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Genes, Patents, and Product Development

Rebecca S. Eisenberg

In the past year, the National Institutes of Health (NIH) has filed patent applications on more than 2750 partial complementary DNA sequences of unknown function. The rationale for the filings—that patent protection may be necessary to ensure that private firms are willing to invest in developing related products—rests on two premises: first, that NIH may obtain patent rights that will offer effective product monopolies to licensee firms, and second, that unless NIH obtains these rights now, firms will be unable to obtain a comparable degree of exclusivity by other means, such as by obtaining patents on their own subsequent innovations. Neither premise is clearly wrong, although both are subject to doubt in view of statements from industry representatives that the NIH patenting strategy will deter rather than promote product development.

Controversy about the impact of patent law on biomedical research is old news to observers of research science. In the 12 years since the U.S. Supreme Court upheld the patentability of genetically engineered organisms in *Diamond* v. *Chakrabarty* (*1*), the Patent and Trademark Office (PTO) has seen a deluge of patent applications covering biotechnology advances of every sort. So why are the recent patent applications on some 2750 partial cDNA sequences from the NIH laboratory of Dr. Craig Venter setting off alarm bells?

A telling distinction between the present controversy and that which erupted around the time of the *Diamond* v. *Chakrabarty* decision is that today it is the federal government that is pushing forward in pursuit of patent protection, while industry representatives are hesitating on the sidelines (*2*, *3*). And although some scientists are raising their voices in a now familiar refrain about the detrimental effects of patenting on scientific communications (*4*), the present controversy seems to be as much about the role of patents in promoting product development as it is about the role of patents in basic research. Opponents argue that the issuance of patents to those who randomly sequence partial cDNAs could undermine the incentives of firms to take up the more costly work of systematically finding genes of interest (*2*, *3*, *5*), whereas NIH asserts that patent protection at this stage may be necessary to ensure that private companies will be willing to develop products related to the partial genes (*6*).

For now, NIH characterizes the filings as an "interim policy" (*7*), suggesting that it

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may decide not to pursue patent rights and inviting debate in the scientific community about how best to proceed (6). But whatever the outcome of such a debate, it is a fair guess at this point that NIH is not the only player in this particular game and that it is therefore beyond NIH's power to call the game off. The technology that allowed NIH to derive the partial cDNA sequences is widely known and within the reach of many laboratories in the public and private sectors. NIH may decide not to claim patent rights in discoveries made by its own scientists but it lacks the power to impose similar forbearance on other institutions. Moreover, even if NIH decides not to pursue patent rights in its own behalf, current regulations of the Department of Health and Human Services require that it allow employees such as Venter to pursue such rights on their own (8).

How NIH proceeds is nonetheless significant, in part because of the sheer numbers of sequences represented in the NIH patent applications and in part because of the central role NIH plays in the Human Genome Project. But regardless of what NIH does, sooner or later the PTO will have to decide how to treat these or similar inventions under the patent laws, and judicial review of its decision is virtually inevitable. Given the high profile of the Human Genome Project, congressional attention to these issues is also a distinct possibility. How should these institutions think about patent rights in these inventions?

Promoting Product Development

According to NIH Director Bernadine Healy, a paramount goal of NIH is to encourage the rapid development of products for disease treatment (6). Will the patent rights it currently seeks further or retard progress toward this goal? NIH takes the position, reflected in government patent policy since 1980 (9), that patenting government-sponsored inventions makes it more likely that those inventions will be developed into useful products in the private sector. The argument is that private firms may be unwilling to commit necessary capital to the development of these inventions unless these firms have exclusive patent licenses to protect their profit margins.

One might question the validity of this argument in light of concerns expressed by some industry representatives that the patent rights NIH seeks would have quite the opposite effect, deterring rather than promoting investment in product development (2, 3). Is the government's patent policy simply misguided or are there circumstances in which it makes sense? In particular, can a persuasive argument be made for patenting partial cDNA sequences of unknown function as a means of promoting technology transfer?

The specific argument that patenting these inventions will promote investment in product development rests on two premises, both questionable but neither clearly wrong. The first premise is that NIH is entitled to claim patent rights that are broad enough to provide effective monopolies for firms seeking to develop and market products related to the sequences. Otherwise, firms will not increase their profits by obtaining licenses under the patents, and the patents will not serve to enhance financial incentives to bring new products to market. The second premise is that unless NIH obtains patent rights now, firms interested in marketing related products will not be able to secure effective monopolies in the future. If these firms could protect their market positions without an exclusive license under an NIH patent, such as by patenting the products they develop, then the NIH patents would not be necessary to promote investment in product development. Taking at face value NIH's claim that its purpose in pursuing patent rights is to facilitate technology transfer rather than to fill the public coffers with revenues from patent royalties, it follows that the patents should be pursued only if they appear to be a necessary and effective means of furthering progress toward that goal. Otherwise, NIH patents will merely add to the thicket of patent rights that firms must negotiate their way past before they can get products on the market.

What Can NIH Patent?

An initial question is thus whether NIH can obtain patent rights that will offer licensees effective commercial protection in markets for related products. The scope of rights conferred by a patent is largely determined by the language of the patent claims, which are initially drafted by the patent applicant (or by his or her attorney) and typically revised and narrowed in response to objections from the PTO. The claims define the patentable inventions arising from the inventor's work. NIH scientists have obtained partial sequences for thousands of cDNAs that correspond to genes expressed in human brain tissue. Like most patent applicants, NIH seeks issuance of a patent on multiple claims of varying scope. At this stage, the application contains claims not only to the partial cDNA sequences as isolated molecules but also to longer sequences that incorporate the partial cDNAs, including the full coding sequences of which they form a part. NIH has not yet filed claims to the proteins for which these cDNAs code, although it may do so in the future. Is NIH entitled to these broad patent rights under present law?

Traditional patent doctrine suggests two grounds for rejecting all of the claims. Both are arguably supported by past decisions of the U.S. Supreme Court, but not by more recent decisions of lower courts. The first is the intuitively appealing argument that patents should not be issued for the discovery of things that exist in nature. Many scientists, and many lawyers, for that matter, are nonplussed at the suggestion that anyone could claim to have "invented" a DNA sequence that forms a part of the human genome or a protein that is expressed naturally in human cells. In fact, there is venerable authority for the proposition that one may not patent "phenomena of nature." A 1948 U.S. Supreme Court decision (10) invalidated a patent claim to a mixed culture of naturally occurring bacteria on the ground that

> patents cannot issue for the discovery of the phenomena of nature. . . . The qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none.

Although this decision has never been overruled, in retrospect it seems to represent a high-water mark in the "phenomena of nature" doctrine. More recently, the Supreme Court has stated that the present patent statute allows patenting of "anything under the sun that is made by man" (1).

One could certainly make a coherent argument that cDNA sequences and the proteins for which they code are not "made by man" but rather are "manifestations of laws of nature," but such an argument is unlikely to prevail in the PTO or in the courts. A substantial body of case law in the lower courts has held that one may patent newly isolated or purified forms of products that exist in nature only in an impure state. These courts have upheld patents on purified chemicals (11) and biologically pure cultures of naturally occurring microorganisms (12). The PTO has issued numerous patents on DNA sequences, and some of these patents have been judicially enforced, although no one has challenged their validity on the ground that they claim phenomena of nature (13). If the courts should hold patents on DNA sequences and proteins invalid on this ground, they would bring down not only the NIH patent applications but also countless other issued patents that support the profit expectations on which the biotechnology industry has been built.

A somewhat narrower ground for rejecting the claims that has received attention in the press is that they lack patentable "utility" because NIH has not identified the

genes that the partial sequences belong to, the proteins those genes code for, or the functions those proteins perform. In *Brenner* v. *Manson*, the Supreme Court relied on the utility requirement in holding invalid a claim to a process of making a novel steroid that had not yet been shown to have any practical use other than as an object of scientific inquiry (*14*). If you cannot patent a new steroid until you have found a use for it, it would seem to follow that you cannot patent a new DNA sequence until you have found a use for it.

NIH has anticipated this objection by identifying several different uses for the sequences. They may be used, for example, as genetic markers, for forensic identification, or for tissue typing. This certainly amounts to a greater showing of utility than was made by the patent applicant in *Brenner* v. *Manson*, although issuance of a patent to NIH in this case might nonetheless seem to violate the spirit of that decision.

What is the purpose of limiting patent protection to useful inventions, and would that purpose be thwarted by issuing a patent to NIH? There is little case law to turn to in answering this question. The utility requirement is rarely invoked in practice, perhaps because few people go to the trouble and expense of seeking patents on useless inventions, and no one is likely to care much if they do. Indeed, the argument against allowing NIH to patent the sequences is not really that these sequences are useless, but rather that NIH does not yet know what they are good for and should not be able to claim patent rights ahead of subsequent researchers who figure it out. It is the as yet undiscovered utility of the sequences, rather than the uses that are disclosed in the patent application, that makes NIH's patent claims worth fighting about.

One could argue, with some support in the language of *Brenner* v. *Manson*, that the function of the utility requirement is to distinguish between basic research, which should stay in the public domain, and applied technology, which may be patented, thereby confining the operation of the patent system "to the world of commerce rather than to the realm of philosophy" (*15*). Under this view, the NIH sequence information might seem too far removed from the world of commerce to be ripe for patent protection. But this is a very difficult line to draw in contemporary biotechnology research, where industrial scientists are often studying the same sorts of problems as their academic and government counterparts. Withholding patents on early research discoveries could backfire if it leads researchers to protect their unpatentable discoveries as trade secrets rather than to dedicate them to the public domain. A decision rejecting the NIH patent claims for lack of utility would conflict with more recent lower court decisions and would probably be unwise as a matter of public policy.

The NIH patent applications are more likely to falter on the more commonplace grounds that the claimed inventions are obvious in light of existing knowledge and that the disclosure is inadequate to support the breadth of the claims. An invention may not be patented if it would have been obvious at the time it was made to a person having ordinary skill in the field in light of existing knowledge (*16*). Whether the sequences that NIH claims are "nonobvious" presents a legal question of some complexity. One approach to this question would allow NIH to claim the sequences if they were derived through a nonobvious method (*17*). NIH scientists have applied conventional automated DNA sequencing technology to randomly selected cDNAs from a commercially available cDNA library. The sequences may well be deemed obvious if other competent investigators would have known how to achieve the same results. Another approach that has been used to determine the patentability of novel chemicals synthesized by conventional means focuses on whether the chemicals have unexpected properties (*18*). The cDNAs may well turn out to have such properties, but the properties that have been identified so far are entirely predictable and may be inadequate to establish the nonobviousness of the sequences at this time.

A further obstacle to the award of commercially effective patent rights to NIH is the requirement that a patent applicant make a disclosure in the patent application that is adequate to justify the scope of the patent claims (*19*). This requirement may present a problem for claims to full coding sequences and proteins that NIH scientists have not yet obtained in the laboratory. The NIH patent application discloses the partial sequences that its scientists have derived but not the full coding sequences of which these sequences form a part or the proteins that the sequences code for.

Although an applicant need not have actually reduced an invention to tangible form before patenting it, it is necessary for the applicant to supply a written disclosure that would enable other skilled investigators working in the same field to make and use the claimed invention without undue experimentation (*20*). Filing an application that includes such an enabling disclosure is deemed a constructive reduction to practice and will support a patent broader in scope than the inventor's actual achievements. Although the NIH application does not disclose either the complete DNA sequences for the genes that have been partially sequenced or the proteins that they code for, it does provide a general description of how to use the partial sequences as probes to find the full genes and how to achieve expression of the full genes once they have been found.

The question of whether an applicant's disclosure is adequate to support the breadth of the claims is specific to the facts of a particular case at a given time, but there is reason to suspect that some of NIH's broader claims will be held invalid under the standards of prior cases. The Court of Appeals for the Federal Circuit, which hears appeals from decisions of the PTO as well as from all federal trial courts in patent infringement cases, has recently used the enabling disclosure requirement to reject broad claims in biotechnology patents. For example, in *Amgen, Inc.* v. *Chugai Pharmaceutical Co.* (*17*), the Federal Circuit considered the validity of Amgen's patent on DNA sequences that encode human erythropoietin. Some of the patent claims were broadly worded to cover not only the actual human erythropoietin gene that Amgen had cloned but also analogous DNA sequences encoding any polypeptide enough like human erythropoietin to share some of its biological properties. In holding these broad claims invalid, the Federal Circuit stated that Amgen's disclosure of how to make only a handful of analogs, whose activity had not been clearly ascertained, did not justify the grant of a patent on every possible analog of a gene that contains 4000 nucleotides. The same court (or the PTO) might well conclude that NIH's disclosure is not adequate to support claims to all sequences encoding any human gene products that include any of the partial cDNA sequences the applicant has identified. On the other hand, the adequacy of NIH's disclosure will be measured against a considerably more advanced state of knowledge in the field than that prevailing at the time of the Amgen filing, making it easier for NIH to establish enablement of broadly worded claims.

Other language in the *Amgen* opinion suggests that the Federal Circuit might be reluctant to award patent rights in a gene to someone who has not yet isolated that gene. Addressing the issue of when rival inventors of the same gene could claim to have first "conceived" of the invention for purposes of establishing priority of invention (*21*), the court held that an inventor who has not yet isolated a gene should not be deemed to have conceived of the invention until he or she is able "to envision [its] detailed constitution . . . so as to distinguish it from other materials, as well as a method for obtaining it" (*22*). The *Amgen* decision suggests that the Federal Circuit

may consider NIH's description of a method for obtaining the full coding sequences inadequate to support patent claims to genes that have not yet been isolated. If so, NIH may be limited to narrower claims to the specific partial cDNA sequences its scientists have identified and readily obtained variations.

Commercially Effective Patent Scope

If NIH's patent rights are so limited, they will probably not be broad enough to offer effective protection to firms seeking to bring related products to market, and NIH's argument for obtaining patents as a means of promoting product development would lose its force.

Generally, the most effective commercial protection is provided by a patent claim on an end product that is sold to consumers. Such a claim confers a right to exclude competitors from the market for the patented product entirely, regardless of how they make it or what they use it for. Somewhat less effective are patent claims on starting materials or processes used in making an unpatented end product. Such claims do not prevent a competitor from making the product from different materials or through a different process or even from using the patented materials overseas and then importing the unpatented end product into the United States (*23*). Such a patent may also be difficult to enforce because of practical problems in detecting and proving infringing activities in the manufacturing process that are not apparent from inspection of the end product as it is sold in the market. Weaker still is a patent that claims products or processes that are used only during product development. Not only is it difficult to detect and prove infringement of such a patent, but often the only effective remedy even for proven infringement will be damages, because an injunction against future use of the invention will not thwart the efforts of a competitor who has already finished using the invention. One could argue for a substantial damage remedy if use of the patented product was an essential step in developing a lucrative product, and if infringement was willful the court has discretion to treble the amount of damages (*24*). But so long as the competitor no longer needs to use the patented invention in the manufacturing stage, an injunction against future infringement would not serve to keep the competitor off the market.

Where do the NIH patent claims fit in this taxonomy? That depends on what products are ultimately sold. If, for example, one of the partial sequences turns out to be part of a gene for a useful protein and that protein is ultimately produced and sold as a therapeutic agent, then the most effective commercial protection would come from a patent claim on the protein itself. A claim to the full gene that codes for the protein (in a recombinant vector or transformed host cell) would be somewhat less effective, offering protection against competitors who use the patented gene in the United States to produce the recombinant protein but not against those competitors who use the gene overseas and then import the unpatented protein into the United States. A claim to the partial cDNA sequence in isolation would offer the most dubious protection, because this product need not be used even in the manufacturing process. The partial sequence might be used in the development stage as a probe to find the full gene, but the remedy for this limited use would not include an injunction against selling the unpatented product that was thereby developed.

A claim to a DNA sequence would offer more effective commercial protection if the sequence itself were a part of the end product rather than just an intermediate for use in the product development or manufacturing stages. A DNA sequence might be a key component of a diagnostic product to detect the presence of disease genes or of a therapeutic product for use in human gene therapy. In these situations, the effectiveness of the claim would depend on whether it covers substitutes for the product that is sold. For example, suppose that one of NIH's patented partial cDNAs turns out to be a portion of a disease gene. The patent would be of little value to a licensee interested in developing a diagnostic test kit to detect the presence of the disease gene if another firm could develop a competing product that uses a different portion of the gene and thereby avoid infringement. NIH attempts to avoid some of these difficulties through a series of patent claims that cover not only the partial cDNAs that its scientists have sequenced, but also allelic variations, complementary sequences, portions thereof, and longer sequences including any of the above. But so far, all we have seen is NIH's wish list, and there are reasons to doubt that the PTO will issue a patent on all that NIH seeks to claim.

Sometimes the effective scope of patent claims is expanded under a rule called the doctrine of equivalents (*25*). This doctrine permits a finding of infringement, even though the defendant's product is outside the literal scope of the patent claims, if the defendant's product substitutes known equivalents for elements of the claimed invention while still performing substantially the same function in substantially the same way to obtain the same result as the claimed invention. Although this doctrine has not yet been applied in a biotechnology context, one might expect it to prevent competitors from avoiding liability for infringement of a claim to a DNA sequence through inconsequential variations in the sequence that do not interfere with the function of a product. But a related doctrine holds that a patent holder may not use the doctrine of equivalents to expand the coverage of the patent to include subject matter that was given up in response to a rejection of broad claims by the PTO (*26*). Because NIH is seeking a patent on broad claims initially, if it fails to persuade the PTO to issue a patent on those claims, it will probably not be able to use the doctrine of equivalents to expand the effective scope of its patent rights

At the very least, it seems fair to say that the first premise of NIH's argument—that it is entitled to patent rights that will offer effective commercial protection to licensees seeking to develop related products—is subject to considerable doubt under current law.

Are The NIH Patents Necessary?

The second premise of NIH's argument for pursuing its patent applications is that unless NIH has exclusive patent rights to offer them, firms may be unwilling to develop related products because they will be unable to protect their profit margins through other mechanisms. The validity of this premise turns on a number of questions that are difficult to assess. Some of these questions are legal and some are empirical.

One empirical question that goes to the core of the government's technology transfer policy is whether the R&D decisions of firms are really influenced by patent rights. There is surprisingly little data on this question (*27*). Even accepting the reasonable assumption that a firm will be more willing to invest in product development if it expects to enjoy a monopoly position in sales of the product, it does not necessarily follow that the firm needs patent rights to secure such a position. The lead-time advantage over competitors gained by being first on the market with a new product may provide adequate incentives for speedy product development. Moreover, Food and Drug Administration regulation can provide a period of de facto exclusivity in a market for a new pharmaceutical product even without patent rights. A 17-year patent monopoly may offer a longer period of exclusivity, but because NIH is seeking patent rights long before related products are ready for market, its licensees will be unlikely to enjoy protected profit margins under the patents for the full 17-year patent term.

Even if patent rights are critical, firms would presumably prefer to protect their

market positions through their own patents rather than through royalty-bearing exclusive licenses from NIH. Will the firms that develop products related to the claimed sequences be able to obtain patents that give them effective monopolies? NIH lawyers argue that once NIH scientists disclosed the partial sequence information, the remaining product development steps may have become obvious and therefore unpatentable.

Did publication of these partial sequences make obvious the full genes to which they correspond or the proteins for which those genes code? The answers to these questions turn on the difficulty and unpredictability of obtaining the desired products. An invention is not made obvious by a disclosure that merely suggests a promising avenue of research to pursue unless the prior art indicates that the effort is reasonably likely to succeed (*28*). The argument for obviousness in this context is that it requires no inventive genius to use the partial cDNAs as probes to find full genes and then to transfer the full genes into expression vectors that direct protein translation in host cells. This technology is all clearly laid out in NIH's patent application and in fact forms the basis for the argument that the disclosure is adequate to enable the claims to the full coding sequences and proteins. On the other hand, one could argue that because NIH gives no indication of what the full coding sequences and proteins are good for, the prior art gives no particular incentive to undertake the effort described in the search for any particular gene or protein, and therefore these subsequent inventions remain nonobvious.

Because the obviousness of an invention is measured against the background of human knowledge at the time the invention is made, this requirement is increasingly difficult to pass as scientific knowledge advances in a field. Even if NIH's disclosure alone does not render obvious all related genes and gene products, it is entirely possible that subsequent inventors who find useful genes and gene products related to the partial sequences will be unable to patent their inventions because other intervening advances will make their inventions obvious by the time they are made. And firms might be more willing to invest in bringing these products to market if they had the protection of an exclusive license under an NIH patent.

In view of this uncertainty, it is worth noting that views expressed to date by industry trade groups generally contradict NIH's hypothesis that patent protection for the sequences may be necessary in order to protect the interests of firms that might develop related products in the future.

The Industrial Biotechnology Association (IBA), a trade association whose members collectively represent 80% of U.S. investment in biotechnology, has recently released a position paper urging that NIH not seek patent protection on DNA sequences whose biological function is unknown but instead place such sequences in the public domain (*2*). Noting that the research to be done by companies in developing products amounts to "more meaningful and costly scientific work" than that done by NIH in deriving the partial sequences, the IBA position paper argues that it would be "unfair to permit the Government to exercise complete control over a product to whose development the Government contributed little." The paper also expresses concern that patents on partial gene sequences of unknown utility will add to the cost of product development, create a risk of infringement litigation, and encourage companies "to abandon current research efforts that are aimed at product development in favor of routine genetic sequencing for the purpose of staking claims to as much of the genome as possible." The Pharmaceutical Manufacturers Association has taken a similar position in a recent letter to the Secretary of Health and Human Services (*3*), expressing the view of its members that "a governmental policy of ownership and licensing of gene sequences would inevitably impede the research and development of new medicines in this country."

More favorable to the position of NIH is a recent statement by the Association of Biotechnology Companies (ABC) (*29*) supporting the decision of NIH to file patent applications directed to the Venter sequences. A careful reading of that statement, however, undermines NIH's justification for filing the applications even while approving of the agency's actions to date. The ABC statement suggests that where NIH has disclosed only a partial sequence without identifying the corresponding protein and its biological activity but nonetheless receives patent rights that are broad enough to cover a full coding sequence or protein developed outside NIH, NIH should extend licenses on a nonexclusive basis. Such nonexclusive licensing "would allow the NIH to receive some financial return" on its investment in genome research without blocking development projects in industry. ABC concedes that under such a nonexclusive licensing strategy the patents could not serve to protect the profit expectations of licensees (*29*):

> Under the proposed non-exclusive licensing program, a given company's ability to obtain any exclusivity will properly derive from its own proprietary position. . . . Whether future patent claims are obtainable . . . is not the concern of the NIH, which should not become engaged in schemes designed to ensure future exclusivity.

But NIH's avowed purpose in seeking patent rights to the Venter sequences is not to receive a financial return but rather to promote product development. By conceding that companies must look to their own patent rights rather than to exclusive licenses from NIH to protect their profit margins, the ABC statement rejects the logic of the NIH strategy that it purports to endorse (*30*).

Perhaps the bleakest possibility of all from the standpoint of industry is that no one will be able to obtain effective patent protection for genome-related products. It may well be that NIH's disclosure is inadequate to satisfy the enablement standard for the broad claims in the application, yet revealing enough to render subsequent related inventions obvious and therefore unpatentable. So far, the companies that have the most obvious financial stake in the issue seem to be willing to bet otherwise. If they are wrong, we may soon find out whether nonpatent incentives are enough to induce firms to exploit the commercial potential of a human genome that remains in the public domain.

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gland tissue in which it was found); Kuehmsted v. Farbenfabriken, 179 F. 701 (7th Cir. 1910), *cert. denied*, 220 U.S. 622 (1911) (upholding validity of patent on acetylsalicylic acid to first inventor to develop process for producing it in sufficiently pure state to render it therapeutically available).
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20. W. L. Gore & Assocs. v. Garlock, Inc., 721 F.2d 1540, 1557 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).
21. Priority of invention depends on the date on which the invention was conceived, the date on which it was actually or constructively reduced to practice, and the diligence of a party who was first to conceive but last to reduce to practice. See 35 U.S.C.A. § 102(g) (West 1984).
22. 927 F.2d at 1206.
23. A recent amendment to the patent statute imposes infringement liability on those who use a patented process abroad and then import the unpatented product of that process into the United States [35 U.S.C.A. § 271(g) (West 1984)], but there is no comparable protection available for holders of patents on products used abroad in an unpatented manufacturing process [Amgen, Inc. v. U.S. Int'l Trade Comm'n, 902 F.2d 1532, 1538 (Fed. Cir. 1990)].
24. 35 U.S.C.A. § 284 (West 1984).
25. Graver Tank & Mfg. Co. v. Linde Air Products Co., 339 U.S. 605 (1950).
26. Kinzenbaw v. Deere & Co., 741 F.2d 383 (Fed. Cir. 1984), *cert. denied*, 470 U.S. 1004 (1985).
27. R. S. Eisenberg, *Univ. Chicago Law Rev.* **56**, 1017 (1989) (see pp. 1030–1033).
28. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987).
29. *ABC Statement on NIH Patent Filing for the Human Genome Project* (Association of Biotechnology Companies, Washington, DC, May 1992).
30. It is interesting to note that the ABC takes a more favorable view of the NIH patent applications than does IBA. ABC is a larger organization than IBA whose roster of voting members includes not only companies that develop products but also numerous law firms and other entities with an interest in biotechnology. One might speculate that these other entities, particularly law firms, have more to gain from a proliferation of patent rights in the human genome than do the companies that need to decide about whether to commit capital to the development of biotechnology products. IBA's voting membership is comprised solely of such companies.

Genome Research: Fulfilling the Public's Expectations for Knowledge and Commercialization

by Reid G. Adler

This article provides a historical perspective for the patenting of gene sequences and describes the fundamentals and evolution of patent law. It summarizes federal technology transfer law and policy and assesses the impacts of patenting on academic research. The patentability of gene sequences is then considered along with potential impacts that published sequence data may have on obtaining patent protection for downstream products. Industry's position on gene patenting is summarized and perspectives from the emerging public record on these issues are presented. The article discussing points at which the filing of patent applications and the licensing of patents may be appropriate. It concludes that technology transfer policies for genome research must be adopted carefully so that they remain viable in a time of rapid technological change.

The public benefits from its support of biomedical research through advances at the frontiers of knowledge as well as through the development of commercial health care products (*1*). While the internationalization of scientific research and the pursuit of patent protection are not incompatible (*2*), the question of when to seek patent protection on gene sequences is a "staggeringly complicated issue" (*3*). The National Institutes of Health (NIH) earlier published several thousand cDNA gene sequences and deposited the clones in an open repository (*4*) but sought patent protection for them as an interim measure. This action protected options, fostered public discussion, and forced no outcome or policy decisions (*5*). Development of appropriate policies will occur at the frontiers of patent and technology transfer law.

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Just as nonscientists involved in science policy must understand the differences between, for example, structure- and function-based research, and the importance of both approaches, scientists involved in technology transfer policy must understand patent law and product development. Other areas of research involving unprecedented amounts of data about informational molecules, such as structure-based (or "rational") drug design, raise similar patent and technology transfer questions. It would be unfortunate if misconceptions about the patent system lead to a self-fulfilling prophesy that international research cooperation will be impaired.

"Gene Patenting" Issues in Perspective

Genes traditionally were identified and cloned through a functional approach, starting with samples having observed biological activities, working backward to isolate and purify the responsible proteins, and then, through the use of degenerate DNA probes, locating the corresponding gene. Once a programmatic decision was made to characterize the human genome through a large-scale structural (in other words, sequence-based) approach, the present debate became inevitable. Wide dissemination of sequence data will encourage research, but due consideration must be given to protecting the market exclusivity necessary for the private sector to risk enormous sums of money in product development efforts. The biotechnology industry is critically dependent upon patent protection to maintain its threatened leadership in highly competitive world markets.

How to apply patent rights to genome research should have been a widely debated question, but it largely went unresolved during the establishment of the human genome project. Although the Office of Technology Assessment (OTA) concluded in 1988 that "genome projects raise no new questions of patent or copyright law," it did not consider how technology transfer principles would apply to sequence data that identified genes (*6*). Contemporaneously, the National Research Council rhetorically considered whether a central agency of the government should own the patents for commercially valuable new DNA clones, but concluded only that genome sequences should not be copyrighted (*7*). Contributing to this lack of foresight may have been an urgency to start the genome program, the absence of any expectation that gene sequences would be identifiable so soon with so little accompanying functional information, a general unfamiliarity with patent law (*8*), and a historical lag in the