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FRAGGING THE PATENT FRAGS: RESTRICTING EXPRESSED SEQUENCE TAG PATENTING USING THE ENABLEMENT-COMMENSURATE-IN-SCOPE-WITH-THE-CLAIMS REQUIREMENT

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I. Introduction

DNA sequences have a dual character in that they are both chemical compositions as well as carriers of information.[1] As a

chemical compound made up of strings of units called nucleotides, DNA, or deoxyribonucleic acid, ultimately ***50** "control[s] the structure and metabolism of living things."[2] As an informational molecule, DNA contains "the detailed instructions for assembling proteins [] in the form of a four-character digital code."[3] In the U.S., while product patent claims on a DNA sequence have focused facially on its chemical composition,[4] it is unclear to what extent such claims may comprise the large quantities of information that a single nucleotide sequence may contain.[5]

Currently, the Patent and Trademark Office (PTO) and the federal courts analyze DNA patent claims using the basic principles of molecular biology and genetics.[6] Under U.S. law, a DNA product patent could cover the DNA sequence ***51** as an isolated and purified chromosomal gene[7] or as a transcribed gene in the form of complementary DNA (cDNA), which is made by reverse transcribing a messenger RNA (mRNA) transcript.[8] Most DNA patents must "(1) identify novel genetic sequence, (2) specify the sequence's product, (3) specify how the product functions in nature--i.e.[,] its use, [and] (4) enable one skilled in the field to use the sequence for its stated purpose."[9] Even a short DNA fragment of a gene might be patentable by satisfying these requirements.[10] In In re Fisher, the seminal case on gene fragment patenting, the U.S. Court of Appeals for the Federal Circuit (Federal Circuit) suggested that an expressed sequence tag (EST), which is generated by sequencing a small number of nucleotides of a cDNA molecule, usually at either end, may be patentable if the patentee identifies "the function for the underlying protein-encoding gene[]."[11] The inventor need only disclose "one utility, that is, teach others how to use the invention in at least one way."[12] More simply, to get a broad product-claim patent on a particular EST, the patentee is not required to "disclose all possible uses,"[13] but merely a "'specific and substantial' use," that is, identify the underlying gene and a resultant protein.[14]

***52** However, a broader view of the underlying science behind the gene should dictate a more limited exclusionary right grant in an EST patent than is now seemingly possible in the United States. Currently, the U.S. patent system does not account fully for the following two scientific facts: that a single gene can code for more than one type of protein and that the sequence of a DNA fragment can match more than one type of gene. Consequently, a broad patent claim on an EST may enable one to assert exclusionary rights over DNA sequences covering many different proteins and fragments thereof or to assert rights over several different genes. To bring U.S. patent law in line with these two facts, the PTO and the federal courts should require patentees to delineate in their patent claims the particular use or uses of the claimed ESTs that are described in their corresponding specifications.[15] Such a requirement need not be implemented through the legislative process as the basis of such a requirement may be developed by the PTO and the judiciary using the current statutory framework.

The PTO and the Federal Circuit missed an opportunity to tighten the drafting of claims for EST inventions in In re Fisher.[16] This case dealt with the patentability of five purified fragments of DNA described as ESTs that "encode proteins and protein fragments in maize plants."[17] The Federal Circuit held that such fragments as disclosed in the patent application were not patentable as the application failed to disclose a specific and substantial utility for the DNA sequences.[18] The court held that the two stated uses for the DNA sequences in the patent application--as research tools to identify polymorphisms or to isolate promoters--were mere hypothetical possibilities.[19] Moreover, the court summarily held that the patent application failed to satisfy the enablement requirement of 35 U.S.C. § 112 for a circular reason--because it failed to satisfy the utility requirement of § 101.[20] The court stated that the utility requirement demands a patent applicant to research and understand a claimed EST to the point where the ***53** patentee identifies "the function for the underlying protein-encoding gene[]" with which the EST would match up.[21]

In a future case, the PTO and the Federal Circuit should go farther in delineating patent law's requirements for an EST patent. In addition to grounding the unpatentability of DNA fragments like those in the In re Fisher case on §§ 101 and 101/112 for lack of utility and enablement, respectively, the PTO and the Federal Circuit should invoke the § 112 enablement-commensurate-in-scope-with-the-claims requirement in such a context. The patent system should acknowledge that the type of DNA sequences claimed in the In re Fisher case are informational molecules with several potential matches to different genes or to a single gene that encodes multiple different proteins. In doing so, the patent system should state that the major reason why Fisher-type product claims to gene fragments are invalid is that the scope of the broad claims in an application does not bear a reasonable correlation to the scope of enablement provided by the specification. To legally claim the ESTs described in In re Fisher, a patentee should be limited to claiming only a specific known use or uses--that is, the DNA sequence coupled to its corresponding known protein or proteins--that are specifically described and enabled in the specification. In other words, the only type of claim to a novel EST that can be enabled with proper disclosure in the specification on how to use the EST with no "undue experimentation" necessary would be a use-type patent claim.[22]

Thus, Part II of this article explores in depth the science behind ESTs. Part III discusses the different ways DNA sequences can appear in patent claims. Part IV discusses the current legal framework for patenting ESTs developed by Congress, the

PTO, and the federal courts. Part V proposes an additional way of restricting the patentability of ESTs in light of the science and the positive law of patents in the U.S.

II. Science Behind ESTs

Genomic DNA acts as a blueprint for making proteins in a cell.[23] In higher organisms, it exists in the nucleus of a cell as several long, tightly wound-up, double-helical strands called chromosomes.[24] Chromosomes contain many genes, ***54** regulatory elements, and intervening sequences.[25] To express a gene on a chromosome encoding a protein, a portion of the chromosome unwinds and the DNA molecule unzips to temporarily form two separate complementary single strands--the coding strand and the antisense strand.[26] The latter serves as a template for making a precursor to mRNA.[27] The precursor mRNA molecule, like its nearly identical DNA coding-strand counterpart, contains both introns, the noncoding intervening sequences of the DNA molecule, and exons, which generally contain the protein-encoding regions.[28] The precursor mRNA molecule then undergoes a process of removing the intronic regions and splicing together the exonic regions to form mRNA.[29] The mRNA transcript then exits the nucleus and enters the cytoplasm of the cell, where a set of ribosomal proteins translate the sequence of nucleotides that make up the mRNA molecule into a sequence of amino acids.[30] In general, a sequential grouping of three nucleotides on the mRNA molecule (a codon) codes for an amino acid, the building block of a protein.[31]

Determining the location of a gene on the genome can be accomplished by examining transcripts.[32] However, as an mRNA transcript is too unstable a molecule to sequence, scientists may make a more stable DNA copy of the mRNA molecule, called complementary DNA (cDNA), and compare the cDNA sequence to the genomic sequence of the organism being studied.[33] From this comparison, scientists may be able to identify the introns that have been spliced out of a sequenced gene and then deduce the amino acid order for the resulting protein.[34]

There are at least two ways to use cDNA to determine the structure of an underlying gene. The classical way is accomplished by high coverage sequencing ***55** of a complete cDNA clone and aligning one or more full-length cDNAs to the genomic DNA.[35] This method is typically used for targeted individual genes.[36] An intermediary method is to perform one-shot sequencing of a library of cDNA clones compiled from a specific tissue type.[37] One-shot sequencing of a cDNA library usually produces short 100- to 800-base-pair gene fragments known as expressed sequence tags (ESTs).[38] ESTs, which are typically sequences obtained from copying the 5' or 3' end of one of the two cDNA strands in its duplex form, "provide information that enable the identification of (partial) exons, either coding or non-coding."[39] As they are able to bind to complementary DNA sequences, ESTs are useful tools in mapping and discovering genes.[40] Introducing a single-stranded EST into a DNA sample taken from the nucleus of a cell may result in a hybridization of the EST to a portion of the DNA being studied, revealing that "the gene corresponding to the EST was being expressed at the time of mRNA extraction."[41]

In practice, the use of ESTs to identify genes in genomic sequences "is non-trivial for a number of reasons."[42] ESTs are typically deposited in databases,[43] which are not comprehensive.[44] EST databases contain many sequencing errors due to the one-shot sequencing methodology,[45] and they typically are compiled from "a large variety of origins that represent a range of subspecies, tissue types, and conditions, thus leading to a heterogeneous sequence view confounded by ***56** polymorphisms and paralogous genes."[46] In spite of this, computer-driven clustering and assembly of multiple combinations of the thousands of ESTs in a database have facilitated the gene identification and analysis process.[47] For example, computer studies using the large human EST databases have revealed that possibly 38% of mRNAs contain alternative splice forms of the originating genes, with 70% of the forms corresponding to exon-deletion events and 30% to exon-insertion events.[48]

The "variety of ESTs provides an ideal resource to examine a number of biological questions concerning gene expression and structure" in a species.[49] Not only can an EST align to a single gene on genomic DNA that may code for more than one protein through alternative splicing of a precursor mRNA transcript,[50] but the EST also may hybridize to genes on different chromosomes in a single species (paralogous genes).[51] Moreover, many proteins are composed of discrete domains that are "evolutionarily mobile, which means that they have spread during evolution and now occur in otherwise unrelated proteins" even within the same species.[52] Hence, an EST may not only match up to one or a combination of exons on a single gene but also to one or a combination of exons on otherwise different, nonhomologous genes in the same species.[53]

The informational value of EST databases can also be revealed across a number of different species. Because ESTs are derived from transcribed regions of a particular genome, ESTs are likely to be conserved across a broad range of different species.[54] As EST databases for most species, including plants, are not ***57** comprehensive enough to be very useful for gene

identification, computer programs have been developed to combine EST databases from distinct species that share a common gene space to predict gene structures.[55] Such models are designed to "tolerate a high percentage of mismatches and insertion[s] or deletions in the EST relative to the genomic template."[56]

Finally, the ESTs derived from one species may match up with newly created genes not found in nature. Scientists have exploited the natural process of exon shuffling, which is the "evolutionary mechanism of recombining exons from unrelated genes," in vitro to create new proteins not known to be found in any living species.[57] Exon-shuffling libraries have been created by recombining a domain-encoding exon (or combination of exons) from one gene with an exon or exons from a different gene.[58] The diversity of such libraries has been increased by further altering the newly created genes through "insertion[s], deletion[s], or changes in the order of the domain-encoding exons."[59]

In sum, there are several ways that an EST, alone or in combination with other ESTs,[60] may be used: 1) it may match up to a single gene with several different protein products; 2) it may match up to several different genes with either similar products (e.g., paralogous genes) or completely different protein products. Moreover, an EST can be used to find genes in the species from which the EST was derived as well as genes found in different species. Furthermore, an EST may match up with a man-made gene unknown to the natural world. Indeed, fully realizing the informational value of an EST, especially in combination with other ESTs in a database, may be impossible at this time.

*58 III. How a DNA Sequence Can Be Patented

There are several different ways to assert rights over DNA sequences. One can patent a discrete segment of DNA molecules that contains all the information necessary for producing a specific protein--in other words, a single gene.[61] Moreover, a single gene, "with, for example, 15 exons could well have a separate patent claim on each of several of these exons, which would have been discovered as expressed gene fragments."[62] There could also be "another claim on the complete expressed sequence discovered by screening a library of expressed gene clones, a separate claim on a promoter sequence and perhaps another on a distant locus control region found to influence the expression of the gene."[63] Furthermore, there could be a patent claim on a fragment of DNA, such as an EST that correlates to a partial exon,[64] or even on the information linking a single nucleotide polymorphism (SNP)[65] to a particular gene.[66]

In addition to the various ways a segment of DNA can be apportioned into a patent claim, there are three different ways of claiming the various parameters of a particular DNA sequence. The broadest way to assert property rights over a DNA sequence is through a product patent claim, which is a claim over the chemical composition (i.e., composition of matter) as well as all uses of that composition.[67] A process patent claim covers the method of making a DNA sequence as well as the sequence that is the product of that method.[68] The more narrow type of patent claim is a use patent claim, which in the DNA context would provide the patentee only with the right to exclude others from using a DNA sequence for a specific purpose.[69] In practice, however, even a use patent claim, which does not include all rights to the DNA sequence itself, may be quite broad if, for example, a use-patent claim for the gene that indicates susceptibility to breast cancer, BRAC1, were to include all diagnostic tests for breast cancer involving the use of the sequence for BRAC1.[70]

***59** Because one can patent different segments of a gene, and one can patent a particular segment with different types of patent claims, it is "apparent that different patents that relate to the same gene often contain claims which overlap."[71] Patents on gene fragments such as ESTs "may extend to subsequent patent applications involving full-length DNA sequences in which the biological function is known."[72] In other words, a patent grant that comprises an EST as a composition of matter and all uses of that composition possibly "would be infringed by a patent application that claimed the full-length gene that included the EST,"[73] arguably even if the EST was derived from a different gene from a different species.[74] Having different entities own patents on individual DNA fragments of a single gene "could lead to the situation where a pharmaceutical company seeking to use a protein [for therapeutic purposes] would infringe any patents held by others that had identified ESTs present in the DNA sequence."[75] On the other hand, if a patentee had a use patent claim over a particular gene fragment, then his right to exclude others from using the particular DNA sequence would extend only to the corresponding protein that is described in the specification and named in the patent claim.[76]

IV. Current Patent Framework for ESTs

The issue of patenting gene fragments such as ESTs came to the forefront in 1991 when the National Institutes of Health

(NIH) filed several patent applications claiming various EST sequences.[77] Even though the NIH ultimately withdrew these applications,[78] private individuals and companies have still attempted to lay ***60** claim to such sequences.[79] Resulting out of such efforts, as well as previous efforts to patent DNA sequences generally, the major requirements for patenting ESTs have developed from the set of legal rules found in the generally technology-neutral patent statute, 35 U.S.C. § 101 et seq., which the PTO and the federal courts have used to produce specific standards and rules for DNA,[80] as described below.

1. The Patentable Subject Matter Requirement: 35 U.S.C. § 101

The Patent Act of 1952, codified at 35 U.S.C. § 101 et seq., provides that: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent . . . ."[81] From this language, courts have devised the broad patentable subject matter requirement, which has been interpreted to mean that "anything under the sun that is made by man" has the potential to be patentable subject matter.[82] Items excluded from patentable subject matter include "laws of nature, physical phenomena, and abstract ideas."[83] Since the seminal case of Diamond v. Chakrabarty,[84] federal courts have held that these exclusions do not encompass DNA molecules that have been isolated and purified through human intervention into forms not found in nature.[85] The terms "isolated" and "purified" have been used interchangeably to mean the "substantial absence of other biological micromolecul[es]."[86] An example of claims on isolated and purified gene fragments is the 1998 grant to Incyte Pharmaceuticals, Inc. giving exclusionary rights over human kinase homologues based on approximately twelve ESTs.[87] ***61** Whether in fragmentary or full-length form, the distinguishing feature of a patentable DNA molecule is its unique structural formula, whose chemistry is distinct from the corresponding DNA macromolecule found in nature.[88] In other words, the proper subject matter for a DNA patent is not raw DNA in its natural state, but rather is limited to DNA modified in some way by human hands.[89]

2. The Novelty Requirement: 35 U.S.C. § 102

Under 35 U.S.C. § 102, a claimed invention must not be anticipated by the prior art to be eligible for patentability.[90] To destroy a claimed invention's novelty, it is not enough to cite prior art disclosing the invention in some form; the cited prior art must contain an enabling disclosure, one that reveals how to make all of the features of the claimed invention in a single reference.[91] In the DNA context, the Federal Circuit held that isolating a DNA molecule without knowing the precise identity of its sequence cannot be considered an adequate enabling description of the invention for § 102 anticipatory purposes.[92] In contrast, a reference that describes millions of DNA molecules, including their structural formulae, can be an anticipatory reference for claims to any one of the listed molecules.[93]

3. The Nonobviousness Requirement: 35 U.S.C. § 103

Even if all elements of a claimed invention are not disclosed in a single § 102 invalidating reference, that § 102 reference can serve as § 103 prior art in combination with other § 102 references.[94] To be invalidating, the prior art must ***62** make the claimed invention "obvious at the time the invention was made to a person having ordinary skill in the art."[95]

For a DNA patent claim, the DNA molecule's sequence structure is one of the elements that would be compared to the prior art in a nonobviousness inquiry.[96] If the sequencing structure of the DNA molecule is not disclosed in the prior art, then, in most circumstances, the invention may be nonobvious.[97] This may be so "even though general procedures leading to the making and use of the molecule are well-known and described in the prior art."[98] For instance, in In re Deuel,[99] the Federal Circuit held that a prior art reference disclosing a protein's amino acid sequence, by itself, did not render its corresponding cDNA sequence obvious.[100] Even combining the amino acid sequence reference with a reference detailing a method of isolating the cDNA molecule was not enough to render the structural formulae of the cDNA molecule obvious.[101] The claimed cDNA molecules were not obvious because the corresponding proteins were large and complex such that "the redundancy of the genetic code permit[ted] one to hypothesize an enormous number of DNA sequences coding for the protein."[102]

In dictum, however, the In re Deuel court suggested that a claimed cDNA molecule might be rendered obvious without a reference disclosing its nucleotide sequence "if there [was] prior art, e.g., a protein of sufficiently small size and simplicity, so that lacking redundancy, each possible DNA would be obvious over the protein."[103] Subsequently, the Board of Patent Appeals and Interferences has permitted patent examiners to issue a § 103 rejection to a small cDNA molecule without a disclosure of its sequence when there existed prior art disclosing the amino acid sequence, a pair of oligonucleotide probes against a claimed DNA ***63** molecule, and a method of using the probes to isolate the DNA molecule.[104] In a similar fashion, a reference citing the DNA sequence of a claimed EST arguably is not necessary for a § 103 rejection if there is prior art disclosing the amino acid sequence of the fragmentary protein domain that is partially encoded by the claimed EST

sequence.[105]

4. The Utility Requirement: 35 U.S.C. § 101

To be patentable, an invention must also be "useful."[106] The Supreme Court determined in Brenner v. Manson[107] that the "basic quid pro quo" of a patent grant is "the benefit derived by the public from an invention with substantial utility."[108] The PTO's Utility Examination Guidelines[109] require at least one "specific, substantial, and credible" utility for a claimed DNA molecule.[110] A "specific" utility means that it is applicable "to the subject matter claimed," rather than "to the broad class of the invention."[111] For example, a specific utility for a claimed gene probe would be its specific DNA target.[112] A "substantial" utility means that the claimed invention has a "real world" use.[113] For instance, using a DNA molecule to assay for a gene that itself has no known use would not be considered a substantial utility.[114] A "credible" utility means the disclosed facts in the specification do not have a serious flaw or inconsistency to a person having ordinary skill in the art.[115] For example, a credible utility for a DNA molecule could be its use as a probe, a chromosome marker, a diagnostic marker, or a forensic marker.[116]

***64** Recently, In re Fisher specifically addressed, for the first time, the § 101 utility requirement for ESTs.[117] This case dealt with the patentability of five ESTs that "encod[ed] proteins and protein fragments in maize plants."[118] The claimed ESTs were "randomly selected nucleic acid molecules isolated from pooled leaf tissue at the time of anthesis," the flowering period in plants.[119] Applicant Fisher disclosed seven potential uses for the claimed ESTs:
(1) serving as a molecular marker for mapping the entire maize genome, which consists of ten chromosomes that collectively encompass roughly 50,000 genes; (2) measuring the level of mRNA in a tissue sample via microarray technology to provide information about gene expression; (3) providing a source for primers for use in the polymerase chain reaction ("PCR") process to enable rapid and inexpensive duplication of specific genes; (4) identifying the presence or absence of a polymorphism; (5) isolating promoters via chromosome walking; (6) controlling protein expression; and (7) locating genetic molecules of other plants and organisms.[120] On appeal from a final rejection by a patent examiner, the Board of Patent Appeals and Interferences (the Board) dismissed these uses as insubstantial because they were all "non-specific uses that [were] applicable to nucleic acids in general and not particular or specific to the nucleic acids being claimed."[121] The Board stated that "[s]omewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between 'utility' and 'substantial utility.'"[122]

The Federal Circuit affirmed the Board's decision, holding that such fragments as disclosed in Fisher's application were not patentable because the application failed to disclose a specific and substantial utility for the subject matter claimed.[123] The court held that the two stated uses on which Fisher focused his appeal--as research tools to identify polymorphisms or to isolate promoters--were mere hypothetical possibilities unsupported by any evidence that the claimed ESTs had been, in fact, useful for such purposes.[124]

Instead, the court required that "an application must show that [a claimed] invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research."[125] Because Fisher admitted that the function for the underlying genes with which the ESTs matched up were ***65** unknown, the court found that "the claimed ESTs act as no more than research intermediates."[126] The court thought that analogizing the claimed ESTs to a research tool like the microscope was flawed because the ESTs are "unable to provide any information about the overall structure let alone the function of the underlying gene."[127] The court noted that the seven asserted uses, as well as the evidence of commercial success, did not distinguish the claimed ESTs from "any EST derived from any organism."[128] Thus, without knowledge of the function of the genes to which the ESTs would match up, the claimed ESTs' value as research tools did not reach the level of "specific" and "substantial" utility required by the patent law.[129]

5. The Disclosure Requirements: 35 U.S.C. § 112

Finally, there are three § 112 requirements for an adequate disclosure of an invention in a patent: best mode, written description, and enablement.[130] First, the best mode requirement is satisfied when the inventor discloses what he subjectively thinks is the best way of carrying out the invention.[131] Second, the written description requirement is satisfied when "the invention as claimed is adequately described to one skilled in the art."[132] For patents claiming a specific DNA molecule, the written description requirement mandates a recitation of the DNA sequence in the specification.[133] Third, the enablement requirement necessitates that the patent application's specification includes indications of how the invention is made and how the invention can be used.[134] There must be sufficient ***66** information in the specification to enable one skilled in the art to make and use the invention without engaging in undue experimentation.[135] Although disclosure of at least one way of making

and using the invention that bears a reasonable correlation to the entire scope of the claims is typically sufficient to satisfy the enablement requirement,[136] more than a single representation or embodiment of an invention may be required to adequately enable broad claims in unpredictable technologies such as biotechnology.[137] For example, the Federal Circuit held that generic DNA sequence claims for "every possible analog of a gene containing about 4,000 nucleotides, with a disclosure only of how to make [the gene itself] and a very few analogs" that would encode any protein "'sufficiently duplicative"' of Erythropoietin were overly broad and invalid for not fulfilling the how-to-make prong of the enablement requirement.[138] As for the how-to-use prong, the Federal Circuit held in In re Fisher that not describing a substantial utility as required by § 101 for a claimed EST--that is, not describing the function of the gene to which the EST would match up--necessarily means that the use prong of the § 112 enablement requirement has not been satisfied because "the enablement requirement of § 112 incorporates [as a matter of law] the utility requirement of § 101."[139]

V. Proposed Solution to Further Restrict EST Patenting

Under the current framework laid out by the In re Fisher court, one could potentially receive a patent on a small gene fragment, such as an EST, if the patentee has identified one corresponding protein and the protein's function. However, when researchers discover other uses for the DNA sequence (e.g., a claimed sequence matches up to the same gene with a different protein product or matches up to different genes either with similar protein products or completely different protein products), "they will not be able to patent those uses without conflict."[140] Because a DNA sequence, even a short one like an EST, contains a vast amount of information, a holder of a broad product-patent may have exclusion rights over later-discovered overlapping sequences and their products.[141] This has ***67** led many commentators to argue for ways "to avoid the negative effect of composition of matter patents on DNA sequence[s,]" such as ESTs.[142]

For example, to limit the scope of the monopoly given to a patentee on a particular DNA sequence, commentators have suggested that Congress take action to alter the patent laws for genetic information patents.[143] One option would be for Congress to define 35 U.S.C. § 101 "utility" for a genetic invention as "'substantial and specific utility that is in currently deliverable form."'[144] In addition to making the definition of utility stricter "to prevent patent owners from later claiming uses not currently available or deliverable," Congress could also further confine novel ESTs to use patent claims so that infringement of an EST sequence claim would only occur with "uses of the EST that are the same or sufficiently similar, under the doctrine of equivalents," to the claimed use.[145]

Another option would be for Congress to prohibit the patenting of genetic material altogether. For example, a bill pending before the U.S. House of Representatives, H.R. 977, states, "no patent may be obtained for a nucleotide sequence, or its functions or correlations, or the naturally occurring products it specifies."[146] Moreover, in the place of using the patent system to grant property rights to novel ESTs, "an EST compulsory licensing system could define the rights held by the owner of the EST and the limited rights to which the EST licensee would be entitled."[147] Such a system, which conceivably would be a single searchable database and run much like the compulsory licensing provision of the Copyright Act, "may provide a way for tracking who owns a particular EST[,] and allowing a for-profit or not-for-profit researcher to pay a fee for use of the EST."[148]

While Congress could narrow the rights asserted over ESTs through implementing specialized statutes in this area, "a number of factors caution against explicitly tailoring the patent system to the needs of particular industries,"[149] ***68** including legal[150] and administrative/economic reasons.[151] Moreover, Congress need not alter the patent statutes because they are flexible enough that the PTO and the judiciary can take into account the science behind ESTs in devising an approach that, in effect, would avoid the negative implications of broad EST patents.[152] The U.S. patent system is well equipped to "tailor[] patent law to the needs of specific technologies" through the application of existing patent standards in a case-by-case, fact-specific manner.[153] For example, while the utility requirement of 35 U.S.C. §§ 101 and 101/112 has lost much of its force in its application to many technological fields, its application by the courts to chemistry and life science inventions, on the other hand, has been robust.[154] In the field of chemistry, for instance, the Supreme Court has required that a molecule or process have "some concrete and terminal application before it can be patented."[155] The utility standard is applied even more robustly to DNA molecules, particularly ESTs: the Utility Guidelines of the PTO require DNA fragment patents to have "'specific,' 'substantial,' and 'credible' applications not found in examination of other technologies."[156] Furthermore, the Federal Circuit in In re Fisher recently ratified the PTO's position by restricting patenting of a DNA fragment, such as an EST, to ***69** situations where at least one use of a corresponding protein is known.[157] In doing so, the Federal Circuit acknowledged that "DNA patents cannot be treated the same as [non-genetic] chemical composition patents since chemical compositions that do not use genetic information are generally based on how the body reacts, whereas DNA patents are based on the code that

dictates how the body will function."[158]

Importantly, as broad EST patents still can be issued even under the current application of the utility requirement, the PTO and the federal courts should further tailor the patent standards to the specific qualities of ESTs that have yet to be addressed. In a future case, the patent system should also acknowledge that the type of DNA sequences claimed in the In re Fisher case are informational molecules with several potential matches to different genes with different protein products or to a single gene that encodes multiple types of proteins.[159] In doing so, the patent system should state that the major reason why Fisher-type product claims to ESTs are invalid is that the scope of the broad product claims does not bear a reasonable correlation to the scope of enablement provided by the specification. Further, even if a patent's specification identifies an underlying protein and its function for a claimed EST in satisfaction of the utility requirement, the patentee should be limited to claiming only a specific known use or uses--that is, the DNA sequence coupled to its corresponding known protein or proteins--that are adequately described and enabled in the specification. This result follows from a facts-specific application of the 35 U.S.C. § 112 enablement-commensurate-in-scope-with-the-claims requirement to EST patent claims. The only type of claim to a novel EST that could be enabled, properly disclosing its use without requiring "undue experimentation," would be a use-type patent claim.[160] Conversely, the scope of enablement provided to one skilled in the art by a patent specification describing an EST could not, practically speaking, be commensurate with the scope of protection sought by a broad composition-of-matter claim to such a sequence.

Thus, the sections that follow show the rationale and framework for employing § 112 enablement to restrict EST patenting. Part A provides an in-depth ***70** analysis of the § 101 and § 112 use-disclosure requirements, particularly the enablement-commensurate-in-scope-with-the-claims requirement. Part B presents reasons why further restricting EST patenting using the enablement requirement of § 112 is desirable. Finally, Part C applies the § 112 enablement-commensurate-in-scope-with-the-claims requirement to small gene fragment patent claims similar to those proposed in In re Fisher.

A. How-to-Use Disclosure Requirements

Descriptions of how to use a claimed invention can be found in various sections of the Patent Act. The written description requirement of 35 U.S.C. § 112 "states what is needed to fulfill the enablement criteria"--to "communicate that which is needed to enable the skilled artisan to make and use the claimed invention."[161] Under the enablement requirement of 35 U.S.C. § 112, the inventor must set forth in the specification information sufficient to enable a person skilled in the relevant art to use the claimed invention.[162] And under the utility requirement of 35 U.S.C. § 101, "an asserted use must show that [the] claimed invention has a significant and presently available benefit to the public."[163]

1. How-to-Use in the Written Description Requirement

The main purpose of the written description requirement is for the applicant to "convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention."[164] As such, the written description requirement is typically used by the Patent Office and the courts to determine who has priority of invention in an interference proceeding[165] or to ***71** determine whether the claimed subject matter is adequately described in the specification as of the filing date sought to avoid a prior art rejection.[166] More generally, however, the purpose of this requirement can be described as "to state what is needed to fulfill the enablement criteria."[167] Viewed this way, both the written description and the enablement requirements of § 112 can be considered "intertwined"[168] even though the written description requirement of § 112 is normally seen and treated as "separate from the enablement requirement of that provision."[169] For both requirements, which are found in the same sentence of the first paragraph of 35 U.S.C. § 112,[170] an explanation of how to make and use the invention is required.[171]

Even where these two requirements meet--at the point of requiring disclosure of how to make and use the claimed invention as of the filing date sought-- there are distinct attributes of each requirement that have developed in the patent law. Determining whether the written description requirement is met is a question of fact.[172] In cases dealing with the written description requirement, "[t]he primary consideration is factual and depends on the nature of the invention and the amount of [detail] imparted to those skilled in the art by the disclosure."[173] Because the written description determination is a fact-intensive inquiry, "[p]recisely how close the description must come to comply with § 112 must be left to case-by-case development."[174] As a result, "the precedential value of cases in this area is extremely limited."[175]

***72** 2. How-to-Use in the Enablement Requirement

On the other hand, although there are underlying factual questions that must be answered in rendering an enablement determination,[176] the enablement requirement is ultimately a question of law.[177] The PTO has the initial burden of proposing a reasonable explanation for a conclusion of nonenablement, and the patent applicant can rebut the presumption of nonenablement with convincing evidence that the specification is enabling.[178] The requirement mandates that the specification describe the invention, which is defined by the construed claims, in such detail as to enable one to make and use it without "undue experimentation."[179] Determining whether any necessary experimentation is "undue"--as opposed to an acceptable level of experimentation--requires application of a reasonableness standard through the weighing of several factual considerations:

(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.[180] Not all of these factors--dubbed the Wands factors[181]--need to be considered when making an enablement determination, as they "'are illustrative, not mandatory. What is relevant depends on the facts."'[182] Finding "any enabled use that would ***73** reasonably correlate with the entire scope of [the] claim is sufficient to preclude a rejection for nonenablement based on how to use."[183] Moreover, a specification typically need only disclose one embodiment of using the claimed invention.[184] However, in more unpredictable technologies, like biotechnology "in which slight changes in amino acid or nucleotide sequences results in highly altered molecular function,"[185] more than one embodiment of using the invention that bears a reasonable correlation to the entire scope of the claim may be necessary to satisfy the enablement requirement.[186] How far one has to go to enable one to use an invention depends on the invention's nature[187] and the scope of the claims.[188] The policy behind § 112 is to force patentees to fully disclose their inventions and to prevent them from "engross[ing] a vast, unknown, and perhaps unknowable area."[189]

For example, in Enzo Biochem, Inc. v. Calgene, Inc.,[190] Enzo Biochem asserted that Calgene, Inc.'s FLAVR SAVR tomato, which was genetically engineered using antisense technology to regulate the expression of an enzyme that facilitates the ripening process of the tomato,[191] infringed its exclusive rights to ***74** genetic antisense technology as delineated in U.S. Patent Nos. 5,190,931 and 5,208,149.[192] These patents, licensed to Enzo, specifically taught the application of antisense technology to regulating the expression of two proteins in E. coli: lipoprotein and outer membrane protein C.[193] Despite the limited disclosure of these patents, the claims were written in such a way as to encompass the general application of antisense technology "in a broad range of organisms," including plants, through general product claims to DNA constructs.[194] However, the Federal Circuit affirmed the decision of the district court and held that broad claims to genetic antisense technology, employed in both prokaryote and eukaryote cells to control gene expression, were invalid as not enabled "because undue experimentation was necessary to practice [it] in cells other than E. coli."[195]

The Federal Circuit applied several of the Wands factors in reaching its decision.[196] With regard to breadth of the claims, the Federal Circuit held that the district court did not err in finding that "'these patents attempt to include the entire universe of cells for the antisense system detailed."'[197] Quoting from a cell-biology textbook, the Federal Circuit next concluded that the district court did not err in finding that antisense technology is a highly unpredictable technology.[198] In response to a challenge to the finding regarding the quantity of experimentation necessary to practice antisense, the Federal Circuit held that the district court was correct in saying that the amount required was quite high because of evidence showing failed attempts to practice the invention in eukaryotes, which were performed "by those of the appropriate level of skill following the methodology disclosed in the specifications" of the patents.[199] The Federal Circuit also agreed with the district court that the specifications of the patents in question provided too few working examples and little guidance on how to control gene expression using antisense technology in cells other than E. coli.[200] Thus, the Federal Circuit ***75** concluded that "the breadth of enablement in the patent specifications [were] not commensurate in scope with the claims, as the quantity of experimentation required to practice antisense in cells other than E. coli at the filing date would have been undue."[201] For this reason, the broad claims to genetic antisense technology, including the product DNA construct claims, were invalidated.[202]

3. How-to-Use in the Utility Requirement

Although questions of 35 U.S.C. § 112 enablement and 35 U.S.C. § 101 utility can be closely related in that "fail[ing] to meet the utility requirement because the invention is inoperative [means] they also fail to meet the enablement requirement because a person skilled in the art cannot practice the invention,"[203] §§ 101 and 112 are also distinct concepts.[204] Whereas the enablement requirement mandates that the specification contain indications of how to use the invention and how the use can be effected, the utility requirement merely mandates that the specification contain one specific, substantial, and credible use

for the invention.[205] Whereas § 112 requires a patent applicant to distinctly claim the subject matter of the invention and to enable one to use the invention as claimed,[206] § 101 does not require the disclosed utility to comport with the scope of the claims.[207] Furthermore, in the instance where a specific, substantial, and credible use is provided in the specification "but the skilled artisan will not know how to effect that use," 35 U.S.C. § 101 has been satisfied but § 112 has not been satisfied.[208]

***76 B. Reasons for Further Restricting Gene Fragment Patenting Using § 112**

Using the enablement-commensurate-in-scope-with-the-claims requirement of 35 U.S.C. § 112 to restrict composition-of-matter patent claims on ESTs to a specific known use or uses for the fragments claimed is ideal for several reasons. From a policy standpoint, broad product patent claims on ESTs are undesirable because they can be used "to block off large areas of research, while simultaneously permitting applicants to obtain protection for the use of the ESTs as research tools" to discover and claim ownership rights over new parts of the genome where the gene fragments may bind.[209] Moreover, commercial products, such as a therapeutic protein or a genetic diagnostic test that incorporate multiple ESTs may be costly or even unfeasible to develop and market if the patents on such fragments were each held by different owners.[210] On the other hand, making it harder to obtain an EST patent may indirectly facilitate more innovation in the biomedical field.[211]

As Judge Rader admitted in his dissenting opinion in In re Fisher, the Patent Office "needs some tool to reject [EST] inventions that may advance the 'useful arts' but not sufficiently to warrant the valuable exclusive right of a patent."[212] Current law only employs the utility requirement of 35 U.S.C. § 101 to forbid EST product claims in the situation where the function of the underlying protein-encoding gene is not understood.[213] Generally, however, "a patentee who identifies a single use for an invention obtains rights over all uses, including ones unknown at the time of patenting."[214] While the In re Fisher decision has addressed the situation in which an EST has no established link to a specific protein, it is still an open question whether a "second generation" or "third generation" EST--one ***77** where its corresponding protein is understood at some level-- could be rejected for failing to satisfy utility or disclosure requirements.[215]

Instead of seizing upon the utility requirement or the written description requirement to reject claims on such molecules, the PTO and the federal courts should employ the enablement requirement to reject ESTs such as those in the In re Fisher case or their second or third generation forms. The utility requirement "lacks any standard for assessing the state of the prior art and the contributions of the claimed advance,"[216] and the precedential value of cases that employ the written description requirement to curb a type of patent claim is "extremely limited."[217] In contrast, the enablement requirement, as a question of law with factual undercurrents, employs several different factors--including the quantity of experimentation, the state of the prior art, and the breadth of the claims--in its analysis and can be used to shape strikingly the law governing EST patents for future PTO office actions and federal court orders.

With a more rigorous application of the enablement requirement to EST patents in place, the patentee of an EST would be limited to claims of only a specific known use or uses that are described and enabled in the specification. In other words, the scope of the patent claim on an EST must be commensurate with the disclosure on how the EST matches up to known genes, corresponding proteins, and their functions. Such an application of the enablement requirement to the sort of ESTs claimed in the In re Fisher case is described in more detail below.

C. Application of the Enablement Requirement to ESTs

The ESTs in In re Fisher were claimed as follows: "A substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 5."[218] The preamble to a claim--e.g., "[a] substantially purified nucleic acid molecule that encodes a maize protein or fragment ***78** thereof"[219]--generally does not function as a limitation on the claim.[220] The exception to this rule is that preamble terminology that is repeated in the body of the claim--the language following the word "comprising"--is usually limiting.[221] Here, a court likely would import the language "substantially purified" to modify the body language "nucleic acid." However, the rest of the preamble language would not be imported as a limitation on the claim because the body otherwise stands as a structurally complete invention. Thus, this claim likely would be construed broadly to include any use of the substantially purified nucleic acids having the sequences disclosed and would not be limited to nucleic acids encoding maize proteins or fragments thereof.

Such a broad patent claim would have allowed Fisher to assert exclusionary rights over the numerous ways that the claimed

ESTs could be used.[222] For example, each claimed EST might match up to an exon or combination of exons of a single gene that ultimately is alternatively spliced into several mRNAs that can be translated into several different protein products. Also, each claimed EST may match up to several different genes with either similar end products (e.g., paralogous genes) or completely different protein products as such genes may all have similar exonic regions at either their 3' or 5' ends. Furthermore, not only can each EST be used to find genes in the species from which the EST was derived, but each fragment may also bind to genes found in different species or even man-made genes unknown to the natural world.[223] In all of these cases, having such a broad patent claim on an EST would have given Fisher the right to exclude others from making or using all fully sequenced genes to which the EST matches up as well as the corresponding proteins or fragments thereof.

The question then becomes this: did Fisher enable a person skilled in the relevant art to use the claimed invention without "undue experimentation" ? Applying the Wands factors, one should say no. First, with regard to the breadth of the claims, Fisher's claimed invention includes 'inter alia, genes, full open reading frames, fusion constructs, and cDNAs' . . . as well as plasmids, naturally-occurring genes, spliced genes, genes with modifications not affecting the encoded protein, fragments of ***79** chromosomes, full chromosomes, collections of chromosomes, genetic regions, etc., comprising one of the EST sequences.[224]

In short, Fisher's claims are broad. Because biotechnology has been found to be a highly unpredictable technology "in which slight changes in amino acid or nucleotide sequences results in highly altered molecular function,"[225] the number of working examples and the quantity of direction provided in the specification also should be quite broad. Yet, Fisher's specification merely describes what may be done with such ESTs--e.g., "as molecular tags to isolate genetic regions, isolate genes, map genes, and determine gene function"[226]--but it does not describe the actual function of all of the protein-encoding genes with which the claimed ESTs would match up. Without such examples, one skilled in the relevant art would have to engage in a high amount of experimentation to determine the myriad of different uses for the claimed ESTs. Thus, the breadth of enablement in Fisher's specification is not commensurate in scope with his claims, as the quantity of experimentation required to figure out the many different ways that the claimed ESTs can match up to different amino-acid-encoding gene combinations, and ultimately the many different types of corresponding proteins with their many varying functions, would be undue.

VI. Conclusion

The inherent nature of ESTs mandates that a patent application claiming such a DNA molecule be rigorously scrutinized such that the use prong of the enablement requirement aligns with the scope of the claims. Merely enabling how to make the EST--i.e., by disclosing the EST's sequence--and disclosing one "substantial" utility--i.e., identifying one gene that matches up to the EST--should not be enough to get a broad product patent claim on the gene fragment. Because there are a myriad of uses for gene fragments, such as ESTs, all such uses should be disclosed in the specification to enable a broad composition-of-matter claim on such a molecule. Doing so is practically impossible at this time. Thus, the EST patentee should be limited to claiming specific uses described in the specification and specifically delineated in the patent claim itself.

Footnotes

a1 J.D. (2006), LL.M. in Biotechnology and Genomics (2006), Sandra Day O'Connor College of Law, Arizona State University. He is currently a judicial law clerk to the Honorable Peter C. Lewis, United States District Court, Southern District of California.

1 Georgios I. Zekos, Nanotechnology and Biotechnology Patents, 14 Int'l J.L. & Info. Tech. 310, 323-24 (2006); Rebecca S. Eisenberg, Re-Examining the Role of Patents in Appropriating the Value of DNA Sequences, 49 Emory L.J. 783, 786-87 (2000).

2 Hitzeman v. Rutter,243 F.3d 1345, 1348 n.1(Fed. Cir. 2001).

3 Lee Strobel, The Case for a Creator 224 (2004) (quoting Dr. Stephen Meyer); see also Jordan Paradise et al., Patents on Human Genes: An Analysis of Scope and Claims, 307 Science 1566, 1566 (2005) (assessing the quality of gene patents and beginning with the assumption that such patents claim the information contained in the human genome).

[4] See, e.g., Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206 (Fed. Cir. 1991).

[5] For example, Joseph J. Rolla, Deputy Commissioner for Patent Examination Policy, has stated that "[w]ith gene patents, the invention is the chemical compound, not 'the information.'" Joseph J. Rolla, Letter to the Editor, Problems in Patenting Human Genes, 308 Science 1868, 1869 (2005). On the other hand, others have pointed out that DNA patents that broadly claim the basic nucleotide sequence "relate to data, not compounds." Jordan Paradise et al., Response to Letter to the Editor, Problems in Patenting Human Genes, 308 Science 1868, 1870 (2005). It has also been argued that because "genes are essentially just genetic information," patenting DNA sequences should be very different from patenting other chemical compounds. Nuffield Council on Bioethics, The Ethics of Patenting DNA: A Discussion Paper 28 (2002), available at http:// www.nuffieldbioethics.org/fileLibrary/pdf/theethicsofpatentingdna.pdf.

[6] See In re Fisher, 421 F.3d 1365, 1367 (Fed. Cir. 2005); Invitrogen Corp. v. Clontech Laboratories, Inc., 429 F.3d 1052, 1058 (Fed. Cir. 2005); In re O'Farrell, 853 F.2d 894, 895-99 (Fed. Cir. 1988); Regents of the Univ. of Calif. v. Eli Lilly and Co., 119 F.3d 1559, 1562 n.1 (Fed. Cir. 1997); and Kridl v. McCormick, 105 F.3d 1446, 1448 n.1 (Fed. 1997), for a discussion of the basics of molecular biology and genetics. The fundamental chemical components of the DNA molecule are the nucleotides. In re O'Farrell, 853 F.2d at 896. The term nucleotide refers to the assemblage of a nitrogenous base, a five-carbon deoxyribose sugar, and a phosphate group. Id. In DNA, there are four types of nucleotides, which contain one of four nitrogenous bases: guanine (G), adenine (A), thymine (T), or cytosine (C). Id. Each base (G, A, T, or C) can only bind to its complement: A binds with T, and G binds with C. Id. at 896 n.5. In its most stable form, DNA is composed of two strings of nucleotides wrapped together in a double-helical configuration. See id. at 896-97. Tightly coiled strings of DNA make up the functional units of heredity called genes, which in turn code for proteins. Id. at 897. DNA expresses genetic information by a two-step process called transcription and translation. See In re O'Farrell, 853 F.2d 894, 897 (Fed. Cir. 1988). In transcription, the double helix unwinds and is transcribed into a single strand of messenger ribonucleic acid (mRNA). Invitrogen Corp. v. Clontech Laboratories, Inc., 429 F.3d 1052, 1058 (Fed. Cir. 2005). The mRNA molecule is composed of three of the same bases as DNA, A, G, and C, but it contains uracil (U) instead of thymine (U's complement is A). In re O'Farrell, 853 F.2d at 897. In translation, the mRNA transcript, which is made inside the nucleus of the cell, moves into the cytoplasm of the cell, where ribosomes and other macromolecules are available to translate the mRNA into a sequence of amino acids that make up a protein. See In re Fisher, 421 F.3d 1365, 1367 (Fed. Cir. 2005). For a more thorough description of the science of genes, see generally T.A. Brown, Genomes (2d ed. 2002), available at http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=genomes.

[7] The PTO's Utility Examination Guidelines state:
A patent claim directed to an isolated and purified DNA molecule could cover, e.g., a gene excised from a natural chromosome or a synthesized DNA molecule. An isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent because (1) an excised gene is eligible for a patent as a composition of matter or as an article of manufacture because that DNA molecule does not occur in that isolated form in nature, or (2) synthetic DNA preparations are eligible for patents because their purified state is different from the naturally occurring compound.
66 Fed. Reg. 1092, 1093 (Jan. 5, 2001).

[8] See Jonathan Kahn, What's the Use? Law and Authority in Patenting Human Genetic Material, 14 Stan. L. & Pol'y Rev. 417, 426 (2003); see also Nuffield Council, supra note 5, at 25 (giving a non-exhaustive list of the many ways that DNA sequences can appear in a patent).

[9] U.S. Department of Energy Office of Science, Office of Biological and Environmental Research, Human Genome Project Information, http:// www.ornl.gov/hgmis/elsi/patents.html (last visited Mar. 19, 2008).

[10] Cf. In re Fisher, 421 F.3d 1365, 1376 (Fed. Cir. 2005).

[11] Id.; see also Rochelle K. Seide & Carmella L. Stephens, Drafting Claims for Biotechnology Inventions, Advanced Patent Prosecution Workshop 2006: Claim Drafting & Amendment Writing 387, 403-04 (P.L.I. 2006).

[12] Utility Examination Guidelines, 66 Fed. Reg. at 1094.

[13] Id.

[14] In re Fisher, 421 F.3d at 1373. Product-claims patents, the broadest type of patents, may enable one to "claim the entire genus of products that function in the same way as the isolated product." Dianne Nicol, On the Legality of Gene Patents, 29 Melb. U. L. Rev. 809, 816 (2005). This type of broad patent can be made by using "comprising" claims. Id. at 819. "Comprising" EST claims allow the patentee to "have rights not only over the EST itself and its use as a research tool, but also the full gene sequence, the proteins for which it codes, diagnostic tests, and even gene therapies that may subsequently be developed." Id.

[15] Some commentators have proposed that gene patents should be restricted to purpose-bound claims, which only give the patentee rights over specific disclosed uses of a product. See, e.g., Nuffield Council, supra note 5, at 66, 71-72 (recommending that the USPTO and similar international patenting bodies limit the scope of product patents to "the uses referred to in the patent claims" whenever the invention only concerns the sequence and not some "derivation or elucidation" of it).

[16] See generally In re Fisher, 421 F.3d 1365 (Fed. Cir. 2005).

[17] Id. at 1367. The ESTs in patent application at issue in In re Fisher were claimed as follows: "A substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 5." Id. (quoting U.S. Patent Application Serial No. 09/619,643, at claim 1 (filed July 19, 2000)).

[18] Id. at 1373.

[19] Id.

[20] Id. at 1378-79.

[21] In re Fisher, 421 F.3d 1365, 1367 (Fed. Cir. 2005).

[22] See In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988). Determining whether a patent specification contains an enabling disclosure on how to use a claimed invention involves weighing several factors including quantity of experimentation, the number of working examples provided, the unpredictability of the art, and the scope of the claims. Id.

[23] See In re O'Farrell, 853 F.2d 894, 896-97(Fed. Cir. 1988); supra note 6 (providing a more detailed description of DNA).

[24] See id. at 896 n.5.

[25] See id. at 897.

[26] See id. at 896 n.5; Enzo Biochem Inc. v. Calgene Inc., 188 F.3d 1362, 1366 (Fed. Cir. 1999).

[27] See Enzo Biochem, 188 F.3d at 1366-67 ("[RNA is] nearly identical in sequence and structure to the DNA coding strand, except that the sugar ribose is used in place of deoxyribose, and the RNA strand contains the base uracil instead of thymine.").

[28] See Amgen Inc. v. Hoechst Marion Roussel, Inc., 457 F.3d 1293, 1298 (Fed. Cir. 2006).

[29] See Enzo Biochem, 188 F.3d at 1366 n.2.

[30] Id. at 1367.

[31] With the degeneracy of the code, more than one mRNA codon can code for most of the 20 different amino acids. Nicol, supra note 14, at 812. Thus, "the same sequence of amino acids can be created from a number of different DNA sequences, also often referred to as a genus." Nicol, supra note 14, at 812. Moreover, a sequential grouping of nucleotides on a mRNA molecule may specify something other than an amino acid--e.g., a start or stop codon. See Brown, supra note 6, at §3.3.2.

[32] See Catherine Mathé et al., Current Methods of Gene Prediction, Their Strengths and Weaknesses, 30 Nucleic Acids Res. 4103, 4104 (2002) (explaining how the information in transcripts can be used to provide information about exon and intron locations).

[33] The Maize Full Length cDNA Project, http:// www.maizecdna.org/outreach/flcdna.html (last visited July 27, 2008).

[34] Id.

[35] See id.

[36] Id.

[37] Mathé, supra note 32, at 4104.

[38] Shivashankar H. Nagaraj et al., A Hitchhiker's Guide to Expressed Sequence Tag (EST) Analysis, 8 Brief Bioform 6, 7 (2007); see also National Center for Biotechnology Information, A Science Primer, Just the Facts: A Basic Introduction to the Science Underlying NCBI Resources (2004), http:// www.ncbi.nlm.nih.gov/About/primer/est.html [hereinafter A Science Primer].

[39] Mathé, supra note 32, at 4104.

[40] A Science Primer, supra note 38; see Mark D. Adams et al., Complimentary DNA Sequencing: Expressed Sequence Tags and Human Genome Project, 252 Science 1651, 1651 (1991).

[41] In re Fisher, 421 F.3d 1365, 1367 (Fed. Cir. 2005).

[42] Volker Brendel et al., Gene Structure Prediction from Consensus Spliced Alignment of Multiple ESTs Matching the Same Genomic Locus, 20 Bioinformatics 1157, 1158 (2004); see Jean-Michel Claverie et al., The Difficulty of Identifying Genes in Anonymous Vertebrate Sequences, 21 Computers & Chemistry 203, 203, 211-13 (1997) (reporting numerous difficulties that can arise in the identification of genes in newly determined sequences).

[43] For example, scientists at the National Center for Biotechnology Information have set up a database of a "great mass of public EST data" called dbEST. A Science Primer, supra note 38. Scientists using dbEST "can access not only data on human ESTs but information on ESTs from over 300 other organisms as well." A Science Primer, supra note 38.

[44] Brendel, supra note 42, at 1157.

[45] Brendel, supra note 42, at 1158.

[46] Brendel, supra note 42, at 1158. Paralogous genes are defined as "two genes or clusters of genes at different chromosomal locations in the same organism that have structural similarities indicating that they derived from a common ancestral gene and have since diverged from the parent copy by mutation and selection or drift." Holmgren Lab, Hedgehog Signaling Glossary (2004), http://www.biochem.northwestern.edu/holmgren/Glossary/Definitions/Def-P/paralogous_genes.html.

[47] See Mathé, supra note 32, at 4107; Brendel, supra note 42, at 1157-58.

[48] David Brett et al., EST Comparison Indicates 38% of Human mRNAs Contain Possible Alternative Splice Forms, 474 FEBS Letters 83, 83 (2000).

[49] Id.

[50] See Brendel, supra note 42, at 1157-58.

[51] See Brendel, supra note 42, at 1158.

[52] Joost A. Kolkman & Willem P.C. Stemmer, Directed Evolution of Proteins by Exon Shuffling, 19 Nature Biotechnology 423, 423 (2001).

[53] See id. For example, mobile domains have been found in the protein cofactors Factor V and Factor VIII. Id. at 426. They both contain "two C domains in the C-terminal regions. This domain, which is also found in the otherwise nonhomologous proteins neuropilin and epithelial discoidin domain receptor 1, is encoded by a symmetric set of four exons." Id.

[54] Catherine H. Pashley et al., EST Databases as a Source for Molecular Markers: Lessons from Helianthus, 97 J. Heredity 381, 381 (2006); see also Ramesh V. Kantety et al., Data Mining for Simple Sequence Repeats in Expressed Sequence Tags from Barley, Maize, Rice, Sorghum and Wheat, 48 Plant Molecular Biology 501, 501-02 (2002). Particularly, ESTs derived from the 5' ends of cDNA molecules "tend to be conserved across species and do not change much within a gene family." A Science Primer, supra note 38. On the other hand, ESTs derived from the 3' ends of cDNA molecules "are likely to fall within non-coding, or untranslated regions (UTRs), and therefore tend to exhibit less cross-species conservation than do coding sequences." A Science Primer, supra note 38.

[55] Brendel, supra note 42, at 1157.

[56] Brendel, supra note 42, at 1157.

[57] Kolkman, supra note 52, at 423.

[58] Kolkman, supra note 52, at 426.

[59] Kolkman, supra note 52, at 426-27.

[60] EST clustering--assembling "overlapping ESTs from the same transcript of a single gene into a unique cluster"--to produce a consensus sequence is one way to reduce redundancy and to reconstruct a single mRNA transcript. Nagaraj, supra note 38, at 6-21. But even a cluster of ESTs may bind alternatively spliced transcripts, paralogues, or related sequences. Id.; see also Ketil Malde et al., A Graph Based Algorithm for Generating EST Consensus Sequences, 21 Bioinformatics 1371, 1371 (2005).

[61] See Nuffield Council, supra note 5, at 4, 25.

[62] For a thorough list of the different ways that DNA sequences can appear in patent claims, see Nuffield Council, supra note 5, at 32.

[63] Nuffield Council, supra note 5, at 32.

[64] In a patent, "EST is a term that defines how the fragment of DNA was obtained and not what it is." Nuffield Council, supra note 5, at 33.

[65] SNPs are "single base pair differences occurring at a frequency of about 1 in every 1000 nucleotides when the genome sequences of many individuals are compared." Nuffield Council, supra note 5, at 33.

[66] Nuffield Council, supra note 5, at 33.

[67] Nuffield Council, supra note 5, at 24.

[68] Nuffield Council, supra note 5, at 24.

[69] Nuffield Council, supra note 5, at 24.

[70] Nuffield Council, supra note 5, at 54.

[71] Nuffield Council, supra note 5, at 32.

[72] Nuffield Council, supra note 5, at 33.

[73] Nuffield Council, supra note 5, at 33.

[74] A Science Primer, supra note 38; see also Pashley, supra note 54, at 381-382.

[75] Nuffield Council, supra note 5, at 33.

[76] See Cynthia D. Lopez-Beverage, Should Congress Do Something About Upstream Clogging Caused by the Deficient Utility of Expressed Sequence Tag Patents?, 10 J. Tech. L. & Pol'y 35, 86 (2005) (proposing that "one way to avoid the negative effect of composition of matter patents on DNA sequence patents is to limit the patent rights granted on DNA sequence claims to only use patents, which do not assert rights over the DNA sequence itself or all unknown uses of it"); see also Joseph P. Pieroni, The Patentability of Expressed Sequence Tags, 9 Fed. Cir. B.J. 401, 412 (2000) (noting how commentators have said that patentees "should be forced to commit uses for their ESTs" in the specification and claims so that other researchers who find new uses for their genes can patent them without interference).

[77] Robert Patrick Merges & John Fitzgerald Duffy, Patent Law & Policy 250-51 (3d ed. 2002).

[78] Paul J. Riley, Comment, Patenting Dr. Venter's Genetic Findings: Is the National Institutes of Health Creating Hurdles or Clearing the Path for Biotechnology's Voyage into the Twenty-First Century?, 10 J. Contemp. Health L. & Pol'y 309, 326 n.* (1994).

[79] Merges & Duffy, supra note 77, at 253.

[80] See generally Dan L. Burk & Mark A. Lemley, Policy Levers in Patent Law, 89 Va. L. Rev. 1575, 1576-79 (2003) (arguing that the patent system is "technology-neutral in theory" but actually "technology-specific" in its application to the broad variety of industries it seeks to foster).

[81] 35 U.S.C. §101 (2006). Having its origins in the patent statue of 1790, the list of subject matters that can be patented has been developed by the legislative branch, whose constitutional power to do so is found in U.S. Const. art. I, §8, cl. 8. See In re Bergy, 596 F.2d 952, 958-59 (C.C.P.A. 1979), vacated sub nom. Diamond v. Chakrabarty, 444 U.S. 1028, aff'd 447 U.S. 303; see also Act of Apr. 10, 1790, ch. 7, §1, 1 Stat. 109, 109-10 (repealed 1793).

[82] Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980) (quoting S. Rep. No. 82-1979, at 5 (1952); H.R. Rep. No. 82-1923, at 6 (1952)).

[83] Diamond v. Diehr, 450 U.S. 175, 185 (1981).

[84] Chakrabarty, 447 U.S. at 310, 318 (holding that a human-made, genetically engineered microorganism is patentable).

[85] See Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206-08 (Fed. Cir. 1991) (holding that isolated and purified DNA molecules are patentable); see also Merges & Duffy, supra note 77, at 104.

[86] Nucleic Acids Encoding a Gap-Associated Protein, U.S. Patent No. 5,731,427 col.7 (filed May 19, 1995).

[87] U.S. Patent No. 5,817,479 (filed Aug. 7, 1996). The basis for granting this patent was the "predicted function of the genes from which the ESTs were derived." Nuffield Council, supra note 5, at 33 n.27.

[88] See Andrew Chin, Artful Prior Art and the Quality of DNA Patents, 57 Ala. L. Rev. 975, 988 (2006).

[89] Merges & Duffy, supra note 77, at 104.

[90] See Chin, supra note 88. Under §102, prior art may include the claimed invention's public use, sale, patenting, or a printed publication describing it. Id. Public use and sale of the claimed invention must occur in the United States, while patents and printed publications of the claimed invention published anywhere in the world may be used as invalidating art. Id. The public use and sale bars are triggered only when such events occurred more than a year before the filing date of the patent application. Id. Patents and other printed publications that have an enabling disclosure of the claimed invention may be considered prior art if they were published prior to the actual date of invention or more than a year prior to the filing date of the patent application. Id.

[91] In re Paulsen, 30 F.3d 1475, 1479 (Fed. Cir. 1994). The Federal Circuit does not require that an anticipating reference contain a specific utility. Impax Labs., Inc. v. Aventis Pharm., Inc., 468 F.3d 1366, 1381 (Fed. Cir. 2006).

[92] Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1207 (Fed. Cir. 1991).

[93] Chin, supra note 88, at 1001.

[94] See Chin, supra note 88, at 1001 ("[Section 103] prior art may include references that could be considered under §102(a), (b), (e), (f), and (g), except that §102(e), (f), and (g) references are excluded if they deal with subject matter co-owned with the claimed invention."). Generally, §103 prior art must either be "in the field of the applicant's endeavor" or "reasonably pertinent to the particular problem with which the inventor was concerned." In re Oetiker, 977 F.2d 1443, 1447 (Fed. Cir. 1992).

[95] 35 U.S.C. §103(a) (2006). The nonobviousness inquiry is a case-by-case determination in which "the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved." Graham v. John Deere Co., 383 U.S. 1, 17 (1966). Obviousness is determined by a person having ordinary skill in the pertinent art (e.g., genetics) at the time of the invention's making. See, e.g., Hybritech v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379 (Fed. Cir. 1986).

[96] Chin, supra note 88, at 1002-03.

[97] Chin, supra note 88, at 1003.

[98] Chin, supra note 88, at 1003

[99] In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995).

[100] Id. at 1557-58.

[101] Id. at 1559.

[102] Id. at 1558.

[103] Id. at 1559.

[104] Ex parte Goldgaber, 41 U.S.P.Q.2d (BNA) 1172, 1179 (B.P.A.I. 1996).

[105] Cf. In re Deuel, 51 F.3d at 1559.

[106] 35 U.S.C. §101 (2000); see also U.S. Const. art 1, §8, cl. 8 (stating that the goal is "[t]o promote the progress of science and the useful arts").

[107] Brenner v. Manson, 383 U.S. 519 (1966) (holding that claimed methods for producing compounds that have no known use lack utility).

[108] Id. at 534.

[109] Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001).

[110] See id. at 1097.

[111] U.S. Patent & Trademark Office, Revised Interim Utility Guidelines Training Materials 5, available at http://www.uspto.gov/web/menu/utility.pdf (last visited July 28, 2008).

[112] Id.

[113] Id. at 6-7.

[114] See id. at 6.

[115] Id. at 5.

[116] Id.

[117] In re Fisher, 421 F.3d 1365, 1369-78 (Fed. Cir. 2005).

[118] Id. at 1367.

[119] Ex parte Fisher, 72 U.S.P.Q 2d (BNA) 1020, 1027 (B.P.A.I. 2004).

[120] In re Fisher, 421 F.3d at 1368.

[121] Ex parte Fisher, 72 U.S.P.Q.2d (BNA) at 1022 (quoting PTO examiner).

[122] Id. at 1026.

[123] In re Fisher, 421 F.3d at 1369-78.

[124] Id. at 1373.

[125] Id. at 1371.

[126] Id. at 1373. As research intermediates, the claimed ESTs "may help scientists to isolate the particular underlying protein-encoding genes and conduct further experimentation on those genes. The overall goal of such experimentation is presumably to understand the maize genome--the functions of the underlying genes, the identity of the encoded proteins, the role those proteins play during anthesis ...." Id.

[127] Id.

[128] In re Fisher, 421 F.3d 1365, 1374 (Fed. Cir. 2005).

[129] Id. at 1376.

[130] See 35 U.S.C. §112 (2006).

[131] See Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1209-11 (Fed. Cir. 1991) (holding that "there is no failure to comply with the best mode requirement for lack of a deposit of the CHO cells, when the best mode of preparing the cells has been disclosed" and enabled).

[132] Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1535-36 (Fed. Cir. 1987), cert. denied, 484 U.S. 954 (1987).

[133] Fiers v. Revel, 984 F.2d 1164, 1170-71 (Fed. Cir. 1993); see Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1567 (Fed. Cir. 1997) (holding that disclosing only a general method for isolating a cDNA molecule and reciting its corresponding amino acid sequence are not enough to satisfy the written description requirement for a claimed cDNA molecule).

[134] Manual of Patent Examining Procedure §2164 (8th ed. rev. 5 2006).

[135] Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed. Cir. 1986).

[136] In re Fisher, 427 F.2d 833, 839 (C.C.P.A. 1970).

[137] Seide & Stephens, supra note 11, at 428.

[138] Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1212, 1214 (Fed. Cir. 1991) (quoting U.S. Patent No. 4,703,008 (filed Nov. 30, 1984)).

[139] In re Fisher, 421 F.3d 1365, 1378-79 (Fed. Cir. 2005).

[140] Lopez-Beverage, supra note 76, at 85-86.

[141] See, e.g., Lopez-Beverage, supra note 76, at 78-83 (warning that granting a patent without sufficiently specific utility can create a monopoly over a vast unknown area and offering as an example the broad and zealously guarded "junk DNA" patents that were granted to Genetic Technologies before anyone really knew the specific function of the DNA claimed).

[142] Lopez-Beverage, supra note 76, at 86.

[143] See, e.g., Lopez-Beverage, supra note 76, at 87-88 (arguing that that the definition of utility could be altered to raise the "standard of credibility required for a claimed utility of a DNA sequence").

[144] Lopez-Beverage, supra note 76, at 87 (quoting Daniel L. McKay, Comment, Patent Law and Human Genome Research at the Crossroads: The Need for Congressional Action, 10 Santa Clara Computer & High Tech. L.J. 465, 495 (1994)) (stating that such a rule would essentially be a codification of the standard applied in Brenner v. Manson, 383 U.S. 519 (1966)); see also Thomas Kiley, Patents on Random Complementary DNA Fragments?, 257 Science 915, 916 (1992).

[145] Lopez-Beverage, supra note 76, at 88.

[146] Genomic Research and Accessibility Act, H.R. 977, 110th Cong. §2(a) (2007).

[147] Lopez-Beverage, supra note 76, at 91.

[148] Lopez-Beverage, supra note 76, at 91.

[149] Burk & Lemley, supra note 80, at 1634. See generally Rochelle Cooper Dreyfuss, Information Products: A Challenge to Intellectual Property Theory, 20 N.Y.U. J. Int'l L. & Pol'y 897, 912-18 (1988) (discussing international ramifications of sui generis legislation with semiconductor chips).

[150] See Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, Legal Instruments--Results of the Uruguay Round, 33 I.L.M. 81, 93-94 (1994) ("[P]atents shall be available and patent rights enjoyable without discrimination to ... the field of technology ...."). However, both the U.S. and the European Union have enacted industry-specific patent rules for particular industries despite this treaty mandate. See Burk & Lemley, supra note 80, at 1634 (observing that such rules may be improper because "the Agreement on Trade-Related Aspects of Intellectual Property Rights ('TRIPs') prohibits member states from discriminating in the grant of patents based on the type of technology at issue.").

[151] Burk & Lemley, supra note 80, at 1634-37 (arguing that having industry-specific patent statutes would be costly to administer, add uncertainty to the legal process, would not be conducive to encouraging innovation, and would not easily accommodate advances in technology).

[152] See Burk & Lemley, supra note 80, at 1674-75 (asserting that the Federal Circuit applies the obviousness and disclosure standards differently in the software and biotechnology industries). But see In re Fisher, 421 F.3d 1365, 1378 (Fed. Cir. 2005) ("Congress did not intend for [the] practical implications [on policy] to affect the determination of whether an invention satisfies the requirements set forth in 35 U.S.C. §§101, 102, 103, and 112."). Nevertheless, the federal courts should and do engage in fact-specific analysis in applying the patent standards, policy reasons notwithstanding. Burk & Lemley, supra note 80, at 1674.

[153] Burk & Lemley, supra note 80, at 1638.

[154] Burk & Lemley, supra note 80, at 1644-45.

[155] Burk & Lemley, supra note 80, at 1644; see Brenner v. Manson, 383 U.S. 519, 534-45 (1966) ("Unless and until ... specific benefit exists in currently available form[,] there is insufficient justification for permitting an applicant to engross what may prove to be a broad field").

[156] Burk & Lemley, supra note 80, at 1645. But see Utility Examination Guidelines, 66 Fed. Reg. 1092, 1098 (Jan. 5, 2001) (requiring PTO examiners to determine if a "specific and substantial utility that is credible" has been asserted for each claimed invention).

[157] See supra Part IV.4.

[158] Lopez-Beverage, supra note 76, at 87. Some commentators have described the In re Fisher decision as a misapplication of established case law on the utility requirement because it treats DNA inventions differently than other sorts of inventions in other technological fields. See, e.g., Thomas Barry, Revisiting Brenner: A Proposed Resolution to the Debate over the Patentability of Expressed Sequence Tags Using the Concept of Utility Control, 35 AIPLA Q.J. 1, 18-19 (2007); Samantha A. Jameson, The Problems of the Utility Analysis in Fisher and its Associated Policy Implications and Flaws, 56 Duke L.J. 311, 322-32 (2006); Diana A. Villamil, Redefining Utility in Determining the Patentability of DNA Sequences, 5 J. Marshall Rev. Intell. Prop. L. 238, 260 (2006).

[159] See supra Part II.

[160] See In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988) (holding that enablement requires the specification to teach how to use the invention without undue experimentation).

[161] Kennecott Corp. v. Kyocera Int'l, Inc., 835 F.2d 1419, 1421 (Fed. Cir. 1987) (describing the written description and enablement requirements as "intertwined") (emphasis added).

[162] Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1371 (Fed. Cir. 1999); Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed. Cir. 1986); Manual of Patent Examining Procedure §2164 (8th ed. rev. 5 2006).

[163] In re Fisher, 421 F.3d 1365, 1371 (Fed. Cir. 2005) (emphasis added).

[164] Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991) (emphasis added and removed). In most circumstances, material contained in originally filed claims is part of the written description and need not be separately described in the specification. See, e.g., In re Koller, 613 F.2d 819, 823-24 (C.C.P.A. 1980). However, the Federal Circuit in Regents of the University of California v. Eli Lilly & Co. "identified a set of circumstances in which the words of the claim did not, without more, adequately convey to others that applicants had possession of what they claimed. 119 F.3d 1559, 1568 (Fed. Cir. 1997). When the name of a novel chemical compound does not convey sufficient structural information about the compound to identify the compound, merely reciting the name is not enough to show that the inventor had possession of the compound at the time the name was written." Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement,66 Fed. Reg. 1099, 1100 (Jan. 5, 2001).

[165] E.g., Fiers v. Revel, 984 F.2d 1164, 1169-72 (Fed. Cir. 1993).

[166] E.g., In re Smith, 481 F.2d 910, 914-15 (C.C.P.A. 1973). A written description requirement rejection may be avoided by seeking "the benefit of the filing date of an earlier-filed foreign or United States application under 35 U.S.C. §119 or 35 U.S.C. §120, respectively, for claims of a later-filed application." Vas-Cath, 935 F.2d at 1560.

[167] Kennecott Corp. v. Kyocera Int'l, Inc., 835 F.2d 1419, 1421 (Fed. Cir. 1987).

[168] Id.

[169] In re Wilder, 736 F.2d 1516, 1520 (Fed. Cir. 1984); see also Vas-Cath, 935 F.2d at 1563 ("The purpose of the 'written description' requirement is broader than to merely explain how to 'make and use.'").

[170] As explained in In re Wright, "[t]he first paragraph of 35 U.S.C. §112 requires that the specification of a patent contain a written description of the claimed invention and the manner and process of making and using that invention in such full, clear, concise, and exact terms as to enable any person skilled in the art to which that invention pertains, or with which it is most nearly connected, to make and use that invention." 999 F.2d 1557, 1561 (Fed. Cir. 1993).

[171] Kennecott, 835 F.2d at 1421 (including instructions on how to "make and use" in the written description requirement); Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed. Cir. 1986) (defining enablement as teaching a skilled artisan to "make and use").

[172] In re Wertheim, 541 F.2d 257, 262-63 (C.C.P.A. 1976). On appeal, compliance with the written description requirement is to be reviewed under the clearly erroneous standard. In re Gosteli, 872 F.2d 1008, 1012 (Fed. Cir. 1989).

[173] In re Wertheim, 541 F.2d at 262 (emphasis added).

[174] In re Smith, 458 F.2d 1389, 1395 (C.C.P.A. 1972). The standard applied by the Federal Circuit for determining whether a written description is sufficient to support a claim under §112 can be described as follows: "where the specification discusses only compound A and contains no broadening language of any kind, [it] might very well enable one skilled in the art to make and use compounds B and C; yet the class consisting of A, B and C has not been described." In re DiLeone, 436 F.2d 1404, 1405 n.1 (C.C.P.A. 1971). See generally Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1560-64 (Fed. Cir. 1991) (discussing the case law on the written description requirement).

[175] In re Driscoll, 562 F.2d 1245, 1250 (C.C.P.A. 1977).

[176] Upon appellate review, the underlying findings of fact are reviewable under the clearly erroneous standard. In re Vaeck, 947 F.2d 488, 495 (Fed. Cir. 1991); In re Wands, 858 F.2d 731, 735 (Fed. Cir. 1988).

[177] In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993).

[178] Id. at 1561-62. Appellate courts review an enablement determination under a de novo standard.

[179] In re Cortright, 165 F.3d 1353, 1356-57, 1360 (Fed. Cir. 1999); see In re Wands, 858 F.2d at 737. As stated by the Federal Circuit, "[n]othing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." In re Wright, 999 F.2d at 1561 (citing In re Marzocchi, 439 F.2d 220, 223 (C.C.P.A. 1971)).

[180] In re Wands, 858 F.2d at 737 (citing In re Forman, 230 U.S.P.Q. (BNA) 546, 547 (B.P.A.I. 1986)); see also Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1370-1372 (Fed. Cir. 1999) (applying the Wands factors in an infringement action).

[181] See Enzo Biochem,188 F.3d at 1371.

[182] Id. (quoting Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1213 (Fed. Cir. 1991)); see also Manual of Patent Examining Procedure §2164.04 (8th ed. rev. 5 2006) (instructing examiners to focus on the factors relevant to the rejection for nonenablement rather than discuss all of the factors). However, "[i]t is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole." Manual of Patent Examining Procedure §2164.01(a) (8th ed. rev. 5 2006) (citing In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988)).

[183] Manual of Patent Examining Procedure §2164.01(c) (8th ed. rev. 5 2006). But "[a]n enablement determination of a claim limited by a particular use should take into account the claim limitation." Id. (citing In re Vaeck, 947 F.2d 488, 495 (Fed. Cir. 1991)).

[184] Seide & Stephens, supra note 11, at 428. But see In re Fisher, 427 F.2d 833, 839 (C.C.P.A. 1970) (affirming a finding of nonenablement where the applicant claimed a "potency" of at least 1.0, but the disclosure only taught how to make a product of potency not "much greater than 2.3").

[185] Albert Wai-Kit Chan & Lauren Korshalla, Biotechnology Patent Practice: The Written Description Requirement of 35 U.S.C. §112 ¶1, and Relevant §101, in Advanced Patent Prosecution Workshop 2007: Claim Drafting & Amendment Writing 125, 134 (P.L.I. 2007).

[186] Seide & Stephens, supra note 11, at 428; see, e.g., Ex parte Hitzeman, 9 U.S.P.Q.2d 1821, 1823 (B.P.A.I. 1987).

[187] In re Nelson, 280 F.2d 172, 184 (C.C.P.A. 1960) (explaining that, in some cases, merely giving an invention a name--e.g., an "adhesive"-- familiar to one skilled in the art could enable its use).

[188] See O'Reilly v. Morse, 56 U.S. 62, 112-13 (1853) (holding that Morse's specification did not enable one to make the broadly claimed use of electro-magnetism for printing letters at a distance).

[189] Brenner v. Manson, 383 U.S. 519, 534 (1966).

[190] Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362 (Fed. Cir. 1999).

[191] Antisense DNA constructs contain the gene of interest in an inverted orientation. Id. at 1366. Inserted in a cell,
[t]he inverted gene sequence is transcribed by an RNA polymerase as if it were the gene sequence in its proper orientation, thereby generating an RNA strand which is complementary to, and thereby able to bind to, the mRNA transcript of the native gene. This RNA strand is known as messenger interfering complementary RNA ('micRNA'), because when it binds the native mRNA, that mRNA cannot be translated. Consequently, the protein for which that gene codes can no longer be produced, and gene expression is thereby blocked.
Id. at 1367-68.

[192] Id. at 1365.

[193] Id. at 1368.

[194] Id.

[195] Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1369 (Fed. Cir. 1999).

[196] Id. at 1370-72.

[197] Id. at 1372 (quoting Enzo Biochem, Inc. v. Calgene, Inc., 14 F. Supp. 2d 536, 569 (D. Del. 1998)).

[198] Id.

[199] Id. at 1374.

[200] Id. at 1374-75. In making an enablement determination, having no working examples "is a factor to be considered, especially in a case involving an unpredictable and undeveloped art.... [I]f all the other factors point toward enablement, then the absence of working examples will not by itself render the invention nonenabled.... To make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims." Manual of Patent Examining Procedure §2164.02 (8th ed. rev. 5 2006).

[201] Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 13677 (Fed. Cir. 1999).

[202] Id.

[203] In re Swartz, 232 F.3d 862, 863 (Fed. Cir. 2000). See also In re Fisher, 421 F.3d 1365, 1378 (Fed. Cir. 2005) (explaining that the

enablement requirement incorporates the utility requirement). In other words, "the factual showing needed to impose a rejection under 35 U.S.C. §101 must be provided if a 35 U.S.C. §112 [enablement] rejection is to be imposed on 'lack of utility' grounds." Manual of Patent Examining Procedure §2164.07 (8th ed. rev. 5 2006).

204 Donald S. Chisum et al., Principles of Patent Law 741 (3d ed. 2004).

205 Manual of Patent Examining Procedure §2164.07 (8th ed. rev. 5 2006). The burden is initially on the PTO to provide evidence that one of ordinary skill in the art would say that the invention lacks utility. Id. To rebut a prima facie showing of lack of utility, the applicant then must provide evidence to support the asserted utility. Id.; see In re Marzocchi, 439 F.2d 220, 223-24 (C.C.P.A. 1971) ("[The PTO] must explain why it doubts the truth or accuracy of any statement in a supporting disclosure and [back] up assertions of its own with acceptable evidence or reasoning ....").

206 Donald S. Chisum et al., Principles of Patent Law 741 (3d ed. 2004).

207 Manual of Patent Examining Procedure §2164.07 (8th Ed. Rev. 5 2006).

208 Id. An invention may be "'highly useful ...,' but the specification may still fail to 'enable any person skilled in the art or science' to use the invention." Id. (citing Mowry v. Whitney, 81 U.S. 620, 644 (1871)). See also In re Nelson, 280 F.2d 172, 184 (C.C.P.A. 1960) (holding that an applicant may satisfy the utility requirement and yet fail to satisfy the enablement requirement).

209 Barry, supra note 158, at 21.

210 Michael A. Heller & Rebecca S. Eisenberg, Can Patents Deter Innovation? The Anticommons in Biomedical Research, 280 Science 698, 698 (1998).

211 Id.

212 In re Fisher, 421 F.3d at 1381-82 (Rader, J., dissenting). Judge Rader proposed that "[t]he proper tool for assessing sufficient contribution to the useful arts is the obviousness requirement of 35 U.S.C. §103." Id. at 1382. Under this proposal, ESTs that have no established links to specific proteins would be considered obvious because they are essentially "[r]andom nucleic acid sequences." N. Scott Pierce, In re Dane K. Fisher: An Exercise in Utility, 6 J. High Tech. L. 1, 76 (2006). The limitation of this proposal is that §103, interpreted in this way, would not provide a means for rejecting a claimed EST that is not completely "random," that is, in the situation where its corresponding protein is understood at some level.

213 See In re Fisher, 421 F.3d at 1376 (holding that a failure to identify the function of the genes underlying claimed ESTs makes an EST patent invalid for lack of utility).

214 Helen M. Berman & Rochelle C. Dreyfuss, Reflections on the Science and Law of Structural Biology, Genomics, and Drug Development, 53 UCLA L. Rev. 871, 893 (2006).

215 Jay P. Lessler et al., Drafting Claims for Chemical, Pharmaceutical, and Biotechnology Patent Applications, 16th Annual Advanced Patent Prosecution Workshop: Claim Drafting & Amendment Writing 247, 261-62 (P.L.I. 2006).
A 'second generation' EST is one where the complete open reading frame (ORF) and the postulated amino acid sequence are disclosed, along with the biological function inferred via consensus sequence(s) and support for a specific, substantial, credible utility.... A 'third generation' EST is similar to a second generation EST, but additionally includes isolation of the protein encoded by the claimed nucleic acid and a determination of the biological activity and function of the protein.
Id.

216 In re Fisher, 421 F.3d at 1382 (Rader, J., dissenting).

[217] In re Driscoll, 562 F.2d 1245, 1250 (C.C.P.A. 1977).

[218] In re Fisher, 421 F.3d at 1367 (U.S. Patent Application '643, supra, note 17, at claim 1).

[219] Id.

[220] Catalina Marketing Int'l, Inc. v. CoolSavings.com, Inc., 289 F.3d 801, 808 (Fed. Cir. 2002) (citing Rowe v. Dror, 112 F.3d 473, 478 (Fed. Cir. 1997)).

[221] Janice M. Mueller, An Introduction to Patent Law 65 (2d ed. 2006).

[222] If his claims were allowed, Fisher would have had "rights not only over the EST itself and its use as a research tool, but also the full gene sequence, the proteins for which it codes, diagnostic tests, and even gene therapies that may subsequently be developed." Nicol, supra note 14, at 819.

[223] See supra Part II.

[224] Brief for Eli Lilly & Co. et al. as Amici Curiae Supporting Respondent at 33, In re Fisher, No. 04-1465, 2004 WL 4996616 (Fed. Cir. Dec. 14, 2004) (No. 04-1465) (quoting Ex parte Fisher, 72 U.S.P.Q. 2d 1020, 1023 (B.P.A.I. 2004)).

[225] Chan & Korshalla, supra note 185, at 134.

[226] Ex parte Fisher, 72 U.S.P.Q. 2d 1020, 1022 (B.P.A.I. 2004).