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Symposium Report

Future Public Policy and Ethical Issues Facing the Agricultural and Microbial Genomics Sectors of the Biotechnology Industry*

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INTRODUCTION

On September 12, 2003, the University of Maryland School of Law sponsored a roundtable discussion on public policy and ethical issues that will likely face the agricultural and microbial genomics sectors of the biotechnology industry in the near future. As this industry has developed over the last two decades, societal concerns have moved from what were often local issues; e.g., the safety of laboratories where scientists conducted recombinant DNA research on transgenic microbes, animals, and crops, to more global issues. These newer issues include intellectual property (IP), international trade, the risks of genetically engineered foods and microbes, bioterrorism, and marketing and labeling of new products sold worldwide. The fast-paced nature of the biotechnology industry and its new developments often mean that legislators, regulators, and society in general must play "catch up" in their efforts to understand the issues, the risks, and even the benefits that may result from the industry's new ways of conducting research, new products, and novel methods of product marketing and distribution.

The goal of the roundtable was to develop a short list of the most significant public policy and ethical issues that will emerge as a result of advances in these sectors of the biotechnology industry over the next 5 to 6 years. A concomitant goal was to provide a set of focused issues for academic debate and scholarship so that policy makers, industry leaders, and regulators would have the intellectual resources they need to better understand the issues and concerns at stake.

Participants at the roundtable included more than a dozen experts in the areas of microbiology, IP, agricultural biotechnology, microbial genomics, bioterrorism, economic development, biotechnology research, and bioethics.[1] These experts came from federal and state government, industry, and academia. The participants collaborated on the development of a comprehensive list of such issues and related questions. This paper describes the process and discussion surrounding the identification of these topics.

BACKGROUND

Early ethical and public policy issues raised by biotechnology

The ethical and public policy issues that have confronted the development of biotechnology have evolved as the technology itself has progressed from

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[1] A complete list of participants appears in Appendix A.

its early days of research, primarily in laboratories at government and academic institutions, to its commercialization in the private sector. In the late 1970s and early 1980s, for example, the primary public policy issues regarding biotechnology were the risks posed to human health and the environment by newly developed organisms such as genetically engineered bacteria and plants and pesticides and the societal risks of the new technology. Risks to human health and the environment included the possibility of the creation of organisms that were treatment resistant or had superior survival skills and thus could displace beneficial existing organisms.[2] Because, at this time, the development of these organisms was still in the research phase and taking place in laboratories, concerns arose about the security of government and academic research institutions and the possibility of organisms escaping from laboratories. In the early 1970s, there was such uncertainty about the risks surrounding the technology that scientists undertook a self-imposed moratorium on rDNA experimentation.[3]

By 1978, there had developed a consensus in the scientific community that the initial environmental and human health risks posed by rDNA research conducted in a laboratory setting had been somewhat exaggerated.[4] However, renewed fears emerged as the technology moved from the laboratory into the field for testing. This became an issue in the early 1980s, when genetically altered organisms were first released into the environment. Initial concerns focused on the potential harms associated with inadvertent conversion of a nonpathogen to a pathogen. This possibility was soon thought to be quite remote, and attention focused on the potential harms to the environment that could result as a consequence of a release of nonpathogenic organisms.[5]

In 1988, when the National Research Council Committee on Mapping and Sequencing the Human Genome strongly urged that a $200 million-a-year effort to map the human genome begin, the debate shifted to the societal risks associated with the technology. In addition to concerns about altering the genetic structure of human beings, critics expressed concerns that the project would lead to genetic discrimination and eugenics or interfere with an individual's right to privacy.[6]

During the early 1990s, scientists began to discover genes related to certain diseases via research on human tissues. As this research began, a number of the foreshadowed ethical and public policy concerns, as well as new issues, emerged. These issues included the rights of individuals to control the use of their tissue, appropriate informed consent for use of human tissue in genetics research, information disclosure to research subjects, and the confidentiality of information gained in the research setting. As genetic tests began to be used in the clinical setting, the privacy of genetic test results and the use of genetic information for purposes of discrimination in employment and insurance became topics of concern.

When scientists began to develop new therapeutic agents that required human subject testing, new issues arose regarding the safety of genetic protocols and the liability of Institutional Review Boards[7] (IRBs) and researchers. This issue was given considerable attention when one research subject died as a result of his participation in a gene therapy trial. As biotechnology products moved from clinical testing into the marketplace, another set of issues

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[2] *See* A.B. Naumann, Federal regulation of recombinant DNA technology: time for a change, 1 High Tech. L.J. 61 (1986).

[3] *See* J.P. Swazey, J.R. Sorenson, and C.B. Wong, Risks and benefits, rights and responsibilities: a history of the recombinant DNA research controversy, 51 S. Cal. L. Rev. 1019 (1978).

[4] *See* H.P. Green, Genetic technology may prompt new legal regime, *Legal Times*, Jan. 18, 1982.

[5] There were different perceptions of the risks associated with such releases. A 1987 report issued by the National Academy of Sciences argued that such risks were minimal. *See* National Academy of Sciences, *Introduction of Recombinant DNA-Engineered Organisms into the Environment: Key Issues* (1987). However, a 1988 report from the Office of Technology Assessment stated:

> Planned introductions of genetically engineered organisms into the environment . . . are not . . . without potential risks. Virtually any organism deliberately introduced into a new environment has a small but real chance of surviving and multiplying. In some small subset of such cases, an undesirable consequence might follow. The complexity of even simple ecosystems makes the precise prediction of such events, and of their consequences, difficult.

Office of Technology Assessment, *New Developments in Biotechnology: Field Testing Engineered Organisms: Genetic and Ecological Issues* 3 (1988).

[6] *See* Human Genome Policy Board recommendations, 7 Biotech L. Rep. 105 (1988).

[7] Institutional Review Boards were established in response to federal regulations governing human subjects research. Virtually all such research conducted at academic medical institutions must be approved by these boards which review research protocols for safety and ensure that research subjects are adequately informed of and consent to the risks to which they may be exposed.

surfaced. These included questions about who should have ownership rights in products when the research and development of such products was largely government supported; whether certain genetically modified organisms or newly identified genes should be patented; and how much control a private company should have over dissemination of its research results when inability to access those results could slow new developments by other researchers and commercial ventures.

During the 1990s, conflicts of interest between government and academic researchers and industry also came to the forefront. Such conflicts occurred in the context of basic as well as clinical research. Academic–industry ties came under closer scrutiny. Issues of academic freedom, freedom to publish, and secrecy, along with conflicts of interest, became the subject of intense debate. In 1995, the National Institutes of Health (NIH) developed regulations that required researchers funded by the National Science Foundation (NSF) or NIH to notify their home institution if they had financial interests or equity above a certain amount in companies that might be affected by their research.[8] In the academic setting, administrators expressed concerns about whether researchers would be able to make decisions in the best interest of the academic institution, and in line with their faculty obligations, if they also had the potential for significant financial gain through participation in a commercial enterprise resulting from their research. In the context of clinical research, concerns have centered on whether physician researchers are acting in the best interests of their research subjects/patients when they have financial incentives to enroll subjects or have financial interests in the outcome of the research.

Also, during the last decade, as agricultural and food products resulting from biotechnology have come into the market, consumer advocates have raised issues regarding labeling. As these products have crossed international boundaries, international treaty issues have also become the focus of discussion.

Regulatory development

According to a 1989 article, the regulation of biotechnology began in 1976 "when the NIH first issued its *Guidelines* to regulate the potential risks of laboratory conducted rDNA research."[9] From 1976 through the late 1980s, the regulatory structure expanded as state and local governments as well as "a number of different federal agencies . . . used a variety of statutes to regulate biotechnology research and product development."[10] At the state and local level, between 1977 and 1982, approximately a dozen local governments passed laws or ordinances regulating biotechnology research. One of the first such localities was the city of Cambridge, Massachusetts, which imposed a 3-week moratorium on all rDNA research and drafted an ordinance to regulate all DNA research conducted in the city.[11] At the state level, during the late 1970s, two states—New York and Maryland—enacted legislation regulating biotechnology research.[12] At the federal level, the industry has been regulated by the NIH, the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), the Occupational Safety and Health Administration (OSHA), and the U.S. Department of Agriculture (USDA).

Early in the industry's development, interested parties also debated public policy and regulatory issues through a handful of court cases. Most of the early judicial involvement in this area was through the National Environmental Policy Act (NEPA). The Act requires federal agencies to prepare environmental impact statements for all "major federal actions" which "significantly affect" the quality of the environment (42 USC §4332). In 1983, the Foundation on Economic Trends, headed by Jeremy Rifkin, used NEPA for the first time to halt rDNA field testing. In *Foundation on Economic Trends v. Heckler* (756 F.2d 143 [D.C. Cir. 1985]), the Foundation sued NIH for its failure to comply with NEPA when it amended its *Guidelines* regulating the potential risks of laboratory conducted rDNA research[13] and approved several deliberate-release experiments, including the release of a genetically altered bacterium (the "ice minus" bacterium) on a crop of potatoes to make them frost resistant. The U.S. District Court for the District of Columbia issued a preliminary injunction preventing the deliberate release and "all future deliberate release ex-

[8] J. Mervis, Science 1995;269:294.

[9] *See* D.E. Hoffmann, The biotechnology revolution and its regulatory evolution, 33 Drake L. Rev. 471, 483 (1988–89).

[10] *Id.*

[11] *Id.* at 537.

[12] *Id.*

[13] *See* National Institutes of Health, Guidelines for Research Involving Recombinant DNA Molecules, 43 FR 60,080 (1978).

periments until a final decision on the merits of the alleged NEPA violations could be reached."[14] On appeal, the U.S. Court of Appeals for the D.C. Circuit upheld the injunction against the ice-minus experiment but overturned the injunction against future releases, finding it overly broad.[15] At the same time, however, the court criticized the NIH for not giving sufficient consideration to the potential environmental impact of these deliberate releases.[16]

In the early years of regulatory development, a debate ensued about whether regulation of this industry, on the one hand, was adequate to control the technology's risks, or whether, on the other hand, it was unduly burdensome. Public opinion fueled the motivation of regulators and policymakers to regulate the industry. A 1987 Harris poll on public perceptions of biotechnology found that 77% said they agreed with the statement that "the potential danger from genetically altered cells and microbes [was] so great that strict regulations [were] necessary."[17] Yet industry was highly critical of the extent of regulation and its complexity and complained of needless delays and confusion as a result of an opaque and fragmented regulatory approach. The debate regarding adequate regulatory control continued throughout the 1990s.

The beginning of the second millennium ushered in increased regulations in this area with heightened concerns about safety and security in the wake of 9/11. While the pendulum has swung in the direction of more regulation, the debate over the appropriate level of regulation will likely continue as pressure from the industry to market its new discoveries mounts and as arguments that the discoveries offer significant potential benefits to society become stronger.

At the same time the regulatory scheme for the biotechnology industry was evolving, the IP landscape changed in ways that have significantly affected the development of this new industry. New IP laws had an especially profound effect on industry and academic relationships. Prior to the early 1980s, technology transfer "was little understood or practiced"; today, it is a major profession within and outside the academic community.[18] The number of patents held by universities has increased dramatically since 1980, when Congress passed the Bayh-Dole Act.[19] That Act, among other things, changed the prior presumption of title in and to any invention developed with government funding from the government to academic institutions.[20] In addition, the Act, in conjunction with the 1980 U.S. Supreme Court decision in the *Chakrabarty* case allowing a live organism (bacterium) to be patented, and with strides in the evolution of genetic engineering concepts, launched universities into an awareness of the economic value of their research-generated technological developments.[21] By allowing universities to hold patents on government-funded research, the law made it much more attractive for private industries to collaborate with universities in research and development of new products as the universities were able to grant exclusive licenses to industry partners. As a result, industry has made available to the public, through the private market, many beneficial new products.

Another significant outgrowth of the Bayh-Dole Act and the development of university technology transfer programs has been the establishment of hundreds of start-up companies based on technology generated in academic laboratories. Many of these start-ups have been in the area of biotechnology. From 1980 to 2001, more than 2900 new companies were based on licenses from academic institutions.[22] Universities often benefit financially from these start-ups, in which they frequently take an equity position.

Future public policy and ethical issues for the biotechnology industry are a matter of intense interest as the industry, with so much to offer in terms of benefit to the private sector and the population at large, begins another phase of development. The role of government as policy maker in this process continues to evolve as new issues emerge and as

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[14] D.E. Hoffmann, *supra*, note 9, at 534.
[15] *Id.*
[16] *Id.* NEPA was used on a number of other occasions by the Foundation on Economic Trends to halt or delay biotechnology development. However, in other cases, the organization was not as successful as it was in *Heckler*.
[17] OTA, *New Developments in Biotechnology—Background Paper: Public Perceptions of Biotechnology* at 81 (1987).
[18] H.W. Bremer, The First Two Decades of the Bayh-Dole Act as Public Policy. Presentation to National Association of State Universities and Land Grant Colleges, Nov. 11, 2001, *available at* www.lnasulgc.org/COTT/Bayh-Dohl/Bremer_speech.htm.
[19] According to a recent article on the subject, in 1979, universities received 264 patents; in 1997, the number had increased to more than 2400. A.K. Rai & R.S. Eisenberg, Bayh-Dole reform and the progress of biomedicine, 66 Law Contemp. Probs. 289 (2003).
[20] Bremer, *supra*, note 16.
[21] *Id.*
[22] *Id.*

government assumes a multitude of new roles in its relations with the industry, including researcher and funder of research, regulator, and promoter of economic development and industry growth. These various governmental roles raise questions about competing objectives. As one author asked, "[c]an government simultaneously promote scientific research and innovation (as scientists want), encourage the growth of an industry that benefits the economy (as the biotechnology industry wants), and protect public health and individual privacy (as the public wants)?"[23]

Current ethical/policy issues

Current ethical and policy issues related to the agricultural and microbial genomics sectors of the biotechnology industry that have received recent attention in the press and trade journals have ranged from the regulation of genetically modified food, protection from bioterrorism and related concerns about scientific freedom, to IP laws and practices and whether they unduly restrict academic research and the development of new genetically based products.

With regard to genetically modified food, in May 2003, the U.S. and the World Trade Organization filed a complaint against the European Union (EU) for its moratorium on the approval of genetically modified (GM) crops.[24] The U.S. alleged that the EU was unnecessarily hindering trade. The EU argued that it is taking a more precautionary stance than the United States. This stance has included passing legislation that requires labeling of GM foods.[25] In contrast, the U.S. has supported the GM food industry, some would say with too little precaution. Since the 1980s, the U.S. regulatory policy has been to focus on the product rather than the process.[26] As a result, the U.S. policy essentially categorizes GM foods as equivalent to conventional foods. In 1992, the FDA's "Statement of Policy: Foods Derived from New Plant Varieties" established a presumption that most GM products are Generally Recognized as Safe (GRAS), thereby skirting the need for stringent regulation.[27] The conflict raises important ethical and public policy issues regarding societal risk and the need for additional regulation. It has already affected, and may further affect, industry development and international trade.

Following September 11, 2001, few public priorities in the United States have taken precedence over antiterrorism initiatives. The vulnerability of the public to the use of biological agents as weapons of mass destruction has become a focus of concern. Beyond considerations of improving readiness and responsiveness to bioterrorist threats, government action has included preemptive measures that implicate basic scientific research. In October 2001, Congress passed the U.S. Patriot Act, which, among other things, included a set of provisions "designed to control access to almost every aspect of science and technology . . . that could conceivably aid terrorists."[28] These provisions included tightened restrictions on foreign students entering the country to study at U.S. colleges and universities and imposition of more responsibilities on educational institutions to report information about their foreign students. Regulations implementing the legislation call for closer oversight of laboratories where researchers are using any of almost 50 specified biological agents. This oversight includes background checks and security clearances for everyone working at the laboratory, as well as unannounced inspections by government agents. Laboratories must also obtain federal approval prior to conducting genetic engineering research that could increase the resistance of an agent to drugs. In a December 2002 statement, the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine argued that the government's policies on foreign students and visitors "in the name of national security have already worked 'serious unintended consequences for American science, engineering, and medicine.' "[29] In response to concerns that the Administration might restrict the publication of "unclassified but sensitive information related to weapons of mass destruction," scientists have argued that such censorship threatens "researchers' abilities to engineer therapies and cures—

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[23] B. Rudolph and L.V. McIntire, eds., *Biotechnology: Science, Engineering, and Ethical Challenges for the Twenty-First Century* (Washington, D.C., 1996).

[24] C.M. Benbrook, Sowing seeds of destruction, *N.Y. Times*, July 11, 2003, at A17.

[25] L. Alvarez, Europe acts to require labeling of genetically altered food, *N.Y. Times*, July 3, 2003, at A3.

[26] E. Marden, Risk and regulation: U.S. regulatory policy on genetically modified food and agriculture, 44 B.C. L. Rev. 733 (2003).

[27] *Id.* at 747–49.

[28] D.J. Kevles, A security clampdown on biotechnology research, 106 Tech. Rev. no. 6 (July 1, 2003).

[29] *Id.*

and that could place the very competitiveness of the nation's biotechnology industry in peril."[30]

With respect to IP concerns, many scientists have been guided by a belief that the scope of a common law-based "research use exemption" to patent infringement was so broad as to insulate from liability virtually all experimentation performed at universities or nonprofit and not-for-profit institutions. The error of that belief was made clear by the Federal Circuit in their 2002 decision *Madey v. Duke University*.[31] In *Madey*, the Court held that use of a patented product or process does not qualify for the experimental use defense "when it is undertaken in the guise of scientific inquiry but has definite, cognizable, and not insubstantial commercial purposes. Use is disqualified from the defense if it has the slightest commercial implication."[32] While the Federal Circuit did not entirely abolish the common law exemption to patent liability, its decision in *Madey* leaves "grave doubt that the common law exemption to patent infringement liability can act as a safe harbor for any academic research effort."[33] In addition to its decision in *Madey*, the Federal Circuit closed an alternative potential safe harbor for academic institutions sued for patent infringement in the more recent decision in *Integra LifeSciences I, Ltd. v. Merck KgaA*.[34] In *Integra*, the Court stated that the provision established by §271(e)(1) of the Hatch-Waxman Act to hold harmless from patent infringement liability any act "to make, use, offer to sell, or sell . . . " a patented invention "solely for uses reasonably related" to the development of a new drug regulated by the FDA was to be very narrowly construed. While it is not clear in the wake of *Integra* what activities will qualify for the statutory exemption, the Federal Circuit held that the provision "does not reach back down the chain of experimentation to embrace development and identification of new drugs that will, in turn, be subject to FDA approval."[35] The implications of these two decisions for academic research institutions and biotechnology developments have not yet been realized, but they may result in a narrowing of the types of research that academic institutions may perform without additional licensing agreements.

Some groups have also raised the issue of IP practices as restricting the development of new genetically engineered crops. In July 2003, a coalition of public sector research institutions published an article in *Science* announcing the formation of the Public-Sector Intellectual Property Resource for Agriculture (PIPRA).[36] The organization, funded by the Rockefeller and McKnight Foundations, argues that the benefits of much publicly funded research come to private industry through university technology transfer programs and subsequently limit universities' flexibility to conduct research. As a result, research into crops with little commercial value, but which may lead to food security for the poor, is being restricted. The agricultural and GM organism sectors of the biotechnology industry are raising these and other concerns about ownership of IP. Additional concerns include bioprospecting and biopiracy,[37] encouraging private-sector technology while maintaining incentives for furthering the public good, and restrictions on the publication of microbial and agricultural genomic data in light of homeland security laws.

PARTICIPANT PERSPECTIVES AND CROSSCUTTING THEMES

Perspectives

The perspectives of the workshop participants reflected both their discipline; e.g., science, ethics, or law, and the organizations with which they were affiliated—governmental agency, not-for-profit research institute, academic research center, or private industry. The governmental bodies represented included federal and state agencies with either a regulatory or an economic development mission. One of the participants worked with a state economic development department whose mission is to attract

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[30] *Id.*

[31] 307 F.3d 1351 (Fed. Cir. 2002), *cert. denied*, 1235 S.Ct. 2639 (2003).

[32] L. Sung and C. Maisano, Piercing the academic veil: disaffecting the common law exception to patent infringement liability and the future of a bona fide research use exemption after *Madey v. Duke University*, 6 J. Health L. Pol'y 256,278 (2003).

[33] *Id.* at 278–79.

[34] 331 F.3d 860 (Fed. Cir. 2003).

[35] L.M. Sung and J.E. Schwartz, *The 2003–2004 Patent Law Handbook*, §4.1 at 155–56 (Thompson/West 2003).

[36] R.C. Atkinson, et al., Public sector collaboration for agricultural IP management, Science 2003;301:174; *available at* www.pipra.org.

[37] *See* Claims of "Bioprospecting" and "Biopiracy" in M. Livingston, The age of frankenfood: a solid overview of how genetic engineering affects our dinner table, *Legal Times*, July 7, 2003, at 21.

new businesses, stimulate private investment, create jobs, encourage the expansion and retention of existing companies, and assist businesses in the state with workforce training and financial assistance.

Several of the workshop participants were from academic or not-for-profit research centers. The specific organizations represented included the J. Craig Venter Science Foundation, the Institute for Genomic Research (TIGR), and the Maryland Biotechnology Institute. The Venter Science Foundation and its four nonprofit research affiliates (including TIGR) have a diverse portfolio of genomics research and policy projects. These range from the sequencing and comparative analysis of mammalian and microbial genomes, including those of pathogens, to the development of a "minimal genome." These affiliates also consider the public policy implications of genomic medicine, IP matters, public understanding of science, and science education. The organizations, collectively, have considerable experience in genome sequencing and analysis of plants, microbes, and animals that are important to agriculture in both the developed and developing worlds. The Center deals with a range of issues involving the use of genomic data generated from its sequencing machines and the software that manipulates that data; e.g., whether they should be protected as IP and licensed or be "open source."

The TIGR is an international leader in genomics. Early on, TIGR's focus was on microbial genomics, and it houses the Pathogen Functional Genomics Resource Center, an NIH-funded center. Over the years, TIGR has expanded its areas of interest and now has a large group that focuses on sequencing and annotation in plant genomics. As a not-for-profit research center that has made billions of basepairs of sequencing information publicly available, the Institute's concerns stem from its mission to disseminate its data to the public as quickly as possible and its worries about obstacles to such dissemination. Related to this basic issue, TIGR has concerns about the use of the information it has made available, specifically, whether subsequent users of the data will place limitations on access to innovations they develop with the data. The Institute also collaborates extensively with both international and national entities. At the international level, collaborators include scientists and governments of economically developing countries, which often express concerns about access to the benefits that are derived from collaborative research. At the national level, the Institute works extensively with academics and must deal with issues of publication and data disclosure.

The University of Maryland Biotechnology Institute (UMBI) consists of several research centers focusing on applications of biotechnology (marine science, agriculture, medicine, virology, and protein structure). The Center for Marine Biotechnology (CMB) focuses much of its research activity on microbial genomics. Several investigators are working on archaebacteria and on novel molecules from organisms that live in unusual environments. Researchers at CMB also are interested in bioremediation, environmental problems, and aquaculture. The Center for Biosystems Research focuses its research on insect vectors and livestock issues, as well as GM crops and plants. While the primary focus of UMBI is research, as a state institution, its second mission is economic development and moving its research from the laboratory to the marketplace. This goal raises numerous issues related to industry–university collaborations, including IP rights.

Another perspective was brought to the table by a research scientist from a for-profit corporation in the business of finding genes and enabling products. The company has formal agreements with a variety of countries for access to biologic materials that are utilized in the company's screening programs and is currently working independently and with strategic partners to develop products for chemical, industrial, and agricultural applications. In addition to these near-term products, the company is advancing its pharmaceutical programs, including new technologies for the discovery of antibody-based therapeutics. Ethical and policy issues for the company have included balancing access to biological diversity with the requirements of local and transnational regulations and conventions, including the Convention on Biodiversity.

Also represented was the office of the Deputy Commissioner for Patent Examination Policy in the U.S. Patent and Trademark Office (PTO). Among other responsibilities, the Deputy Commissioner provides staff assistance in establishing patent examination and documentation policy standards for the Commissioner for Patents and is the authority on patent laws, rules, and examining practice and procedure; provides direction for the establishment of new rules, practices, and procedures; and reviews and revises the *Manual of Patent Examining Procedure*. The Deputy Commissioner also provides

support, representation, advice, and direction on technical matters relating to the International Patent Classification System and other international documentation-related standards. Recent policies established by the Commissioner relevant to agricultural and microbial genome developments include the new examination guidelines for the utility and written description requirements for patentability. The Office is involved in an international effort to harmonize the substantive requirements of patent law. The Office is also working on projects with the European and Japanese patent offices to generate greater mutual understanding and possible convergence of views on the patenting of genomic and proteomic inventions. Several other participants also had backgrounds in IP or provide IP advice to clients.

Two participants direct academic centers focusing on issues related to bioterrorism. The Center for Health and Homeland Security at the University of Maryland and the Center for Deterrence of Biowarfare and Bioterrorism at the University of Louisville are among a handful of academic centers, established after 9/11, devoted to this issue. Both Centers draw on the resources available at their respective universities to provide expertise and advice to local, state, and national government agencies seeking to address a broad range of problems and policies pertaining to the nation's war on terrorism. Each Center serves as a focal point for research and helps to develop and support programs within its university in conjunction with other private and governmental agencies. Both Centers have assisted or are assisting their communities to improve their infrastructure for bioterrorism preparedness and have been involved with preparedness training exercises. Both Centers are also located at universities where researchers are working with organisms that could be used for bioterrorism, such as anthrax and smallpox.

A representative from Department of Energy (DoE) Office of Science, Program of Biological and Environmental Research also participated in the discussion. The DoE's mission includes the advancement of the "national, economic and energy security of the United States," the promotion of "scientific and technological innovation in support of that mission," and the "environmental cleanup of the national nuclear weapons complex."[38] The Office of Science manages fundamental research programs in basic energy, biological and environmental sciences, and computational science. In addition, the Office is the federal government's "largest single funder of materials and chemical sciences, and it supports unique and vital parts of U.S. research in climate change, geophysics, genomics, life sciences, and science education."[39]

In 1994, DoE began the Microbial Genome Project, a spin-off of the Human Genome Project, to sequence the genomes of microbes, primarily prokaryotes. Unlike the human genome, which took several years to complete, many microbial genomes can be sequenced completely in weeks or months and, with recent advances in sequencing technologies, even days. As of April 2003, DoE had funded the sequencing of the genomes of about 100 microbes, most of them by the Joint Genome Institute. These data, in addition to those from many viruses and higher organisms such as yeast and the roundworm, are available in public databases and are being used by academic, medical, and industrial scientists to make comparisons not previously possible.[40]

Cross-cutting themes

At the roundtable, participants expressed a number of common concerns. These centered largely on access to genetic information and IP issues but also included the environment and public health, disparities between developed and developing nations, and regulatory balance.

Scientific freedom/access to data/publications

Participants representing academic and research institutions expressed concerns about disclosure of scientific breakthroughs, data access, and IP. One participant from an academic research center commented that when dealing with faculty, scientific freedom is a significant issue and one of recurring challenge. Institutions dedicated to the development of products and processes derived from their research face new obstacles in the post-9/11 environment, where there is a heightened sensitivity to

[38] U.S. Dept. of Energy Mission Statement, *at* www.energy.gov/engine/context.do?BT_CODE=AD_M.
[39] U.S. Dept. Of Energy, Office of Science, *at* www.energy.gov/engine/content.do?BT_CODE=OF_POS.
[40] *See* U.S. Dept. of Energy, Microbial Genome Program, *at* www.sc.doe.gov/ober/microbial.html.

confidentiality, what is considered "secret," what information can be shared, and what can be published.

Several roundtable participants also expressed concerns about publicly funded genome research projects. These projects typically come with requirements for timely release of the data into the public domain, either by distribution on the institution's own Website or in a public database such as GenBank. Once these data are released, researchers at large can use them freely in their own studies or for their own publications. Questions raised by these arrangements include (1) who owns the data? (2) what incentives exist for scientists to participate in these projects if the scientist(s) directly involved in the sequencing project will continue to be "scooped" on publications? (3) should we balance the public release of such data with the interests of the scientists/collaborators in publishing whole genome or chromosome analysis of such projects? (4) what role do, or should, academic journals play in accepting publication from scientists who have not generated the data on which their manuscript relies? and (5) should we simply have Web-based information for one and all to use? If so, how will that impact the protection of IP, which in this context has been in the patent rather than copyright area?

Another concern was the monitoring of how data are being used after completion of a sequencing project not under publicly funded guidelines. Participants were not aware of any guidelines for non-government-funded organizations to monitor the use of sequence data. Data release policies are based on guidelines from the funding agencies, and all sequence data are available over the Internet. There are no assurances that the data will be used in a beneficial way.

Public/private collaborations

A second theme to emerge was the need for guidelines for public/private collaborations. Participants concerned about this topic asked what role the federal government agencies should play in fostering public/private collaborations in the area of genetic research and product development and to what extent we should allow the industrial organizations that collaborate with government and not-for-profits to restrict publication and dissemination of research results and IP rights. A number of federal agencies are now trying to determine whether they should assert control over databases generated from collaborative efforts they fund to ensure that access will be made available to the public at large. At least one participant felt that such an approach seemed "counterintuitive." "For the government to have a heavy-handed approach to what would otherwise be a public library or public databank," he remarked, "may mean that when we get on a commercial Website and want access to a public database that was generated by or with support from the federal government, we may have to click on a license that is pages long to ensure that we do not seek IP protection based on the fruits of information gleaned from the database." However, he acknowledged that the government may believe it is necessary to adopt a "defensive IP strategy to ensure public access downstream."

The representative from the PTO clarified that in order to procure a patent on an invention, one must satisfy the enablement and written description requirements. These requirements include submission of a written description of the invention that is sufficient enough that one who is skilled in the field can recognize that the researcher is actually in possession of what he/she is trying to protect. The "enablement requirement" is an attempt to ensure that one who is skilled in the technology could make the invention and use it on the basis of the disclosure as well as knowledge of the art. If a skilled artisan would need undue experimentation in order to be able to practice the invention, the disclosure is insufficient.

These questions and issues struck a chord for those working with academic research centers. One participant shared the experience that collaborations with external parties have been an issue at her institution for a number of years. Even simple things such as material transfer agreements to foster collaborations between people who are not in the same institution become problematic points of negotiation—one side puts on conditions that the other finds unacceptable, and ultimately, the research "can't happen because the materials can't be transferred." Another participant reported that he thought this was a problem, but that it was also a natural consequence of universities playing a much greater role as entrepreneurs and actors in the marketplace. Others pointed out the impact that recent judicial decisions in the area of IP law may have on this issue by limiting the experimental use defense and allowing researchers to use patented technology and innova-

tions without a license in only very narrow circumstances.

Another participant commented that these collaborative initiatives raise questions about when the work is sufficiently completed to become part of the public domain. One participant spoke of the need to distinguish between different types of data—raw sequence information from a genome sequencing project may not be protected by patent or copyright, and it makes sense to put this data in the public domain as soon as possible.

Intellectual property

A third, and related, theme was that of IP rights. The debate about the appropriate balance between public access and commercial exclusivity depends in large part on the scope of IP rights, particularly patent rights. Participants questioned whether the current IP laws provide sufficient predictability for researchers. Limited pertinent jurisprudence on the scope of patent rights to genomic inventions leaves a void that creates uncertainty. Although the PTO has granted patent rights to inventions in genomics, few such patents have been litigated. Accordingly, little guidance exists about whether seemingly broad patents on early-stage research will be upheld by the courts or struck down as overreaching.

Several participants voiced concerns about how IP laws might impact new developments in agricultural biotechnology and microbial genomics. Some questioned whether our current IP regime made sense for this new technology. Others pointed out the significance that IP rules have for economic development.

One participant expressed concern about patent thickets, pointing out that if we do not consider options such as patent pooling,[41] we may find that companies in the U.S. are less able to conduct research and development. Another participant agreed this was an issue worthy of further study but thought it was more likely to be an issue on the human genomics side than on the animal, plant, and microbial side. For example, he asserted, even if we had cost-effective techniques to sequence people's genomes and screen for mutations and alleles, we would "run into an instant infringement thicket because there are hundreds of patents covering 'one-off genetic test methods.'" Several participants asserted that we need to examine ways to address this very likely problem, whether through government licensing, patent pooling, or other means. This scenario may be worse in the genomics sector, where "mom and pop" shops have patented genetic testing methods, than in the semiconductor industry, which lacks the "mom and pop" shop culture.

Participants raised a number of issues and questions about IP rights, including:

- How IP and publication rights should be coordinated within public/private collaborations and whether patent pooling arrangements can be established to facilitate such collaboration or would run afoul of U.S. antitrust laws;
- How universities and research institutions can protect their subject matter and whether, in light of recent court decisions, we need a broader experimental use infringement exemption;
- Whether patenting and licensing practices for "platform" technologies are overly restricting or delaying the development of products of public health and agricultural significance;
- Whether PIPRA establishes a framework for other scientific sectors to follow, or whether this type of IP management is applicable only to the agricultural sector and how the interests of small commercial end-users of agricultural technology can be protected. In multi-institutional projects to develop new genetically engineered crops, should any one institution have the right to own the IP developed, or should the IP be assigned to the consortium to ensure that it is ultimately made available to the public?

In addition, some asked whether the goals and effectiveness of the Bayh-Dole Act should be reevaluated. The original intent of the Bayh-Dole Act was to spur the commercial development of academic

[41] The PTO, in a recent paper, defined patent pools as agreements "between two or more patent owners to license one or more of their patents to one another or third parties" or, alternatively, as "[t]he aggregation of intellectual property rights which are the subject of cross-licensing, whether they are transferred directly by patentee to licensee or through some medium, such as a joint venture, set up specifically to administer the patent pool." J. Clark, et al., "Patent Pools: A Solution to the Problem of Access in Biotechnology Patents?" USPTO (Dec. 5, 2000) *citing* J. Klein, An Address to the American Intellectual Property Law Association on the Subject of Cross-Licensing and Antitrust Law (May 2, 1997), *reprinted at* http://www.usdoj.gov/atr/public/speeches/1123.htm.

inventions and increase the range of products in the marketplace. Perhaps we need to examine whether the Act is accomplishing these ends or whether there are unintended consequences such as the spread of IP rights to cover more basic research activities.

Bioterrorism

Several workshop participants acknowledged that the threat of bioterrorism on the one hand and the need to develop effective means of mitigating this threat on the other poses unique ethical challenges for modern science. The rapid pace of genome sequencing in the public and private sectors, coupled with growing understanding of the mechanisms of pathogenicity and the biology of disease-causing microorganisms, have created information with the potential to be misused. As a consequence, scientific organizations at all levels are being forced to balance the obligation of scientists to publish and disseminate new discoveries with the risks of doing harm by making that information available to individuals or entities who will use it to create new or more harmful weapons. One participant commented that dual-use technologies may engender particularly difficult decisions. For example, sequencing and gene synthesis technologies may be used for biological warfare or bioterrorism purposes, as well as for the development of new therapeutics. As an example, he mentioned the technologies that permitted the recent (July 2003) production of a poliovirus.

This discussion raised questions about whether scientists or funding agencies should have the right to restrict public access to certain genome projects (e.g., *Bacillus anthracis*, smallpox) for national security reasons. Several participants commented that there have already been disturbing examples where federal agencies have interfered with publications, even doctoral dissertations, arguing that certain information must be stripped from the articles prior to public dissemination. Participants all expressed concerns about the costs of excessive secrecy to beneficial new products.

The lack of clarity about what is or is not "too risky" to publish and the lack of widely accepted guidelines on this issue was also thought to be an obstacle to new developments. One participant commented that some groups such as the Monterey Institute have made a start at laying out a conceptual framework; however, until there is better guidance in this area, "a good deal of potential publications may get caught up in some kind of review cycle, and we may become so conservative that we don't move forward with the scientific literature at a fast enough pace to cure diseases."[42]

Federal policies that tie receipt of funding to restrictions on information dissemination are also problematic for many research institutions. For example, one participant reported that her university prohibits researchers from accepting classified research projects and funding to engage in activities accompanied by restrictions on their ability to publish.

The two workshop participants who direct academic centers that focus on bioterrorism articulated concerns, not only about GM organisms and their potential use as weapons of bioterrorism, but also about the broader implications of security policies that affect civil rights and create fear and suspicion. As one participant stated, "it is clear that post 9/11, we live in a new era, an era of fear—fear of foreigners who could be terrorists and fear of scientific information that could be misused by terrorists. The consequence is that we, in the scientific and academic communities, are now subject to new levels of public scrutiny that are manifest in the regulations governing visas for foreign students and visiting scientists and security clearance requirements for those with access to microorganisms and toxins (select agents) that are considered high-risk biothreats which might be used by terrorists."

One participant asserted that this public scrutiny has at times been very heavy handed, especially in the areas of immigration, detention, and environmental information. In fact, it has been so heavy handed that there has been a backlash against the U.S. Patriot Act, which expanded the U.S. government's surveillance and law enforcement powers to increase the government's ability to fight bioterrorism. At the time of the workshop, approximately 200 city councils (including those of Baltimore and

[42] Shortly after the roundtable was held, the National Academies of Science issued a report entitled, "Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma." The report helps define areas of potentially high risk in the life sciences that should be given additional scrutiny. The NAS report also proposed a framework of filters that would help protect the life sciences against potential misuse. The report is available at www.nap.edu/books/0309090778.

Philadelphia) had voted either to have the Act declared unconstitutional within the confines of their jurisdiction or instructed police officers not to follow it. Three state legislatures (Hawaii, Alaska, and Vermont) had also passed laws preventing the enforcement of the Act.

Another participant argued that scientists have an important role in educating both the public about the need for regulations to prevent bioterrorism and policy makers about crafting such regulations so that they do not impede scientific research and progress: "We, in the scientific community" he asserted,

> "need to explain to the public and policy makers that the best defense against the threat of bioterrorism is to advance the research agenda against infectious diseases so that we have the vaccines, therapeutics and diagnostics needed to combat emerging and reemerging infectious diseases as well as "plagues" that may be introduced by terrorists. We need to make clear that biomedical research is an international endeavor and the battle against infectious diseases must be global. We also have an obligation to engage in a dialog with the national security community so that we understand the threats and vulnerabilities of our new world and can engage in activities—some of which will involve constraint and adherence to the new regulatory mandates—that will reduce the threat of the misuse of the life sciences by terrorists."

This participant further argued that for public policy reasons, we need to (1) define what is dangerous information and should be kept secret; (2) determine appropriate investments in biodefense; (3) balance security with the advancement of science; and (4) establish a dialogue between the scientific and national security communities.

Industry and economic development

Several workshop participants articulated concerns about economic development and the impact of biotechnology on the agricultural and food industries. The ability to genetically modify plants and crops has dramatically changed the modern food sector and the range of players in the "value chain." One participant commented that "it used to be that the farmer was the initial player in the food production system; now, there are at least three players prior to the farmer. They include very small biotechnology companies, large life science companies, and universities. The world in terms of agriculture is much more complicated than it was even a decade ago. The technology is very sophisticated. In addition, there has been a rapid increase in private R&D in this area. Previously, most of the innovation in this sector was done through public funding, mostly federal dollars. Agriculture is now starting to look much more like a traditional high-tech industry. There have been a number of mergers and a good deal of consolidation and vertical integration in the industry so that today, there are basically a half dozen major life science companies." Companies such as DeKalb and Pioneer have been bought up by bigger players such as Monsanto and Dupont. Many of the new players were formally large chemical companies that have taken over the life science enterprise."

This industry sector has experienced a consistent and rapid escalation in patent filings. These patents are for GM seeds as well as for processes that, for example, remove fat or add vitamins to traditional crops. In the mid 1980s, after the PTO began allowing patents on this type of innovation, filings increased significantly. Prior to that time, researchers did not think these developments were eligible for patent protection. After the U.S. Supreme Court decision in *Diamond v. Chakrabarty*, which reiterated the patentable subject matter standard as "anything under the sun made by man," little debate remains about the scope of patent-eligible subject matter.[43] But this area is generating new patent issues, and the granting of patents for items such as GM seeds, for example, is creating new marketing challenges for producers. Every bag of GM seed is now accompanied by bag-tag and seed wrap licenses. As a result, the seeds are not sold but licensed. If the seeds were sold, the patent would be exhausted, and the buyer could then do whatever he/she wanted with the product. This practice has created policy issues in a number of states where there have been efforts to outlaw such licenses. These prohibitory

[43] Any doubt about the availability of utility patent protection for plants and seeds was laid to rest in the 2001 Supreme Court decision *J.E.M. Ag. Supply, Inc. v. Pioneer Hi-Bred Int'l., Inc.*, 534 U.S. 124, 122 S.Ct. 593, 60 USPQ2d 1865 (2001).

efforts appear to be based on concerns that the new large life science companies are changing the way business has been done and a fear that the licensing process will affect traditional business dealings.

Another reaction to the use of GM seeds is illustrated by recent pollen-drift lawsuits. This litigation is arising from claims that GM organisms have crossed into neighboring fields. Although the legal implications of such claims are unclear, these events may have undermined early scientific assurances that fears of the spread of GM organisms were unwarranted.

Underlying these actions is a concern that the new technology is transforming economies. Although, in the end, the new technology may result in lower costs, it is displacing the need for some types of labor. An example given by one roundtable participant was the labor pool that was needed less than 10 years ago in the Midwest to detassel corn each summer. Now, there is male-sterile corn that does not have tassels. The new innovation may cost less in the long run, but it has the short-term impact of putting an entire group of people out of work. States and countries need to think about transition strategies for laborers when one technology displaces another. One speaker commented that he thought the potential for transforming economies was much greater in the agricultural sector than in the medical industry.

Participants also discussed whether there was a need for policies to expedite economic development. For example, should a state assist in establishing the infrastructure that would allow environmental and industrial applications to be better tested in the environment? Such an infrastructure might include fast-tracking permitting processes or facilitating industrial partnerships that would allow the use of "brown" fields. The infrastructure would permit some of the new technology to surmount obstacles related to proof of principle, which is often challenging and burdensome in terms of paperwork and other regulatory hurdles.

Public health and environmental perspective

Several participants spoke about public health and environmental concerns related to agricultural and microbial genomics. One participant asserted that we need to develop timely and effective environmental risk-assessment protocols that can both assure the public of environmental safety and allow responsible development of new biotechnology products intended for use in the open environment. Such protocols are especially needed for trees and microbial products.

A second participant echoed this concern, stating that we need to consider the impact of new microbes on the ecosystem. In the U.S., most view the biotechnology industry as medical biotechnology; i.e., the development of novel gene-based biologics for therapeutic and diagnostic purposes. In Europe, at present, biotechnology is synonymous with GMO applications. The so-called "third wave" of biotechnology, industrial and environmental biotechnology, is growing in momentum and potential in terms of its impact on our daily lives. Largely confined at present to improving efficiencies in industrial synthesis processes and bioremediation applications, future applications involving non-confined (or open) systems of GMOs require serious consideration. The potential solutions that these applications can provide to society are as enormous as some of their potential to make unanticipated alterations in our ecosystem. Microbial and synthetic cells, as well as products derived from them, will find broader application in the production of new materials, nonconventional fuels, and environmental clean-up. It will be crucial to understand how these organisms and their products will interact with our environment. These developments will require new modes of research such as closed micro-ecosystems (beyond containment), that allow testing of the influence of natural genetic pressures on these organisms, as well as how they will ultimately adapt and perform in an open ecosystem.

Related to this point, another participant mentioned the need to guard against inadvertent development of new organisms that may become pathogens or antibiotic resistant. She commented that "transposable elements have been slow to move around in the population and transfer genes such as those associated with antibiotic resistance (e.g., the *Enterococcus faecalis* genome). Plasmids are known to contain genes for antibiotic resistance and are capable of spreading these genes through populations quite rapidly. Microbes have their own ways of exchanging DNA, such as through transformation, allowing them to acquire free DNA from their environments. Competent species can take up random and non-random pieces of DNA."

Participants also pointed out that new public health regulatory issues will arise as a result of new therapeutics for animals and humans. While most are certainly aware of the issues surrounding the current and anticipated consumer-directed GMOs in produce and dairy applications, whole new developments for the use of plant-based technology platforms are under way. Some of these include the production of human and animal therapeutics. These plant-based platforms are serving, and will serve, both as cost-effective production methods and as combined therapeutic and delivery vectors. The possibilities of new recombinant therapeutic proteins produced and delivered in this manner will stretch our current concepts of Good Manufacturing Practices (GMP) and other FDA-regulated aspects of therapeutics for human use. The reality of edible biodefense vaccines or low-cost therapeutic alternatives that address compliance issues in developing nations, as well as the transformation of farming communities into biomanufacturing enterprises for the pharmaceutical industry, are months to a few years—not decades—away.

International issues

Participants' international concerns focused, in large part, on U.S. relationships with economically developing countries from which unique natural resources are taken or that collaborate with U.S. scientists on research projects. A number of participants mentioned that they, or the organization for which they worked, had dealt with other countries that want to lay claim to any benefits that come from biotechnology products that are derived from their natural resources. One participant said "You have countries that are being advised by groups that tell them . . . this is your resource, they sell it for this much and you should be entitled to all of that." The representative from a for-profit agricultural biotechnology company discussed his company's practices in this area. He commented that, "in order to facilitate access to unique environments while at the same time acknowledging the legitimate rights of stakeholders, the company has entered into agreements that provide for sharing of value created by its biosampling activities in accordance with the Convention on Biological Diversity (CBD). These agreements have been founded on principles consistent with the CBD: (1) the conservation of biological diversity; (2) the sustainable use of its components; and (3) the fair and equitable sharing of the benefits derived from utilization of genetic resources.

"If bioprospecting is to be successful," he remarked, "the parties involved must have realistic and congruent views regarding how value will be created, and how much of that value should fairly be shared."

One participant commented that in these cases, the issue often boils down to upfront negotiation and whether the researchers will gain access to the resources. In most cases it can be dealt with as a simple royalty issue. There was considerable concern about the imbalance between the U.S., which has the tools—the educational communities and the scientific expertise—to develop raw materials into valuable therapeutics or other products, and the countries which may have the natural resources but none of the tools. Another participant argued that what is at stake here is determining contributions to value and deciding how value can be shared in a way that is fair to both sides. He also pointed out that there are few standards in use by which to assess fairness in this context.

A number of participants felt that we needed to encourage scientists to carry out research relevant to developing countries and that this new technology should be used to assist less-developed countries. Others agreed that these were important questions, especially with respect to GMO seeds and crops that might alleviate starvation and hunger in some economically developing countries. Genetically modified seeds and crops are now being developed that are drought and insect resistant and can be used to alleviate food shortages. To the extent there are obstacles to less-developed countries using these technologies (because of cost or having only small plots of land), one participant suggested that our country should develop policies to overcome these barriers. Another added: "We need to provide incentives for industry to be a partner in collaborating and sponsoring research for smaller crops and developing countries."

Other participants pointed out that cost is often an obstacle with patented products, but that there are institutions, such as the Consultative Group on International Agricultural Research (CGIAR), working to take patented technologies in this area and turn them into public goods.

Another participant commented that this area is "ripe with overgeneralization because one has to as-

sess each of these potential crops individually. The cost-benefit analysis for each is very different. Examples are golden rice and Roundup Ready® soybeans. Golden rice is solving so many instances of vitamin A deficiency that it is considered very cost effective. Roundup Ready soybeans are a great innovation but not necessarily the solution to world hunger."

Public education

Several participants noted a need for communication with the public regarding genomics and biotechnology. Participants felt that without such communication and education, the public will not trust new developments and will not understand the benefits research in this area can provide. Issues such as utilization of natural resources from developing countries have attracted the attention of global activist groups. One participant stated that "developing means for scientists in academia, government, and the private sector to interact with the public in constructive ways to further the understanding of biotechnology will be critical in avoiding the kinds of polarized debates that now surround agricultural biotechnology. Separating sensationalistic concerns and issues from legitimate ones is a matter of critical importance in ensuring reasoned discussions."

Another participant shared this concern, stating that as we move into the 21st Century with advances in technology development in all fields, the intellectual demands on policy makers and the public at large will increase dramatically. One can argue that public perception, or misperception, can have as dramatic an impact on society as the improper implementation of a biotechnology application. In Europe, public activist groups have reacted negatively and vocally to GMOs—with a negative impact on trade between the US and the EU. He asked how the EU might have responded to the introduction of GMOs if educational institutions had taken an early lead. This participant went on to say that "[O]ne cannot equate education with promoting one opinion or another. Appropriate public education, a mix of science and ethical issues, would allow consumers to reach an informed opinion. From this collective knowledge, balanced public policies will be possible. At present, we rely too heavily on a system of 'advisory panels of experts' in policy decision-making. While they serve an essential role, the breadth of biotechnology developments and their potential implementation across a spectrum of industries will make sole reliance on this system logistically difficult in years to come."

A third participant stated that education of the public should be one of our highest priorities. She related her experience over the last 7 years in outreach and education programs for minority populations as relates to the Human Genome Project:

> The level of misunderstanding and lack of communication of scientific information to the public is amazing for a milestone as significant as the completion of the sequencing of the human genome. Although most funded projects that are associated with microbial and agricultural genomics have some requirement for an education and outreach component, this invariably results in training and further education of junior scientists who already have an understanding of the science involved in genome sequencing and the applications that are possible from this process. More attention should be given to the education of lay people either through radio, television or newspapers. Such education may reduce some of the public's misconceptions about these various scientific issues.

Another participant added that the public needs to be better informed about the overall benefits of biotechnology and the pace of their implementation, both of which may be more limited than is typically perceived. He asserted that the expectations of the public in the U.S., Europe, and developing countries about these issues may be unrealistic.

Several participants also mentioned the need to educate regulators who are attempting to balance concerns about homeland security with scientific freedom. If they do not appreciate the costs and benefits of their actions, they may implement policies that have significant negative impacts on the research enterprise. One participant expressed the view that this was a short-term problem; the longer-term issue, he argued, is the education of the public and how we function as a democratic society. "Do we let an uninformed public make decisions about what kind of technology can go forward?" he asked. He referred to a study conducted by the Office of Technology Assessment in the late 1980s about public perceptions of biotechnology. The survey asked "Do you favor or not favor genetic mod-

ification of organisms?" Eighty percent of the respondents said "absolutely not." The survey then asked, "What if you do it [genetic modification] through conventional breeding and cross-breeding?" Approximately the same percentage opposed that. Then the survey asked, "how about genetic modification if it will save the life of your child?" Here, the response was 97% in favor.

One participant commented that a negative byproduct of an uninformed public on these scientific issues is that lawmakers do not pay close attention to them. He added that "there is a great deal of good research . . . showing that policy development on these complex topics is dominated by the stakeholders who get together and work it out. The legislators don't give it the same kind of attention they might give crime legislation or an issue on which there is much more focused public attention."

Forum issues

A final crosscutting theme addressed by participants was the appropriate forum for dealing with the variety of issues brought to the fore by this new technology. One participant stated, "There is currently no body that, from a global perspective, is going to be able to wrestle with these types of questions. And it does not appear that any one entity at this time is equipped to be able to ultimately resolve these things to anyone's satisfaction." Even on the private sector side, another participant commented, the large seed-producing companies have not spoken with one voice on these issues and are paying the price for it. "Now," he said, "the GMO debate is wrapped up in the world trade debate, and it has become a big-company versus the Third World issue" rather than one about the risks of the technology and the problems it can address. The debate has become extremely polarized. "Hopefully," he went on to say, "the microbial genomics industry will be able to learn some lessons from agricultural genomics and move forward in a more productive way."

FUTURE PUBLIC POLICY AND ETHICAL ISSUES IDENTIFIED BY ROUNDTABLE PARTICIPANTS

The crosscutting issues identified above were reviewed by the participants and used to develop the following list of public policy and ethical issues most likely to confront the industry over the next half decade. Along with each issue, participants raised a series of questions for consideration. The issues are *not* listed in order of importance.

Public access to public information

- Privatization: Do we need rules regarding access to genetic data developed with public funds? Should limits be placed on the types of restrictions the private sector can place on this information?
- Funding concerns: Are sufficient financial resources being made available to facilitate research and development for public benefit without the necessity of commercial exclusivity considerations? What might be the role of charitable entities in this regard?
- National security issues: Is there a need to better define what kind of information is "too risky" or "too dangerous" to be published, so scientists can take that into account when deciding what research to pursue?

National security *v.* biotechnology development:

- Achieving an appropriate balance: How do we balance concerns about national security with the need for openness as part of the process essential for research and development of new products? How much should we be investing in biodefense?
- Bioterrorism: How do we balance concerns about bioterrorism with the need to develop effective means to prevent and mitigate such threats?

International collaborations

- Access to natural resources: How can we foster collaborations with countries that have natural resources that may benefit all countries through technological development and provide a fair return to the country of origin? Should the U.S. adopt the CBD or some modification of it so that commercial entities in this country have some guidelines for such collaborations? If not, should private sector actors voluntarily comply with the Convention?
- "North/South" issues: How can we reconcile the interests of economically developing coun-

tries with those of the more industrialized nations with regard to IP enforcement concerns?
- Biopiracy: How can we protect against the unauthorized export of natural resources for purposes of R&D by foreign private companies?
- Technology transfer: Do we need guidelines to determine value and appropriate compensation for agreements between commercial entities and developing nations? Similarly, should we develop guidelines for relationships between public and private entities regarding access to publicly funded data collection and allocation of benefits resulting from developments based on the data?

Movement of U.S. research and development to foreign countries

- U.S. economic development: Is the U.S. losing economic benefits as a result of IP rules and biotechnology regulations that encourage private companies to move their research and development operations overseas?

Optimal IP/use regimes for microbiological/agricultural inventions

- Reconciliation of disparate legal regimes: Do we need to reevaluate the current U.S. IP regime and its appropriate application to agricultural and microbial genomics? Should policy makers rethink what would be the optimal IP regime for agricultural innovation and agricultural biotechnology?
- Patent issue rate: As a policy matter, how should we deal with the fact that competing patents in this area are issuing at a phenomenal rate? Do we need to establish patent pooling policies?
- Navigating patented landscapes: Is there a need to scrutinize the existing patent landscape? Are we encountering or likely to encounter patent "thickets" in the agricultural or microbial genomics areas, as we have in the pharmaceutical area? Should we continue to allow early-stage patenting, or should there be more stringent patentability requirements?
- Absence of a common law research use exemption to patent infringement and scope of 271(e) clinical use exemption: Should there be such an exemption? What should be its scope? Do we need clearer guidelines for research institutions? Does the current situation; i.e., a lack of clarity regarding a research exemption, increase academic transaction costs or create a chilling effect on academic research? Do we need federal legislation on this issue?

Competing economies

- Cultural/value issues: The development of agricultural biotechnology affects family farmers, who have been a staple of the American heritage. How can traditional family farmers continue to exist in light of the innovations of the new technologies, which may lead to transgenic, high-tech livestock and crops?

Regulation of biotechnology applications

- Regulatory approach: What regulations will we need to respond to the multiple impacts of new biotechnology applications on public health through the development of new foods, crops, microbes, and therapeutics?
- Environmental impact: Can we develop timely and effective environmental risk assessment protocols for ensuring environmental safety? GMOs raise issues of genetic containment. How can we assure that GMOs released into the environment are not or do not become pathogens or disrupt the ecosystem by competing with existing species?

Global food supply

- World hunger: Should agricultural biotechnology continue to be used to address world hunger? Are there ways we can encourage the application of the technology for this purpose? In particular, can we encourage government agencies and industrial sponsors to fund crop development that may be of interest only to developing countries? Can we provide incentives for transfer of knowledge and technologies to less developed countries to assist them address food shortages and lack of therapeutic interventions?

GMOs

- Labeling issues: The lack of globally agreed on labeling standards has created significant trade

problems for U.S. food manufacturers. Should we pursue uniform global labeling requirements that assure consumers of the content of products they purchase?

Education/public information

- Forum and content: Both consumers and regulators need to be educated about biotechnology and national security and the legal and ethical issues raised by its application. What are the best forums for discussion between scientists, regulators, lawyers, and ethicists about these issues?

Research funding prioritization

- Allocation of research funds: Are we allocating our research budget appropriately? Has shifting the funding priorities from basic research to homeland security affected progress on new developments that could benefit the public health and welfare?

Industrial/environmental applications

- Role of government: Should governments support the development of infrastructures for companies to test new GMOs or agricultural biotechnology products? Should we restrict the ability of companies to test these products in economically developing countries?

PRIORITY ISSUES—THE CONSENSUS OF THE GROUP

On the basis of the comprehensive list of questions above and their discussions, the roundtable participants were asked to identify the top three to five policy/ethical issues they thought were priorities that policy makers, academics, and industry should address over the next few years. Despite their divergent backgrounds, the group members agreed relatively quickly on the following list:

1. Public access to publicly funded research results: Should we establish policies that ensure public access to research outcomes that resulted from publicly funded projects and thereby limit the ownership rights by commercial enterprises?
2. Harmonization of laws and regulations: Is there a need for common regulations regarding labeling and risk reduction across international borders so that new GM products can be imported and exported with assurance that the products are meeting global standards for safety? How might the disparity in the enforcement of IP rights in various countries be reconciled to address the respective national concerns about the appropriate balance between public access to research outcomes and commercial exclusivity?
3. Natural resources disparity: How should we address the concerns of economically developing countries that arise when commercial enterprises extract natural resources from those countries and use sophisticated biotechnological processes to develop profitable products? What is a fair allocation of the benefits from these products?
4. Bioterrorism: What are the costs to innovation and development in the agricultural and microbial genomics sectors of the biotechnology industry as a result of our current focus on national security and bioterrorism? How do we address bioterrorism without slowing innovation and development in the biotechnology industry?
5. Public education: How can we educate the public, policymakers, and regulators about biotechnology, its relevant impacts, and the competing interests at stake?

Participants raised the issue of legal harmonization, both in the context of IP and public health and safety regulations and in the context of natural resource/expertise disparities. The group agreed that the technology has become so global that the U.S. cannot act alone in national regulatory oversight without considering how the decisions affect the rest of the world.

The participants all felt that issues arising from disparities in natural resources and technological expertise between the U.S. and economically developing countries deserved significant attention as a policy matter over the next few years. For the most part, this issue has been addressed by private actors in the U.S. We now must think about whether we need a national policy or guidelines on this topic.

CONCLUSION

This paper represents an initial step in identifying the public policy and ethical issues that are likely to confront the agricultural and microbial genomics sectors of the biotechnology industry over the next half decade. The topics were identified as a result of a discussion among experts from many disciplines, including science, law, ethics, business, and public policy. The multidisciplinary composition of the group contributed to the breadth of the range of issues discussed and may have resulted in a more comprehensive list of issues than would have been identified by individuals from a single discipline. These topics are likely to come to the attention of policymakers over the next several years and are deserving of additional background research, debate, and development. Policymakers, industry, and academic leaders in the field may find them a useful focus for further discussion, thought, investigation, or scholarship. Some, but not all, may require legislative action at the state or federal level. Others may benefit from industry guidelines or collaborative agreements. Finally, others, such as public education, may require funding and incentives for implementation.

APPENDIX A
ROUNDTABLE PARTICIPANTS

Reid Adler is General Counsel at the J. Craig Venter Science Foundation.

Ronald Atlas is Graduate Dean and Professor of Biology as well as Co-Director of the Center for the Deterrence of Biowarfare and Bioterrorism at the University of Louisville.

Michael Brown is the Director of Technology Transfer and Senior Counsel at The Institute for Genomic Research (TIGR) in Rockville, Maryland.

Michael Greenberger is the Director of the Center for Health and Homeland Security and a professor at the University of Maryland School of Law.

Peter Heifetz is a Research Fellow at the Diversa Corporation in San Diego, California.

Marian Jackson is Vice President for Academic Affairs at the University of Maryland Biotechnology Institute (UMBI).

Jay P. Kesan is Professor of Law at the University of Illinois College of Law and a registered patent attorney.

Larry Mahan is Director of Biosciences & Advanced Technologies in the Department of Business & Economic Development for the State of Maryland.

Karen Nelson is an Associate Investigator at The Institute for Genomic Research (TIGR) in Rockville, Maryland.

Karen Rothenberg is Dean of the University of Maryland School of Law and founder of the School's Law & Health Care Program.

Linda Therkorn is a Patent Examination Policy Advisor in the Office of the Deputy Commissioner for Patent Examination Policy at the U.S. Patent and Trademark Office.

Mary Webster. At the time of the workshop, Mary Webster was an Assistant Professor at the University of Maryland School of Law and Director of the Maryland Intellectual Property Legal Resource Center (MIPLRC).

The Workshop organizers and co-chairs were **Professor Lawrence M. Sung** and **Professor Diane E. Hoffmann** of the University of Maryland School of Law.

Daniel Drell, Program Manager, Department of Life Sciences, U.S. Department of Energy, also attended the roundtable and offered comments on a number of the issues.

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