Journal of Health & Life Sciences Law
June, 2011

***106** PATENT PROTECTION IN MEDICINE AND **BIOTECHNOLOGY:** AN OVERVIEW

Stephen W. Chen [FNa1]
Marina Len [FNa2]
Seth D. Levy [FNa3]

: The law has long needed to respond to the development of modern technologies. Patent law continues to evolve in an effort to keep pace with scientific advancement, while attempting to remain true to certain fundamental principles intended to foster innovation. This article summarizes important requirements surrounding patentability of an invention, including the written description requirement, patentable subject matter, novelty, and obviousness. For each patentability requirement, leading cases are highlighted to illustrate evolution in the law emphasizing the manner in which broadening or narrowing of patentability requirements can traverse gaps between legal principles and technological advancement. Key focuses are the impact of recent case law on medicine and biotechnology and predictions for future developments.

KEYWORDS: Patent, Invention, Inventor, Requirements for Patentability, Biotechnology, Medicine, United States Patent and Trademark Office (USPTO), Novel, Obvious, Written Description

***108 Chen, Len, and Levy: Patent Protection**

CONTENTS

***109 Introduction**

In the midst of the current recovery from a global recession, technology innovation is increasingly viewed as a vital catalyst toward renewing economic growth in knowledge-based economies. [FN1] In the United States, the creation, commercialization, transfer, and diffusion of high-value technology has a remarkable track record in spurring economic growth. [FN2] A vital ingredient for all these activities is a strong intellectual property regime, with patents acting as a key driver of research innovation, a critical step toward pursuit of market opportunities, and an important resource for the sharing of knowledge with the public.

Nevertheless, there is disagreement about the metes and bounds of what should qualify for U.S. patent protection or how vigorous enforcement of existing patents should be. Some object to certain types of patents on a variety of moral, ethical, or religious grounds. These issues can be particularly pronounced when dealing with the commercialization of products and services in medicine and biotechnology. Perhaps such conflicts are inevitable given the variety of interests at stake, the fast pace of technological development, and the lengthy process for regulatory approval. At the heart of the U.S. patent system is the United States Patent and Trademark Office (USPTO), which provides a central function of substantively examining patent applications and determining whether a patent should be issued. Disputes over patent rights are handled in legal institutions such as the Court of Appeals for the Federal Circuit (CAFC), which has exclusive, appellate jurisdiction for patent matters. Both institutions have remained remarkably nimble in the face of a rapidly evolving technology landscape.

***110** This article is intended largely as a primer for those interested in learning more about fundamental principles governing what is patentable under U.S. law, with an emphasis on the medical and biotechnical arts. Within this context, more challenging technological areas are provided to illustrate occasional rifts with an existing legal principle and how some recent cases have attempted to traverse the gap. This article is organized along a basic framework of the requirements for patenting an invention:

- Is it adequately described, and does it work?
- Is the category of subject matter eligible for patent?
- Is it new and unique?
- Is it a meaningful advance in technology?

Patent claims delineate the specific features of an invention, and much like a fence around a piece of land, define the boundaries of the patent owner's property right. Patentability requirements must be satisfied during the prosecution of a patent application and may also serve as a basis to challenge the validity of an issued patent in litigation. Ultimately, an applicant satisfying these requirements receives an exclusive, time-limited right to exclude others from making, using, offering for sale, selling, or importing the patented invention in the United States for the period from the date a patent is awarded to the date that is approximately 20 years from the date on which the underlying patent application was filed with the USPTO. [FN3] This right to exclude others provides an ability for the patent owner to enforce the patent against others infringing the claims of the patent.

***111 Written Description and Enablement**

A central premise of the U.S. patent system is that innovation is promoted by the grant of exclusive private rights to inventors for their creations, in exchange for the voluntary disclosure and sharing of technologies with the public. In this regard, a patent can be thought of as a contract between the inventor and the government. Inventors obtain the right to exclude others from making, using, offering for sale, selling, or importing a patented invention for a specified period of time within the U.S. borders. In exchange, the patent applicant must disclose and share the invention, thereby providing an immediate public benefit of disclosing new technologies to the world and a later benefit when the invention becomes available in the public domain upon the patent's expiration. Within this quid pro quo exchange, the essence of what the inventor provides is information on the claimed invention. As such, the exchange's value is realized more fully if there are conditions placed on the information's volume, detail, and clarity that the applicant must provide in the patent application.

Three separate requirements under 35 U.S.C. § 112, ¶1 ensure that applicants submit sufficient detail and clarity in a patent application for a claimed invention: (i) that it has an adequate written description, (ii) that it is enabled without undue experimentation, and (iii) that it sets forth the best mode of using the invention. Given that the ultimate purpose of these three requirements is to ensure a substantive and meaningful disclosure by a patent applicant, there has been some confusion about whether written description and enablement are indeed, separate and independent requirements. However, the CAFC has clarified recently that written description and enablement are separate requirements that must be individually satisfied, with each fulfilling a particular role in determining validity of an issued patent. [FN4]

***112** Written description requirement

A patent application must contain an adequate written description of the invention as defined in the claims. [FN5] The primary rationale behind the written description requirement is to ensure that the applicant had actually invented the claimed subject matter as of the filing date by requiring an applicant to memorialize the description of a claimed invention when filing the patent application. The focus on the time of the patent application's filing also guards against overreaching by applicants seeking to patent subject matter not originally contemplated when filing. In short, the written description requirement provides an important role toward ensuring an applicant possessed the claimed invention when he filed his application.

How is possession evaluated within the written description requirement's context? In the recent leading case of Ariad Pharmaceuticals v. Eli Lilly and Company, the CAFC clarified that possession of an invention is not satisfied by an applicant's ability merely to submit extrinsic documentary evidence supporting claims of possessing an invention at the time of filing. Instead, an objective inquiry into the "four corners" of the patent application is necessary to establish whether possession is shown in the patent applicant's disclosure. [FN6] Applying an objective standard requires use of a hypothetical character known as a person having ordinary skill in the art (PHOSITA). The particulars of a PHOSITA are described more fully in Level of ordinary skill in the art, but the general description is a person of ordinary ability and expertise in the ***113** relevant field of technology. [FN7] The central question with respect to the written description requirement is whether a disclosure would convey to a person of ordinary ability and expertise

that the applicant possessed the invention at the time of filing.

In Ariad, the CAFC rejected the notion that written description is satisfied by simply providing sufficient information for one to make and use a claimed invention. Rather, the CAFC found that Ariad's patent claims for methods of treating human disease by reducing activity of NF-kB, a transcription factor involved in immune response and inflammation, did not fulfill the written description requirement. The patent disclosed three broad classes of NF-kB inhibitors, but without disclosure of specific molecules capable of reducing NF-kB activity, the patent did not contain a written description sufficient to convey possession of the claimed invention. Through the Ariad decision, the CAFC's clarification of the meaning of possession within the written description context suggests applicants should describe fully, including specific examples of their inventions within the disclosure of the filed application to satisfy the written description requirement.

Because the test for an adequate written description, as articulated in Ariad, appears to focus tightly on the concept of possession, one might imagine that clear evidence of actually possessing a claimed invention at the time of filing would strongly support a determination of satisfying the written description requirement. However, this is not necessarily so, as demonstrated in the case of Enzo Biochem v. Gen-Probe. [FN8] In Enzo, the patent owner sued the defendant for allegedly infringing a patent directed to nucleic acid probes for the detection of specific species of bacteria. The defendant sought to invalidate the patent's claims on the basis of failing to meet the written description requirement. The patent owner actually possessed the invention at the time ***114** of filing the patent application, having placed the biological materials in a public depository, referencing the deposits by public accession numbers provided in the patent specification, and thereby making the contents accessible to the public. The Enzo court determined that the process of depositing biological materials was a format compatible with the written description requirement and the deposit provided factual evidence of the patent owner's actual possession of the claimed invention. However, this did not necessarily mean the disclosure's written description was adequate. [FN9] If a PHOSITA would not be able to glean from the disclosure what the claimed subject matter was, its purpose, or significance, then actual possession still would fail to satisfy the written description requirement. A patent applicant must describe fully the claimed invention for the sake of conveying possession to satisfy the written description requirement. However, possession of a claimed invention at the time of filing does not necessarily satisfy the requirement unless adequately described.

The seemingly inconsistent notion of the written description requiring a demonstration of possession, unsatisfied even by a showing of a claimed invention's actual possession, makes sense when recalling the multiple policy rationales motivating the requirement. Recall that although one objective is for the inventor to demonstrate he or she actually invented what is claimed, a secondary objective of the written description requirement is to guard against overreaching by applicants seeking to patent subject matter originally not contemplated when filing. Requiring patent applicants to disclose the purpose and uses of their claimed inventions fully protects against later attempts to claim technology features unanticipated or unappreciated when the patent application originally was filed.

***115** For example, in the field of biotechnology, the CAFC has held that when gene material has been defined only by a statement of function or result, such a statement alone does not adequately describe the claimed invention. "[A]n adequate written description of genetic material 'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." [FN10] In Regents of University of California v. Eli Lilly, the CAFC held that the written description requirement for supporting claims directed to DNA, such as DNA of recombinant plasmids or genetically modified recombinant prokaryotic microorganisms, requires specificity, such as the recitation of the sequence of nucleotides that make up the DNA. [FN11] A generic recitation of DNA, even if accompanied by the name of the protein it encodes, is not sufficient to satisfy the written description requirement. [FN12]

In 2004, the CAFC revisited the written description requirement and its role in determining an invention's patentability. In University of Rochester v. G.D. Searle & Company, the court considered the validity of claims directed

to methods of reducing inflammation by "selectively inhibiting PGHS-2 activity in a human ... by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product ..." [FN13] The University of Rochester sued Pfizer for infringement of the patent, alleging that the patent covered Pfizer's COX-2 inhibitor, Celebrex®, and Bextra®. Pfizer successfully moved for summary judgment on grounds that the disputed patent claims were invalid for failure to satisfy the written description requirement. The Rochester court found the patent claims invalid, in part because the patent failed to describe any "non-steroidal compound that selectively inhibits the activity of the PGHS-2 gene," and the inventors did not contemplate such compounds ***116** at the time of filing. [FN14] Again, the CAFC reiterated that the specification must set forth enough detail to provide a meaningful disclosure, allow a PHOSITA to understand what is claimed, and to confirm that the inventor invented what is claimed.

Enablement requirement

In addition to meeting the written description requirement, an applicant's disclosure must be enabling. The enablement requirement is satisfied by teaching a PHOSITA how to make and use the full scope of the claimed invention. Courts have interpreted this to mean that the patent disclosure must enable a PHOSITA to make or carry out the claimed invention without undue experimentation. This requirement imposes a condition on the patent applicant to provide sufficient detail and guidance for the public to make and use a disclosed invention. The degree of experimentation held to be undue (i.e., too extensive to consider the disclosure "enabling") turns on a set of factors set forth by the CAFC in In re Wands (known as Wands factors). These factors are based on the type of technology at issue and the state of the art at the time the application was filed. In total, there are eight Wands factors, with all factors balanced together and without any dispositive single factor. The following example should provide a sense of the workings of the Wands factors and the contours of the enablement requirement.

Is the technology predictable or unpredictable?

The first factor is whether the technology is considered predictable. The mechanical and electrical arts generally are considered predictable. It is often the case in the mechanical arts that if one version of the invention is described sufficiently, the assumption is that a PHOSITA could predict fairly easily how to implement variations of that invention. However, this predictive assumption generally is not applied to ***117** inventions in the biological arts, which are usually considered unpredictable. For instance, even a minor change in the physical structure of a molecule or compound can result in a major change in its function.

Some inventions involve different types of components, some of which may be mechanical and others biological. For example, DNA chips used for screening the genetic makeup of humans are created by layering nucleic acid probes on silicon chips. Certain components of these inventions are mechanical in nature and considered within the predictable arts. Other components are based on physiology and considered unpredictable in nature. In such situations, courts have preferred that the issue of enablement is considered individually for each component, rather than categorizing the invention as a whole, because classifying a hybrid device as mechanical or biological may be difficult. [FN15] Instead, classifying specific components as predictable or unpredictable provides a more convenient set of categories to classify the elements of a claimed invention.

What are the breadth and subject matter of the claims?

The next consideration is whether the degree of enablement is proportionate to the breadth of the claims. A simple rule of thumb is that the more subject matter a patent applicant seeks to claim, the more guidance, examples, and details he or she must provide to satisfy the enablement requirement. The applicant is entitled to a right to exclude others from practicing only that which is commensurate with the extent of the inventive contribution disclosed in the patent application. "The boundary defining the excludable subject matter must be carefully set: it protects the inventor, so that commercial development is encouraged; but the claims must be commensurate in scope with the inventor's contribution." [FN16]

***118** This issue often arises in the life sciences when a patent claims a broad list of members constituting a genus. Within the context of patent law, a genus is a form of generally claiming the features of multiple species, wherein species are specific members within the genus. A brief illustrative example of a genus is something such as fruit produce, wherein apples and oranges are species within the fruit genus. In a common scenario in biotechnology or chemical cases, a patent applicant seeks to claim a compound generically because the applicant's technology may focus on the new and important use of a class of chemicals, the application of which was previously unknown or unappreciated in the past. However, having tested only a few of the compounds and forced with presenting their compelling, yet incomplete results in a patent application disclosure, the applicant may not have sufficient species members to claim the larger genus of compounds because some species members have not been tested and thus are not enabled. There is no requirement to test each and every member of a genus, but how many species is "representative" to claim an entire genus? Unfortunately, no bright-line rule exists to strictly define how many examples (species) are sufficient to support a claim directed to a genus. Instead, courts rely on an objective analysis of whether the examples provided are sufficient to teach a skilled artisan to make and use the full scope of the invention, as claimed.

Future developments in the technology

The next factor, which can be particularly challenging for rapidly evolving life sciences technologies, is how to evaluate the later emergence of different versions of a claimed invention not in existence when the application was filed. In a classic case of patent claims possibly encompassing "after-arising" technology, in Chiron Corporation v. Genentech, Chiron sued Genentech for its sale of Herceptin®, a humanized antibody directed to target HER2 antigens, a cell membrane surface localized receptor associated with aggressive types of breast cancers. [FN17] ***119** Chiron's disputed patent claims were directed to HER2 antibodies, but had been filed in the 1980s when mouse monoclonal antibodies were in existence, but humanized antibodies were not yet routinely available. Whereas humanized antibodies are immunologically compatible with human subjects, mouse monoclonal antibodies do not necessarily possess such human immunocompatibility. On an appeal before the CAFC, the Chiron court accepted a broad definition of "antibody," because humanized antibodies were stated expressly as falling within the definition of antibody, as provided in the Chiron patent. However, the Chiron court nevertheless found that, for an unpredictable and "nascent technology" such as antibody engineering, the enabling disclosure must provide a "specific and useful teaching" as a PHOSITA would have little or no knowledge apart from the instructions set forth in the application. Applying the Wands factors, the court concluded that the creation of a humanized antibody, such as Herceptin®, would have required undue experimentation based on the Chiron patent disclosure. The Chiron patent failed to provide guidance on leading modern genetic engineering techniques that were needed to produce humanized antibodies, a technology field that was unpredictable, not routine, and limited to only a small number of specialists. Although Chiron illustrates an important principle--that there is no absolute bar against earlier patent claims reaching "after-arising" technologies--this is limited to the extent that the patent disclosure must enable the later technologies sufficiently.

Other issues with enablement

Most recently, the CAFC has invalidated patents for lacking "full scope" enablement. In Pharmaceutical Resources v. Roxane Laboratories, the patent at issue covered a therapeutic composition comprising a "surfactant." [FN18] Surfactants are compounds that reduce the surface tension of liquids or between liquids and solids, thereby increasing the ***120** contact of two materials. Surfactants often are used in detergents, wetting agents, emulsifiers, foaming agents, and dispersants. In the pharmaceutical industry, surfactants are used to develop liquid pharmaceutical compositions.

The claimed invention was interpreted to cover all surfactants generally. However, the defendants introduced evidence demonstrating that only surfactants having less than 0.030 percent weight by volume would work, and that surfactant concentrations over 0.030 percent would not work, thereby leading the court to conclude that the "number of inoperative combinations is significant when assessing the experimentation that a [PHOSITA] would need to prac-

tice the claimed invention." The court noted that the specification contained only three working examples, which would "not provide an enabling disclosure commensurate with the entire scope of the claims."

However, the enablement requirement prohibiting patenting if undue experimentation exists does not mean no experimentation is expected from a PHOSITA reading a patent specification. Courts also will consider the presence or absence of the scientific theory underlying the invention, such as the mechanism of action, when applying the Wands factors. In Johns Hopkins University v. Cellpro, the patent at issue was directed to the genus of CD34 antibodies. [FN19] The patent disclosed methods of producing CD34 antibodies, a preferred immunogen, and a description of the biochemical mechanism by which the antibody attaches to the antigen. The court found this disclosure sufficiently enabled the claimed invention, holding that:

> The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction ***121** in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. [FN20]

Best mode

In addition to satisfying the written description and enablement requirements at the time of filing, a patent applicant must disclose the best way known to him or her of carrying out the invention. Unlike the preceding requirements for patentability, which are consistent thematically with the patent laws of other industrialized countries, the best mode requirement is unique to U.S. patent law.

The rationale behind the best mode requirement is to prevent an applicant from obtaining a patent while concealing from the public the preferred method of carrying out the claimed invention. For example, if an invention can be carried out using a generic form of a compound, but is carried out most efficiently with a specific form of that compound, the specific form of the compound must be disclosed in the specification.

Courts have interpreted the best mode requirement to involve a two-part test with a subjective and an objective inquiry. [FN21] The subjective inquiry is based on a consideration of the applicant as of the filing date: Did the applicant consider one particular mode or method of carrying out the invention better than others? [FN22] Courts have found that corporate knowledge or knowledge within the scientific community should not be considered. Likewise, a patent application need not be updated to disclose later-developed methods to satisfy the best mode requirement. [FN23] The second phase of consideration is the objective inquiry: If a best mode does exist, has it been enabled sufficiently, such that a skilled artisan could make and use the best mode of the invention ***122** without undue experimentation? Is the undisclosed material or step covered by the claim? If the material or step is not covered by the patent, it need not be disclosed. In fact, although the best mode must be included, it need not be pointed out as such.

In 2002, the CAFC presented a comprehensive review of best mode analysis in Bayer AG and Bayer Corporation v. Schein Pharmaceuticals. [FN24] Bayer owned a patent with claims directed to the antibiotic ciprofloxacin. Defendant Schein alleged that the patent was invalid for failure to disclose the best mode of carrying out the claimed invention. In particular, Schein pointed to Bayer's failure to disclose the inventor's preferred mode of making a novel, synthetic compound used as an intermediate in the synthesis of the claimed invention. This intermediate compound was not recited in the claims, although it was adequately disclosed in the specification.

The CAFC noted at the outset that the court had held claims to be invalid only for failure to satisfy the best mode requirement on seven occasions, and that these cases could be grouped into two categories: (i) failure to adequately disclose a preferred embodiment and (ii) failure to disclose preferred aspects of making or using the claimed invention where the undisclosed matter materially affected the properties of the invention. Although this presented a case of the latter category, the Bayer court rejected defendant Schein's argument that the inventor's preferred method of making the intermediate was significant. In particular, the preference did not materially affect the properties of the

ciprofloxacin product and, as such, the court readily concluded that "not every preference constitutes a best mode of carrying out the invention." [FN25]

***123** Summary

The written description, enablement, and best mode requirements remain among the more challenging areas of patent law, as illustrated by the CAFC's recent clarification of the two separate concepts. Under an evolving framework, it is easy to imagine an expanding number of cases making issue of these disclosure requirements, and bright-line rules contemplating the high complexity of medical technologies and biotechnology inventions may be appropriately difficult to establish.

Subject Matter Eligibility

The types of inventions eligible for patent protection are set forth in 35 U.S.C. § 101, wherein a patent may be obtained for any one of four categories of potentially patentable subject matter, including "new and useful [1] process, [2] machine, [3] manufacture, or [4] composition of matter, or any new and useful improvement thereof." Working definitions and examples help to flesh out these categories in greater detail, but courts generally have construed potentially patentable subject matter very broadly to implement a Constitutional command to support progress of new and useful technologies and to best effectuate legislative intent. [FN26] As an example, the legislative history of the 1952 Patent Act vividly declares that U.S. patents are available for "anything under the sun that is made by man." In this sense, patent applicants traditionally have found expansive opportunities to fit an invention within one of the four statutory categories of 35 U.S.C. § 101.

However, it is clear that 35 U.S.C. § 101 only identifies subject matter that is potentially patentable. An invention still must clear the hurdles of related statutory provisions, including 35 U.S.C. § 102 (novelty), ***124** § 103 (non-obviousness), and § 112 (written description, enablement, and best mode), among several others, to achieve patentability. Recent judicial decisions have clarified further the boundaries of 35 U.S.C. § 101 to provide important limits on what can be patented in the information age.

Potentially patentable subject matter

A survey of definitions provides a useful framework to evaluate the scope of potentially patentable subject matter categories under 35 U.S.C. § 101. Generally speaking, the categories can be described as follows:

- **Process**--Essentially a method in which a series of steps accomplishes a particular result. Examples include a method of isolating a protein or a method of detecting the presence or absence of a sequence in a patient's DNA.
- **Machine**--Typically describes a physical apparatus with moving parts. Examples include an imaging scanner or a pulse oximeter.
- **Composition of Matter**--Includes chemical compounds, biomolecules, purified substances, or mixtures of them. Examples include a DNA gene vector or a drug molecule.
- **Manufacture**--Perhaps the broadest category. Includes tangible human-made products. Far-ranging examples could be anything from a surgical knife to an intravenous fluid bag.

The broad scope of these definitions should demonstrate that, as a starting point, 35 U.S.C. § 101 can encompass virtually all products one uses in his or her daily life and the manner in which they are used. For the purposes of potential patentability, there is no requirement for an invention to fall neatly within one of these four statutory categories. A corollary to this rule is that a patent applicant can claim multiple categories ***125** for different inter-related features of a single invention. [FN27] This is a key benefit for patent owners, because it potentially allows patent claims directed not only at the main aspect of a single invention, but also claims directed to features and uses derived from the surrounding inventive concept.

Perhaps best illustrating the far reach of 35 U.S.C. § 101 was the landmark case of Diamond v. Chakrabarty, which required the U.S. Supreme Court to address the issue of whether living creatures, including genetically engineered organisms, could qualify as patentable subject matter. [FN28] In Chakrabarty, custom-designed bacteria capable of digesting a variety of petroleum components had been rejected by the USPTO as nonpatentable subject matter because the invention was a living organism. Affirming a lower court decision overruling the USPTO rejection, the Chakrabarty court favored a broad interpretation of 35 U.S.C. § 101 to include inventions such as the genetically engineered bacteria involved in the dispute. The Chakrabarty opinion emphasized that the question of utmost importance was whether the invention was a product of human intervention; the fact that the invention under dispute was a living creature in this case was "without legal significance."

Despite these far-reaching definitions, 35 U.S.C. § 101 is not without limit, as described further below.

Nonpatentable subject matter and boundary conditions

A second viewpoint to consider in evaluating the boundaries of 35 U.S.C. § 101 entails exploring some well-settled categories of what is not eligible for patent protection in the United States. This includes laws ***126** of nature, natural phenomenon, ideas, unapplied mathematical algorithms, and products of nature. Attempts to patent Einstein's special theory of relativity ($E=MC^2$), a bare mathematical proof, or a newly discovered lizard species in Africa--all would fail to qualify for patent protection in the United States.

Two principles appear to govern judicial decisions, excluding these categories from eligibility for a patent. First, these categories center on discovery of previously unrecognized phenomenon and laws of science and nature, in contrast to inventive activity for which generation of new ideas and applying them in a useful manner are deemed worthy of patent protection. In essence, it is the distinction between discovery and invention. Second, strong public policy reasons exist to prohibit parties from obtaining exclusive use of fundamental scientific phenomena, as other members of the public would face stiff challenges in assembling the necessary building blocks to advance technological progress. Awarding patents for such basic discoveries could hinder the progress of innovation that is meant to reside at the heart of patent law.

Purified forms of natural products

Given that products of nature are nonpatentable subject matter, it may surprise some that isolation or purification of those natural products is potentially patentable subject matter. Confusion about that distinction often may serve for more misunderstood controversies surrounding patents, such as whether DNA can be patented or whether naturally-produced substances in the human body, like insulin, should be eligible for patent protection. In this regard, a general principle guiding the boundary between patentable and nonpatentable subject matter for natural products is the role of human intervention (patentable) and something that is solely the handiwork of nature (nonpatentable). A stroll through legal history informs this discussion and further demonstrates a long history of granting patents on purified forms of natural products in the United States.

***127** The origin of modern law governing patentability of purified forms of natural products was set forth in Parke-Davis & Company v. H. K. Mulford Company. [FN29] In this early case, an accused infringer attacked the validity of a patent claiming a purified form of adrenaline obtained from the adrenal glands of animals, where it is naturally formed. Although other crude preparations of dried and powdered glands existed at the time, the purified adrenaline was practically free of the gland tissue and provided improved safety, stability, and efficacy. These features of the claimed composition made it "for every practical purpose a new thing commercially and therapeutically"; and because it was sufficiently different from its nonpurified counterpart, there was sufficient justification for upholding the patent's validity.

A further illustration of this principle in more modern technology is the case of In re Bergy. [FN30] The USPTO had denied a patent applicant's claimed invention of a purified culture of a microorganism that produced the antibiot-

ic lincomycin on the basis that the culture was merely a product of nature. The court of Customs and Patent Appeals reversed the rejection in deciding that a pure culture, such as the Bergy applicant's, was something not found in nature and was produced only in the carefully controlled conditions of a laboratory. The commercial uses of the purified bacterial culture were more analogous to chemical reactants and reagents than "horses and honeybees or raspberries and roses." [FN31]

DNA patents

The analogy of purified products of nature as similar to man-made chemical compounds also guides the rationale for granting patents on human genetic materials because isolated DNA is a discrete chemical compound and similarly cannot be found in a purified state in ***128** nature without meticulous human intervention. Surprisingly, two cases frequently cited for the patentability of DNA did not address directly whether isolated DNA was patentable within the context of 35 U.S.C. § 101. [FN32] The lack of a direct, appellate court holding on the issue has not gone unnoticed and has provided an opportunity for parties to challenge DNA patents, as discussed further below. [FN33]

Nevertheless, applicants have interpreted Chugai and Fiers (alongside two decades of CAFC and Supreme Court law) to mean that isolated DNA is patentable subject matter under 35 U.S.C. § 101. DNA patents were issued in the early 1990s, perhaps following the wake of Chakrabarty, discussed earlier, where the question of utmost importance was the role of human intervention in establishing patentability under 35 U.S.C. § 101. [FN34] Despite this apparently well-settled precedent, certain forms of DNA patents have come under increased scrutiny in recent years.

Increasing scrutiny of isolated DNA as patentable subject matter

In a recent case stirring great controversy over the patentability of DNA, the plaintiffs in Association for Molecular Pathology v. USPTO (Myriad) seized on the alleged gap in the law with regard to isolated DNA patentability under 35 U.S.C. § 101. [FN35] In this district court decision, claims from several Myriad Genetics patents directed at compositions and methods of using BRCA 1/2 breast and ovarian cancer susceptibility genes (i.e., DNA sequences encoding a protein) were ***129** found to be invalid. In the first category of "compositions of matter," the district court found that isolated DNA encoding BRCA 1/2 and related sequences did not possess "markedly different characteristics" from their natural counterparts. Central to this assertion was the view that the core property of both natural and isolated DNA is coding of specific information for a protein. This ruling diverges sharply from the long-standing principles behind Parke-Davis, Bergy, and Chugai, which call attention to properties of purified substances as a chemical compound, with structural and functional differences conferring patentable weight over a naturally-occurring product. In the district court's view, DNA as an information-carrying element makes natural and isolated DNA indistinguishable, as both forms encode information for the same protein. The district court judge in Myriad also invalidated claims directed at a diagnostic method, discussed further in Patentability of diagnostic methods post-Bilski. The case is currently undergoing appeal before the CAFC.

While the public eagerly awaits an appeal ruling to determine whether Myriad rests on sound legal principles, one take-home point should be made clear. Even in its broadest form, the divergent ruling of Myriad nevertheless appears to recognize that a DNA molecule can be patented if it imparts markedly different characteristics in function and properties, such as a variation in the form of the translated protein. Broad generalizations of genes or junk DNA as unpatentable are inaccurate in the sense that the specific properties of the isolated fragment of DNA in question will speak to the eligibility for patentable subject matter. This concept is more fully illustrated below in the form of very short fragments of DNA known as expressed sequence tags (ESTs).

Shorter ESTs may lack utility

On a slightly different tack than the type of DNA under dispute in Myriad, ESTs are not protein-encoding genes and may or may not be junk DNA without any apparent function or usefulness. In In re Fischer, ***130** the USPTO denied an application claiming five ESTs for lack of utility. [FN36] The utility requirement, a separate and distinct

patentability criterion under 35 U.S.C. § 101, excludes the claimed invention from patent eligibility if an invention is not useful or inoperable. [FN37]

The applicants claimed that the ESTs were useful because of their role in tagging genetic fragments for detection and measurement, and that this feature was used in their laboratories for measuring expression levels of certain genes and detecting genetic variations. Despite this purported utility, the Fischer court affirmed the USPTO's rejection on the basis that, without a substantial and credible utility, such as presenting a described function for a particular gene associated with the EST, there was no presently particular benefit to the public.

As these cases show, the underlying rationale behind why certain DNA patents may or not be patent eligible are very different. The properties and uses of an isolated piece of DNA will help to inform whether it is eligible as potentially patentable subject matter.

Human reproductive cloning and embryonic stem cells

An entirely different rationale is presented for excluding certain types of technologies, such as human embryonic stem cells and cell cloning technologies, from patent eligibility: social morality. Aside from a long-discarded "moral utility" requirement aimed at denying patents on gambling machines and deceptive or fraudulent devices, modern U.S. patent law is almost completely agnostic to morality considerations when it comes to patentability.

Human embryonic stem cells involve particularly tricky moral and ethical issues given their original isolation technique requiring destruction of embryos. These unique cells can form virtually every cell type in the human body, creating therapeutic avenues through a type of cloning ***131** known as therapeutic cloning, wherein cells compatible with a specific patient's immunological profile are created and subsequently administered to treat numerous afflictions involving cell death or disease (e.g., diabetes, cardiac and liver diseases). Concerns arise from the potential of deploying embryonic stem cell technology in reproductive cloning where the primary aim is asexual reproduction or replication of individual humans, which raises a quandary of moral and ethical problems. Some foreign nations have enacted laws to specifically prohibit patenting of technologies involving embryo destruction and/or reproductive cloning or have found them to be unpatentable in their general prohibitions rejecting claimed inventions that are against social morality. [FN38]

Although U.S. law is lacking in this respect, there has been a specific prohibition in the USPTO for awarding patents for claims that could encompass a human being. Notwithstanding the Chakrabarty decision and other patent grants for multicellular organisms, the USPTO has taken the position that "[i]f the broadest reasonable interpretation of the claimed invention as a whole encompasses a human being, then a rejection under 35 U.S.C. § 101 must be made indicating that the claimed invention is directed to nonstatutory subject matter." [FN39] Some commentators have noted that despite these apparently clear statements on the issue, the USPTO may lack the authority to not grant patents on humans. [FN40] Indeed, a virtual firestorm erupted in 2002 when a patent issued to the University of Missouri claimed reproductive cloning techniques without specific exclusion of humans from the claimed ***132** subject matter. [FN41] In response to issuance of the Missouri patent, Congress repeatedly attempted to limit the USPTO's authority to issue such patents--without success. [FN42]

Absent Congressional action, human embryonic stem cells and their tremendous potential for therapeutic cloning uses remain patentable technology under 35 U.S.C. § 101. Public policy concerns are likely to extinguish attempts to patent humans or reproductive cloning.

Pioneering technologies defy convenient categorization

Within these two opposite ends of potentially patentable subject matter--that is, the seemingly broad mandate of § 101 as opposed to its judicially-recognized boundaries--judges at the CAFC and the U.S. Supreme Court have grappled with establishing a clear framework for pioneering technologies that defy convenient categorization under

35 U.S.C. § 101. Patenting is on the rise for business methods, DNA fragments, primate embryonic stem cells, digital computing processes, and diagnostic methods. Although the subject matter of many innovations is of important value in a modern, knowledge-based information society, some attempts to obtain patent rights have proved to be controversial, particularly at the margins where ideas may not produce useful and tangible results, or public policy concerns necessitate careful tailoring of the limits of patentability.

Bilski: "Machine or transformation" not the sole test for patentability

Although process inventions are a prescribed category of patentable subject matter, the intangible aspects of performing a series of steps to complete a particular task have required additional criteria to evaluate patent eligibility. Until recently, the primary test was the ***133** machine-or-transformation (MOT) test, wherein a process invention is eligible for patent protection if "(1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing." [FN43] The rationale behind such a requirement is to prevent patenting of laws of nature, ideas, purely mental processes, or methods achieving no tangible effects.

However, the Supreme Court recently ruled that MOT is not the sole test for eligibility of patentable subject matter under 35 U.S.C. § 101. [FN44] In Bilski, the claimed invention involved a method of hedging risk in commodities trading. As an initial matter, the Bilski court rejected a categorical exclusion of business method patents from patent eligibility, observing that 35 U.S.C. § 101 and related statutory provisions contemplated their existence as potentially patentable subject matter. The court also continued to support a broad interpretation of 35 U.S.C. § 101, finding that the statutory language of the provision defined process as "process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material." Relying on the ordinary meaning of the statutory language, the Bilski court found no reason for necessarily imposing MOT as the sole test for determining patentability of processes, particularly in view of potential barriers stifling new and unexpected technologies.

The MOT test has been an important test in the biotechnology and medicine areas for determining patent eligibility. Bilski's recognition of the MOT test's continuing vitality suggests that the patentable subject matter landscape remains largely the same as before. Nevertheless, the Bilski court's determination that MOT is not the sole test for determining subject matter eligibility under 35 U.S.C. § 101 raises interesting new questions about what other tests may emerge.

***134** Patentability of diagnostic methods post-Bilski

Very recently, the CAFC decided the case of Prometheus v. Mayo, which involved a dispute over the patentability under 35 U.S.C. § 101 of a diagnostic-related method related to inflammatory bowel disease. [FN45] Prior to the Supreme Court's Bilski decision, the CAFC had affirmed the patentee's claims directed to a method of improving therapeutic efficacy as passing muster under the MOT test. On appeal, the Supreme Court remanded the case to the CAFC after the Bilski ruling, providing a valuable opportunity to re-evaluate the outcome under the same facts, but in a post-Bilski world. The result? First, the CAFC rejected the contention that the Bilski decision required adoption of a "complete preemption" test as a replacement to the MOT test. Under the suggested complete preemption test, a patentee's effort to own completely the entire range of useful applications for ideas or natural laws would be akin to patenting the ideas or natural laws themselves and thereby be ineligible for patentable subject matter under 35 U.S.C. § 101. Instead, the CAFC noted that the Bilski decision affirmed the continuing utility of a MOT test and merely required adoption of other tests as alternative avenues of inquiry for determining 35 U.S.C. § 101 eligibility. Next, the CAFC noted that a complete preemption test could be one useful alternative avenue alongside the MOT test and applied both tests to claims of the disputed patent. The CAFC found that the patent claims satisfied the MOT test, just as it had determined in its first decision. More importantly, the CAFC applied the complete preemption test in again reaching the determination that the claims were patentable subject matter under 35 U.S.C. § 101, as the use of "specific means of treating specific diseases using specific drugs" was inconsistent with the notion of complete preemption as directed to a particular and specific application. [FN46] Because the construed claims ***135** satis-

fied both the MOT test and the complete preemption test (with either one sufficient to establish 35 U.S.C. § 101 eligibility), the CAFC again affirmed the claims as capturing patentable subject matter.

Although perhaps unsatisfying for those seeking greater guidance, the CAFC's decision in Prometheus provides some important lessons as an early indicator of the scope of 35 U.S.C. § 101 after Bilski. First, confronted with the challenge of workable tests outside of MOT, the CAFC appears at least open to the suggestion of alternatives as indicated by its application of the complete preemption test, with the important caveat that any such test be consistent with its own and Supreme Court patent law jurisprudence. Second, Prometheus may be of limited reach with respect to diagnostic claims. The disputed patent claims in Prometheus were construed by the CAFC as treatment methods with claim language reciting a first step of administering a compound and later measuring the compound's presence in the blood. It is unclear how the notion of "specific means of treating specific diseases using specific drugs" would apply to diagnostic methods that do not possess an analogous "administration step" in the claim language or cannot be characterized as treatment methods.

Similar issues over patentability of diagnostic methods were raised in the previously discussed Myriad case. In addition to finding isolated DNA unpatentable, the district court also weighed in on a second category of "method" (i.e., process) claims directed at "analyzing" and "comparing" DNA sequences from normal, test, and disease samples. According to the district court, the method claim at issue did not recite any transformative steps, such as an express determination step comparing normal, test, and disease samples, and without mention of a detection apparatus, thereby failing to be tied to a particular machine. The court also rejected the notion that routine steps used for the isolation and preparation of DNA sequences were transformative, as the essence of the procedure was mere data-gathering without any transformative effect. In the district court's opinion, such methods were ***136** merely ideas untethered to any machine, lacking a transformative step, and unpatentable. This case is currently undergoing appeal and framing this 35 U.S.C. § 101 dispute over patentability requirements for diagnostic method claims will allow the CAFC to revisit the existing limits for diagnostic methods patent protection. [FN47]

Summary

From this review of 35 U.S.C. § 101, we can ascertain that what qualifies as potentially patentable subject matter is markedly less than the mental imagery arising from "anything under the sun that is made by man." Broad interpretation of this provision is likely to continue to avoid stifling creation of the new, unpredictable, and evolving technologies invented every day. Nevertheless, broad approaches toward patenting a wide array of pioneering technologies merit further refinement, and some otherwise new and useful ideas and discoveries may not merit patent protection without tangible forms of application and embodiments.

Novelty and Loss of Right

A central tenet of U.S. patent law is to award a patent only for novel inventions defined under 35 U.S.C. § 102. Although generic use of the term novelty conveys a general sense of new and unique subject matter, patent novelty under 35 U.S.C. § 102 is a more limited technical definition reached by applying a series of facts through seven different subsections, 35 U.S.C. § 102(a) to (g). A helpful starting point toward organizing the various subsections is to recognize that 35 U.S.C. § 102 is actually two provisions in one. A first set, 35 U.S.C. § 102(a), (e), and (g), includes what one might call true novelty provisions with a central inquiry directed at identifying the existence of public disclosures ***137** that exactly describe the applicant's invention. These provisions approximate what one might imagine when thinking of novelty: Has anyone described the claimed invention before in public? If so, then the existing disclosure is a prior art reference that destroys the novelty of a claimed invention because it has already been invented and shared with the public by someone. A second set of provisions, 35 U.S.C. § 102(b), (c), and (d), involves asking: Has the patent applicant performed an affirmative act, such as selling, patenting, or voluntarily sharing the invention in a publication or an oral presentation, before filing the application? If so, this triggers a loss of right to obtain a patent through the applicant's own act of selling, patenting, or sharing the invention as prior art references against them-