BRIEF AND ADDENDUM FOR APPELLEE, DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

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

In re DANE K. FISHER and RAGHUNATH V. LALGUDI

Appeal from the United States Patent and Trademark Office,
Board of Patent Appeals and Interferences.

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STATEMENT OF RELATED CASES

No other appeal connected with patent application 09/619,643 has previously been before this or any other appellate court.

Monsanto, the real party in interest here, has six other appeals pending in this Court that present the same legal issue on analogous facts that will likely be directly affected by this Court's decision in this case: *In re Kovalic*, No. 05-1007; *In re Lalgudi*, No. 05-1010; *In re Byrum*, No. 1011; *In re Anderson*, No. 1012; *In re Adab*, No. 05-1013; and *In re Boukharov*, No. 05-1014. An unopposed motion for stay of further proceedings has been filed in each of these related appeals.

STATEMENT OF THE ISSUE

Does substantial evidence support the Board's finding that the five claimed nucleic acid molecules (ESTs) do not have a specific and substantial utility as required by 35 U.S.C. § 101?

STATEMENT OF THE CASE

Appellants Dane K. Fisher and Raghunath V. Lalgudi ("Fisher") filed a patent application claiming compounds and compositions related to molecules derived from maize (corn) plant tissue. The application included a "Sequence Listing" disclosing partial sequences for 32,236 nucleic acid molecules extracted from corn plants. Original Claim 1 was directed to nucleic acid molecules, Claim 2 to proteins, and Claims 3-7 to transformed plants. Each claim required a selection from 4,013 different nucleic acid sequences. The examiner required restriction to a smaller set of distinct inventions under 35 U.S.C. § 121. Fisher elected the first five sequences. Each sequence comprises approximately 300 or 400 nucleotides.

The patent examiner rejected Claim 1 on three grounds, two of which the Board of Patent Appeals and Interferences (Board) affirmed: (1) 35 U.S.C. § 101 for lack of utility; and (2) 35 U.S.C. § 112, first paragraph, for lack of enablement

based on the finding of lack of utility. Thus the enablement rejection stands or falls with the utility rejection. Fisher appeals.

STATEMENT OF THE FACTS

A. The Invention Involves Five ESTs Derived From Corn.

1. Technical Background.

Fisher claims nucleic acid molecules. An explanation of nucleic acid technology appears in *In re O'Farrell*, 853 F.2d 894, 896-898 (Fed. Cir. 1988). The following summary relies on the explanation in *O'Farrell*, supplemented with illustrations from an introductory textbook.[1]

In nature, cells use the long polymeric molecule DNA (deoxyribonucleic acid) as a specification for the primary structure of the proteins that form important cell structures and carry out cell activities. The subunits, or monomers, in the DNA polymer chain are called nucleotides, and their order or sequence is what determines the order or sequence of amino acids in proteins. The diagram on the facing page shows common graphic representations of DNA at increasing levels of detail from top to bottom, from DRLICA at inside cover. AD40.

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[1] KARL DRLICA, UNDERSTANDING DNA AND GENE CLONING, (John Wiley & Sons, New York 1992). AD38-46. Citations to this brief's addendum are abbreviated "AD__," citations to the joint appendix are "A__," and citations to Fisher's blue brief are "Br. at __."

A nucleotide consists of a nitrogen-containing ring, called a base, linked to a 5-carbon sugar that has a phosphate group attached. DNA is composed of only four nucleotides which differ from each other in the base. The four bases that characterize those nucleotides in DNA are adenine (A), guanine (G), cytosine (C), and thymine (T), usually referred to by the initials A, G, C, and T. The structure of a DNA molecule is typically represented by writing the initials A, G, C, and T in the order or sequence the bases are found on a strand of DNA, listing them from the 5'–>3' direction. *See e.g.*, Fisher's SEQ ID NO:1 at A125.

In a cell, the DNA is sequestered in the nucleus and exists mainly in the form of a very long double stranded helix, comprising two strands hundreds of thousands of nucleotides long. The two strands in the helix are complementary to each other: each A on one chain is paired with a T on the complementary chain, and each C is paired with a G. Thus, the base pairs are linked as follows:

A -- T
C -- G
G -- C
T -- A

(For a more detailed representation, see DRLICA. AD43). There are typically several distinct double stranded helices in any cell, and the distinct helices are referred to as chromosomes. A chromosome is a long chain of nucleotides in a

definite order or sequence, typically hundreds of thousands of nucleotides long, and it contains many sub-sequences, or genes, that code for proteins. Cells particular to a given organism have the number of chromosomes associated with that species. For example, corn has ten chromosomes. A421-22.

DNA molecules do not participate directly in the synthesis of proteins.

In order to produce a protein, the DNA sequence encoding a protein, *i.e.*, a gene, is transcribed as a molecule of RNA (ribonucleic acid). An RNA molecule has a sequence complementary to the gene sequence read off the DNA molecule. Thus, the sequence of the DNA is reflected on the RNA, except that the base uracil (U) appears in the place of thymine (T), and where the sugar in DNA is deoxyribose, the sugar in RNA is ribose.

Since the RNA is usually a genetic transcription that carries a sequence coding for a protein, it is called a **m**essenger or mRNA. mRNAs are typically some thousands of nucleotides long, and move from the nucleus where they are first transcribed, to organelles called ribosomes which translate the nucleotide sequence message into an amino acid sequence, thereby synthesizing a protein. The cartoon on the facing page from DRLICA (inside back cover) illustrates a messenger RNA being transcribed in the nucleus, moving to the cytosol, and being translated by a ribosome into a new protein. AD41.

Proteins are also polymeric molecules, but they are chains of amino acids, not nucleotides. To translate the mRNA, from a code written in nucleotides to a molecule containing instead a sequence of amino acids, a ribosome "reads" the mRNA code three nucleotides at a time. Nucleotides taken three at a time are a "codon," and code for an amino acid. Each triplet of three nucleotides is a codon that specifies one of twenty different amino acids. Since four nucleotides can be combined in triplets to form a total of 64 codons, there are many redundant codons; but three codons are called termination, or stop, codons because they signal the ribosome to stop translating the mRNA and release the finished protein. In standard reference works, the genetic code is shown in table form, *e.g.*, DRLICA at 35. AD45. The diagram on the facing page, DRLICA at 24, illustrates the triplet nature of a codon in relation to the single amino acid coded for by the triplet. AD42.

At any moment, a living cell can be synthesizing mRNA for expressing hundreds or thousands of different proteins. In a laboratory, mRNA from a cell can be extracted for the purpose of experimentation. One of the standard techniques is to "reverse" transcribe the mRNA back into DNA. The product of this reverse transcription is called **c**omplementary DNA, or cDNA. A diagram

summarizing the derivation of mRNA and cDNA from genomic DNA is shown in *In re Deuel*, 51 F.3d 1552, 1553-55 (Fed. Cir. 1995), and reproduced here:

As noted in *Deuel*, collections of cDNA molecules can be stored in "libraries," *i.e.*, cells that contain cDNAs. *Id*. As also observed in *Deuel*, the molecules present in cDNA libraries may be of unknown function and chemical structure, and the proteins which they encode may be unknown. *Id*.

2. Fisher's ESTs.

Fisher derived nucleic acid molecules from corn leaf cells. The specification explains that a cDNA library was prepared using maize, *i.e.*, corn, leaves as source material. A106-07.

Fisher sequenced portions of randomly selected clones in several cDNA libraries and listed the 32,236 partial sequences in the "Sequence Listing" section of the specification (filed in electronic form rather than on paper, A122[2]). A36.

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[2] The Office printed a "Raw Sequence Listing" which shows several initial entries in the Sequence Listing. A125-32. The Office uses the short Raw Sequence Listing form to confirm the absence of formatting errors in the listing, or

The short sequenced strand of DNA is called an EST (or **e**xpressed **s**equence **t**ag). That is, an EST is a short strand of DNA which is part of a cDNA.

The specification explains that ESTs "are short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones." A28. That is, a portion of the cDNA molecule was sequenced and the partial sequence serves as an identifying tag for that molecule.

The claim on appeal reads:

> 1. 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.[3]

A169. Thus, claim 1 covers compounds that contain any of one (or more) of the five named ESTs. SEQ ID NO:1 through 5 are from the library designated

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to inform applicants of formatting errors in the listing.

[3] The SEQ ID NO: format is an international standard for disclosing nucleic acids in patent disclosures. Since nucleic acid molecules do not usually have unique names, nucleic acid molecules described by sequence are each assigned a sequence identifier number (SEQ ID NO) to allow for easy reference. Details of the convention are explained in 37 C.F.R. § 1.821 *et seq*. Essentially, the rules require a patent application to include a look-up table called a "Sequence Listing" where each nucleic acid molecule disclosed by sequence is assigned a unique SEQ ID NO.

LIB3115, A106, and are short sequences of randomly selected clones in the library. A28. SEQ ID NO:1 through 5 list 429, 423, 365, 411, and 331 nucleotides respectively. A125-26. For example, SEQ ID NO:1 is:

A125.

Each claimed molecule contains at least the number of nucleotides in the referenced SEQ ID NO, and may contain additional nucleotides. In other words, the five ESTs recited by sequence, and the related five source cDNAs in the library, are species within the genus of molecules now claimed. The genus comprises any nucleic acid molecule that encodes a maize protein, or a fragment thereof, where the molecule contains one of the five recited sequences.

B. The Board Decision.

The Board affirmed the examiner's finding that the invention does not meet the utility requirement, and thus affirmed a corresponding rejection based on lack of enablement. A2. The Board reversed the examiner's finding that the claim was not supported by an adequate written description. *Id*. Before discussing the rejections, the Board construed the claim.

1. Claim Construction.

The Board construed Claim 1 as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, that encodes a maize protein or fragment thereof. The nucleic acid molecule comprises at least a sequence of nucleotides selected from SEQ ID NO:1 through 5 without internal alterations, and may comprise additional nucleotides or other molecules at either end. A4-5. The claim encompasses, among other things, genes, full open reading frames, fusion constructs, and cDNAs. *Id*.

2. Review Of Precedent Under 35 U.S.C. § 101.

The Board reviewed controlling precedent interpreting the utility requirement, including *Brenner v. Manson*, 383 U.S. 519 (1966) and later decisions by the CCPA and this Court: *In re Kirk*, 376 F.2d 936 (CCPA 1967); *In re Jolles*, 628 F.2d 1322 (CCPA 1980); *Cross v. Iizuka*, 753 F.2d 1040 (Fed. Cir. 1985); *In re Ziegler*, 992 F.2d 1197 (Fed. Cir. 1993); and *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995). A5-12.

The Board determined that in the "context of contemporary chemistry," "where little or nothing is wholly beyond the pale of 'utility,'" § 101's utility requirement should not be given its "broadest reach." A7 (quoting *Brenner*, 383 U.S. at 530). Second, rather than a *de minimis* standard, § 101 requires a

utility that is substantial, that is, "a specific benefit exists in currently available form." A13 (quoting *Brenner*, 383 U.S. at 534-35). Third, the Board noted that the *Brenner* standard has been held to mean that vague general disclosures of "useful in research" or "useful as building blocks of value to the researcher," or that an applicant is "on the way to discovering a practical utility," would not meet the standard. A13. Finally, the Board noted that since *Brenner*, this Court and its predecessor have used the phrases "substantial utility" and "practical utility" interchangeably. A5 n.3.

3. The Board Found That Fisher's Currently Asserted Utilities Do Not Satisfy The Utility Requirement of § 101.

The Board first addressed the two asserted utilities that had received the most attention in briefing: (1) that the claimed nucleic acids could be employed as marker nucleic acids to identify polymorphisms (A13-15), and (2) that the claimed nucleic acid molecules could be used as probes or primers to isolate nucleic acid molecules of other plants and organisms (A15-19). The Board acknowledged that obtaining genetic heritage information by detecting the presence or absence of polymorphisms would fall within the broad reach of the word "utility," but that absent further information about the gene corresponding to a given EST, such utility was insubstantial. A14-15. While the threshold level of knowledge of the

gene required for "substantial utility" may be difficult to ascertain, the Board held that "no knowledge" was safely below that threshold. A15.

As to using the claimed molecules as probes or primers to isolate other nucleic acid molecules from different plants and organisms, the Board asked what substantial use such other molecules would have. A16. Finding no answer to the question, and finding that the specification does not relate any plant trait to the claimed molecules, the Board found that probing for other molecules that have no known use did not represent a substantial utility for a probe or primer. *Id*.

Fisher argued that the claimed molecules provide appropriate useful starting points for a chromosome walk to isolate a promoter active in leaves at the time of anthesis, or a promoter active in leaves. A16. The Board found the specification did not provide an expectation of successfully using any of the disclosed molecules to isolate such promoters. A16-17. There was no evidence that claimed molecules are tissue or cell-type specific, or developmentally or environmentally regulated, or expressed only at the time of anthesis and thus capable of isolating a promoter active only at the time of anthesis. A17-18.

The Board considered Fisher's arguments about additional utilities: (1) introduction of the claimed molecules into a plant or a plant cell (either as sense or antisense inhibitors), which plant or cell can then be used to screen for

compounds such as a herbicide, A20; (2) use of the claimed molecules to measure the level of mRNA in a sample via microarray technology and use as molecular markers, A20-21; (3) and use of the claimed molecules as molecular markers or probes, A23-24. The Board found that none of the suggested uses provided a specific or substantial benefit in currently available form. Nothing in the specification indicates how the results of the proposed experiments can be interpreted as meaningful. Instead, further experimentation is needed to determine functions and properties of the claimed molecules. A21. The Board considered the situation directly analogous to that in *Brenner*. A22-23.

The Board also rejected Fisher's arguments that the usefulness of ESTs could be inferred from the existence of a multimillion dollar industry in the U.S. related to ESTs. Given Fisher's failure to provide any evidence as to the specific "use" of ESTs responsible for the growth of this industry, the Board assumed that it was based on the use of EST databases, clone sets, and microarrays, and found the attribution of a single EST to such a dataset did not amount to a "substantial use." A24.

In essence, all of the alleged utilities could be asserted for any EST but none currently provide a specific use for the claimed ESTs. A19. The Board reasoned that not every utility will satisfy § 101, even if the utility is shared by a class of

inventions. *Id*. For example, if it was unknown that a new compound was an analgesic, an application disclosing that the compound could be used as a paperweight would not satisfy § 101, even though that utility is shared by a large class of inventions including other analgesics, namely, those whose physical embodiments have mass. *Id*.

Finally, the Board determined that the examiner's enablement rejection was a consequence of the finding of lack of utility, and thus affirmed it. A25.

SUMMARY OF THE ARGUMENT

Section 101 requires that a specific and substantial utility for any claimed invention must be known or disclosed. The utility must be currently available, and a patent does not issue if the requirement for a currently available specific and substantial utility is not met.

Monsanto is claiming molecules containing five ESTs derived from corn, but discloses no specific and substantial utility for any of them. Some of the proposed utilities involve using the claimed ESTs to find their binding partners, mates, or complements, but no specific and substantial uses for those objects are disclosed. Some of the proposed utilities would use the claimed ESTs to find other molecules that might be more or less close to the EST on a chromosome, but there are no specific and substantial utilities for those other molecules are

disclosed. In short, all of the proposed utilities are simply methods of investigating what to do with the claimed molecules or the others that could be found.

As asserted in the specification, the utilities alleged are the same for anyone of the thousands of corn ESTs Monsanto discloses. Moreover, these same utilities could similarly be asserted for any EST from any other plant or animal. For example, the fact that any EST can act as a probe that can base pair with its complement somewhere is not disputed, but these non-specific assertions are true for any EST from any organism. The Board should be affirmed because Monsanto does not identify any specific and practical benefit for using any of the five claimed ESTs.

Apart from its lack of legal support, Monsanto's position in this case would be poor patent policy with unfortunate consequences for the genetics field in general and the future of corn production in particular. If Monsanto were to obtain patent protection for the thousands of corn sequences that its automated tools have identified, it would obtain the very sort of "monopoly of knowledge" that the Supreme Court has warned "should be granted only if clearly commanded by the statute." *Brenner*, 383 U.S. at 534.

ARGUMENT

A. The Standard Of Review.

Whether an application discloses a substantial utility for an invention is a question of fact. *Ziegler*, 992 F.2d at 1200; *Cross*, 753 F.2d at 1044 n.7. "If the application fails as a matter of fact to satisfy 35 U.S.C. § 101, then the application also fails as a matter of law to enable one of ordinary skill in the art to use the invention under 35 U.S.C. § 112." *Ziegler*, 992 at 1201; *Brana*, 51 F.3d at 1564 n.12. This Court upholds the Board's decisions on factual matters if there is substantial evidence in the record to support the Board's findings, and it reviews the Board's legal conclusions *de novo*. *In re Gartside*, 203 F.3d 1305, 1316 (Fed. Cir. 2000).

B. Section 101 Requires Disclosure Of A Specific And Substantial Utility.

The PTO and Fisher agree that a patent may not be granted on an invention unless a substantial utility for the invention is known or disclosed. *Brenner*, 383 U.S. at 535; *Fujikawa v. Wattanasin*, 93 F.2d 1559, 1563 (Fed. Cir. 1996); Br. at 31. It is also undisputed that § 101 requires that an invention provide a "specific benefit" in currently available form. *Brenner*, 383 U.S. at 534-35; Br. at 30. That an invention belongs to a class of things that are the subject of serious scientific investigation is not enough to meet the requirement. *Brenner*, 383 U.S. at 532. Thus, being the object of scientific research is not sufficient; what is

necessary is that the invention have a currently available specific and substantial use. *Brenner*, 383 U.S. at 535.

The parties dispute whether Fisher has satisfied the requirement for disclosing a specific and substantial utility in currently available form. The PTO's view is that Fisher's utilities are similar to the generalized, nebulous assertions of "biological activity" that were insufficient in *Kirk*. There, the CCPA affirmed rejections under §§ 101 and 112, based on the failure to disclose a specific benefit, and explained:

> As this court stated in *Diedrich*, [318 F.2d 946, 949 (CCPA 1963)] quoting with approval from the decision of the board:
>
> > We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.
>
> As the Supreme Court said in *Brenner v. Manson*: "*** a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Kirk, 376 F.2d at 942 (emphasis added).

1. The Required Practical Utility Must Have A Specific Purpose.

While the threshold of utility is not high, a patent applicant is required to disclose at least one substantial use. For practicality, the use and its associated benefit must be identified specifically. The leading case holds that "useful" is not given its broadest reach, even in chemistry "where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of 'utility'–if that word is given its broadest reach." *Brenner*, 383 U.S. at 530.

Based on well-known dicta from an early circuit decision by Justice Story, Fisher instead proposes a minimalist meaning for "useful." Br. at 28-29. That is, all the law requires is that the invention "should not be frivolous, or injurious to the well-being, good policy, or good morals of society"; the word useful is in "contradistinction to mischievous or immoral." *Id.* (quoting *Lowell v. Lewis*, 15 F. Cas. 1018 (C.C. Mass. 1817)).

When Manson made the same argument based on Justice Story's dictum, the Supreme Court rejected it. *Brenner*, 383 U.S. at 532-33 (citing Note on the Patent Laws, 3 Wheat.App. 13, 24, and the *Lowell* and *Bedford* cases). The *Brenner* Court rejected the minimalist position as "plac[ing] such a special meaning on the word 'useful' that we cannot accept it in the absence of evidence that Congress so intended." *Brenner*, 383 U.S. at 533.

In the almost 200-year old circuit case that Fisher relies on, the accused infringer of a patent on a water pump (Lewis) defended by arguing that the patented pump was not a useful invention because the patented pump worked no better than other pumps. *Lowell v. Lewis*, 15 F. Cas. 1018, 1019 (C.C.D. Mass. 1817). According to Lewis, if the patented pump did not supersede common pumps already in use, the patent should not have issued. Justice Story rejected the idea an invention must be better than things already in use to be patentable. *Id*. It was undisputed that the patented water pump worked, and Lewis himself admitted that the accused pump "is useful in a very eminent degree." *Lowell*, 15 F. Cas. at 1019. Thus, Justice Story instructed the jury that the issue was whether the accused pump was the same as the patented pump, and "the abstract question [the meaning of useful] seems hardly of any importance in this cause." *Id*. Accordingly, Justice Story's comments suggesting that useful only means not frivolous, injurious, mischievous or immoral were dicta.

Fisher's contention that Justice Story's dicta has continued vitality and somehow applies to chemical inventions, despite the express repudiation in *Brenner*, may stem from Fisher's erroneous attribution of Story's view to the Supreme Court in *Evans v. Eaton*, 16 U.S. 454, 518 (1818). Br. at 29 (quoting *Evans*). The sentence Fisher attributes to the Supreme Court is not in *Evans*, nor

was "useful" an issue in the *Evans* case. We have found no evidence that the Supreme Court ever adopted the position that Fisher attributes to *Evans*. *Evans* was reported in 3 Wheaton, and the sentence Fisher quotes is in 3 Wheaton, Appendix, Note II on the Patent Laws, *i.e.*, a note contributed to 3 Wheaton by Justice Story himself, not by the Court.[4]

Finally, the minimalist view that useful means only not frivolous or insignificant and not injurious to morals, health or good order of society that Fisher proposes is also in conflict with the well-settled principle that inoperable inventions are not patentable because they are not practical. *E.g.*, *Beidler v. U.S.,* 253 U.S. 447, 453 (1920) (when a patent issues on an inoperable machine, the patent is invalid because "it fails to disclose a practical and useful invention."); *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1358 (Fed. Cir. 1999).

2. After Notice And Comment, The PTO Adopted Reasonable Interpretative Guidelines That Were Followed In This Case.

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[4] Justice Story alone was the author of Note II. Craig Joyce, "Wheaton v. Peters - The Untold Story Of The Early Reporters," 1985 Sup. Ct. Hist. Soc. Y.B. 35, 51 ("For volume 3 of Wheaton's Reports, Story prepared two more marginal notes, both on common law subjects, and a seventeen-page dissertation on the patent laws for the appendix.").

From time to time, the PTO updates its patent examination practice to ensure that the agency's interpretation of the § 101 utility requirement properly implements the law according to precedent. On two recent occasions (the first beginning in 1994 and the second in 1998), the Office focused on the utility standard and held public hearings, sought public comment, and issued formal instructions to its patent examiners in the form of examination guidelines published in the Federal Register. The guidelines were incorporated in the MANUAL OF PATENT EXAMINING PROCEDURE. The pertinent pages of MPEP § 2107 are provided in this brief's addendum. AD15-23.

The first revision was made in 1995 after spontaneous public comment suggested that the Office may have been demanding overly rigorous evidentiary showings of efficacy for pharmaceutical inventions. The resulting guidelines indicated that the Office would accept assertions of utility if they were specific and credible, and if the record did not show evidence to the contrary.

The second revision was prompted by advances in DNA technology. By 1992, DNA technology advanced to a point where thousands of nucleic acid compounds could be derived from nature in bulk. Found mRNAs could be copied and stored as cDNAs, and random portions of the cDNAs could be sequenced and called ESTs. ESTs were often said to simply represent not only the cDNA but also

a fragment of a chromosome (although this is not necessarily correct in every case).

Questions about whether ESTs could, would or should be patentable attracted considerable public attention during the 1990s. For example, while agricultural geneticists speculated that a genomics patent based only on a sequence "could crumble in court," many nevertheless filed patent applications. A382. In 1998, the PTO published proposed examination guidelines, held public hearings on the subject, and requested public comment.[5] *See* Request for Comments on Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1 "Written Description" Requirement; Extension of Comment Period and Notice of Hearing, 63 Fed. Reg. 50887 (Sept. 23, 1998). AD1-3. In addition, the PTO invited comment on specific questions relating to ESTs:

> 10. Is there any basis in law or fact for treating expressed sequence tags (ESTs) differently than any other nucleic acid under the written description requirement?
>
> 11. Are there additional issues related to other statutory requirements of Title 35 invoked in the patenting of ESTs? If so, please set forth those issues separately and specifically.

63 FR at 50888. AD2.

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[5] Copies of Federal Register notices cited in this brief are provided in the Addendum.

Responses from the public suggested that ESTs disclosed with only bare structural information (as in this case) were subjects for experiment and investigation, but lacked practical applications. The Office reconsidered the issues and revised its examination guidelines to ensure that the Office would give due consideration to the Supreme Court's "substantial" criterion for utility. *See* Revised [Interim] Utility Examination Guidelines; Request for Comments, 64 Fed. Reg. 71440 (Dec. 21, 1999), AD4-6; and Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001), AD7-14.

Reasonable agency interpretations carry "at least some added persuasive force." *U.S. v. Mead Corp.*, 533 U.S. 218, 234-35 (2001) (discussing *Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944)); *Bayer AG v. Carlsbad Technology, Inc.*, 298 F.3d 1377, 1381 (Fed. Cir. 2002) (deference to PTO interpretative decision applying Uruguay Round Agreements Act proper under *Skidmore*); *Blacklight Power, Inc. v. Rogan*, 295 F.3d 1269, 1273 (Fed. Cir. 2002) ("agency actions are entitled to judicial respect when they are reasonably taken and in accordance with the 'specialized experience' of agency officials and the 'validity of its reasoning'" (quoting *Skidmore*, 323 U.S. at 139-40)). For example, this Court has considered PTO guidelines in cases involving the written description requirement and found them persuasive. *E.g.*, *Enzo Biochem v. Gen-Probe*, 323 F.3d 956, 964 (Fed. Cir.

2002) ("We are persuaded by the Guidelines on this point and adopt the PTO's applicable standard for determining compliance with the written description standard"); *Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2004).

The PTO's utility guidelines state that the utility requirement applies to patents in all technologies, and the PTO published examples of how patent examiners should examine claims in a broad array of technologies. The "Revised Interim Utility Guidelines Training Materials" are accessible at the PTO website (<www.uspto.gov/web/menu/utility.pdf>). The patent examiner in this case followed the guidelines and instructions in the training materials. A224-43.

The PTO "utility" example most pertinent to the present case is Example 9, "DNA Fragments," pages 50-53. AD24-27. In Example 9, DNA fragments having no disclosed utility other than serving as objects of further research are found to lack a specific practical utility. AD26.

In contrast, Example 10 presents a DNA molecule disclosed as having a complete "open reading frame" or "ORF." AD27-29. An ORF is the region of a cDNA that is sufficiently complete as to code for an entire protein. In Example 10, the sequence of the ORF is said to have a significant degree of similarity to the sequence of a known DNA that encodes a useful protein, *i.e.*, a ligase (a kind of enzyme) that catalyzes bond formation. Because ligase activity is relatively non-

specific, the finding of significant sequence similarity supports a fair inference that the new DNA likely codes a new ligase having the same use. AD14. Inferring utility based on structural similarity is reasonable in appropriate circumstances. *E.g.*, *Brana*, 51 F.3d at 1567 ("evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility"). Thus, whereas Example 9 would not satisfy the utility standard, Example 10 would.

C. Fisher's Asserted Uses Are Not Specific and Substantial.

1. The Asserted Utilities Are Investigational Tests That Yield More Compounds Lacking Practical Uses.

Fisher found over 32,000 nucleic acid molecules in corn cells and disclosed fragmentary sequences for the molecules. Based on the disclosure of only random short fragments of structural information for each molecule, Fisher seeks to patent any nucleic acid comprising one of the first five fragmentary sequence structures from the list of over 32,000.

If more were disclosed, some of the claimed molecules might meet the utility requirement, but the present specification does not disclose that any specific

substantial benefits are currently available. Fisher may be "on the way to discovering a practical utility," but is not there yet. *Ziegler*, 992 F.2d at 1203.

The proposed possible uses are so general that they have no specific meaning. Indeed, the specification provides no specific use concerning any one of the over 32,000 distinct structures disclosed, and always mentions them in batches of thousands together. The same proposed investigational uses would apply not only to the over 32,000 ESTs Fisher discloses, and to the over 600,000 ESTs disclosed in Monsanto's related appeals, but also to any ESTs derived from any organism.

As objects of lacking any specific substantial use, the molecules lack practical applications and do not meet the utility requirement. A22. To the extent that the claimed molecules might be considered intermediates for finding more molecules, "[i]t is not enough that the specification disclose that the intermediate exists and that it 'works,' reacts, or can be used to produce some intended product of no known use. Nor is it enough that the product disclosed to be obtained from the intermediate belongs to some class of compounds which now is, or in the future might be, the subject of research to determine some specific use." *Kirk*, 376 F.2d at 945.

Reviving an argument rejected by the majority in *Kirk*, Fisher argues that the claimed molecules are research tools like microscopes and other instruments. Br. at 39; see *Kirk*, 376 F.2d at 961 (Rich, J., dissenting) (arguing that chemical compounds such as Kirk's steroids were like research tools, such as microscopes, laboratory balances, and spectrophotometers, and therefore met the requirement for utility). However, the claimed molecules do not have a function analogous to a microscope. A15. A microscope has the specific benefit of magnifying other objects clearly. ESTs for anonymous genes do not have an analogous specific use, and therefore don't meet the requirement for a currently available specific benefit.

The *Kirk* majority also rejected the dissent's argument that any chemical compound is *per se* useful as an intermediate to make other compounds of yet unknown use for research purposes. *Kirk*, 376 F.2d at 945. As indicated in MPEP § 2107.01, the generalized label "research tool" is not helpful in identifying a specific, substantial utility because it indicates context but not practicality. AD19.

A more apt analogy is that Fisher's ESTs are akin to a manufactured copy of a portion of one's fingerprint. Six billion people have different fingerprints and presumably a copy of a fragment of a fingerprint could be used in a biometric device, as for example, a comparative standard. While machines for reading

fingerprints, and methods for fingerprinting, and computer programs for matching fingerprints may all be patentable, a copy of a portion of one's fingerprint is not because there is no specific benefit to the individual fingerprint. Similarly, whereas methods for making cDNAs, methods for random sequencing, robots for implementing the methods, and computers for comparing the ESTs may be patentable, until a specific benefit is identified for an EST, an individual EST is not useful under § 101.

Fisher argues that the specific sequence of each EST makes its use specific because it would likely bind only its complement. It is not disputed that the EST may bind its complement, but there is no specific reason for using the EST to bind its complement. To the extent that more sequence data could be acquired by using the ESTs as probes, that result would likely be true for any scrap of DNA derived from nature, but it confers no specific benefit. Again using the fingerprint analogy, even though one person's fingerprint would match only one person's finger, that in and of itself does not warrant patenting individual plastic reproductions of fingerprints under the utility standard merely because each one is different.

None of Fisher's proposed utilities provide a specific and substantial or practical benefit. The Board correctly found that Fisher's arguments only stand

for the proposition that the claimed molecules are useful simply "because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean." A22. We will now respond to Fisher's various arguments as to why any EST has utility and is thus patentable.

None Of The Claimed Molecules Currently Marks Anything Specific

When the location of a sequence is identified by position on a chromosome, the sequence embedded in the chromosome can serve as a marker, analogous to how a landmark might mark a physical location. Fisher argues the claimed molecules can serve as molecular markers on a genetic map. Br. at 36. However, there is no disclosure in Fisher's specification showing that any of Fisher's ESTs is currently known to mark anything.

The deficiency in Fisher's disclosure is highlighted when compared to prior art in the record. For example, Hake et al., A419-26, show diagrams of the ten corn chromosomes, with some known markers indicated. A422-23 ("Figure 31.1 . . . Markers considered suitable for lineage and mutant analyses are indicated"). Assuming that Fisher's ESTs would map to single chromosomes, Fisher's disclosure does not provide information analogous Hake's disclosure illustrating suitable markers, because Fisher has yet to disclose where or what the claimed molecules could mark.

Fisher also asserts that the claimed molecules can serve as molecular markers for genes of interest. Br. at 37. Fisher's specification fails to disclose a gene of interest and is a sharp contrast to prior art in the record. A16. By comparison, an example of markers for genes of interest may be seen in Kurata et al., A304-14, which lists specific, mapped rice genes of interest and displays specific, related chromosome maps. A306-10. In contrast, Fisher's specification provides only general allegations about ESTs.

Measuring The Level Of mRNA For The Molecules Is Use-Testing, Not A Practical Application, Because Such Measurements Have No Specific And Substantial Significance

Fisher proposes that the claimed molecules can be used to measure the level of mRNA in a sample, Br. at 36, and detect and monitor the quantitative levels and patterns of mRNA found in a particular cell or tissue sample, Br. at 37. According to Fisher this provides information pertinent to detecting expression changes in plant traits of interest, *e.g.*, drought stress. *Id*. However, there is no disclosure that any of SEQ ID NO:1 through 5 has a relation to a specific plant trait of interest. A20. None of the claimed molecules were disclosed to detect any traits of interest. Further experimentation is needed to determine if any of the claimed molecules have any relation to a trait of interest, and if the results would be likely to lead to practical applications for the claimed molecules. A21. Only after

successful experimentation led to the discovery of some practical benefit would any benefit of monitoring mRNA levels with SEQ ID NO:1-5 be revealed. In other words, the suggestion is not a currently available utility, but is instead just another research proposal.

Using The Molecules As Primers Is Non-Specific Probing Of Unknowns With Another Unknown

Fisher alleges that the claimed molecules are a source of primers, Br. at 36, that would enable the rapid and inexpensive duplication of a specific target gene, Br. at 38. No target gene has been identified. If the genes associated with the cDNA sources of SEQ ID NO:1-5 are intended as targets that might be obtained by using the claimed molecules as intermediates, those genes themselves are not disclosed to be useful. A16. Using the molecule to obtain more molecules whose uses are unknown is not a practical utility. Intermediates leading to more compounds of unknown use are not useful. *Kirk*, 376 F.2d at 945. As to using the claimed molecules as probes or primers to isolate other nucleic acid molecules from different plants and organisms, the Board found there was no indication of a practical use for other molecules that might be found. A15. In view of the specification's failure to answer this question, and its failure to relate any plant trait to the claimed molecules, substantial evidence supports the Board's finding

that probing for other molecules that have no known use did not represent a substantial utility under § 101. A15-16.

Searching For Polymorphisms Is Non-Specific Use-Testing

The allegation that the claimed molecules could be used for finding polymorphs is a suggestion to begin research, *i.e.*, use-testing, to see if polymorphs exist. Fisher has not disclosed that any such polymorphs, if found, would have any substantial use.

The Board found that detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. A14. It reasonably found that knowing whether a polymorphism is present or not has no meaning in the absence of any disclosure of an effect for a related gene. A15.

Polymorphisms are alternate forms of a gene. *See, e.g.*, GLOSSARY OF GENETICS,[6] defining "genetic polymorphism" as the regular and simultaneous occurrence in the same population of two or more "alleles" or "genotypes." AD36. According to the GLOSSARY, at least six kinds of genetic polymorphism have been described. Fisher does not disclose that any of SEQ ID NO:1-5 occur as two or more alleles or genotypes, but simply discloses that research can be done

[6] GLOSSARY OF GENETICS, 5th Ed., Springer-Verlag, Berlin (1991). AD30.

to find out if alleles or other genotypes exist. Fisher does not disclose any specific benefit to any polymorphisms that might be discovered.

The GLOSSARY further defines "allele" as one of two or more alternate forms of a gene. AD32-33. If the nucleotide sequence difference changes the amino acid sequence in the protein that a gene codes for, the different proteins would be different allelic forms or "morphs." The GLOSSARY distinguishes seven different kinds of alleles or morphs: amorphs, hypomorphs, hypermorphs, antimorphs, neomorphs, isoalleles, and unstable alleles. AD32-33. Fisher does not disclose any alternate forms for SEQ ID NO:1-5, but simply indicates that research could be done to find out if they exist. On the current disclosure, before any discovered polymorphs could be recognized as useful, one would have to know a practical utility of the presently claimed compounds for comparison. Fisher discloses no specific use for any molecule and there is no practical way to assess the benefit of finding polymorphs. None of SEQ ID NO:1-5 is disclosed as suggesting an inference of a specific use for a polymorph if one were found.

Isolating Promoters Is Non-Specific Experimentation

Fisher argues that the claimed molecules can be useful starting points for a chromosome walk to isolate promoters. Br. at 38. However, the Board found the specification did not provide an expectation of successfully using any of disclosed

molecules to isolate such promoters. A16-17. There was no evidence that claimed molecules are tissue or cell-type specific, or developmentally or environmentally regulated, or capable of isolating a promoter active only at the time of anthesis. A17-18.

Chromosome walking is a general procedure that starts with a piece of DNA from a chromosome. The initial piece of DNA allows one to start wherever that piece binds a complement on the chromosome and then "walk" to neighboring regions of the DNA. One then acquires pieces of those neighboring regions to learn their sequences. Thus, instead of getting the EST's complement, walking allows one to find fragments next to the EST or its complement. Here, Fisher discloses no reason why starting at any of the disclosed randomly sequenced EST starting points provides any specific benefit. A16.

Any EST or any fragment of any cDNA would do as well. Indeed, even Fisher's preferred embodiments are all stated generally in terms of "SEQ ID NO:1 through SEQ ID NO:32236" with no specific disclosure concerning any of them. A44-45. Fisher discloses nothing about the utility of the other DNA fragments that might be marked, found, or probed, whether one learns the sequence or not. A23-24. In this regard, the proposed utility is not a practical utility because the proposal is to find or make more compounds whose utilities are unknown.

Brenner, 383 U.S. at 535 (a process for making compounds of unknown utility is not patentable); *Kirk*, 376 F.2d at 945 ("It is not enough that the specification disclose that the intermediate exists and that it 'works,' reacts, or can be used to produce some intended product of no known use."). The proposed utility is similarly not specific since it is true not just for the five ESTs but for any EST. Assuming that a promoter for a cDNA represented by one of SEQ ID NO:1-5 were found, it would promote expression of a compound having no practical utility.

Controlling An Unknown Protein's Expression Level Is A Nebulous, Non-Specific Proposal

Fisher argues that the claimed molecules can control the expression levels of protein, Br. at 36, to allow study of protein expression pattern and gene protein function [sic], Br. at 38. However, Fisher disclosed no association between any of SEQ ID NO:1-5 and any protein whose expression could be controlled. Thus, any such utility is hypothetical and not currently available.

No specific and substantial benefit regarding protein expression to be controlled is disclosed or readily apparent. A20. Moreover, each of SEQ ID NO:1-5 is theoretically translatable into several potential pieces of protein but Fisher did not disclose which theoretical translation is a maize protein. The examiner found that none of six possible reading frames for SEQ ID NO:5 and its

complement could code for a protein because every potential reading frame was peppered with termination or stop codons. The Board noted that the examiner's finding was uncontested. A20 n.5.

The Board's observation concerning six potential reading frames refers to the fact that Fisher did not disclose if the first nucleotide in each recited sequence is in position one, two, or three, of a codon. Thus, the identity of any "real" maize protein associated with the fragmentary ESTs remains undisclosed, because Fisher did not disclose the reading frame. *See, e.g.*, *O'Farrell*, 853 F.2d at 897-98 ("Synthesis of a particular protein requires that the correct register of *reading frame* be maintained as the codons in the RNA are translated") (emphasis in original). The cartoon on the facing page, DRLICA at 24, illustrates a selected reading frame being translated into a unique amino acid sequence for a protein. AD42. If the reading frame is shifted, the content of the message is changed and the amino acid sequence of the resulting protein is changed. *O'Farrell*, 853 F.2d at 897. Thus, given the absence of any reading frame information for Fisher's molecules, there is only a one-in-three chance of guessing which reading frame on Fisher's ESTs codes for a maize protein.

Assuming that one of skill in the art went through the motions of using the claimed molecules to attempt to control protein expression, there is no disclosure

of an experimental parameter to monitor. A20. The corn leaves were likely expressing at least 2,177 mRNAs at the time Fisher collected the mRNA. A107 (cDNA library LIB3115 was the source of SEQ ID NO:1 through 2177). Thus, the leaves may have been potentially producing over 2,177 different proteins. Fisher's specification does not identify what change in protein expression should be observed, since there is no disclosure of what, if any, specific change to monitor. The suggestion is another example of use-testing.

The Board considered Fisher's arguments about introducing the claimed molecules into a plant or a plant cell (either as sense or antisense inhibitors), and attempting to use the plant or cell as a screen, but correctly concluded that no such utility was made currently available by the disclosure. A20. *Kirk*, 376 F.2d at 941 ("the nebulous expressions 'biological activity' or 'biological properties' . . . 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 [*Diedrich*]").

Locating Other Genetic Molecules Is Simply Expanded Use-Testing, Not A Practical Utility

Fisher argues that the claimed molecules can be used to locate genetic molecules of other plants and organisms, Br. at 36, to allow comparative studies of located genes and their functions between organisms, Br. at 38. As with all of Fisher's other proposed utilities, assuming the claimed molecules could be used to find similar molecules, finding similar molecules having no disclosed specific use is not a practical benefit. Studying the found molecules would be yet more of the kind of investigation the *Brenner* court characterized as "use-testing," but not a patentable utility. *Brenner*, 383 U.S. at 535. The proposal does not provide a specific or substantial benefit in currently available form. Nothing in the specification indicates how the results of the proposed experiments can be interpreted as meaningful. Instead, further experimentation is needed to determine a practical application for the claimed molecules. A21.

2. Section 101 Requires A Specific Practical Use, Not Commercial Success.

Fisher argues that ESTs have a real world value as part of a multi-billion dollar industry, and ought to be patented because the people who buy them find them useful. Br. at 40-41. Relying on precedent involving infringement cases,

Fisher argues there is a nexus between utility and commercial success because people rarely if ever invest large sums of money in useless inventions. Br. at 41-42. The Board correctly rejected Fisher's argument. A24. The proposition that utility is proven by the extent to which an invention has gone into general use is not the accepted standard. *McClain v. Ortmayer*, 141 U.S. 419, 427-28 (1891) ("That the extent to which a patented device has gone into use is an unsafe criterion, even of its actual utility, is evident from the fact that the general introduction of manufactured articles is as often effected by extensive and judicious advertising, activity in putting the goods upon the market, and large commissions to dealers, as by the intrinsic merit of the articles themselves") (emphasis added). The Court was concerned that if the generality of sales were made the test of patentability, a party who secured a patent on a trifling variation might secure an exclusive right "without in fact having made the slightest contribution of value to the useful arts." *Id*. Thus, the Court acknowledged that while entry into general use might be evidence of utility in a doubtful case, it was not conclusive. *McClain*, 141 U.S. at 429.

No evidence suggests a nexus between sales and any of the molecules now claimed. A24. Assuming that nucleic acids such as those claimed could be sold, the sales would not establish that the molecules have a currently available

practical utility. Instead, the literature Fisher that references, Br. at 41, indicates that batches of ESTs of unknown significance are sold for the purpose of finding targets worthy of further development, not because the individual ESTs have any specific currently available benefit. *See, e.g.*, A352 ("Through this alliance, JT gains access to a . . . drug lead discovery system"), or A365 ("to identify and validate screening targets"). Further, the claims are not directed to EST databases, clone sets, or microarrays. A24.

To rebut the Board's finding that Fisher is not claiming clone sets, Fisher argues that he is precluded from claiming sets of ESTs by the PTO's restriction requirement. Br. at 42. However, it was Fisher's choice to present a claim directed to ESTs selected in the alternative, and not a claim to a clone set. In this application, Fisher never presented a claim to a clone set. Fisher's original Claim 1, for example, read "[a] substantially purified nucleic acid molecule . . . selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:4013." A114. The Board correctly found that the single data point any of the claimed molecules

would provide, *e.g.*, as one in thousands on a microarray, is not a substantial use.[7] A24.

This Court's precedent rejected the theory that sales of new compounds are conclusive of practical utility. The dissent in *In re Joly*, 376 F.2d 906, 917-924 (CCPA 1967) (Smith, J., dissenting) argued forcefully that offers to sell compounds evidenced that any compound was useful because it would be used for experiments. In *Kirk*, the majority also rejected the dissent's argument that a compound is *per se* useful when chemists could experiment with it or use it as a building block to make more compounds lacking a specific use. *Kirk*, 376 F.2d at 959 (Rich, J., dissenting).

Although Fisher criticizes the Board for requiring disclosure concerning the coding function of the underlying gene, Br. at 38, the Board did not go that far. The Board required disclosure of at least one practical utility, but did not require that Fisher disclose the coding function or the natural function of any coded protein. Many patents issue for genetic molecules having a specific and

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[7] If an EST is considered as an intermediate for making an end product microarray, the Board's finding is consistent with law in other contexts concerning the patentability of intermediates. For example, when an intermediate used to make an end product is shown to contribute the feature that makes the end product unexpectedly superior to prior art, the intermediate may satisfy the contributing cause test for overcoming a case of *prima facie* obviousness against the intermediate. *In re Magerlein*, 602 F.2d 366, 372-73 (CCPA 1979).

substantial utility, where the genetic molecule's natural coding function, if any, is unknown or undisclosed. Well-known examples include patents on probes that have a specific and substantial use in diagnosing infection by detecting DNA from a specific infectious microorganism in a patient sample. In those cases, nature's use for the specific portion of microorganism DNA in the probe may be unknown.

Here, the Board correctly followed precedent that one may not patent a compound on allegations of use so nebulous as to be meaningless, leaving others to discover a practical use. The "undefined spectrum" of disclosure that Fisher complains of, Br. at 33, is not a new concept, but as no specific benefit is disclosed, the Board correctly found the claimed molecules are not anywhere on the "spectrum." A15-16. Mere discovery of a new compound for research is not enough to place the compound over the threshold of specific practical utility.

D. Fisher's Proposed Rule That Any Nucleic Acid Derived From Nature Must Be *Per Se* "Useful" Would Negatively Impact The Art.

1. Patentable Compounds Have A Specific And Substantial Utility, Whether They Are Designed Prospectively Or Derived From Natural Compounds.

In all technologies, inventions are found useful or not useful depending on the evidence for utility. *Fujikawa*, 93 F.3d at 1564. Mechanical and electrical inventions are often designed "prospectively," with an intent to provide a specific

benefit, or solve a specific problem. The name of the invention often states the utility, *e.g.*, a screwdriver or a relay switch. Sometimes chemical inventions are made prospectively, by design, with a specific goal in mind, *e.g.*, an enzyme inhibitor designed and made to fit the known dimensions of an enzyme active site to thereby block the enzyme's activity, with a resultant industrial use or pharmacological benefit.

In contrast, some chemical inventions are derived from nature, *e.g.*, when mRNA molecules are found in plants and copied as cDNA molecules. If nothing at all is known about how to use such molecules, they are objects of research or investigation. They can be studied by a variety of tests, and the test results may or may not lead to later discovered practical applications. When the compound is a fragment of genetic material, a common first test might be sequencing, just as any chemist finding a new compound might first learn the structure of the new compound. If the structure of the new compound reveals a similarity to another compound already known to have a utility, it may be reasonable to impute a similar utility to the newly discovered molecule, depending on the facts. *E.g., Brana*, 51 F.3d at 1567. That is not the case here.

In the pharmaceutical arts, practical utility may be shown by adequate evidence of pharmacological activity. *E.g.*, *Cross*, 753 F.2d at 1043 (noting

Board's holding that "[t]ests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use."). Thus, on the spectrum of disclosure, the demonstration of specific pharmacological effects may be enough, without a disclosure of a further therapeutic use.

In the polymer art, the disclosure of the structure and some physical properties for a new polymer were not enough to support a finding of utility. *Ziegler*, 992 F.2d at 1203. Although Ziegler described the new polymer as "plastic-like," the disclosure of descriptive properties failed to establish that a specific and substantial utility was available.

Assuming that Fisher's ESTs belong to a class of compounds that is the subject of serious research, that alone does not provide a currently available practical utility. Rather than being practical, Fisher's proposed utilities are actually testing methods that put the discovered molecules through various standard routines applied to <u>any</u> newly discovered EST. In *Brenner's* term, the claimed molecules are objects of "use-testing." *Brenner*, 383 U.S. at 1042.

The claimed molecules may correspond to genes with "knowable" functions, as Fisher argues, Br. at 36, but Fisher does <u>not</u> know and did not disclose the functions. Even if the natural function of a gene becomes known, that

does not necessarily mean that a specific benefit would then be available for isolated molecules containing fragments of the gene. One cannot get a patent now based on a specific practical and substantial utility discovered later. *Ziegler*, 992 F.2d at 1203. Whatever the present value of a future utility is, it is not a currently available specific and substantial utility.

When the Supreme Court declined to extend patents to compounds lacking a "degree of specific utility," it was concerned that a patent not engross a vast area of technology without a compensating benefit to the public. *Brenner*, 383 U.S. at 1041-42. The Court found "absolutely no warrant" for granting patents on a chemical compound whose "sole 'utility' consists of its potential role as an object of use-testing." *Id*. at 1042. Even considering the scope of investigational testing suggested by over 200 documents purportedly incorporated by reference, the specification fails to identify even one specific practical use for any of the claimed compounds.

2. If Fisher Is Correct, Any EST Would Satisfy § 101.

In the field of plant genetics, it is reasonable to expect that issuing a patent on Fisher's compounds now would hurt, rather than help, progress in the field. Under Fisher's attenuated construction of "useful," any EST would be patentable under § 101 based on the theory that it would likely base pair with a chromosome.

Accordingly, thousands of patents could issue just from Fisher's specification, unless the prior art happens to disclose the same random fragmentary sequences, which is highly unlikely. Similarly, thousands or tens of thousands of patents on ESTs would issue for every plant or animal.[8] The result of a minimalist standard would be that patents would issue in this field on the results of structural analysis, coupled with the assumption that any EST is useful because it likely binds somewhere on a chromosome.

Other problems will arise as well. For example, it easy to see that if Fisher's EST is a random fragment of a cDNA, and another party discloses a different EST of the same cDNA, both could obtain patents covering the same cDNA, but § 101 states that only one patent can issue on an invention. For each of the genes, or fragments thereof, that is the subject of a patent claim held by someone else, a license would have to be negotiated. Each overlapping patent claim would be an extra "tollbooth" for the same cDNA. The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

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[8] In CHEMICAL WEEK, December 23-30, 1998, Peter Fairly reported on *The Genomics Race*. A379-86. According to the article, several companies, including Monsanto, were intending "to tie up as much intellectual property as quickly as possible" involving ESTs from corn and other crops. A382. The report also noted the debate in the industry over whether simple sequencing would be enough to support a patent. *Id*.

> [I]n rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." . . . To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230 (1964) (citations omitted).

What Fisher discloses is a plan for learning more about the invention, not a currently available benefit. A specific benefit is yet to be discovered and disclosed. The biochemical testing procedures Fisher proposes as utilities might allow those of skill in the art to learn such things as where an associated gene might be on a chromosome, or whether there are similar compounds in other organisms, or whether an associated gene is expressed at a particular time in the life cycle of the organism, or expressed more in some tissue than others. But the same is likely true for any nucleic acid extracted from any living cell and copied into cDNA, including not only Fisher's 32,000 ESTs, but also the over 600,000 ESTs derived from corn and other plants listed in Monsanto's six related appeals, as well as any ESTs associated with any of the millions of organisms in existence.

Fisher's compounds can be used in research procedures which may or may not lead to later discoveries of practical uses, and may lead to the discovery of other compounds of unknown utility. "It is not enough that the specification disclose that the intermediate exists and that it 'works,' reacts, or can be used to

produce some intended product of no known use. Nor is it enough that the product disclosed to be obtained from the intermediate belongs to some class of compounds which now is, or in the future might be, the subject of research to determine some specific use." *Kirk*, 376 F.2d at 945.

E. The Specification Fails To Teach How To Use The Invention.

The how to use prong of § 112 incorporates as a matter of law the requirement that the specification disclose a practical utility for the invention. *Ziegler*, 992 F.2d at 1200. Thus, this Court should also affirm the Board's legal conclusion that the claims are not enabled, because the claimed molecules do not have a specific practical utility. *Ziegler*, 992 F.2d at 1201. *Accord*, *Chiron v. Genentech*, 363 F.3d 1247, 1254 (Fed. Cir. 2004) ("Nascent technology, however, must be enabled with a 'specific and useful teaching.'" (quoting *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1368 (Fed. Cir. 1997)).

CONCLUSION

Substantial evidence supports the Board's finding that the claimed compounds do not have a specific and substantial utility. Thus, this Court should affirm.

Respectfully submitted,

December 7, 2004

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PROOF OF SERVICE

I hereby certify that on this 7th day of December, 2004, I served the foregoing BRIEF AND ADDENDUM FOR APPELLEE, THE DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE upon counsel by causing two copies to be delivered by FederalExpress to:

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December 7, 2004

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The claim on appeal

1. 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.

A169.

ADDENDUM

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