04-1465
(Application No. 09/619,643)

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

In re DANE K. FISHER and RAGHUNATH V. LALGUDI

APPEAL FROM THE UNITED STATES PATENT AND TRADEMARK OFFICE, BOARD OF PATENT APPEALS AND INTERFERENCES, APPEAL NO. 2002-2046

BRIEF OF GENENTECH, INC. AS AMICUS CURIAE SUPPORTING AFFIRMANCE AND SUPPORTING THE UNITED STATES PATENT AND TRADEMARK OFFICE

Jeffrey P. Kushan
Kathi A. Cover
David L. Fitzgerald
Sidley Austin Brown & Wood, LLP
1501 K Street, N.W.
Washington, D.C. 20005
202-736-8000

Attorneys for Genentech, Inc.

CERTIFICATE OF INTEREST

Counsel for *Amicus Curiae* Genentech, Inc., certifies the following:

1. The full name of the *amicus* that we represent is:

GENENTECH, INC.

2. The name of the real party in interest that we represent is:

GENENTECH, INC.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the *amicus curiae* that we represent are:

ROCHE HOLDINGS INC. owns approximately 56 percent of the issued common stock of GENENTECH, INC.; GENENTECH, INC. remains an independent, publicly traded company.

4. The names of all law firms and the partners or associates that appear for the *amicus* now or are expected to appear in this Court are:

Jeffrey P. Kushan
Kathi A. Cover
David L. Fitzgerald
SIDLEY AUSTIN BROWN AND WOOD LLP

12-15-04.
Date

Kathi A. Cover

TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

STATUTES & RULES

OTHER AUTHORITIES

STATEMENT OF GENENTECH'S INTEREST AND AUTHORITY FOR FILING

Genentech, Inc., the world's first biotechnology company, uses human genetic information to identify and develop new pharmaceutical products to address significant unmet medical needs. The more than 900 United States patents granted to Genentech cover not only its products, but also technologies relevant to the commercial-scale production, isolation, purification and formulation of the therapeutic proteins that are often the central component of these products. Patent protection enables Genentech to recoup its significant investments in research and development – more than $700 million each year – and to deliver effective returns to its shareholders. Genentech also respects the legitimate intellectual property rights of others, paying millions of dollars annually to other intellectual property owners to license patents and other intellectual property rights.

This Court's pronouncements on the patentability requirements for gene sequences are critically important to Genentech's business and to the biotechnology industry as a whole. As both a patent holder and a consumer of information produced by others, Genentech presents a balanced industry perspective regarding the implications of this singularly important issue.

The Parties have consented to Genentech's filing of this brief, which Genentech respectfully submits pursuant to Federal Rule of Appellate Procedure 29(a).

ARGUMENT

In Genentech's experience, two factors are essential to creating a patent environment that fosters innovation in the biotechnology sector.

First, the environment must promote the rapid and fluid flow of information concerning the results of basic research. This information flow has proven to be particularly important with respect to information obtained by sequencing human genetic material. Genentech often pays significant fees to access private databases of human genomic information to supplement the information it generates or obtains from publicly accessible sources, such as from the Human Genome project.

The other essential requirement is a patent system that rewards the biotechnology innovator that has delivered – through its patent disclosure – an invention with present and concrete value. In human genomics particularly, this goal is served by requiring that patents be awarded only to the innovator who delivers an invention with a definite, specific, and currently available utility, and that patent rights be commensurate with the inventor's contribution.

Fisher and Lalgudi ("Fisher") dismiss the statutory utility requirement as a nominal formality of the patent system, when in fact it plays an important role in

regulating which applicants should and do receive patents. Fisher's opinion may stem from the fact that for inventions in fields of technology having little scientific uncertainty, deficiencies under 35 U.S.C. § 101 arise infrequently. In the field of genomics, however, this is not the case.

I. THE ROLE OF THE STATUTORY UTILITY REQUIREMENT IN THE FIELD OF GENOMICS

To understand the effect of utility standards on the biotechnology industry, it is essential to appreciate the impact of the incredible volume of information about the human genome that entered the public domain during the 1990s. This information was generated through the coordinated efforts of hundreds of researchers under the leadership of the Human Genome Project.[1]

The availability of "raw" genomic information, in both public and private databases, fueled a period of intense research and commercial development unparalleled in the biotechnology sector. It also triggered a flood of patent applications seeking to identify and stake claims to commercially significant genes. The commercial pressure to file applications placed strains on the patent system and on the industry.

---

[1] The Human Genome Project was an "international 13-year effort, formally begun in October 1990 and completed in 2003, to discover all the estimated 20,000-25,000 human genes and make them accessible for further biological study. Another project goal was to determine the complete sequence of the 3 billion DNA subunits (bases in the human genome)." *See* http://www.ornl.gov/sci/techresources/Human_Genome/project/hgp.shtml.

Some applicants elected to pursue patents before they had completed even the most basic investigations needed to establish what a gene did and how it could be exploited in a "useful" manner.[2] Often, the patent applications were filed with nothing more than a computer-generated analysis of all or part of the sequence of a gene.[3] Other applicants refrained from filing applications until they had performed enough experimentation to reasonably characterize the biological functions, roles or activities of the genes and their expression products.[4] Genentech adopted the latter approach because it came to appreciate the magnitude of the scientific

---

[2] For example, in June of 1991, the NIH announced that it had filed patent applications for more than three hundred DNA sequences having no known function. To many in the industry, "the very notion of blindly patenting sequences without knowledge of what they do was outrageous. . . . This conduct could only be seen as a preemptive financial claim on a truly meaningful discovery someone else might yet make." James D. Watson, DNA: THE SECRET OF LIFE 180 (Alfred A. Knopf 2004). Amid significant public outrage and internal conflict, NIH eventually withdrew its applications.

[3] *See, e.g.*, Julian David Forman, *A Timing Perspective on the Utility Requirement In Biotechnology Patent Applications*, 12 Alb. L.J. Sci. & Tech. 647 (2002). EST patent applications "typically involve the use of high-throughput DNA sequencing[, which] is an automated process that produces DNA sequences at a relatively rapid rate. . . . Producing DNA sequences in this manner does not seem to require a great deal of ingenuity on the part of researchers . . . ." *Id.* at 660.

[4] "'The task of identifying the biological function of a gene is by far the most important step in terms of both its difficulty and its social benefit, one of the primary objectives of the United States patent system should be to ensure that this step 'merits the most incentive and protection.'" Donald J. Zuhn, Jr., *DNA Patentability: Shutting the Door to the Utility Requirement*, 34 J. Marshall L. Rev. 973, 980 (Summer 2001) (quoting the president of the Human Genome Organization) (citations omitted).

uncertainty regarding the role or biological functions of a gene for which only the sequence is known. This uncertainty, in turn, creates significant questions about potential uses of the gene or its expression product.[5]

Genomic research thus presents unique circumstances for the utility requirement that bear careful consideration. In most technologies, a practical application for an invention can be easily and definitively identified in the patent disclosure, often simply by describing the characteristics of the invention. In the field of genomics, however, a person of skill in the art usually cannot ascertain the specific use or application of a newly sequenced gene until more research is done. Without adequate information regarding the biological function or role of a gene, it can be difficult to ascertain how to use the gene in a way that delivers "real world" value to the public – the question central to whether an invention is "useful" within the meaning of 35 U.S.C. § 101.

Within the context of genomics research, the bounds of the utility requirement are being tested in ways never before considered. This case presents the Court with its first opportunity to review the standards set by the Patent and

[5] As a matter of commercial prudence, Genentech filed several "EST" patent applications, similar to those filed by NIH, at the beginning of the genomics era. Ultimately, Genentech did not pursue any of those applications.

Trademark Office in its Utility Examination Guidelines[6] – which it has applied to thousands of applications since 1999 – and, more fundamentally, to interpret the statutory requirement of usefulness as applied to gene sequences.

Clarity regarding the utility requirement for inventions arising from genomics research is essential. The cost and business disruption of litigating patents of questionable validity is tremendous.[7] These costs and disruptions would be multiplied if this Court adopts the standard proposed by Fisher, under which innumerable open-ended claims based on ESTs would be granted.

The standard that Fisher proposes would also give rise to a perverse economic equation. Under its perspective, patents will be granted to applicants who make only insubstantial contributions toward identifying potential new products. A different party must then expend significant amounts of money and effort to determine why a sequence or its expression is "useful" and then how to commercially exploit this additional finding. In this equation, the "innovators" who discover an invention with "real world" value nonetheless will be beholden to

---

[6] The Utility Examination Guidelines were first promulgated in 1995. *See* 60 Fed. Reg. 36263-02 (1995). They were subsequently revised and issued in 2001. *See* 66 Fed. Reg. 1092-02 (2001). The PTO has also published training materials to further illustrate how it is applying these guidelines.

[7] One commentator has estimated that litigation costs in biotech patent cases range between $1 million and $10 million for each party. John P. Walsh et al., Effects of Research Tool Patents and Licensing on Biomedical Innovation, PATENTS IN THE KNOWLEDGE-BASED ECONOMY 285, 315 (The Nat'l Academies Press 2003).

the owners of those patents. And since any one full-length gene might be subject to rights derived from several independent EST patents, a drug developer might have to obtain licenses from an array of patent owners, each owning one or more patents, and each imposing its own terms and conditions. As one commentator has observed, "[t]he large royalties demanded by gene-finding monopolies tip the economic balance against drug development; cloning a drug target [as might be covered by a claim to a DNA sequence] is at most 1 percent of the way to an approved drug."[8] Patents issued on inventions that are yet to be made are harmful to the biotechnology industry and the public, because they effectively extinguish commercial interest in developing new drugs or diagnostic products based on genomic information.

II. GENENTECH ENDORSES THE PATENT OFFICE'S UTILITY GUIDELINES AND THEIR APPLICATION TO REJECT FISHER'S CLAIMS

The requirement that a claimed invention have a specific and substantial credible utility, as described in the 2001 Utility Examination Guidelines, is well-grounded in Supreme Court and Federal Circuit precedent. Application of this precedent compels affirmance of the rejection of Fisher's claims.

[8] Watson, *supra*, at 183.

A. Supreme Court and Federal Circuit precedent require an inventor to identify a specific and substantial credible utility for a claimed invention.

The Guidelines are based on the seminal decision of *Brenner v. Manson*, 383 U.S. 519 (1966), where Justice Fortas stated that a patent is "not a hunting license" nor "a reward for the search, but the compensation for its successful conclusion." *Id.* at 536. The Court ruled that

> [t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with *substantial utility*. Unless and until a process is refined and developed to this point – *where 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.

Id. at 534-35 (emphases added).

The Supreme Court's conclusion applies with particular force to claims for gene sequences. An open-ended claim to any nucleic acid comprising a particular nucleotide sequence allows the patent holder to gain control over any use of every gene containing that sequence, every recombinant protein made by expressing those genes, and in practical terms, every potential drug target within that group of proteins. An open-ended claim thus allows an applicant "to engross what may prove to be a broad field." *Id.* at 535. To justify such a reward, the Guidelines adopt *Brenner's* standard, requiring that a claimed invention have a *specific* and *substantial* utility in *currently available* form.

An important component of the Court's holding in *Brenner* was that an asserted utility for an invention must be specific to what is being claimed. The Court rejected as insufficient the patent applicant's general assertion that its "steroidal" compounds would find a use in the conduct of further research. *Id.* at 531-32 (rejecting assertion that claimed compound was likely to have the same utility as a similar compound of the same class). This is precisely the type of "generalized" (non-specific) utility cited by Fisher for its ESTs. Courts have followed *Brenner's* mandate concerning the requirement for specificity in an asserted utility, rejecting putative utilities that are described in terms "so general as to be meaningless." *See, e.g., In re Kirk*, 376 F.2d 936, 942 (C.C.P.A. 1967) (asserting that compound was useful because it had "biological activity"); *In re Brana*, 51 F.3d 1560, 1565 (Fed. Cir. 1995) (asserting utility based on "antitumor activity").[9]

The requirement for specificity is particularly important with respect to claims to genes. As a general matter, it is rarely scientifically plausible to assert that a biological function of a particular sequence can be presumed exclusively because a similar function was demonstrated previously for a different gene (or

[9] The court in *Brana* did find, however, sufficiently specific utility based on the additional description by the applicant of specific tumor models and data comparing the claimed compound to known therapeutic agents having defined activities against the same tumor models.

small number of genes) bearing some structural similarity to the gene or gene fragment at issue. *Cf. Brenner*, 383 U.S. at 532 (rejecting asserted utility because there was no basis for believing that two similar compounds would have similar tumor-inhibiting characteristics).

Consistent with *Brenner*, the Guidelines instruct examiners that assertions that a claimed sequence is useful as a "gene probe" or "chromosome marker" should not be considered sufficiently specific if the applicant has not disclosed sufficient information about the DNA target. Similarly, the PTO instructs examiners that a general statement regarding "diagnostic" utility is insufficient if no disclosure has been made of a particular condition that can be diagnosed using the sequence. *See* Revised Interim Utility Guidelines Training Materials, pp. 5-6.

The Guidelines also require that any asserted utility be "credible" to a person skilled in the art. This standard, like the requirement for specificity, is well-founded in this Court's precedent. Credibility does not demand an excessive degree of scientific certainty. *See, e.g., Fujikawa v. Wattanasin* 93 F.3d 1559, 1565 (Fed. Cir. 1996) ("a rigorous correlation need not be shown in order to establish practical utility; 'reasonable correlation' suffices."); *In re Brana*, 51 F.3d at 1566, (overturning a rejection because the claims did "not suggest an inherently unbelievable undertaking or involve *implausible scientific principles*" (emphasis added)). Instead, as these decisions confirm, an asserted utility should be accepted

as credible if it is scientifically plausible. "Assuming that sufficient reason to question the statement of utility and its scope does exist," a rejection for lack of utility is proper and "can be overcome by suitable proofs indicating that the statement of utility and its scope as found in the specification are true." *Ex parte Balzarini*, 21 U.S.P.Q.2d 1892, 1895 (Bd. Pat. App. & Int. 1991). According to the Guidelines, an applicant can rely on evidence such as test data, affidavits, or expert declarations to support its assertion of utility. 66 Fed. Reg. 1092-02, 1098. *See also In re Jolles*, 628 F.2d 1322 (C.C.P.A. 1980) (applicant submitted evidence of testing in mice to support an asserted utility that the claimed composition was useful in treating humans).

Credibility is particularly important when an applicant asserts that an invention *may* be useful for some purpose. This kind of speculative assertion necessarily requires careful scrutiny to determine whether it is scientifically reasonable. *See, e.g., Ex parte Balzarini*, 21 U.S.P.Q.2d at 1895 (reviewing evidence to determine whether *in vitro* testing of HIV infected cells would reasonably indicate success during *in vivo* testing).[10]

[10] As discussed in section III.B, *infra*, the credibility requirement becomes particularly important when an applicant asserts utility based on "homology."

B. Fisher's claim is not supported by a specific and substantial credible utility.

Applying this precedent and the Guidelines to Fisher's patent application shows that the applicant has failed to establish the requisite utility for its claimed nucleic acids. Fisher identifies eight possible uses for its claimed sequences. But in each case, additional research would be required to determine whether a "real world" value specific to any particular sequence exists.[11] Without more information, Fisher's ESTs are nothing more than tools that might be used to discover something that may, or may not, lead to an invention with practical utility. *Cf. In re Ziegler*, 992 F.2d 1197 ,1203 (Fed. Cir. 1993) ("The utility of a chemical compound may not reside in its 'potential role as an object of use-testing.'" (quoting *Brenner*, 383 U.S. at 535)). Fisher's asserted utilities therefore do not meet the developmental or timing requirement stated in *Brenner*, which ensures that an inventor has brought an invention to a point that others can in fact make some use of it, and that it provides presently existing benefit to the public. *See* 383 U.S. at 535 (a specific benefit must be "in *currently* available form") (emphasis added). The purported benefit of the invention must be "actual, not merely potential . . . [and] directed to the immediate practical utility of [the disclosed] product." *In re Ziegler*, 992 F.2d at 1202.

---

[11] *See generally* PTO Br. at 27-37.

Moreover, Fisher has not identified anything other than already well-known potential uses that could be true for any EST. Fisher has therefore done nothing to further the *quid pro quo* of the patent grant contemplated by the Constitution or by Congress. In this regard, Fisher's asserted utilities are like the purported utility at issue in *In re Kirk*, 376 F.2d 936. There, the court rejected the applicant's assertion that the claimed compounds "'have present and useful biological activity of a nature known for analogous steroidal compounds,' and that 'one skilled in the art would know how to use the compounds of the claims to take advantage of their presently-existing biological activity.'" *Id.* at 939. The Court found that "the nebulous expressions 'biological activity' or 'biological properties' appearing in the specification convey no more explicit indication of the usefulness of the compounds and how to use them than did the equally obscure expression 'useful for technical and pharmaceutical purposes' unsuccessfully relied upon by the appellant in *In re Diedrich*, [318 F.2d 946 (C.C.P.A. 1963)]."[12] The Court also

[12] The Court also rejected Kirk's effort to cure the deficiencies of its applications by submitting an affidavit showing that three of the claimed compounds actually did possess "useful" biological properties. As the Court observed:

rejected Kirk's claim that compounds were useful as "intermediates," observing that "appellants have not disclosed or otherwise shown that any 6-methyl aromatic steroid which can be produced from their intermediates possesses activities in common with those commercial members of the aromatic steroid series." *In re Kirk*, 376 F.2d at 944 n.9. Similarly, in *Ziegler*, this Court affirmed the finding that Ziegler's German application, from which Ziegler sought to claim priority in an interference, did not establish a sufficient utility because "at best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." 992 F.2d at 1203.

In this respect, it is also important for this Court to contrast the putative utilities advanced by Fisher to what it actually claims as its "invention." The appealed claim seeks rights in any nucleic acid that "comprise" the recited ESTs. The claim is not limited to the ESTs, per se. If Fisher is entitled to any patent

---

> While that affidavit may show that three of appellants' claimed compounds do in fact possess specific ... activity or usefulness ..., [i]t is what the compounds are *disclosed to do* that is determinative here. [I]t is appropriate to note that the specification does not even intimate that the claimed compounds [have] the specific [ ] activities mentioned in the affidavit. With respect to the eighteen androstanes that are disclosed, ... [t]here is no suggestion which androstanes are of value [on account of their biological properties], or what biological properties make them useful.

In re Kirk, 376 F.2d at 941 (emphasis added).

rights, they should be commensurate in scope with what Fisher presents as its "invention" – namely, a claim limited to the specific ESTs that Fisher alleges can be used as a research tool or in a database system. *See Ex parte Balzarini*, 21 U.S.P.Q.2d at 1894 (disclosure of utility must be commensurate in scope with the subject matter sought to be patented). In other words, at most, Fisher would be entitled to claims limited to the specific ESTs themselves (i.e., nucleic acids *consisting* of the referenced sequences). Fisher is not entitled to dominant rights in "downstream" inventions to be discovered later using the disclosed EST tools (*e.g.*, genes and expression constructs). Because Fisher has not identified a credible and specific utility for such downstream inventions, Fisher has not met the requirements of 35 U.S.C. § 101 for the claims presented in the application.

III. THE PTO'S GUIDELINES APPROPRIATELY FOCUS ON THE SUFFICIENCY OF A "PROSPECTIVE" UTILITY

It is settled law that an applicant need not have actually reduced an invention to practice to secure a patent. Even in unpredictable arts, such as chemistry or biology, it is appropriate to describe new uses for compounds that are adequately supported in prospective terms – that is, without having actually tested the uses in the laboratory or the clinic. The Utility Guidelines provide a structured approach for examiners to assess whether a disclosure of prospective utility is closer to the extreme of an inevitable consequence of known facts or, on the other hand, to that of a blind (or hopeful) guess about the properties of a new compound. The

situations discussed below, which are relevant to Fisher's claims as well as to many other applications in biotechnology, illustrate how the Guidelines properly direct the application of the requirements of precedent in the new technological context of genomics.

A. A diagnostic utility for a new compound cannot be realized absent a disclosure of at least one specific disease or condition to be diagnosed.

Applicants claiming novel genes or gene fragments often assert that patentable utility resides in the use of the materials to diagnose disease. Probes corresponding to certain gene sequences can in fact be used to screen tissue samples for certain cancers, for example. But such an asserted diagnostic utility is only credible – and the diagnostic method will only work – if it is known that abnormal cells express the particular gene in a manner that is measurably distinct from the way it is expressed in normal cells. Arriving at this kind of diagnostic insight is no simple matter. A single tissue type may contain thousands of genes and produce thousands of proteins under various conditions and at different times. Pinpointing which genes are abnormally expressed in a malignancy – not for reasons unrelated to the cancer – often requires significant and substantial research.

Identifying a specific diagnostic utility thus requires knowing more than just the sequence of a gene. At a minimum, there must be some reasonable basis for correlating its expression – and more particularly, the *relative* degree of expression

between normal and abnormal cells – with the presence or absence of disease. Accordingly, the Guidelines instruct examiners that a specific diagnostic utility requires at least the identification of a condition that can be diagnosed using a *particular* sequence. Revised Interim Utility Guidelines Training Materials, p. 6.

The law does not require an overly rigorous correlation between gene expression and a specific indicator of disease to credibly establish a specific diagnostic utility. Instead, as *Cross v. Iizuka* makes clear, when a claimed chemical compound – such as a nucleic acid – is asserted to be useful for diagnostic purposes, there must be a reasonable correlation, based on credible scientific evidence, between the compound and the putative diagnostic use. 753 F.2d 1040, 1050-51 (Fed. Cir. 1985). Thus, when an applicant describes the structure of a new compound but provides no specific factual basis for making such a correlation, the applicant is only guessing that the compound *might* have the asserted utility. This provides no "immediate benefit to the public," *id.* at 1051, and thus fails to establish a credible specific utility.

B. A predicted utility based on sequence homology will be specific and credible only in rare circumstances.

Many applications filed in the last decade rely, substantially or exclusively, on "sequence homology" information to establish the utility of a newly discovered nucleic acid or polypeptide sequence. Sequence homology information characterizes the degree of structural similarity between a given nucleic acid or

polypeptide and one or more previously discovered and characterized nucleic acids or polypeptides.[13] Such comparisons can provide insights that are useful for understanding the functions or roles of a newly discovered gene. The value of homology information for establishing patent utility, however, depends on both the biological significance of the homology (i.e., whether, standing alone, it would be considered sufficiently informative of function or activity of the newly identified gene), and on what the homology information is relied upon to establish in the patent application.

An asserted utility based only on sequence homology relies on the *presumption* that because a deduced gene sequence is "homologous" to previously characterized gene(s), it will possess the same or similar biological properties, and will be similarly "useful." In some circumstances, this presumption may be justified. For example, where a gene appears to belong to a family of known genes, and where every known member of the family encodes a protein that exhibits essentially the same biological functions (*e.g.*, human type I (α and β) interferons), one skilled in the art would generally consider it reasonable to conclude that the new gene encodes a protein of like function.

---

[13] Many polypeptides possess structurally similar regions. Such polypeptides are often grouped into protein "families." In many protein families, possession of the "signature" region (or domain) does not unequivocally confirm the existence of specific biological functions.

In most cases, however, this presumption is not justified. Where an identifiable family of genes encodes proteins having widely divergent functions (*e.g.*, the TGF-β receptor superfamily, which includes proteins involved in activities ranging from scar formation to development of embryonic heart to bone growth), membership in that family – standing alone – usually will not establish that the newly discovered protein does possess or exhibit the same specific biological functions as the other members of the protein family. And while sequence analysis algorithms can often recognize structural "motifs" that characterize proteins having a generic type of enzymatic activity (*e.g.*, a kinase (phosphorylates proteins) or serine protease (degrades protein molecules)), this information about a "generic" activity usually will not identify the molecules with which the new enzyme interacts. In other words, establishing the likely existence of a generic activity does not necessarily describe a specific utility for an otherwise uncharacterized protein product.

Thus, the mere fact that a protein or nucleotide sequence encoding it has a certain degree of homology with a known protein or gene sequence rarely establishes, by itself, that the new protein actually has the properties or functions that make the old protein "useful." In essence, a demonstration of homology –

which is done using computer-based comparisons of the new and old sequences – is nothing more than a predictor of *possible* utility.[14]

An inference of biological properties necessary to establish utility of a compound which is based exclusively on structural similarity is proper only if that information is known to be sufficiently predictive of specific functions or activities of other molecules in the same class. In *Brenner*, the Court rejected the contention that structural similarities between the claimed steroids and compounds known in the art reasonably established that the new compounds would be useful for the same purposes where those skilled in the art did not recognize a predictable correlation between structure and function. *See* 383 U.S. at 532 ("the presumption that adjacent homologues have the same utility has been challenged in the steroid field because of 'a greater known unpredictability of compounds in that field'").

The specificity and credibility of an asserted utility based on sequence homology thus should be assessed in light of factual considerations such as the degree and nature of the homology, the existence or non-existence of a correlation between identified functions and corresponding homologous structural elements,

[14] Sequence comparison algorithms only "see" the sequences they are comparing, not the biological environments in which the genes or proteins are found. Sequence homology almost always indicates an evolutionary relationship, but it is an unreliable indicator of conserved function. The extent to which similar structure predicts similar function depends on the selection pressures on the evolution of particular genes and the biological systems in which they are found – information which is simply not derivable from sequence data.

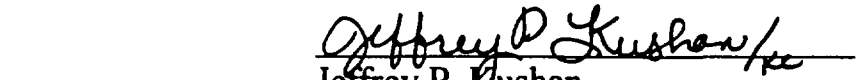
and the current knowledge and understanding of a person of ordinary skill in the art. *See, e.g., Brenner*, 383 U.S. at 532; *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1385 (C.C.P.A. 1974) (utility of claimed compound established based on generally recognized property of closely related compound). Thus, according to the methodology set forth in the Guidelines, if an asserted utility is based solely on homology, it may be appropriate for the examiner to reject the relevant claims with reliance on a scientifically valid explanation as to why a person of ordinary skill in the art would be skeptical of the asserted utility. *See, e.g., Ex parte Balzarini*, 21 U.S.P.Q.2d at 1894. This places the burden on the applicant to then establish the credibility of the asserted utility.

CONCLUSION

Genentech believes that a substantial and credible utility that is specific to a particular claimed gene sequence must be disclosed to meet the requirements of 35 U.S.C. § 101. It will be the rare case that utility for such a sequence can be credibly demonstrated in the absence of at least some experimental demonstration of the biological functions or the biological role of the claimed gene or its expression product. Genentech accordingly believes that the PTO's Utility Guidelines appropriately require a showing of a substantial and specific credible utility in a patent application claiming a genomic-related invention.

Genentech respectfully submits that this Court's endorsement of the standards reflected in the PTO Guidelines is vital to the continued advancement of the biotech industry. Because Fisher's claims do not meet these standards, the Patent Office's rejection of these claims should be affirmed.

Respectfully submitted,



Jeffrey P. Kushan
Kathi A. Cover
David L. Fitzgerald
Sidley Austin Brown & Wood LLP
1501 K Street, N.W.
Washington, D.C. 20005
202-736-8000
Attorneys for Genentech, Inc.

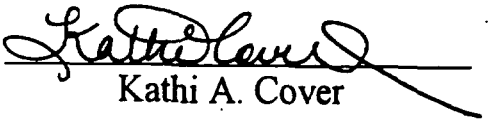
December 15, 2004

CERTIFICATE OF SERVICE

I, Kathi A. Cover, certify that on this 15th day of December, 2004, I caused two copies of the foregoing *Brief of Genentech, Inc. As Amicus Curiae Supporting Affirmance And Supporting The United States Patent And Trademark Office* to be served by Federal Express upon the following:

John M. Whealan
Office of the Solicitor
Crystal Park II
Room 714
2121 Crystal Drive
Arlington, VA 22215

William G. McElwain
Wilmer Cutler Pickering Hale and Dorr LLP
1455 Pennsylvania Avenue, NW
Washington, D.C. 20004



Kathi A. Cover

CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitations of Federal Rule of Appellate of Procedure 32(a)(7)(B). The brief contains 5,000 words, excluding those parts of the brief exempted by Rule 32(a)(7)(B)(iii).

This brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type style requirements of Federal Rule of Appellate Procedure 32(a)(6). The brief has been prepared in a proportionally spaced typeface using Microsoft Word, Times New Roman font, 14 point size.

Kathi A. Cover