FOREWORD:

THE PROMISE AND PERIL OF BIOTECHNOLOGY

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Recent years have seen unprecedented growth in biotechnology and its potential applications to human health. Genetic engineering techniques such as recombinant DNA technology have made possible the mass production of life-saving pharmaceutical products that previously could only be derived from biological samples. The identification of the genetic component of many diseases, such as breast cancer, has spurred the development of screening mechanisms for vulnerable populations. Advances in pharmacogenomics and gene therapy suggest the tantalizing possibility that drugs can be tailored for specific responsive populations—and that some patients’ conditions might ultimately be cured by “repairing” faulty genes. In light of the recent mapping of the

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1Biotechnology is defined as “the collection of industrial processes that involve the use of biological systems.” ROBERT C. KING & WILLIAM D. STANSFIELD, A DICTIONARY OF GENETICS 41 (5th ed. ‘97). For purposes of this Symposium, the processes with which we are concerned are those related to health care.

2Recombinant DNA technology describes a variety of “techniques for joining DNA molecules in vitro and introducing them into living cells where they replicate.” Id. at 291. In the pharmaceutical context, recombinant technology may be used to create cells that express a naturally-occurring substance, often one that cannot be mass-produced in a synthetic manner. See, e.g., Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., 927 F.2d 1300, 1310 (Fed. Cir. 1991) (addressing patent dispute over recombinant technology used to produce the red blood cell stimulator erythropoietin, which previously could only be collected by purifying large quantities of human urine).

3See generally Karen H. Rothenberg, Breast Cancer, the Genetic “Quick Fix,” and the Jewish Community: Ethical, Legal, and Social Challenges, 7 HEALTH MATTERS 97 (1997) (describing issues raised by discovery of the BRCA1 gene).

4See, e.g., Mark A. Rothstein & Phyllis Griffin Epps, Ethical and Legal Implications of Pharmacogenomics, 2 NATURE REV. GENETICS 228 (2001) (describing the uses and dangers of pharmacogenomics); Jesse D. Goldner, Dealing with Conflicts of Interest in Biomedical Research, 66 J. L. MED. &
human genome—and the recent debate over human cloning—the biotechnology revolution is likely to continue.5

Yet the promise of biotechnology will also bring challenges—challenges to the medical, scientific, and patient communities, and to the legal and regulatory structures that govern the development and commercialization of these new biological tools. The ability to identify and manipulate genetic material will stretch our previous assumptions about what can (and should) be protected by patent law, and whether tissue donors have any right to share in the benefits of the discoveries they help create. The necessity of examining large numbers of genetic samples will raise questions regarding patient’s motivations for assisting in research efforts, and whether existing law adequately protects patient interests. The burgeoning number of commercially available biotechnology products will force the Food and Drug Administration (“FDA”) to reevaluate its traditional approach to pharmaceutical regulation. And in a competitive marketplace where allegations of widespread misconduct already exist, the potential for the development of genetically tailored pharmaceutical products will increase pressure on manufacturers to recoup their investments from a significantly smaller customer base.

The authors in this Symposium address the challenges posed by biotechnology in the health care fraud, regulatory, and patent protection contexts. While recognizing the enormous potential for medical advances, each author acknowledges the ways in which biotechnology stretches the boundaries of traditional health care and intellectual property regulation. Finding the balance is a difficult task; lack of regulation may leave millions of patients vulnerable to abuse, while overly restrictive laws pose the risk of freezing the industry in its current undeveloped state. The suggestions, made by these authors, and their careful analyses of the problems, will go a long way toward helping us achieve that balance.

In the 2002 Jenkins & Gilchrist Health Law Lecture, Assistant United States Attorney James Sheehan addresses the challenges facing biotechnology in the pharmaceutical context.6 Sheehan looks to biotechnology as a potential solution to a problem that plagues traditional pharmaceutical treatment: the fact that many drugs simply don’t work for the patients for whom they are prescribed.7 Sheehan attributes this problem to our continued adherence to an “old industrial way” of standardized pharmaceutical regulation.8 The traditional system has a number of advantages, including standardized research and development, mass production, marketing, and regulation of pharmaceutical products, and the ability to standardize dosing regimens. But the standardized approach also has significant disadvantages, including a large number of adverse effects, non-compliance with drug regimens due to side effects, the inability to identify which patients will respond to a drug, and the failure to adjust drug regimens based on subsequent data.9 Biotechnology’s potential for “customizing” drugs—by determining which patients will respond to each product, and at what dose—offers great promise in alleviating these problems.

In Sheehan’s view, however, biotechnology’s promise is shadowed by the specter of fraud—a particularly insidious type of fraud posing a threat to vulnerable patient populations. Rather than involving clear violations of positive law obligations, this new fraud focuses on “breach[es] of good faith and fair dealing as understood in the community[,] involving a deception or breach of trust.”10 In order to identify such community boundaries, Sheehan suggests that we look to the broader ethical standards governing science and medicine.11 Whereas traditional medical fraud has involved issues

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7 Id. at 13-14.

8 Id. at 15.

9 Id. at 15-16.

10 Id. at 17. Of course, pursuing such “new fraud” may require the utilization of a broader range of anti-fraud laws than are currently in vogue. For example, the government’s primary health care fraud weapon, the Civil False Claims Act (“FCA”), can be invoked only where the defendant submits a monetary “claim” to the government. 31 U.S.C. §3729(a). While failure to comply with underlying legal duties may at times violate the FCA, courts generally require that compliance with such obligations be expressly linked to the government’s payment of the claim. See John H. Krasner, Health Care Providers and the Proactionary Paradigm: Government Harm Under the Civil False Claims Act, 36 GA. L. REV. 121, 175-81 (2002) (analyzing false certification arguments). Thus, fraud actions based on more amorphous “breaches of trust” might have to be brought under other causes of action, such as the traditional conspiracy or false statements laws. See, e.g., 18 U.S.C. §§371 (prohibiting conspiracies) & 1001 (prohibiting false statements).

11 Sheehan, supra note 6, at 18.
of billing and reimbursement, Sheehan believes that fraud in the biotechnology era will focus more broadly on what happens to patients in these health care settings.

This new type of fraud will encompass a wide range of impermissible activities, including reckless endangerment of patients and the provision of medically unnecessary tests and treatment. Sheehan is particularly interested in fraud that occurs in the research context, where patient-subjects may be unaware of the dangers, risks, and financial incentives involved in clinical studies. Despite the difficulties of prosecuting research fraud, Sheehan indicates that federal law enforcement officials plan to pursue these cases. The potential for biotechnology fraud is significant.

Professor Michael Malinowski addresses one of Sheehan's initial assumptions: that recent advances in genetic profiling will enable us to determine which patient populations will benefit from individual drugs, and perhaps even tailor drugs to individual patients. Malinowski argues that the pharmaceutical industry is under unprecedented competitive pressures due to the growing influence of the generic drug industry and to challenges involving global patent harmonization. Pharmaceutical companies have responded by devoting an increasing amount of money to research and development ("R&D") activities. Like Sheehan, Malinowski argues that traditional R&D activities—a focus on clinical trials—leave significant gaps in our ability to treat individual patients. In contrast, recent advances in genetic testing have made it possible to screen large patient populations, offering unprecedented precision in prescription drug delivery.

As Malinowski demonstrates, however, this shift from mass-produced, mass-market pharmaceutical products to a "tailored" approach has a number of implications for the relationships between patient-subjects and health care providers. As scientists focus on the intricacies of individual gene function, they are likely to seek access to greater numbers of biological samples and family history information. In addition to intellectual property disputes, competitive pressures will raise concerns about our ability to protect human subjects from the financial conflicts of interest that entangle researchers and academic institutions. As biotechnology increases the pace of new therapeutic developments, the line between "research" and "treatment" increasingly will become blurred.

Outside of the research context, the ability to use genetic testing to profile large patient populations will also challenge health care competency—both that of individual health care providers and of the governmental agencies charged with regulating these new products. These advances also will work significant changes to the health care market: drug prices will rise to incorporate the costs of genetic profiling and monitoring activities, and to enable pharmaceutical companies to recoup their R&D costs from smaller target populations. Malinowski ends his article with a call for the legal, medical, and scientific communities to work together to develop criteria to guide the development, application, and reimbursement of these new technologies.

Professor Lori Andrews addresses biotechnology from another perspective, exploring one of the difficult intellectual property questions posed by recent biotechnology breakthroughs: should researchers be permitted to obtain gene patents, thereby attaining the right to exclude others from using that genetic material? Andrews grounds her analysis in the basic premise of the patent laws: a monopoly is granted to a patent holder only in exchange for the benefit
the public receives from the disclosure of the patented invention.\textsuperscript{21}
Many substances, such as “products of nature,” are not patentable because the public would not gain any new knowledge in exchange.\textsuperscript{22} While courts have upheld patents of isolated and purified forms of naturally occurring substances, it is not clear that genetic material, standing alone, meets the criteria for patentability. Moreover, restricting access to diagnosis and treatment involving genetic information—the practical effects of patent exclusivity—may have enormous social costs in the health care context.\textsuperscript{23}
Andrews argues that the very exclusivity rights that make patents so attractive pose significant obstacles for the advancement of science and medicine. As a practical matter, the possibility of obtaining patent protection creates an impediment to research by giving researchers incentives to hoard samples and delay publication of results in an attempt to protect their patent rights (and hence their commercial interests).\textsuperscript{24} Similarly, the costs of obtaining a license may prevent others from engaging in further research using a patented gene sequence, including studies needed to confirm the veracity and utility of the original discovery.\textsuperscript{25} Patents also interfere with the traditional scientific process of “cumulative investigation” by forcing researchers to pay for costly access to samples, databases, and other necessary information—costs that will be reflected in the price of the resulting products.\textsuperscript{26} And the pressure to quickly patent new genetic discoveries, long before the functions of the patented sequences can be established, may lead to the granting of “submarine” patents that can unexpectedly derail ongoing research related to those sequences.\textsuperscript{27}
In addition to these broader scientific concerns, gene patents also affect the delivery of health care services. The fact that one company holds the patent on a gene associated with a particular disease may prevent other researchers from engaging in future research in solving that disease, particularly where the patent holder refuses to license competing laboratories to test for the gene.\textsuperscript{28} Gene patents also raise the cost of new technology—technology that often is discovered through publicly-funded research.\textsuperscript{29} The high costs of the resulting diagnostic tests may ultimately restrict patients’ access to these useful new technologies, including the very patients who made that research possible.\textsuperscript{30} Gene patents may also give physicians an incentive to commercialize genetic discoveries derived from their patients, thus interfering with the physician’s duty to consider the patient’s interest paramount to their own.\textsuperscript{31}
Andrews notes several possible policy alternatives for addressing these problems. First, gene patents may be vulnerable to litigation, both by patients who were not informed of their physicians’ patent aspirations and by critics who oppose the basic principle of patenting genetic material. Second, Andrews argues that it would be possible for Congress to ban gene patents altogether, as it once banned patents on health inventions.\textsuperscript{32} Short of an outright ban, Congress could enact limited restrictions on patent rights to give health care providers and scientists access to patented genes for treatment, testing, or research purposes. Third, Andrews suggests that we explore the possibility of creating “patent pools,” through which researchers and health care providers could purchase blanket licenses for access to certain genetic discoveries.\textsuperscript{33} Similarly, the government might impose a compulsory licensing scheme, forcing patent holders to permit researchers and health care providers to purchase access to the patented gene sequences.\textsuperscript{34} Finally, Andrews highlights ongoing efforts to strengthen the rights of tissue donors in the discoveries to which they contribute.\textsuperscript{35} Although being open to the possibility that donors should be granted a property interest in patents, Andrews notes that this approach will not resolve the broader controversy regarding gene patents (particularly those de-

\textsuperscript{21} Id. at 67-68.
\textsuperscript{22} Id.
\textsuperscript{23} Id. at 69.
\textsuperscript{24} Id. at 80.
\textsuperscript{25} Id. at 81.
\textsuperscript{26} Id. at 83.
\textsuperscript{27} Id.
\textsuperscript{28} Id. at 85.
\textsuperscript{29} Id. at 78.
\textsuperscript{30} Andrews, supra note 20, at 91. Andrews offers the example of families who participated in a large genetic testing program for Canavan disease, only to have the patent holder later attempt to restrict other laboratories from testing for the gene.
\textsuperscript{31} Id. at 93. See, e.g., Moore v. Regents of the University of California, 793 P.2d 479 (Cal. 1990) (refusing to grant leukemia patient a property interest in his cells, which were used by his physicians to create a lucrative patented cell line, but finding that patient might have a cause of action for breach of informed consent and fiduciary duty).
\textsuperscript{32} Andrews, supra note 20, at 96-101.
\textsuperscript{33} Id. at 101-103.
\textsuperscript{34} Id. at 103.
\textsuperscript{35} Id. ( ) at 104.
rived from more common genetic sources). Regardless of the alternative chosen, however, Andrews stresses the need for a policy to assure that patented genetic material remains accessible to patients and researchers and is used to promote positive social advances.

Professor Cynthia Ho expands on Andrews' final policy query: what rights should patients have in biotechnological inventions based on their genetic material? Ho argues that patients who contribute to genetic research may not be aware the research could lead to patented discoveries that confer exclusive rights on the patent holder. Ho traces the roots of such misconceptions to widespread patient misunderstanding, including the mistaken assumption that doctors and researchers are immune from commercial interests, and to general misconceptions about the nature of patent protection. The reality, of course, is quite different: biotechnology is highly commercialized, making new technologies extremely expensive—and perhaps inaccessible to the very patients whose genetic contributions made those discoveries possible.

Despite arguments that patients deserve to share in the profits from these discoveries, Ho argues that the patent laws are not designed to protect mere sources of scientific information or ideas. Patents protect "inventors" who make discoveries regarding the substances they study, such as identifying the function of a particular genetic sequence (rather than simply identifying the existence of a genetic anomaly). Under current law, patients do not engage in any inventive activities that would grant them a role in the conception of the patented discovery; their mere genetic material, existing in its natural state, is not patentable subject matter.

Given these restrictions, can patients ever hope to share in the scientific discoveries made with their genetic information? While acknowledging the policy arguments in favor of amending the laws of joint inventorship to recognize a role for patients, Ho argues that current legal interpretations regarding the rights of joint inventors—as well as opposition from corporate interests—make this an un-

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41 Id., supra note 37, at 145-47.
42 Id. at 151-52.
43 Id. at 153.
44 Id. at 155-60, 163-66.