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THE FATE OF GENE PATENTS UNDER THE NEW UTILITY GUIDELINES

¶ 1 The United States Patent and Trademark Office (PTO) recently finalized its patent utility guidelines.¹ Promulgated by the PTO, the new guidelines will be used by patent examiners in determining whether a claimed invention should be awarded patent protection² and will be used by patent applicants and attorneys who file patent applications. The guidelines focus primarily on the utility standards for gene and gene fragment patents, an issue that was featured in the PTO's 1999 Revised Interim Utility Guidelines³ and has been the subject of considerable public debate.

¶ 2 The patenting of genetic sequences implicates a number of policy issues, ranging from individual privacy concerns to controversies over who should control the use of DNA sequences. In promulgating the new guidelines, however, the PTO predictably focused more on technical issues than on these larger policy issues. For instance, the PTO considered (and largely rejected) technical arguments supporting an overall prohibition on gene patents. These arguments included contentions that (1) the process of discovering genes is merely an obvious extension of already available technology,⁴ and (2) an inventor should not be given a patent when he discloses only a single useful function for a particular gene.⁵ While these arguments primarily focused on technical reasons for the exclusion of gene patents--i.e., reasons having to do with novelty, utility, and non-obviousness--their rejection by the PTO may have been based on larger policy concerns.

¶ 3 The utility of gene fragments presents particular problems. The use of DNA pieces as molecular probes is perhaps the most controversial issue addressed by the new guidelines. Proponents of gene patents argue that even gene fragments, pieces of DNA also known as express sequence tags (ESTs),⁶ should be patentable because these fragments are regularly used as molecular probes to search for complete genes.⁷ Others argue that ESTs should be unpatentable as long as their utility is limited to research--that is, before the final physiological function of the EST is discovered. The new guidelines attempt to resolve these competing positions by upholding the general concept that genes can be patented, but raising the utility bar for the patenting of gene fragments. Although the PTO's position that some ESTs can be patented thus strikes a balance in terms of policy, the technical framework chosen by the PTO

leaves a number of questions unresolved.

¶ 4 This iBrief first describes the backdrop of the Utility Examination Guidelines. It then explains the PTO's standard for determining utility of genetic material, as set out in the 1999 Revised Interim Utility Guidelines and the newly-released final guidelines. Finally, this iBrief critically analyzes the final guidelines as they pertain to gene patents.⁸

Background: The Gene Patent Controversy

¶ 5 The controversy over gene patents emerged when Dr. Craig Venter, CEO of Celera Genomics, sent 20,000 gene sequences to the PTO, claiming patents to the sequences and to procedures that would be used to diagnose disorders with the genes. The PTO denied these applications, suggesting that simply finding DNA sequences and claiming their use as a research reagent was not sufficient for a patent. The PTO thus indicated that it required the inventor of a gene to show a level of utility beyond the gene's use as a research tool.

¶ 6 The standard of utility wielded by the PTO, however, has been far from clear. For example, the PTO recently issued a patent to Human Genome Sciences (HGS) in Rockville, Maryland claiming the gene for CCR5, a receptor that binds protein molecules termed "chemokines" at the surface of CD4+ leukocyte cells.⁹ HGS was issued a patent on the CCR5 gene, its protein, and fragments of DNA for locating the gene. But the patent does not disclose the function of the particular claimed protein. The specification discloses the chemical building blocks that made up the gene and its protein, information that was deduced by homology studies between the new CCR5 and known chemokine receptors and G-proteins. The specification also discloses a wide variety of uses for known chemokines, including inflammation, immune reactions, allergies, and arthritis.¹⁰ The specification further discloses a number of biological functions for known G-proteins, including dopamine receptors, protein kinases, and adenylate cyclase.¹¹ Yet, significantly, the specification does not disclose the function of this particular protein.

¶ 7 Such function was later published in 1996 by independent researchers at the National Institutes of Health (NIH), who reported that CCR5 works as a co-receptor in binding HIV.¹² Having performed the necessary research to identify the co-receptor's function, NIH contended that it was their group, rather than HGS, that made the "discovery."¹³ But HGS was issued the patent, despite not being the first group to identify the gene's role in HIV and not doing any of the research to show that role. The net effect, of course, is that HGS can now exclude other groups, including the NIH group, from using the gene in HIV treatment.

¶ 8 As the example of the CCR5 patent indicates, the PTO's standard for gene utility has been unevenly applied. In 1995, the PTO established "Utility Examination Guidelines" for training its examiners to review biotechnology patent applications in an attempt to bring clarity to the standard.¹⁴ Under the 1995 standard, an invention that had a "credible" utility could be patented. If not credible, then the invention could still be patented if it had a "well-established" utility. Under this standard, examiners began to more freely issue patents that covered genetic material.¹⁵ But this practice was criticized extensively, and in 1999 the PTO issued its Revised Interim Utility Guidelines¹⁶ with the intent of tightening the standard and restricting the issuance of gene patents.¹⁷

The Rise of 2001 Utility Examination Guidelines

¶ 9 The key issue in patenting genetic material has always revolved around the utility of the claimed genes and fragments. The 1999 Revised Interim Utility Guidelines established a heightened standard for utility, at least under the "credible utility" test. Under the 1999 standard, "credible utility" was not sufficient without an additional showing of "specific" and "substantial" utility. The policy of this heightened standard was based on the PTO's adoption of the US Supreme Court's position in *Brenner v. Manson* that a patent is not given as a reward for the search of an invention's utility but, rather, a reward for actually discovering that utility.¹⁸

¶ 10 Accordingly, the 1999 Revised Interim Utility Guidelines retained the structure of two different tests for utility, either of which, if satisfied, was sufficient for a showing of statutory utility. The first test under the 1999 guidelines was, like the 1995 standards, whether or not the invention had a "well-established utility."¹⁹ Yet the 1999 standards differed from the 1995 standards in that a "credible" utility was no longer sufficient by itself. If the invention did not have a well-established utility, the second test was applied, namely whether the invention had a utility that was "specific," "substantial," and "credible."²⁰

¶ 11 In response to comments, the PTO issued its final version of the utility guidelines in January 2001.²¹ The 2001 Utility Examination Guidelines follow the 1999 Revised Interim Utility Guidelines in adopting the structure of two alternative tests for showing utility. These two tests are the "specific, substantial, and credible" utility test and the "well-established utility" test.

The "Specific, Substantial, and Credible" Utility Test

¶ 12 The definitions of "specific, substantial, and credible" under the new guidelines are the same as those described in the 1999 Revised Interim Utility Guidelines' Training Materials issued to patent examiners. Under both the 1999 and 2001 guidelines, a utility is "specific" when it is particular to the subject matter claimed.²² For example, a fragment of nucleic acid that has a claimed utility as a gene probe or chromosome marker would not pass the "specific utility" hurdle without also identifying the particular gene or chromosome target.²³ Unless it discloses its target, the fragment is no more useful than any random fragment of nucleic acid.²⁴ Similarly, stating that a gene is useful as "a diagnostic" is ordinarily not sufficiently specific without also identifying the condition that is diagnosed.²⁵

¶ 13 In addition, both the 1999 and 2001 guidelines establish that a "substantial utility" is one that defines a "real world" use.²⁶ The PTO's test for determining "real world" use is whether further research is required to identify an immediate benefit.²⁷ For example, a nucleic acid does not have a substantial utility if it is only useful for studying its own properties. By contrast, a nucleic acid used to identify genes that have a known link to a specific disease would satisfy the "real world" use requirement, even if a cure for the disease does not become available for many years. The "real world" requirement is designed to prevent the granting of patents if further research must be performed before the genetic material can be used for a specific purpose or benefit.²⁸ This rule derives from the US Supreme Court's position in *Brenner* that a chemical or a chemical process is not sufficiently useful if its only use is as an object of scientific research.²⁹

¶ 14 The 2001 guidelines also adopt the PTO's past position that any asserted utility must be a "credible" utility, a standard determined by whether a person with ordinary skill in the art would accept that the invention "is currently available for such use."³⁰ Such a standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion.³¹ For instance, a nucleic acid used as a probe for a particular gene would likely satisfy the credibility requirement because nucleic acids are commonly used as probes.³²

The "Well-Established Utility" Test

¶ 15 While the 2001 Utility Examination Guidelines essentially adopt the "specific, substantial, and credible" test from the 1999 Revised Interim Utility Guidelines, the same is not entirely true for the "well-established utility" test.³³ Importantly, the "well-established utility" test has now been expanded to incorporate the "specific, substantial, and credible" standard. In other words, although the new guidelines theoretically still employ two separate, alternative

tests, in reality an applicant seeking to qualify under just the "well-established utility" test must now satisfy the "specific, substantial, and credible" standard as well.

¶ 16 Under the 1999 guidelines, gene fragments were evaluated based on the "specific, substantial, and credible" test because, as noted by Stephan Kunin of the PTO, "at the present time, there is no well-established utility for these fragments."³⁴ The distinction between a "well-established utility" and a utility that is not "well-established" was ambiguous under the 1999 guidelines. This ambiguity is seen in the PTO's suggestion that a protein that limits the production of a second protein of well-known identity was sufficiently "well-established,"³⁵ while a protein used to identify a second protein of not-so-well known identity was not sufficiently "well-established."³⁶ The critical feature apparently was not the new protein's function as a locator, but whether the located product had been known for a while.

¶ 17 Despite the PTO's position that gene fragments are not patentable if useful only as probes, the 1999 version did not entirely foreclose the possibility that fragments might, over time, develop the status of possessing "well-established utility" and thereby qualify as patentable inventions. This possibility is foreclosed, however, because the 2001 guidelines formally import the "specific, substantial, and credible" test into the test for a "well-established utility."³⁷ Thus, under the 2001 guidelines, any patent claim to a gene fragment must satisfy the "specific, substantial, and credible" test in order to establish utility under any circumstances.

Ambiguities in the New Guidelines

¶ 18 As described above, there is an essential tension between those who believe that genes (and gene fragments) are patentable if they have research utility, and those who argue that genes are not patentable until their final physiological function is discovered. This is not just a technical issue; it is also a policy issue. If the PTO allows any sort of utility to meet the standard for patentability, it could result in an influx of gene patents that would ultimately stifle genetic research. On the other hand, setting the utility hurdle too high could create insufficient incentive for scientists who rely on patents to create funding for further research.

¶ 19 The new guidelines attempt to resolve this tension by requiring that any application for a gene patent show that the gene's utility is "specific, substantial, and credible." The PTO's heightened utility policy for gene patents aims to ensure that genes can be patented, but not before their physiological use is discovered. Despite the worthiness of this compromise, however, the framework chosen by the PTO is not airtight, leaving a number of questions unresolved.

Why Can't ESTs Become "Well-Established" as Probes?

¶ 20 The new guidelines adopt the position that the genetic sequences known as ESTs are not of sufficiently "well-established" utility if they are only useful as probes, chromosome markers, or other research tools. Under the new guidelines, ESTs can never have a well-established utility because, by definition, they do not satisfy the specific and substantial utility tests.

¶ 21 Yet, the conceptual difference between a "well-established" utility and a not "well-established" utility under the 1999 guidelines was more a matter of how long the use has been known than the relative level of public benefit derived from the use.³⁸ ESTs are used as tools in genetic research because they bind to and identify longer pieces of DNA,³⁹ a process that has become important to the biotechnology industry over the past few years as a primary means of identifying and characterizing DNA. ESTs can be used as probes whether they ultimately find a target or not, unlike chemicals whose only utility depends upon the actual exhibition of biological activity.⁴⁰ Furthermore, a probe that successfully locates a gene that codes for a specific protein has performed its task, regardless of how the protein functions in a living system.

¶ 22 Accordingly, the PTO has acknowledged that ESTs can pass as "credible" inventions because "those skilled in the art recognize that [ESTs] could potentially have utility in a variety of credible contexts, e.g., as probes, chromosome markers, diagnostic tools, and forensic tools."⁴¹ Why this recognized use of ESTs to locate genes could not eventually lead to a finding of well-established utility is not immediately clear under the new guidelines.

Why are EST Probes Not of "Specific" Utility?

¶ 23 Another problem in the new guidelines is the requirement of specific utility. When evaluating an asserted utility, the PTO will ask whether that utility is common to any member of a general class.⁴² If so, then the asserted utility is not "specific" enough, as may be seen where the asserted utility of a newly discovered protein is its use as a source of amino acid nutrients. The new guidelines, however, do not articulate why inventions useful mainly as discovery tools (for instance using ESTs as gene probes) are not considered to have "specific utility."⁴³

¶ 24 Indeed, while it is true that any gene can be fashioned into a probe, not all probes can successfully locate any given gene. A probe is, by its definition, specific to a limited number of genes. Thus, the PTO's position that the use of ESTs as probes is not of "specific utility" appears

inconsistent with its rationale.

Why are EST Probes Not of Substantial Utility?

¶ 25 Finally, the new guidelines do not appear to take into account case law governing the standard for substantial utility. One argument the PTO uses against allowing probes to be patented is that an invention must have more substantial utility than merely for use in further experiment upon itself. This argument was enunciated in *Brenner v. Manson* and re-stated in subsequent federal circuit cases. The *Brenner* Court stated emphatically that an invention was not patentable if its only use was that it might be an "object of scientific research."⁴⁴ The Court of Customs and Patent Appeals applied the language from *Brenner* and disallowed patents that claimed compounds used in intermediate processes of making final compounds where the utility of the final compounds was not known.⁴⁵ By implementing this language in the 2001 Guidelines, the PTO significantly eliminates applications where the claimed utility is only that the invention can be used for further study of its own utility (presumably such further study would be used to determine any other uses of the invention).

¶ 26 Yet the PTO has not recognized that patents have been granted for products with anti-tumor effectiveness demonstrated only in laboratory animals--where the animals themselves were mere objects of scientific research.⁴⁶ Other cases have similarly found sufficient utility even where the invention could not readily be used by anyone.⁴⁷ Indeed, many compounds demonstrated only by animal testing to be useful are not immediately beneficial to humans as espoused by the guidelines.⁴⁸ Therapeutics and other inventions with uses established solely through animal studies are patentable because they will "marshal resources and direct the expenditure of effort to further in vivo testing of the most potent compounds, thereby providing an immediate benefit to the public."⁴⁹ This effect--the inspiring of in vitro testing--is precisely one of the effects of allowing a patent on an EST probe.

¶ 27 Furthermore, a long held pre-*Brenner* case law standard supports judging the utility of an invention on whether or not the public derives a benefit from the invention, regardless of how slight the benefit.⁵⁰ DNA fragments are widely used as probes, markers, and diagnostics in the biotechnology industry, playing key roles in drug and disease discovery processes. Indeed, these fragments enable researchers to find the genes associated with physiological functions. The discovery of such functions readily benefits the public. Accordingly, such tools could satisfy the pre-*Brenner* case law standard.

What Utility Should an Applicant Disclose?

¶ 28 Despite these ambiguities in the tighter standard for EST patents, an applicant can successfully gain a patent on an EST if he can satisfy the "specific, substantial, and credible utility" test. This test was derived from federal circuit precedent⁵¹ with the intent to ensure that all patents have "real world" utility⁵² and to limit the extension of patents involving molecules with utility that is applicable to any member of that molecule's class.⁵³ Accordingly, an applicant for a gene fragment patent must disclose more than the DNA sequence of the fragment, more than the sequence of the complete gene, and more than the size of the protein product that comes from the gene.

¶ 29 Such additional information should probably include⁵⁴ a particular biological reaction involving the protein product,⁵⁵ or it might include a disease or other cellular mechanism to which the complete gene is correlated.⁵⁶ Alternatively, an EST may be patentable if its gene is shown to be homologous to a gene in another species.⁵⁷ Furthermore, even if the gene product itself is not known, a claimed DNA fragment that "hybridizes near a disease-associated gene or has a gene-regulating activity" may have sufficient utility.⁵⁸ However, if the sole utility stated or implied for the claimed EST is for use in locating a full gene, protein, or some other molecular target, utility will likely not be sufficient absent knowledge of the physiological process of the target molecule.⁵⁹

¶ 30 But the decision of what utility to disclose is complicated in at least three ways. First, no training materials have yet been published with the 2001 Utility Examination Guidelines. Presumably, the 1999 Revised Interim Utility Guidelines' Training Materials will be used by patent examiners until new materials are issued, but whether revised training materials will differ from the existing training materials is not yet clear.

¶ 31 Second, applicants should be aware that the 1999 Training Materials and other writings by the PTO have been interpreted to leave significant discretion to the PTO to evaluate utility. One of the PTO's primary threshold questions is, of course, whether or not the asserted utility requires "additional knowledge" before the invention can be practiced. Under this principle, at least one member of the PTO has interpreted the new guidelines to authorize the rejection of an EST patent for lacking a wide range of information, including the following:⁶⁰

- the sequence of the corresponding complete mRNA sequence, protein coding sequence or genomic sequence;
- whether there are sequence polymorphisms linked to the corresponding genomic location;
- the function of the protein encoded by the corresponding mRNA;

- the phenotype of a mutation in the corresponding gene;
- the tissue distribution of the corresponding mRNA and tissue-specific expression levels;
- the map location of its corresponding genomic sequence.

¶ 32 Any of the above could be very difficult to determine for a given EST. Yet, not knowing the complete mRNA sequence of the EST certainly does not preclude the inventor from identifying the protein product, nor does it prevent the inventor from discovering the physiological role of the protein.

¶ 33 Third, the new guidelines do not clearly articulate, nor do the 1999 Training Materials suggest, a standard for how closely an EST must correlate with a particular physiological condition. In other words, the line between speculation and genuine correlation is not entirely clear. As noted previously, the CCR5 patent discloses the chemical building blocks of the new gene and protein, yet the disclosure does not demonstrate a particular function for the particular protein. Rather, the specification assumes by homology studies that the new CCR5 is, at first, a G-protein and, second, that it will bind chemokines. If such is the activity, then a variety of diseases would be implicated, including cancer, blood disorders, allergies, and arthritis.

¶ 34 The PTO was urged during the last comment period to include an anti-speculation standard in the Guidelines that would limit gene or gene fragment patent coverage to the specific uses actually disclosed in the application.⁶¹ The PTO refused to adopt such a standard, noting that the concept is inconsistent with the patent statute's provision that only one utility need be shown to warrant a patent for an invention.⁶² Thus, in adhering to the integrity of US patent law, the PTO has shifted the question back to Congress for a standard as to speculative and non-speculative utilities. Until that standard is clarified, patent applicants will likely have considerable leeway in proposing possible utilities of genes and proteins. Given that the incentive for inventors is to speculate widely as to the utility of claimed genes, fragments, and proteins, the increased number of patent applications for genetic material could force the PTO to clarify its position.

Conclusion

¶ 35 Although the debate over whether genetic material should be patentable may not be resolved any time soon, the 2001 Utility Examination Guidelines tend to reinforce the PTO's disfavor of granting patents for genes and fragments of unknown utility. Nevertheless, the lack

of clarity and uniformity in the new guidelines suggest that, while the PTO's stricter utility standards may serve its policy goal of limiting (but not eliminating) gene patents, loopholes exist with respect to technically demonstrating the utility of genetic materials. If the PTO issues new training materials, these may help resolve questions as to what evidence inventors should disclose when applying for gene patents. For now, applicants should consider disclosing a particular physiological process or clinical condition that may be implicated by the gene's protein product. Such information will likely establish sufficient "specific, substantial, and credible" utility for not only the protein, but also for its corresponding gene and the EST used to locate the gene.

Footnotes

1. Utility Examination Guidelines, 66 Fed. Reg. 1092 (2001), *available at* http://www.access.gpo.gov/su_docs/aces/aces140.html (last visited Feb. 9, 2001).

2. *See* The Patent Act, 35 U.S.C. §101 (2000), *available at* <http://www4.law.cornell.edu/uscode/35/101.html> (last visited Feb. 9, 2001) (a patent may only be issued for an invention if that invention is "useful").

3. *See* Revised Interim Utility Examination Guidelines; Request for Comments, 64 Fed. Reg. 71440 (1999), *available at* http://www.access.gpo.gov/su_docs/aces/aces140.html (last visited Feb. 9, 2001) [hereinafter *Revised Interim Utility Guidelines*].

4. *See* Utility Examination Guidelines, 66 Fed. Reg. at 1095 (Comment 13).

5. *See* Utility Examination Guidelines, 66 Fed. Reg. at 1094 (Comment 5).

6. Gene fragments are pieces of DNA that are smaller than a complete gene.

7. *See* Utility Examination Guidelines, 66 Fed. Reg. at 1094 (Comment 9) ("The disclosure of a DNA sequence has inherent value... possible uses for the DNA appear endless").

8. The PTO has addressed the patentability of genes and gene fragments through the written description and enablement requirements of the US patent law. *See* 35 U.S.C. §112 (2000), *available at* <http://www4.law.cornell.edu/uscode/35/112.html> (last visited Feb. 9, 2001).

9. U.S. Patent No. 6,025,154 (Feb. 2000), *available at* <http://164.195.100.11/netacgi/npParser?Sect1=PTO1&Sect2=HITOFF&d=PALL&p=1&u=/netahtml/srchnum.htm&r=1&f=G&l=50&s1='6,025,154'.WKU.&OS=PN/6,025,154&RS=PN/6,025,154> (last visited Feb. 9, 2001).

10. *See id.*

11. *See id.*

12. *See* Christopher C. Broder et al., *HIV-1 Entry Co-Factor: Functional DNA Cloning of a Seven-Transmembrane, G Protein-Coupled Receptor*, *SCIENCE*, May 10 1996, at 872.

13. J. Madeline Nash, *Who Owns The Genome? Battle Pending*, CNN.com, at <http://cgi.cnn.com/ALLPOLITICS/time/2000/04/10/genome.html> (April 10, 2000) (noting that the NIH scientists who nailed down the link between CCR5 and AIDS have questioned why HGS should profit from their hard work).

14. *See* Utility Examination Guidelines, 60 Fed. Reg. 36263, 36264 (1995), *available at* http://www.access.gpo.gov/su_docs/aces/aces140.html (last visited Feb. 9, 2001).

15. DNA is genetic material and is made of small molecules called "nucleotides" that are bonded together in a long chain. A DNA sequence refers to the linear sequence of its nucleotides and is determined by well-documented analyses. ESTs are pieces of DNA that have been randomly isolated and sequenced. Usually, ESTs are isolated well before their parent gene is discovered and before the encoded protein is discovered.

16. *See* Stephen G. Kunin, *Written Description Guidelines and Utility Guidelines*, 82 PAT. & TRADEMARK OFF. SOC'Y 77, 96-97 (Feb. 2000) (stating that the Revised Interim Utility Guidelines address more pointedly the issues of specific and substantial utility, while retaining the same standard for credible utility as found in the 1995 guidelines).

17. Revised Interim Utility Guidelines, 64 Fed. Reg. at 71440.

18. *See* *Brenner v. Manson*, 383 U.S. 519, 536 (1966) (stating that "a patent is not a hunting license. It is not a reward for the search but compensation for its successful conclusion").

[19.](#) See Utility Examination Guidelines, 60 Fed. Reg. at 36264; see also Revised Interim Utility Guidelines, 64 Fed. Reg. at 71440.

[20.](#) See Revised Interim Utility Guidelines, 64 Fed. Reg. at 71441; see also *Brenner*, 383 U.S. at 534-35 (1966) (denying a patent application for a steroid compound for failure to state a substantial utility). But see *In re Kirk*, 153 U.S.P.Q. 266, 266 (C.C.P.A. 1967) (Rich, J., dissenting) (arguing that the *Brenner* utility standard is mere dicta and was not intended to be applied "unwittingly by future lower court expansion of its dicta").

[21.](#) Utility Examination Guidelines, 66 Fed. Reg. at 1092.

[22.](#) See Training Materials at p. 5.

[23.](#) *Id.*

[24.](#) *Id.*

[25.](#) See Training Materials at p. 6.

[26.](#) See Training Materials at p. 6 (stating that a therapeutic method of treating a known disease and methods of identifying compounds that correlate with known diseases pass the utility hurdle).

[27.](#) See Kunin, *supra* note 16, at 98.

[28.](#) *Id.*

[29.](#) See *Brenner*, 383 U.S. at 535.

[30.](#) See Training Materials at p. 5.

[31.](#) See *id.*

[32.](#) See Kunin, *supra* note 16, at 98.

[33.](#) However, the PTO has noted that proteins of well-established utility also happen to satisfy the specific, substantial, and credible test. See, e.g., Training Materials at Example 8 (tyrosine kinase inhibitor not only has a well-established utility but also passes the specific, substantial, and credible test).

[34.](#) See Kunin, *supra* note 16, at 98.

[35.](#) See Training Materials at Example 8 (stating that a newly discovered compound that inhibits enzyme Z is of sufficient "well-established" utility because enzyme Z is a tyrosine kinase, a well-known enzyme).

[36.](#) See, e.g., Training Materials at Example 5 (stating that a protein useful only for locating protein Y is not of sufficiently well-established utility because protein Y is known to be in blood but nothing more is known about it).

[37.](#) Compare Utility Examination Guidelines, 66 Fed. Reg. at 1098 ("an invention has a well-established utility (1) if a person of ordinary skill in the art would immediately appreciate why it is useful . . . and (2) the utility is specific, substantial, and credible") with Revised Interim Utility Guidelines, 64 Fed. Reg. at 71441 ("an invention has a well-established utility if a person of ordinary skill in the art would immediately appreciate why the invention is useful").

[38.](#) Compare Training Materials at Example 8 (stating that a newly discovered compound that inhibits enzyme Z is of sufficient "well-established" utility because enzyme Z is a tyrosine kinase, a well-known enzyme) with *id.* at Example 5 (stating that a protein useful only for locating protein Y is not of sufficiently well-established utility because protein Y is known to be in blood but nothing more is known about it).

[39.](#) The identification process works simply, as the probe emits light with a distinguishable wavelength after it binds to a target.

[40.](#) Such chemicals were rejected by the court in *In re Kirk*.

[41.](#) See Training Materials at p. 5.

[42.](#) See Training Materials at p. 7 (stating that any DNA molecule could be used as fuel, but the statute is not intended to allow a patent for this non-specific use).

[43.](#) See, e.g., Training Materials at Example 5 (claiming that a protein was not substantially useful where its main utility was for locating a second protein of unknown functionality).

[44.](#) *Brenner*, 383 U.S. at 535.

[45.](#) See *In re Joly*, 376 F.2d 906, 908 (C.C.P.A. 1967) (denying application for patent covering intermediate compound in producing steroid); see also *In re Kirk*, 376 F.2d at 936 (rejecting vague claims referring only to "biological activity" as the utility).

[46.](#) *In re Kirk*, 376 F.2d at 948 (Rich, J., dissenting).

[47.](#) See *Nelson v. Bowler* 206 U.S.P.Q. 881, 881 (C.C.P.A. 1980) (upholding showing of "pharmaceutical activity" in a lab animal to be sufficiently useful despite not demonstrating specific therapeutic application nor identifying a human application); see also *Cross v. Lizuka*, 753 F.2d 1040, 1040 (Fed.Cir. 1985) (stating that a claim to an invention inhibiting thromboxane synthetase is sufficiently useful based solely on in vitro tests).

[48.](#) See Training Materials at Example 9.

[49.](#) *Cross*, 753 F.2d at 1051.

[50.](#) See *In re Nelson*, 280 F.2d 172, 178-180 (C.C.P.A. 1960) (stating that "however slight the advantage which the public have received from the inventor, it offers a sufficient reason for his compensation") (citing ROBINSON ON PATENTS (1890)); see also *Lowell v. Lewis*, 1 Mason 182 (Fed. Case. No. 8568, 1817) (claiming "if it be more or less useful is... of no importance to the public. If it be not extensively useful it will silently sink into contempt and disregard").

[51.](#) See Kunin, *supra* note 16, at 77 (arguing that new guidelines were written in response to comments asserting that practice of granting EST patents was contrary to case law).

[52.](#) "Real world" derives from US Supreme Court language in *Brenner v. Manson*. See *id.* at 90 (stating that "real world" utility has come to imply an association with a disease or physiological process or condition).

[53.](#) See Training Materials at Example 9 (claiming that the use of a DNA fragment as a probe is not sufficiently useful because the use as a probe is generally applicable to all DNA fragments).

[54.](#) The recommendations of this section are based on the "Response to Comments" accompanying the 2001 *Guidelines*, the 1999 *Training Materials*, and other writings from the PTO.

[55.](#) See Training Materials at Example 8 (stating that a protein kinase performs a well-known role in known biological reactions; its gene could be sufficiently useful to be patented and,

therefore, a gene fragment used to locate said gene would presumably also be sufficiently useful).

[56.](#) *See, e.g.*, Training Materials at Example 9 (stating that an EST probe is not substantially useful because the cellular mechanism of the corresponding protein is not disclosed); *see also* Training Materials at Example 5 (stating that a newly discovered protein might be sufficiently useful if it were correlated with heart disease or some other physiological condition).

[57.](#) *See* Utility Examination Guidelines, 66 Fed. Reg. at 1096 (arguing that a reasonable correlation between the sequence of a newly found fragment or complete gene with the sequence of a known gene from a different species establishes homology between the two genes, possibly also establishing the utility of the new gene).

[58.](#) Utility Examination Guidelines, 66 Fed. Reg. at 1095.

[59.](#) *See* Training Materials at Example 5 (stating that a protein useful in locating a second protein is not sufficiently useful absent a showing of the physiological significance of the second protein).

[60.](#) *See* Kunin, *supra* note 16, at 98.

[61.](#) *See* Utility Examination Guidelines, 66 Fed. Reg. at 1095 (Comment 11).

[62.](#) *See id.*