators limited their freedom to use and share the Cre-lox animal.[35]

> DuPont asked that anyone using Cre-lox methods send the company prepublication copies of their scientific reports. The company also tried to acquire commercial rights to future inventions that might arise from experiments involving a Cre-lox animal. In addition, DuPont's lawyers warned researchers not to share Cre-lox mice with colleagues unless the recipient agreed in advance to DuPont's terms.

Fortunately, that company position of reach-through rights has now been abandoned for academic researchers. In commenting on a landmark agreement between DuPont Pharmaceuticals Company and the Public Health Service, Paul Friedman, the President of the company, emphasized the company's commitment to the "wide dissemination of this valuable technology to the academic community".[36] Dr. Maria Freire, Director of NIH's Office of Technology Transfer, who was involved in this important negotiation summarized the position of NIH with the comment, "We hope that the agreement will serve as a prototype for how a commercial organization can put a technology into the academic domain."[36]

## Bayh-Dole Act

How did all this happen? Why do you need a license to obtain a reagent from a colleague at another university? Has the culture of credit among scientists changed? Should investigators think about patenting their discovery or invention rather than publishing it in a scientific journal? Have you contacted your Technology Transfer Office? Have you signed the Material Transfer Agreement? These and many analogous questions are raised as a consequence of the major changes resulting from passage of the Bayh-Dole Act about 20 years ago.[37]

For many years, government-sponsored research, especially through NIH and NSF grants, led to an outpouring of exciting scientific results which were all in the public domain. There appeared to be little incentive for commercial development of the new technologies. As a consequence according to the metaphor in the seminal article by Garrett Hardin, entitled "The Tragedy of the Commons," the great discoveries were available to all, but no one benefited.[38] Hence Congress began encouraging research institutions to patent discoveries arising from federally-funded research and to transfer the technology to the private sector. This action by Congress in 1980 took the form of the Bayh-Dole Act and the Stevenson-Wydler Innovation Act. Their purpose was to promote the economic development of the products of federally funded research, thereby benefiting the public through commercialization of advances in research and technology. In effect, these acts provided incentives for private parties to develop useful products from research results that might otherwise not have been exploited. Through these laws, recipients of government funding can elect to retain title to their inventions, but the laws impose the obligations to promote utilization, to encourage commercialization and to encourage public availability of the products.

By and large, the Bayh-Dole Act has been remarkably effective, especially in the area of biotechnology, an industry which originated from the science of NIH-funded research. But it appears now that we have gone to the other extreme. Privatization, though helping in overcoming the Tragedy of the Commons, could lead, according to Heller and Eisenberg, to another tragedy—"The Anticommons in Biomedical Research".[39]

As Eisenberg has pointed out, these statutes (the Bayh-Dole Act and the Stevenson-Wydler Act) encourage research institutions to patent discoveries made through government-sponsored research.[40] This turning to patents rather than simply publishing results constituted a major

change in policy for scientists and non-profit research institutions. Thirty years ago, most scientists thought that the best way to obtain utilization of the results of publicly-sponsored research was to make them freely available through publications in scientific journals. Now it is recognized that if published research results are available to anyone who wants them, they may not attract sufficient commercial interest to warrant development into useful products. As a consequence, institutions performing federally funded research are increasingly obtaining patents and offering licenses to private companies. Experience over the last 20 years has demonstrated that this change in culture, from publications to patents and licenses, has been accompanied by significant impediments to the ongoing research in universities and other non-profit institutions.

## Intellectual Property

A by-product of the Bayh-Dole Act and the increasing use of patents and licenses by universities has been the focus on intellectual property rights and interests of the public and private sectors. The contrasting views over intellectual property was summarized in the Introduction to the Summary of a Workshop on Intellectual Property Rights and Research Tools in Molecular Biology, as follows:

> University scientists complain that the eagerness of private firms to preserve intellectual property poses a threat to open scientific communication, that the prospect of obtaining patents influences research agendas, that overly broad patents stifle research, and that licensing practices impede access to and use of genetic materials and DNA technology. Yet few scientists today would voice wholesale opposition to patenting itself; scientists' concern is more likely to be how to ensure access to patented inventions on reasonable terms. Representatives of the private sector have a different list of complaints, including the overeagerness of university technology transfer managers to file patent applications, their overestimation of the value of their intellectual property, the underestimation of the additional investment required to turn a research discovery into a product, and their readiness to grant exclusive, rather than non-exclusive, licenses.[41]

Regrettably, increasing commercialization of research results has blurred the distinction between "research tools" and "products." As a

consequence, we have witnessed the patenting and licensing of basic research tools, such as PCR and Cre-lox, which historically were exchanged freely and directly among scientists without licenses, material transfer agreements or memoranda of understanding. Whereas investigators used to devote little thought to a financial return when their lab was involved in constructing a plasmid or a mutant protein, now the perspective is different.

## Research Tools

As a result of complaints from scientists involved in biomedical research, a working group was established by the Director of NIH in order to devise remedies for the increasing difficulties and delays in gaining access to research tools. In their report on June 4, 1998, the group enumerated the more significant problems and their recommendations for resolving them.[42] They also pointed out the sometimes conflicting goals and obligations of NIH. On the one hand, NIH has a strong interest in facilitating the use of research tools in both the public and private sectors. At the same time, NIH is required to promote commercial development and widespread availability of discoveries derived from NIH-funded research. The working group noted that "case by case negotiations for permission to use research tools and materials create significant administrative burdens that delay research." The members of the working group, in their discussion of problems, stated that:

> Institutions that seek to retain a competitive advantage from their propriety research tools are generally unwilling to make them freely available. In order to minimize risks of competitive harm they may seek to limit who has access to the tools, restrict how they are used, and restrict or delay disclosure of research results.

The final and very important problem cited by the group was:

> License mechanisms by which tool providers seek to profit from the future discoveries of tool users often involve future royalty obligations or rights to future intellectual property.

In proposing remedies, the working group made a series of recommendations:

- NIH should promote free dissemination of research tools without legal agreements whenever possible, especially when the prospect of commercial gain is remote.

- NIH should promote use of the Uniform Biological Materials Transfer Agreement (UBMTA) and the development of other standard agreements to reduce the need for case-by-case review and negotiations.

- NIH should develop and disseminate guidelines for recipients of NIH funds as to reasonable terms in licenses and MTA's, addressing both importing of research tools from other institutions and exporting of research tools created with NIH funds.

In response to this report of the working group, NIH published a notice in the *Federal Register* on May 25, 1999, describing a proposed policy for sharing biomedical research resources, and the final notice, entitled, "Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Research Resources," appeared on December 23, 1999.[43] It is difficult to believe that there could be opposition to the stated principles: Ensure Academic Freedom and Publication; Ensure Appropriate Implementation of the Bayh-Dole Act; Minimize Administrative Impediments to Academic Research.; and Ensure Dissemination of Research Resources Developed with NIH Funds. But it is in the Guidelines for Implementation that we can expect vigorous protests such as the comment of a biotech executive who termed the action "an unmitigated disaster" and called it "Varmus's revenge".[44] Just as those from the industrial marketplace and from technology transfer offices of major research universities will oppose the NIH rules (or damn them with faint praise such as "a good step"), the scientists in academia will complain that the guidelines do not go far enough toward achieving the tool sharing principles. Clearly the "devil is in the details." Reconciling the mandate of the Public Health Service policies and that of the Bayh-Dole Act will continue to pose problems that are not resolved by the new NIH guidelines. Many research scientists in academia recognize the increasingly onerous barriers to free and open exchange of scientific information and materials resulting from the creation of material transfer agreements and establishment of technology transfer offices on university campuses. They yearn for the return to the era where collegiality and sharing took precedence over commercial considerations.

## Summary

It is clear that impediments to the free exchange of materials, ideas, and results are attributable in part to each of the constituencies involved in the research enterprise. At the one extreme, some scientists increasingly are not sharing the products of their research. They are aided and abetted in this withholding by the universities in which they work. The widespread installation of technology transfer offices with the hoped for goal of developing revenues is contributing to the barriers which defy the openness essential in institutions responsible for creating and dispensing knowledge. As a result of their interactions with industry, both the scientists and the universities are responsible for imposing additional curbs leading to the new secrecy. The merging of academia and industry is bound to introduce serious problems since their goals and functions are so disparate. Finally, the interplay of diverse political forces leads to government policies which are frequently in conflict with one another. Some policies lead to seemingly unnecessary burdens on scientists thereby interfering with research activity. More importantly, other actions of government prevent important types of federally funded biomedical research which could be of enormous value to our citizenry. A resolution of the contrasting goals of the Public Health Service calling for sharing and those of the Bayh-Dole Act which lead to privatization is sorely needed. Also a reappraisal of our patent policy regarding organisms and genes is essential, so that patenting of materials with unknown functions like expressed sequence tags (EST) is not permissible. In considering the culture change in our research institutions, one is reminded of the comment of H.L. Mencken:

> "If they say it's not about money, it's about money."

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