Future Public Policy and Ethical Issues Facing the Agricultural and Microbial Genomics Sectors of the Biotechnology Industry: A Roundtable Discussion

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I. Executive Summary

On September 12, 2003, the University of Maryland School of Law's Intellectual Property and Law & Health Care Programs jointly sponsored and convened a roundtable discussion on the future public policy and ethical issues that will likely face the agricultural and microbial genomics sectors of the biotechnology industry. 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, international trade, 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 five to six years. More concretely, by "most significant" the conveners meant the types of issues that would come to the attention of members of Congress or state legislators during this time frame and for which they would be better prepared if they had well researched and timely background information. 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. The goal was not to provide answers to any of the issues or problems, simply to identify those topics that deserve our attention as a society. Some of the issues may benefit from legislation at the federal or state levels, others may be more appropriately addressed by the private sector.

Participants at the roundtable included over a dozen experts in the areas of microbiology, intellectual property, 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 were asked to come to the roundtable with a written statement of the top three to five public policy/ ethical issues they viewed as most likely to be significant to the industry and to policy makers over the next several years.

At the roundtable, participants collaborated on the development of a comprehensive list of such issues and related questions. Through a facilitated discussion, they narrowed this list down to the following:

I. **Public Access to Publicly Funded Research Results** – Should we establish policies that ensure public access to biotechnology research outcomes that resulted from publicly funded projects and thereby limit ownership rights by commercial enterprises in such outcomes?

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

II. **Harmonization of Laws and Regulations** – Is there a need for common regulations regarding labeling and risk reduction across international borders so that new genetically modified products can be imported and exported with assurance that the products are meeting global standards for safety? How might the disparity in enforcement of intellectual property rights in various countries be reconciled to address respective national concerns about the appropriate balance between public access to biotechnology research outcomes and commercial exclusivity?

III**. Natural Resources Disparity** – How should we address 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 benefits from these products?

IV. **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 industry?

V. Public Education – How can we educate the public, policy makers and regulators about biotechnology, its risks and benefits and the competing interests at stake?

This paper describes the process and discussion surrounding the identification of these topics.

Support for the Roundtable:

Support for the roundtable and the preparation of this report was provided by a grant from the Department of Energy's Office of Biological and Environmental Research. The report is being distributed to policy makers, regulators, and directors of academic centers who deal with the development and regulation of this sector of the industry.

Sponsoring Programs:

The University of Maryland School of Law's
Intellectual Property Law Program
Law & Health Care Program

The Maryland Intellectual Property Legal Resource Center

II. Introduction

a. Background

i. 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 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 facing government regarding biotechnology were the risks posed to human health and the environment by newly developed organisms such as genetically engineered bacteria, 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 new organisms that were treatment resistant or had superior survival skills and thus could displace other beneficial existing organisms. 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 recombinant-DNA (R-DNA) experimentation.[2]

By 1978, there had developed a consensus in the scientific community that the initial environmental and human health risks posed by R-DNA research conducted in a laboratory setting had been somewhat exaggerated. 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 the 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.[3]

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

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[2] 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).

[3] 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). A 1988 report from the Office of Technology Assessment, however, 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).

concerns about altering the genetic structure of human beings, critics expressed concerns that the project would lead to genetic discrimination and eugenics or could interfere with an individual's right to privacy.[4]

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 individual rights 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 by FDA, new issues arose regarding the safety of genetic protocols and the liability of institutional review boards[5] (IRBs) and researchers. This issue was given considerable attention when one research subject died as a result of his participation in a gene therapy research trial. Then, as biotechnology products moved from clinical testing into the marketplace another set of issues 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 research as well as clinical research. Academic-industry ties came under increased 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.[6] In the academic setting, concerns centered on 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.

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[4] *See* Human Genome Policy Board Recommendations, 7 BIOTECH L. REP. 105 (1988).

[5] 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 risks and ensure that research subjects are adequately informed of and consent to the risks to which they may be exposed.

[6] J. Mervis, 269 *Science* 294 (1995).

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

ii. 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 R-DNA research."[7] 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."[8] 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 three-week moratorium on all R-DNA research and drafted an ordinance to regulate all DNA research conducted in the city.[9] Other localities passing similar ordinances included Princeton, New Jersey; Amherst and Boston, Massachusetts; and Berkeley, California. At the state level, during the late 1970s, two states -- New York and Maryland-- enacted legislation regulating biotechnology research.[10] 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).

Public policy and regulatory issues were also debated early on in the industry's development 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 U.S.C. Sec. 4332). In 1983, the Foundation on Economic Trends, headed by Jeremy Rifkin, used NEPA for the first time to halt R-DNA 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 R-DNA research[11] and approved several deliberate release experiments including the release of a genetically altered bacteria (the "ice minus" bacteria) to 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 experiments and “all future deliberate release experiments until a final decision on the merits of the alleged NEPA violations could be reached.”[12] 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. At the same time, however, the court

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[7] *See* D.E. Hoffmann, "The Biotechnology Revolution and its Regulatory Evolution," 33 *Drake Law Review* 471, 483 (1988-89).
[8] *Id.*
[9] *Id*. at 537
[10] *Id.*
[11] *See* National Institutes of Health, *Guidelines for Research Involving Recombinant DNA Molecules,* 43 Fed. Reg. 60,080 (1978).
[12] D.E. Hoffmann, *supra* note 7 at 534.

criticized the NIH for not giving sufficient consideration to the potential environmental impact of these deliberate releases.[13]

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 policy makers to regulate the industry. A 1987 Harris poll on public perceptions of biotechnology found that "more than three-fourths of the public (77 percent)" said they agreed with the statement that "the potential danger from genetically altered cells and microbes [was] so great that strict regulations [were] necessary."[14] Yet industry was highly critical of the extent of regulation and its complexity. According to one author, industries were confronting needless delays and confusion as a result of a complex and fragmented regulatory approach. For example,

> Genentech reportedly encountered needless delays and expenses while USDA and FDA argued for more than a year over which agency should regulate the company's new bovine interferon. The agencies were unable to decide whether the product was a "veterinary biologic" under USDA's jurisdiction or a "new animal drug" under FDA's control.
>
> Advanced Genetic Systems complied with all of NIH's testing requirements in order to inject a genetically engineered bacterium that would reduce the risk of frost into the bark of fruit trees . . . in Oakland, California only to find that EPA approval was required instead.
>
> After two years of review and field tests, USDA's Animal and Plant Health Inspection Services licensed Biologic Corporation's pseudo rabies swine vaccine for commercial use. Because the vaccine was not reviewed through the Department's Recombinant Advisory Committee, however, its license was withdrawn and it required additional testing.[15]

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 increased 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 that the regulatory scheme for the biotechnology industry was evolving, the intellectual property landscape changed in ways that have significantly affected the

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[13] *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*.

[14] OTA, NEW DEVELOPMENTS IN BIOTECHNOLOGY--BACKGROUND PAPER: PUBLIC PERCEPTIONS OF BIOTECHNOLOGY at 81 (1987).

[15] P. Huber, *Biotechnology and the Regulation Hydra*, 90 TECH. REV. 57 (Nov. 1987).

development of this new industry. New intellectual property 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 of the academic community.[16] The number of patents held by universities has increased dramatically since 1980 when Congress passed the Bayh-Dole Act.[17] The 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.[18] 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.[19] 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 new and beneficial products.

Another significant outgrowth of the Bayh-Dole Act and the development of university technology transfer programs has been the establishment of hundreds of new start-up companies resulting from technology generated in academic laboratories. Many of these start ups have been in the area of biotechnology. From 1980 to 2001, over 2,900 new companies were formed based on licenses from academic institutions.[20] Universities often benefit financially from these start-ups in which they frequently take an equity position.

Future public policy and ethical issues for the biotech 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 government assumes a multitude of new roles in its relationship to the industry including researcher and funder of research, regulator, and promoter of economic development and the growth of the biotechnology industry. 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)?"[21]

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[16] 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.

[17] According to a recent article on the subject, in 1979 universities received 264 patents; in 1997, the number had increased to over 2,400. A.K. Rai & R.S. Eisenberg, "Bayh-Dole Reform and the Progress of Biomedicine," 66 *Law & Contemp. Probs.* 289 (2003).

[18] Bremer, *supra* note 16.

[19] *Id.*

[20] *Id.*

[21] B. Rudolph and L.V. McIntire, eds., BIOTECHNOLOGY: SCIENCE, ENGINEERING, AND ETHICAL CHALLENGES FOR THE TWENTY-FIRST CENTURY (Washington, D.C. 1996).

iii. Current Issues in the News

As background and a starting point for discussion, readings on several topics relevant to this issue, as reflected in recent media coverage or trade journals, were identified by the workshop organizers. Some of them were provided to workshop participants. The topics and relevant news items included the following:

- *The Regulation/Import & Export of 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 against the approval of genetically modified (GM) crops.[22] 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.[23] 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 end product rather than the process. [24] 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.[25] 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.

- *Restriction on Scientific Freedom*- 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).[26] The organization, funded by the Rockefeller and McKnight Foundations, argues that the benefits of much publicly-funded research comes to private industry through university technology transfer programs and subsequently limits 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 genetically modified organism sectors of the biotechnology industry are raising these and other concerns about ownership of intellectual property. Additional concerns include bioprospecting and biopiracy,[27] 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.

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[22] C.M. Benbrook, *Sowing Seeds of Destruction,* N.Y. TIMES, July 11, 2003, at A17.
[23] L. Alvarez, *Europe Acts to Require Labeling of Genetically Altered Food,* N.Y. TIMES, July 3, 2003, at A3.
[24] E. Marden, *Risk and Regulation: U.S. Regulatory Policy on Genetically Modified Food and Agriculture,* 44 B.C. L. REV. 733 (2003).\
[25] *Id.* at 747-49.
[26] R.C. Atkinson, et.al., *Public Sector Collaboration for Agricultural IP Management,* 301 SCIENCE, 174, July 11, 2003, www.pipra.org.
[27] *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.

- *Genetically Engineered Microorganisms for Bioremediation* - The Department of Energy's Natural and Accelerated Bioremediation Research (NABIR) Program seeks to develop genetically engineered microorganisms to clean up radionuclides and metals in subsurface environments. The process raises numerous policy and ethical concerns including intellectual property rights, community consent for the use of bioremediation strategies, public safety and the need for long term stewardship of sites where contaminants have been stabilized.[28] A primary challenge is the predictability of bioremediation process performance. A report from a NABIR Workshop states that "[i]n some cases, predictability is limited by the lack of fundamental knowledge about microbial community structure, composition, functions, and dynamic changes under different environmental conditions; and in other cases, by the lack of accurate parameter estimation. Current methods for measuring and evaluating the effectiveness of bioremediation are too cumbersome. Rapid, simple, reliable, quantitative and cost-effective tools that can be operated in real-time and in field-scale heterogeneous environments for assessing bioremediation endpoints are needed."[29]

- *Efforts to Combat Bioterrorism* – Following September 11, 2001, few public priorities in the United States have taken precedence over anti-terrorism 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."[30] These provisions included tightened restrictions on foreign students entering the country to study at U.S. colleges and universities and increased responsibilities on educational institutions to report information about their foreign students. Regulations implementing the legislation call for increased oversight of laboratories where researchers are using any of almost 50 specified biological agents. This oversight includes background checks and security clearances of everyone working at the laboratory as well as unannounced inspections by government agents. Labs 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.'"[31] In response to concerns that the administration might restrict the publication of "unclassified but sensitive information

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[28] *See* http://www.science.doe.gov/grants/LAB00_21.html

[29] J. Zhou, D.P. Chandler and F.J. Brockman, Report on the NABIR Workshop: Application of Genomic Technology to Bioremediation, Dec. 5-7, 1999, available at www.161.gov/nabir/generalinfo/workshop_reports/Genom_tech.pdf

[30] D.J. Kevles, "A Security Clampdown on Biotechnology Research," 106 *Tech. Rev.* no. 6 (July 1, 2003).

[31] *Id.*

related to weapons of mass destruction, scientists have argued that such censorship threatens "researchers' abilities to engineer therapies and cures—and that could place the very competitiveness of the nation's biotechnology industry in peril."[32]

- *Intellectual Property – Research Exemption from Patent Liability* –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 non-profit and not-for-profit institutions. The error of that belief was made clear in a 2002 decision of the Federal Circuit. *See Madey v. Duke University,* 307 F.3d 1351 (Fed. Cir. 2002), *cert. denied,* 1235 S.Ct. 2639 (2003). 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." [33] While the Federal Circuit did not abolish the common law exemption to patent liability entirely, 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."[34] 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 very recent decision of *Integra LifeSciences I, Ltd. v. Merck KgaA*, 331 F.3d 860 (Fed. Cir. 2003). In *Integra*, the Court stated that the provision established by Sec. 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 be considered to meet 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.

b. Goals and Objectives of the Roundtable

The purpose of the Roundtable was to bring together a small group of experts from the biotechnology industry, government and academia who would attempt to reach consensus on the "most significant" public policy and ethical issues that will confront the biotechnology industry (microbial genomics and agricultural sectors) over the next half decade. By "most significant" the workshop organizers intended to include either issues that would come to the attention of

[32] *Id.*
[33] L. Sung & 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).
[34] *Id.* at 278-79.
[35] L.M. Sung & J.E. Schwartz, THE 2003-2004 PATENT LAW HANDBOOK, § 4.1 at 155-56 (Thompson/West 2003).

members of Congress or state legislators during this time and/or issues that might be the focus of federal or state legislation. Development of the list of issues was to be a collaborative effort taking into account the various competing interests at stake including public safety, economic development, ownership of intellectual property, and international relations and trade, and was to reflect the various backgrounds of the workshop participants: industry, intellectual property, economic development, regulation, public interest, scientific development, and academic research. The work product developed from the roundtable was to be distributed to relevant policy makers, trade associations, public interest groups and others that might benefit from its content.

A concurrent goal was to provide a document that would serve as the basis for academic debate and a spur to scholarship so that policy makers, industry leaders and regulators would have a set of intellectual resources to help them better understand the issues and concerns at stake.

III. Participant Perspectives and Crosscutting Themes

In preparation for the workshop, each participant was asked to write: 1) a brief description of his or her perspective and that of his/her organization on microbial or agricultural genomics research and development; 2) the participant's view of the three to five most pressing public policy and ethical issues facing the microbial and agricultural genomics sectors of the biotechnology industry; and 3) the reasons behind the participant's chosen priorities. At the workshop, the participants elaborated on their written statements. This section of the report includes a description of the range of participant perspectives, either as expressed in writing or orally at the roundtable, and the common and cross-cutting themes that emerged across perspectives as priorities for policy focus.

Perspectives

The perspectives of the participants reflect both their discipline, e.g., science, ethics or law, and the organization with which they are affiliated – governmental agency, not-for-profit research institute, academic research center, private industry. Governmental agencies included federal and state agencies with either a regulatory or economic development mission. For example, one of the participants works with Maryland's Department of Business and Economic Development (DBED). DBED's mission is to attract new businesses, stimulate private investment and create jobs, encourage the expansion and retention of existing companies, and provide businesses in Maryland with workforce training and financial assistance. The Department promotes the State's many economic advantages and markets local products and services at home and abroad stimulating economic development, international trade and tourism. In carrying out its mission, the Department funds new technology development from both a seed grant and equity investment stage. As a result, the Department is heavily involved in strategic partnering issues domestically and internationally and with academic institutions as well as private industry.

A number of the workshop participants came to the table with a research/ education perspective either as part of an academic research center or a not-for-profit institution. The

specific organizations represented by participants in this category 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 pathogens, to the development of a "minimal genome." These affiliates also consider the public policy implications associated with genomic medicine, intellectual property matters, and the public understanding of science and education. In addition, the Center for the Advancement of Genomics, one of the affiliates, publishes an online news magazine about genomics research around the world. 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 intellectual property and licensed or should be "open source."

The Institute for Genomic Research (TIGR) is an international leader in the genomics field. Early on, TIGR's focus was on microbial genomics and it houses the Pathogen Functional Genomics Resource Center, an NIH-funded Center dealing with microbial genomics. Over the years, the Institute has expanded its areas of interest and now has a large group that focuses on sequencing and annotation in the plant genomics field. As a not-for-profit research center that has made billions of base pairs 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 obstacles to such dissemination. Related to this basic issue, the Institute has concerns about the use of the information that it has made available, specifically, whether subsequent users of the data will place limitations on access to innovations that they develop with the data. One of the participants from TIGR stated that the Institute questions whether there should be more control of what others are doing with the information that is generated and made publicly available by sequencing centers like TIGR. Without the reach-through rights and other provisions that preclude individuals from using that information, he asserted, "a number of both for-profit and not-for-profit entities could take the data, file patents on it and preclude others from using it until they take licenses to do so. In our role as an academic institution," he said, "we're putting the data out there for the public good and hoping that it will be used to benefit everyone."

The Institute also collaborates extensively with both international and national entities. At the international level, collaborators include scientists and governments of economically developing countries that 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 different 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 focusing on novel molecules that can be discovered from the organisms that live in very unusual environments. Researchers at CMB are also interested in bioremediation,

environmental problems, and aqua-culture. The Center for Agricultural Biotechnology recently changed its name to the Center for Biosystems Research. The change reflects the Center's interest in insect vectors and livestock issues as well as genetically modified crops and plants. In Maryland, chicken farming is a significant industry and the Center has a large chicken vaccine program. While the primary focus of UMBI is research, as a state institution, a second mission is economic development and moving its research from the laboratory to the marketplace. This raises numerous issues related to industry-university collaborations, including intellectual property rights.

Another perspective was brought to the table by a research scientist from Diversa, a for-profit corporation in the business of finding genes and enabling products. Diversa has formal agreements with a variety of countries for access to biologic materials that are utilized in the company's screening programs. The company is currently working independently and with strategic partners to develop products for chemical, industrial, and agricultural applications. In addition to these near-term products, Diversa is advancing its pharmaceutical programs, including new technologies for the discovery of antibody-based therapeutics. Diversa is currently receiving funding from the Department of Defense (DOD) and NIH to apply its technologies for generating and optimizing antibodies to biodefense applications. Issues for Diversa have included balancing access to biological diversity with the requirements of local and transnational regulations and conventions including the Convention on Biodiversity. The company is also following the global debate about genetically modified organisms in order to understand the viewpoints of groups with differing interests in, and opinions regarding, the uses of biotechnology in industry and health care.

Another participant provided a unique perspective as a representative of the Deputy Commissioner for Patent Examination Policy in the U.S. Patent and Trademark Office. Among other things, 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 on establishment of new rules, practices and procedures; reviews and revises the Manual of Patent Examining Procedure; and 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 issuance of 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 currently working on projects with the European Patent and Japan Patent offices to generate greater mutual understanding and possible convergence of views on the patenting of genomic and proteomic inventions.

Several participants also had backgrounds in intellectual property or provided intellectual property advice to clients. One participant directs the Maryland Intellectual Property Legal Resource Center. The Center, a collaborative effort between the University of Maryland School of Law and the Montgomery County Department of Economic Development, provides, and trains law students to provide, legal advice and information on intellectual property issues to start-up high tech and biotech companies in Maryland.

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, focusing on this issue. Both Centers draw on the resources available at their respective universities in different disciplines 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 respective university and in conjunction with other private and governmental agencies. Both Centers have assisted or are assisting their communities 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.

Support for the Roundtable was provided by the Department of Energy's Office of Science, Program of Biological and Environmental Research. A representative from D.O.E. also participated in the discussion. D.O.E.'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."[36] 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."[37] The Office's Biological and Environmental Research Program has divisions in Life Sciences, Medical Sciences and Environmental Sciences. The Life Sciences Division manages a diverse portfolio of research including, but not limited to:

- Genomes to Life Research – This program uses new genomic data and high through-put technology to identify biotechnology solutions for energy production, environmental cleanup, carbon sequestration, and biothreat defense.

- Human Genome Research – This research continues after the mapping of the Human Genome to create and apply new technologies and resources in comparative genomics and to study the use of model systems and information management for identifying genes and their regulatory elements within the human genome.

- Microbial genome research- This project was initiated to characterize and exploit the genomes and diversity of microbes with potential relevance for energy production, bioremediation, and global climate issues.

- ELSI research – This research focus was established to anticipate and address ethical, legal and social implications arising from genome research.[38]

[36] U.S. Dept. of Energy Mission Statement, *at* www.energy.gov/engine/context.do?BT_CODE=AD_M.
[37] U.S. Dept. Of Energy, Office of Science, *at* www.energy.gov/engine/content.do?BT_CODE=OF_POS.
[38] *See* U.S. Dept. of Energy, Life Sciences Division, *at* www.sc.doe.gov/ober/lsdabout.html.

In 1994, D.O.E. 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 completely sequenced 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, in addition to many viruses and higher organisms such as yeast and the roundworm, are available in public databases and are being actively used by academic, medical and industrial scientists to make comparisons not previously possible.[39] According to DOE's website:

> Through the study and understanding of a diverse group of microbes, solutions are nearer for DOE mission challenges in environmental cleanup, medicine, agriculture, industrial processes, and energy production and use. . . . For example, *M. jannaschii's* ability to produce methane may have implications for new forms of fuel generation, and *Deinococcus radiodurns* has potential for cleanup of toxic mixed-waste sites containing radionuclides, in addition to heavy metals and organic solvents, because it can survive extremely high levels of radiation and repair its own radiation-damaged DNA. Understanding the genome sequence of *B. anthracis*, which causes anthrax, will promote faster detection methods and new treatments.[40]

Cross Cutting Themes

In both their written and oral comments, participants expressed a number of common concerns. These are grouped by themes below.

Scientific Freedom/ Access to Data/Publications

A number of participants representing academic and research institutions expressed concerns about disclosure of new scientific breakthroughs, data access, and intellectual property. 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 current post 9/11 environment where there is a heightened sensitivity to "confidentiality, what's secret, what's not secret, what you can share, and whether you can publish your data." According to a number of participants, these are very practical and serious issues for the scientific community.

A representative from TIGR commented that publicly funded genome research projects present a number of issues related to data access and publications. These genome projects typically come with requirements for timely release of genome data into the public domain, either by distribution on the institution's own website or in a public database such as Genbank. Once this data is released, researchers at-large can freely use it in their own studies or for their own publications. Questions raised by these arrangements include:

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[39] *See* U.S. Dept. of Energy, Microbial Genome Program, *at* www.sc.doe.gov/ober/microbial.html.
[40] *Id.*

- Who owns the data?
- What incentives exist to continue large genome projects if the scientist(s) directly involved in the sequencing project will continue to be "scooped" on publications?
- How 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?
- What role do, or should, academic journals play in accepting publication from scientists who have not generated the data on which their manuscript relies?
- Should we simply have web-based information for one and all to use? If so, how will that impact the protection of intellectual property, which in this context has been in the patent rather than copyright area?

Another participant asked the question, "Who is the watchdog for how data is being used post-completion of a sequencing project when it is not under publicly funded guidelines?" This participant went on to say, "[t]o the best of my knowledge there are no current 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 is available over the internet. We can only assume and hope that the data is going to be used in a beneficial way."

Public/Private Collaborations:

A second theme to emerge was a need for guidelines for public/private collaborations. Participants concerned with this issue raised the following questions: 1) What role should federal government agencies play in fostering public/private collaborations in the area of genetic research and product development?, and 2) To what extent should we allow the industrial organizations that collaborate with government and not for profits to restrict publication and dissemination of research results and intellectual property rights? One participant characterized this problem as one of "downstream exclusivity." He acknowledged that a number of federal agencies are now trying to determine whether they should assert control over databases generated from collaborative efforts that they fund to ensure that access will be made available to the public at large. This participant commented that it seems "counter-intuitive" for the government to "have a heavy-handed approach" to what would otherwise be a public library or public databank but that the government may believe it is necessary to adopt a "defensive intellectual property strategy to ensure public access downstream." As a result, "when we get on a commercial web-site 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 intellectual property protection based on the fruits of information gleaned from the database."

Linda Therkorn from the U.S. Patent and Trademark Office (USPTO) clarified that in order to procure a patent on an invention, one must satisfy the enablement and written description requirements. These are ways, she said, "of preventing people from claiming downstream inventions when they haven't quite gotten there yet." 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 based on 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 that collaborations with external parties has been an issue at her institution for a number of years and continues to grow. Even simple things like 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 shared 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 intellectual property law may have on this issue by limiting the experimental use defense and allowing researchers to use patented technology and innovations 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. 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 intellectual property (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. One participant asked whether or not the current IP laws provide sufficient predictability to researchers. Limited pertinent jurisprudence on the scope of patent rights to genomic inventions leaves a void that creates uncertainty. Although the USPTO has granted patent rights to inventions in genomics, few such patents have been litigated. Accordingly, little guidance exists about whether seemingly broad patents to 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 participants questioned whether our current IP regime made sense for this new technology. Others pointed out the significance that IP rules have on economic development. One participant shared that in late 2003, the Prime Minister of Japan raised intellectual property to essentially cabinet-rank status and set up a strategic infrastructure for IP. In establishing this heightened visibility for IP the Prime Minister remarked that Japan lacks both natural resources and cheap labor and therefore has no choice but to innovate and establish an IP regime that encourages and rewards innovation. This participant suggested that the U.S. may want to be more strategic about its IP policy. Others pointed out that while it is the practice in Japan to "patent everything," the Japanese are less likely to sue for patent infringement. On the other hand, because the patent field is so tight in Japan, there is little freedom to operate.

One participant commented that we are starting to experience the obstacles of patent thickets in this country as well. 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 said that this was an issue worthy of further study but that 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 against different genetic mutations and alleles, we would "run into an instant infringement thicket because there are hundreds of patents that are 'one-off genetic test methods.'" Several participants asserted that we need to examine different methods 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 semi-conductor industry which lacks the "mom and pop" shop culture.

Specific questions raised by participants regarding intellectual property included the following:

- How should IP and publication rights be coordinated within public/private collaborations? Can patent pooling arrangements be established to facilitate such collaboration? Will such arrangements run afoul of U.S. antitrust laws?

- How are universities and research institutions going to be able to protect their subject matter? In light of recent court decisions, do we need a broader experimental use infringement exemption?

- Are patenting and licensing practices for "platform" technologies overly restricting or delaying the development of products of public health and agricultural significance?

- Does PIPRA establish a framework for other scientific sectors to follow, or is this type of IP management only applicable to the agricultural sector? How can the interests of small commercial end users of agricultural technology be protected? For example, in multi-institutional projects to develop new genetically engineered crops, should any one institution have the right to own intellectual property developed from the project, or should the IP be assigned to the consortium to ensure that it is ultimately made available to the public?

- Should the goals and effectiveness of the Bayh-Dole Act be reevaluated? The original intent of the Bayh-Dole Act was to spur the commercial development of academic inventions and increase the range of products in the marketplace. Is the Act

[41] The USPTO, 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.

accomplishing these ends? Are there unintended consequences of the Act such as the spread of IP rights to more basic research activities? Do these consequences outweigh the benefits of the Act, or can it be restructured to correct them?

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 the potential for this information to be misused. As a consequence, scientific organizations at all levels are being forced to examine the issues raised by attempting to fairly and ethically 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 create 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) synthesis of a polio virus.

This discussion raised questions about whether scientists or funding agencies should have the right to restrict public access to certain genome projects for national security reasons (e.g., *Bacillus anthracis*, smallpox, etc.). 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. In one case, a doctoral student at George Mason University was told that his dissertation had to be purged of considerable information. As a result, it may be difficult for his committee to evaluate his work.

Participants discussed whether the scenario now was any different than it was during the time when scientists were working on the development of nuclear weapons. One participant commented that

> "[a] huge difference between physics and bioscience is that in the early days of the 20th century, theoretical physics was done openly by an academic community and generated extraordinary excitement . . . . It was when a decision was made to try and build the Manhattan Project that the federal government built a fence around it. The fence wasn't around the physics but around the effort to build a device. In bioscience it's . . . too late to do that. Biology is out there, it's widespread. . . . Another difference is that in the arena of bioterrorism we are often talking about therapies for diseases and if the information does not get disseminated people will die."

Another participant affirmed this view stating that "fifty-plus years of NIH, NSF and other agency funding have established that openness in bioscience works. We get results. We get new developments in medicine. We get benefits to the economy. It's incredibly successful. And that

leads to the issue of a cost-benefit calculation . . . What is the cost of excessive secrecy in terms of what you give up from the bioscience enterprise. . .?"

Another speaker expressed concern regarding the lack of clarity about what is or is not "too risky" to publish and the lack of widely accepted guidelines on this issue, although some groups like the Monterey Institute have made a start at laying out a conceptual framework. As a result, he said, "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 which tie receipt of funding to restrictions on information dissemination are also problematic for many research institutions. For example, the Maryland Board of Regents has a policy that prohibits the University from accepting classified research and from accepting funding to do things that restrict an academic's ability to publish.

The two workshop participants who direct academic centers that focus on bioterrorism articulated concerns not only about genetically modified 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 Baltimore and 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 both educating the public about the need for regulations to prevent bioterrorism and educating policy makers about crafting such regulations so that they do not impede scientific research and progress: "We, in the scientific community" he asserted,

[42] 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.

> "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 biotech 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 like DeKalb and Pioneer have been bought up by bigger players like 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 genetically modified seeds as well as for processes that, for example, remove fat or add vitamins to traditional crops. In the mid 1980s, after the USPTO began allowing patents on these types of innovations, filings increased significantly. Prior to that time, researchers did not think these types of 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

[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).

granting of patents to items such as genetically modified seeds, for example, is creating new marketing challenges for producers. Every bag of genetically modified 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. One participant suggested that it might be helpful to think about this with an analogy to the sale of CDs where the CDs are sold but then replicate themselves at night. In the case of seeds, a purchaser can regenerate the genetically modified seed. The seller cannot capture the value of the seed into the future unless he sells a license. This practice has created policy issues in a number of states where there have been efforts to outlaw these kinds of licenses. These prohibitory 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 the accepted customs of traditional business dealings.

Another reaction to the use of genetically modified seeds is illustrated by recent pollen drift law suits. This litigation is arising from claims that genetically modified 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 genetically modified 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 ten 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.

Another speaker pointed out an analogy between the licensing of genetically modified seeds to capture downstream benefits and efforts of U.S. researchers to use natural resources from economically developing countries and the developing country's desire, in effect, to license such uses.

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 very challenging and burdensome in terms of paperwork and other regulatory hurdles.

Public Health & 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. This is especially needed for trees and microbial products.

A second participant echoed this concern, stating that we will 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 in 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 to our ecosystem. Microbial and synthetic cells, as well as products derived from them, will find broader application in the production of new materials, non-conventional fuels, and environmental clean up. It will be crucial to understand how these organisms and/or their products will interact with our environment. These developments will require new modes of research such as closed micro-ecosystems (beyond containment), that allow for testing 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 the 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 underway. 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 years -- not light years -- 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." Peter Heifetz, from Diversa, discussed his company's practices in this area:

> "In order to facilitate access to unique environments while at the same time acknowledging the legitimate rights of stakeholders, Diversa has entered into agreements that provide for sharing of value created by its biosampling activities in accordance with the Convention on Biological Diversity (CBD). Diversa has formed sample collection partnerships with research institutes and researchers in locations such as Alaska, Australia, Bermuda, Costa Rica, Ghana, Hawaii, Iceland, Indonesia, Kenya, Mexico, the Meadowlands Superfund site, Russia, South Africa, and Yellowstone National Park.[44] These partnerships 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. Diversa believes very strongly in the notion that responsible bioprospecting can benefit all, and is strongly opposed to "biopiracy" -- the unauthorized taking and exploitation of natural biological resources. How to manage the expectations and interests of all stakeholders in the bioprospecting process is a critical issue. If bioprospecting is to be successful, 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. Another participant stated that, "[I]t is contrary to the U.S. ethic when a country, that simply provided a sample [natural resource], claims the benefits of the knowledge that someone else applied to develop the sample into a valuable product. We need to understand that this is a U.S. perspective, i.e., to ask how anyone can hold us up for reach-through royalties on an item that they simply supplied. The international community thinks 'this is our natural resource, the only thing we have that we can make money on because we don't have the biotechnological community to go out and develop the sample into a drug or other valuable product.'" 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.

[44] Since the Roundtable in September, 2003, Diversa has added two additional collaborators: Puerto Rico and the San Diego Zoological Society.

Another participant asserted that the situation we are facing now parallels the one we faced at the time of the Industrial Revolution:

> "This is old history, [he said] . . . with a new set of clothes, albeit a more complicated set of clothes, because we're talking about microbial genomes and agriculture, . . . truly things that can have long-term effects on the economic development of a country. The fact that it's not copper coming out of the mountain, but rather some odd microbe that might cure cancer, does not mean it is not similar. We can now see where we had our failings as a first world country in dealing with the developing countries historically because our capabilities superceded theirs. We assumed that our policies would have spill-over benefits to those countries through the creation of employment. These were downstream benefits. I see this as a parallel situation [to what we are now facing with the biotech industry]. It's just new to biotechnology because the industry is coming out of its own infancy. It's been business-driven . . . with heavy pressures to produce because of all the funding that it's received. We have a little history revisited here where we have a chance to create policy anew. We should learn from our failed global policies in other revolutions, both economic and industrial, and think more carefully about our relationships with these other countries."

One participant asked, "How do we ensure that scientists carry out research that is relevant to developing countries and that this new technology is used to assist lesser developed countries? What policies can be enacted to encourage these outcomes?" Others agreed that these were important questions especially with respect to genetically modified seeds and crops that might be used to alleviate problems of starvation and hunger in some economically developing countries. Another participant commented that "the reality is that there are tens of thousands of people today who are dying of lack of food. This is a disgrace in the 21st Century. Genetically modified seeds and crops are now being developed that are drought resistant and insect resistant and can be used in these other countries to alleviate food shortage problems. To the extent there are obstacles to lesser developed countries using these technologies (because of cost, or having only small plots of land) perhaps 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), that are 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 assess 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 expressed the need for public communication 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 that 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 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." He then asked, "Is this being done well or poorly by those responsible for communicating with the public? What checks and balances exist or should exist to preserve the objectivity and credibility of the watchdog role?"

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 the resulting 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 provide 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 seven 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 miscon-ceptions 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 are not educated about 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 modification of organisms?" Eighty (80) percent of people 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.

Another participant advised caution when talking about "educating the public" because it can be interpreted as "getting them to agree" with what the government or scientists want to do. In some cases, she said, "it's not an issue of education, it's actually a difference in people's value systems."

Several participants shared their experiences with public education projects or programs to improve the dialogue on these issues between scientists and non-scientists. One participant mentioned a multimillion dollar effort by the American Society of Microbiologists to put on a multipart television series with the idea that you could educate the public on these issues enough to enter the debate in the course of a week. He believes that at least, in part, this effort was not successful because education on this topic cannot be a one time event -- continuous education is critical. This participant also mentioned his experience on the Recombinant DNA Advisory Committee (RAC) which included scientists, public members, theologians, and attorneys. He found that the format worked very well, but that ultimately the public believed that the non-scientists were co-opted by the scientists.

A number of participants expressed the need to educate students earlier and better about these types of scientific issues. A participant from TIGR volunteered that much of the Institute's federal funding includes a requirement that they engage in public education. As a result, scientists at TIGR reach out to students in elementary, junior and senior high schools and talk to them about genomics, what is going on in the field of research, and new developments in the area. He expressed the view that the funding agencies are taking the need for public education very seriously; that they see it as part of their mission.

Participants also discussed the need to educate students about more than basic science. They agreed that, in addition, students should be learning about the ethical and legal issues associated with new technologies.

Finally, 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 as crime legislation or as 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 point in 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."

IV. 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 upon the types of restrictions the private sector can place upon 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 such as The Wellcome Trust and The Bill & Melinda Gates Foundation 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 that researchers 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 Convention on Biological Diversity or some modification of it so that commercial entities in this country have some guidelines for these types of collaborations? If not, should private sector actors voluntarily comply with the Convention?*

- "North/South" Issues – *How can we reconcile the interests of economically developing countries with more industrialized nations as regards intellectual property enforcement concerns?*

- Biopiracy – *How can we protect against the unauthorized export of natural resources for purposes of research and development 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 intellectual property 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 re-evaluate 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 ag-biotech?

- Patents issuing at a phenomenal 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 may affect family farmers who have been a staple of 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 cows, other 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 only be of interest 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 upon labeling standards have created significant trade problems for U.S. food manufacturers. Uniform labeling requirements would 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 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? Have shifting 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 ag-biotech products? Should we restrict the ability of companies to test these products in economically developing countries?*

V. Priority Issues – The Consensus of the Group

Based on the comprehensive list developed above and the prior discussion, 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. The group, despite their divergent backgrounds, agreed relatively quickly on the following list:

I. Public Access to Publicly Funded Research Results – Should we establish policies that ensure public access to research outcomes in this area that resulted from publicly funded projects and thereby limit ownership rights by commercial enterprises in such outcomes?

II. Harmonization of Laws and Regulations – Is there a need for common regulations regarding labeling and risk reduction across international borders so that new genetically modified products can be imported and exported with assurance that the products are meeting global standards for safety? How might the disparity in enforcement of intellectual property 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?

III. Natural Resources Disparity – How should we address 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 benefits from these products?

IV. 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?

V. Public Education – How can we educate the public, policy makers 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 intellectual property 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 it affects the rest of the world.

One participant commented that both homeland security and public access to publicly-funded information are on the agenda for this session of Congress: "Whether they are short-lived or whether they have a longer life, there is no question that they are currently front and center." As a scientist, he said, "I'm less aware of the intellectual property issues. At least I'm not hearing about them in the hallways that I frequent. From what I've heard today, however, it is clearly an item that needs to be put on someone's agenda."

The participants all felt that issues arising from disparities in natural resources and technological expertise between the U.S. and economically developing countries were ones that 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.

Finally, the group agreed that public education is vital in this area and that policy makers should develop strategies to encourage public education on these issues.

VI. Conclusion

This paper represents an initial step at identifying the handful of 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 identified were a result of a

discussion among experts from a wide range of disciplines including science, law, ethics, business, and public policy. The multidisciplinary composition of the group contributed to the broad range of issues discussed and may have resulted in a more representative list of issues than what would have been identified by individuals from a single discipline. These topics are likely to come to the attention of policy makers over the next several years and are deserving of additional background research, debate and development. Policy makers, industry and academic leaders in the field may find them a useful focus for further discussion, thought, investigation and/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.

VII. Appendix A

Roundtable Participants

Reid Adler is General Counsel at the J. Craig Venter Science Foundation. The Foundation is the support organization for the Center for the Advancement of Genomics, a not-for profit policy center dedicated to advancing science through education of the general public, elected officials, and students; the Institute for Biological Energy Alternatives; The Institute for Genomic Research; and the J. Craig Venter Science Foundation Joint Technology Center. Several of these affiliate organizations undertake a fair amount of genomic research in the microbial area and the agricultural sector. The Foundation provides administrative support, organizational policy development, and research activities for these various Centers and Institutes and also carries out investment management and fund-raising activities on behalf of each. In addition to this internal support, the Foundation is exploring new ways to obtain external support to foster science education and scientific innovation. Mr. Adler's professional focus includes legal issues related to human subjects research, intellectual property, collaborative genomics research with developing countries and corporate governance. Prior to joining the Foundation, from 1994 to 2002, Adler was a Partner at two international law firms with a practice focus on intellectual property law and technology transfer. From 1989 to 1993 he served as Director of the NIH Office of Technology Transfer. He received his B.S. in Chemistry from the University of Maryland, and J.D. from George Washington University. Mr. Adler was a law clerk to the Honorable Giles S. Rich, U.S. Court of Appeals for the Federal Circuit, and a Fellow at the Max Planck Institute for Foreign and International Patent, Copyright and Competition Law in Munich, Germany.

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. He is Past President of the American Society for Microbiology (ASM) and served as co-chair of the ASM Task Force on Biological Weapons. He is currently a member of NASA's Planetary Protection Board and the FBI Scientific Working Group on Bioforensics. He previously served on the NIH Recombinant Advisory Committee. He is author of nearly 300 manuscripts and 20 books. He is a fellow in the American Academy of Microbiology and has received the ASM Award for Applied and Environmental Microbiology, the ASM Founders Award, and the Edmund Youde Lectureship Award in Hong Kong. He regularly advises the U.S. government on policy issues related to the deterrence of bioterrorism. Atlas received his B.S. degree from the State University at Stony Brook and his M.S. and Ph.D. degrees from Rutgers University. He was a postdoctoral fellow at the Jet Propulsion Laboratory where he worked on Mars Life Detection. His early research focused on oil spills and he discovered bioremediation as part of his doctoral studies. Later his research focused on the molecular detection of pathogens in the environment which form the basis for biosensors to detect biothreat agents.

Michael Brown is the Director of Technology Transfer and Senior Counsel at The Institute for Genomic Research (TIGR) in Rockville, MD. TIGR, founded in 1992, is a not-for-profit research institute with primary research interests in structural, functional and comparative analysis of genomes and gene products from a wide variety of organisms including viruses, eubacteria (both pathogens and non-pathogens), *archea* (the so-called third domain of life), and

eukaryotes (plants, animals, fungi and protists such as the malaria parasite). Since its founding, TIGR has sequenced over 50 organisms -- more than any other single research center. Brown oversees the Institute's intellectual property and technology transfer activities and serves as its legal counsel. In this capacity he routinely interfaces with federal government agencies, including NIH, USDA, DOE, NSF, and DOJ, academic and not-for-profit institutions, and industry, in the negotiation of agreements, establishment of collaborations, data access, publication issues, in and out licensing, and intellectual property matters. Mr. Brown received his J.D. from the University of Maryland School of Law.

Michael Greenberger is the Director of the Center for Health and Homeland Security and a professor at the University of Maryland School of Law. He teaches intellectual property, contracts, constitutional law and a course entitled "Homeland Security and The Law of Counterterrorism." Prior to joining the Law School faculty, Professor Greenberger was a partner for over 20 years in the Washington, D.C. law firm of Shea & Gardner, where he served as lead counsel and argued cases before the U.S. Supreme Court, eight federal circuit courts of appeals, four state supreme courts and various other federal and state trial courts. In 1999, Greenberger began service as Counselor to U.S. Attorney General Janet Reno and then became the Justice Department's Principal Deputy Associate Attorney General, in which capacity he reported to the Attorney General and the Associate Attorney General about the supervision of five of the Department's six litigating divisions (civil, tax, civil rights, antitrust, and environment). He was also responsible for several counterterrorism projects, including organizing a nationwide counterterrorism war game on behalf of the Attorney General in which most of the Clinton administration cabinet participated. Professor Greenberger has written about, and appears frequently in the media on, counterterrorism issues. He is a graduate of Lafayette College and the University of Pennsylvania Law School.

Peter Heifetz is a Research Fellow at the Diversa Corporation in San Diego, CA. Diversa is a publicly traded biotechnology company that utilizes genomics to discover and optimize molecules from the environment, primarily from microbial sources. Prior to joining Diversa Corporation in early 2003, Heifetz was the head of plant-made biopharmaceutical research for Syngenta Plant Science as well as the Director of Consumer Health at the Torrey Mesa Research Institute (formerly the Novartis Agricultural Discovery Institute, a genomics institute of the Novartis Research Foundation). Heifetz began his industry career in 1995 at Ciba-Geigy Corporation, which became Novartis in 1996. Heifetz's academic background is in molecular genetics and biochemical engineering. He received his B.S., M.S., and Ph.D. from Duke University. His research has focused on recombinant protein expression in plants and microalgae, the molecular biology of chloroplast gene expression, and applications of protein therapeutics in mucosal immunology.

Marian Jackson is Vice President for Academic Affairs at the University of Maryland Biotechnology Institute (UMBI). UMBI is a center for intensive research into the basic science of biotechnology and its application to human health, the marine environment, agriculture, and protein engineering/structural biology. Established in 1985 by the State of Maryland, UMBI's five centers conduct research and training that provide a core of expertise and facilities to advance the state's scientific and economic development. UMBI emphasizes collaboration with industry, other research institutions, and federal laboratories; and sponsors training workshops,

short courses, symposia, and seminars throughout the year. As Vice President for Academic Affairs, Dr. Jackson is responsible for faculty matters, program development, conflicts of interest, and interface with the Institute's Office of Research and Development. Dr. Jackson received her B.S. from Cornell University in Biology with a focus on Genetics and both her M.S. and Ph.D. in Genetics from the Albert Einstein College of Medicine.

Jay P. Kesan is Professor of Law at the University of Illinois College of Law and a registered patent attorney. He writes and teaches in the areas of intellectual property and law. During the past several years he has focused attention on teaching and writing about various issues related to agricultural biotechnology including intellectual property and plant variety protection for various ag-biotech innovations. In addition to his faculty position at the College of Law, he holds positions at the Department of Electrical & Computer Engineering and the Institute of Government & Public Affairs. Prior to going into law, Kesan worked at the IBM T.J. Watson Research Center and published numerous scientific papers and obtained several patents. He received his J.D. *summa cum laude* from Georgetown University and his Ph.D. in electrical & computer engineering from the University of Texas at Austin.

Larry Mahan is Director of Biosciences & Advanced Technologies in the Department of Business & Economic Development for the State of Maryland. In this capacity, Dr. Mahan oversees programs of business development and strategic partnering for one of the largest industry clusters of technology companies in the U.S. These activities include national and international corporate location and strategic partnering projects as well as in-state business incubation, expansion and retention. Dr. Mahan is also an accomplished senior scientist with over 16 years experience in basic medical research, an author of over 100 published articles and abstracts and holder of four U.S. patents. His expertise spans cellular and molecular biology, neuroscience, pharmacology, immunology and biochemistry. Dr. Mahan received his Ph.D. in 1984 in Physiology and Pharmacology from the University of California, School of Medicine. In 1985, he was a recipient of the nationally competitive Pharmacology Research Associate Traineeship award at the National Institutes of Health.

Karen Nelson is an Associate Investigator at The Institute for Genomic Research (TIGR) in Rockville, MD. Her areas of research include microbial genomics of species of environmental and agricultural significance, lateral gene transfer and studies in extremophiles. Dr. Nelson received her Ph.D. from Cornell University and her M.Sc. from the University of Florida. She has published extensively in the field of microbial genomics. In addition, since 1997, Dr. Nelson has been involved in community outreach programs to minority populations throughout the United States on the implications of the Human Genome Project.

Karen Rothenberg is Dean of the University of Maryland School of Law and founder of the School's Law & Health Care Program. Dean Rothenberg received both her B.A. and M.P.A. from Princeton University's Woodrow Wilson School of Public and International Affairs and received her law degree from the University of Virginia School of Law. Prior to joining the faculty at Maryland, she practiced with the Washington, D.C. law firm of Covington and Burling and has worked with a variety of health and medical organizations. She served as president of the American Society of Law, Medicine and Ethics, as a member of the Institute of Medicine's Committee on "Legal and Ethical Issues relating to the Inclusion of Women in Clinical Studies,"

and on a number of NIH panels, including several on the ethical, legal and social implications of new developments in genetics. She also served as co-editor-in-chief of the *Journal of Law, Medicine & Ethics*, as a member of the NIH Recombinant DNA Advisory Committee, the National Action Plan for Breast Cancer, the American Bar Association's Coordinating Group on Bioethics and the Law and on the Advisory Council to the National Institute of Child Health and Human Development. She currently serves on the Editorial Board of the *Journal of Law, Medicine and Ethics*, on the Association of American Law Schools Committee on Academic Freedom and Tenure, and as a Fellow of the American Bar Foundation. She has written numerous articles on such topics as AIDS, women's health, genetics, right to forego treatment, emergency care, and the new reproductive technologies. She also completed a series of studies on legislative approaches to genetic information in both health insurance and workplace contexts which were published in *Science*.

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 (USPTO). In this capacity she edits the Manual of Patent Examining Procedure, a reference manual for patent examiners and practitioners. Ms. Therkorn has had an active role in a number of biotechnology patent policy issues during the past five years. She has co-authored several articles including *Reach-Through Claims in the Age of Biotechnology*, 51 Am. U. L. Rev. 609 (2002) and the Utility Examination Guidelines and Written Description Guidelines and associated training materials. She has worked on several Trilateral (USPTO, European Patent Office and Japan Patent Office) projects in biotechnology, including several comparative studies. Ms. Therkorn has worked for the USPTO since 1986. Prior to joining the Deputy Commissioner's staff in 1996, she was a primary patent examiner in the chemical arts. Ms. Therkorn earned her J.D. with honors in 1991 from the George Washington University National Law Center and a B.S. in Chemistry in 1985 from Rensselaer Polytechnic Institute.

Mary Webster is Assistant Professor at the University of Maryland School of Law and Director of the Maryland Intellectual Property Legal Resource Center (MIPLRC). The MIPLRC, a joint initiative of the University of Maryland School of Law and the Montgomery County Department of Economic Development, was established in early 2002 to provide low-cost intellectual property services and other legal assistance to start-up high technology companies and explore emerging ethical, legal and policy issues in the field of high-technology and intellectual property. Professor Webster has eighteen years of combined experience in microbiology and patent law. Beginning with a career as a molecular virologist, she has specialized in biotech patent law for the past ten years. Her law career has included work in private practice, a clerkship at the Federal Circuit, and in-house counsel in commercial and not-for-profit settings. A registered patent attorney, she holds a B.S. in bacteriology from the University of Wisconsin, an M.S. in microbiology from the University of South Florida, and a J.D. from the Washington College of Law at American University.

The Workshop organizers and co-chairs were Lawrence M. Sung and Diane E. Hoffmann.

Lawrence Sung is currently a partner with the law firm of Preston Gates Ellis & Rouvelas Meeds LLP in Washington, D.C. specializing in intellectual property law and a part time Law School Professor at the University of Maryland School of Law. Prior to joining Preston, Gates, in

the fall of 2003, he was Assistant Professor and Director of the Intellectual Property Law Program at the University of Maryland School of Law, teaching courses in patent law, licensing and technology transfer and biotechnology law. A registered patent attorney, he received his Ph.D. in microbiology from the U.S. Department of Defense-Uniformed Services University of the Health Sciences and his J.D. from American University, Washington College of Law. Following a judicial clerkship with the U.S. Court of Appeals for the Federal Circuit, he specialized in biotechnology patent litigation with several law firms. Before joining the faculty at Maryland he taught at the George Washington University Law School, the American University, Washington College of Law, and the Northwestern School of Law of Lewis & Clark College.

Diane Hoffmann is Associate Dean and Director of the Law & Health Care Program at the University of Maryland School of Law. From 1987 – 1990, she held an appointment with the University of Maryland Biotechnology Institute's Program on Public Issues in Biotechnology. At the School of Law she has taught a seminar on Biotechnology and the Law and authored articles on the regulation of biotechnology and on legal and ethical issues in genetic testing. She was instrumental in the development of the Maryland Intellectual Property Legal Resource Center, conducting and authoring a "needs assessment" for its establishment. Currently Professor Hoffmann is working on a research project to determine how judges are using health related genetic test results in the court room. Her research and teaching focus on issues at the intersection of health law, policy and bioethics. She is also founder of the Maryland Health Care Ethics Committee Network. Prior to joining the law school faculty, Hoffmann worked as a policy advisor to the Massachusetts Secretary of Environmental Affairs and practiced health, environmental and food and drug law at the Washington D.C. office of Dewey, Ballantine, Bushby, Palmer & Wood. Hoffmann received her J.D. from Harvard School of Law, her M.S. from Harvard School of Public Health and her A.B. from Duke University.

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 discussed.

Other attendees included Teresa LaMaster, Managing Director, Clinical Law Program, University of Maryland School of Law, and University of Maryland School of Law students Lauren Axley and Kristina Wirth.