No. 2008-1184
(Serial No. 09/667,859)

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

IN RE MAREK Z. KUBIN and RAYMOND G. GOODWIN

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

BRIEF OF *AMICUS CURIAE* BIOTECHNOLOGY INDUSTRY ORGANIZATION SUPPORTING APPELLANTS AND REVERSAL

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UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

IN RE KUBIN, 2008-1184

CERTIFICATE OF INTEREST

Counsel for *Amicus Curiae*, Foley & Lardner LLP, certifies the following:

1. The full name of every party or amicus represented by me is:

Biotechnology Industry Organization

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) is:

Biotechnology Industry Organization

3. The parent companies, subsidiaries (except wholly-owned subsidiaries), and affiliates that have issued shares to the public, of the party or amicus curiae represented by me are:

None

4. The names of all law firms and companies and the attorneys that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

STATUTES

I. STATEMENT OF IDENTITY, INTEREST, AND AUTHORITY OF *AMICUS CURIAE* UNDER F.R.A.P. 29(C)(3)

Innovation in biotechnology affects many facets of human existence. For example, biotechnology research into agriculture has increased harvests worldwide through the creation of higher yields, and pest and herbicide resistant crops. Biotechnology is responsible for new therapies to treat heart disease, cancer, AIDS, stroke, septic shock, diabetes, anemia, cystic fibrosis, multiple sclerosis, lupus, kidney disease and liver disease. Many more inventions, however, have yet to make the transition from foundational knowledge to practical and safe solutions for health, nutrition, and energy needs. These benefits from biotechnology depend upon a patent system in which the biotechnology industry and its investors need not fear that innovations will be invalidated as obvious merely because they are combinations of pre-existing technologies or result from the use of known production methods.

The Biotechnology Industry Organization ("BIO") is a trade association with over 1,150 companies, academic institutions, and biotechnology centers involved in the research and development of healthcare, agricultural and environmental products. BIO's members file thousands of patent applications each year directed to, inter alia, nucleotide sequences, peptides, vectors, plasmids, cell lines,

screening and treatment methods, and manufacturing processes. Predictable patent protection, in particular, patent protection for compounds, is often considered a prerequisite to adequate investment in the often risking and lengthy development of biotechnology-based products. Whether the Board erred in finding Kubin's claim 73 obvious under 35 U.S.C. § 103, and in restating this Court's precedent regarding the patentability of chemical compounds, are of vital interest to BIO's members. Accordingly, BIO submits this brief to help this Court understand that claim 73 is patentable and explain why BIO believes discarding this Court's precedent will negatively impact innovation in the biotechnology industry.

Amgen, Inc., assignee of the application at issue in this case, is a member of BIO, but has not contributed to the filing of this brief.

BIO obtained consent from both parties to file this *amicus* brief.

II. BACKGROUND

This appeal originated in a decision of the United States Patent and Trademark Office ("USPTO"), Board of Patent Appeals and Interferences ("Board") upholding a final rejection of the claims pending in U.S. Patent Application No. 09/667,859. *Ex parte Kubin*, 2007 WL 2070495 (Bd. Pat. App. & Interf.).

III. SUMMARY OF THE ARGUMENT

Amicus supports reversal of the Board's decision to affirm the final rejection of claim 73 as obvious under 35 U.S.C. § 103(a).

The Board erred in failing to follow controlling legal authority, in particular *In Re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995). The Board misinterpreted KSR as weakening the legal principles announced by *Deuel*. The Board's decision is based on a novel legal theory lacking any precedent in patent law, that is, that obviousness may be based purely on the route the inventor takes to arrive at the invention, where the structure of the invention was not predictable as a combination of known structural elements. This novel legal theory could severely limit the patentability of future inventions that utilize known methods in their discovery. In particular, new biochemical entities (*e.g.*, nucleotides, peptides, vectors, and plasmids) could be considered obvious despite their nonobvious structures, because such biochemical entities would be considered the obvious result of the use of a known research method.

IV. ARGUMENT

A. THE BOARD ERRED IN IGNORING *DEUEL* AS CONTROLLING AUTHORITY AND IN NOT CONSIDERING STRUCTURAL SIMILARITY

The Board committed legal error by failing to apply the holding of *Deuel* to this case. The Board's reasoning is contrary to what *Deuel* requires. *Deuel* held that the obviousness of claimed DNA molecules must focus on the claimed compounds themselves, as defined by their structure, which generally requires consideration of structural similarity:

> Because Deuel claims new chemical entities in structural terms, a *prima facie* case of unpatentability requires that the teachings of the prior art suggest *the claimed compounds* to a person of ordinary skill in the art. Normally a *prima facie* case of obviousness is based upon structural similarity, *i.e.*, an established structural relationship between a prior art compound and the claimed compound.

Deuel, 51 F.3d at 1557-58 (emphasis in original). In emphasizing structural similarity as the proper basis for determining obviousness, this court rejected an obviousness determination based on the method used for arriving at the claimed DNA molecules:

> The PTO's focus on known methods for potentially isolating the claimed DNA molecules is also misplaced because the claims at issue define compounds, not

> methods. . . . "[T]he issue is the obviousness of the claimed compositions, not of the method by which they are made."

Deuel, 51 F.3d at 1559 (quoting *In re Bell*, 991 F.2d 781, 785 (Fed. Cir. 1993)). In the instant case, the Board equally failed to consider any structural features of the claimed NAIL cDNAs, instead basing obviousness on the methods available for isolating NAIL cDNA.

> Thus, an obvious method of obtaining a single nucleic acid molecule encoding NAIL may be all that is required to show that the presently claimed genus of nucleic acid molecules is unpatentable under § 103.

A7. In so doing, the Board squarely applied the reasoning that *Deuel* rejected. This is legal error.

1. The Board's Reliance On "Factual Differences" And "Increased Level Of Skill In The Art" Is Unfounded

The Board justified ignoring *Deuel* by referring to alleged factual differences and increased level of skill in the art. A7.

Regarding the level of skill in the art, the Board did not explain the alleged advance in the level of skill in the art since *Deuel*. The application at issue in *Deuel*, 07/542,232, was effectively filed in 1990, while Valiante, Mathew, and Sambrook, the principal references relied on by the Board in the present case, have

filing and publication dates of 1994, 1993, and 1989, respectively. The Board did not explain what in these references supports a proposition that an advance in the level of skill took place during the intervening years, nor did the Board explain how such an advance is relevant to the application of *Deuel* to the facts of the present case.

Further, the Board appears to have quoted *Wallach* out of context. The Board quoted *Wallach* as follows for the statement the "state of the art has developed [since] *In Re Deuel*"):

> Regardless of some factual similarities between *Deuel* and this case, *Deuel* is not controlling and thus does not stand in the way of our conclusion, given the increased level of skill in the art and the factual differences. *See In re Wallach*, 378 F.3d 1330, 1334, 71 USPQ2d 1939, 1942 (Fed. Cir. 2004) ("state of the art has developed [since] *In re Deuel*").

A7. However, as can be seen from the following complete quote, *Wallach* does not support the premise that advanced skill in the art renders *Deuel* non-controlling:

> [W]e agree with Appellants that the state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it, and that one of ordinary skill in the art at the time the '129 application was filed may have therefore been in possession of the entire genus of DNA

> sequences that can encode the disclosed partial protein sequence, even if individual species within that genus might not have been described or rendered obvious. *Cf. In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995).

In re Wallach, 378 F.3d 1330, 1333 (Fed. Cir. 2004). Insofar as it pertains to obviousness, the above quote at most stands for the proposition that the level of skill in the art had advanced enough that a given amino acid sequence may render obvious the genus of all DNA sequences, but not the individual DNA species, encoding that amino acid sequence. This is a far cry from the present facts.

In the present case, the prior art disclosed the isolated NAIL (p38) protein, characterized by its molecular weight and, functionally, by its antibody binding affinity to mAb C1.7, as well as the merely "cumulative" teaching of the corresponding mouse gene and gene product. A4-A5. Unlike the circumstances in *Deuel*, the prior art in the present case lacked even a partial amino acid sequence. *See* A5.

Regarding factual differences, the Board did not explain which facts differed such that the Board could justifiably ignore *Deuel*. Indeed, the facts of this case provide no basis for distinguishing *Deuel*. The absence of a prior art amino acid sequence for NAIL is instructive when evaluating similarities and differences between this case and the facts in *Deuel*. In *Deuel*, the examiner reasoned that a

skilled person could have used the preexisting partial amino acid sequence for HBGF to (1.) design a gene probe, and then (2.) screen a DNA library in accordance with established cloning methods to (3.) isolate the claimed nucleotide sequences. *Deuel*, 51 F.3d at 1556.

In the present case, there was no preexisting amino acid sequence. Thus, compared to *Deuel*, a skilled person starting with Valiante's isolated p38 protein, and armed with the generic laboratory techniques taught by Sambrook and the commercially available C1.7 antibody, would have had to go through the additional steps of (1.) purifying p38 and (2.) obtaining its partial amino acid sequence before being able to (3.) design gene probes, (4.) screen DNA libraries and (5.) isolate the claimed nucleotide sequences. *See* A5 (neither DNA nor protein sequences disclosed in the prior art). Clearly, the distance between the prior art and the invention of Kubin's claim 73 is substantially farther away from the facts of *Deuel* and, as noted above, *In re Wallach* provides no support for the Board's decision to ignore binding precedent.

Accordingly, the Board erred in relying on "factual differences" and "increased level of skill in the art" without substantial evidence in support.

2. The Board Erred In Concluding That *KSR V. Teleflex* Weakened The Holding Of *Deuel*

The Board justified ignoring *Deuel* by concluding that KSR "cast doubt" on *Deuel*:

> Appellants heavily rely on *Deuel*. (*See, e.g.*, Br. 19.) To the extent *Deuel* is considered relevant to this case, we note the Supreme Court recently cast doubt on the viability of *Deuel* to the extent the Federal Circuit rejected an "obvious to try" test. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, ___, 82 USPQ2d 1385, 1394, 1396 (2007) (citing *Deuel*, 51 F.3d at 1559). Under *KSR*, it's now apparent "obvious to try" may be an appropriate test in more situations than we previously contemplated.

A8. The above quote suggests that *KSR* referred to *Deuel* in discussing "obvious to try." As explained below, *KSR* cited *Deuel* only once, in summarizing this court's decision; *KSR* never mentioned *Deuel* in its analysis of "obvious to try."

As explained below, *KSR* related to whether it would have been "obvious to try" a combination of known components, not "obvious to try" known methods to arrive at completely unknown structure. The latter is the situation here.

The Board committed legal error in ignoring *Deuel*.

B. *DEUEL* REMAINS BINDING PRECEDENT AND WOULD REQUIRE HEARING EN BANC TO OVERTURN.

The Supreme Court opinion in *KSR* did not affect the holding of *Deuel*. *KSR* related to obviousness of combinations of known components to directly yield predictable structures. Specifically, the issue in *KSR* was whether a claim to a vehicle control pedal was obvious over the combination of two prior art references separately disclosing components that, when combined, directly yield the claimed pedal.

In contrast, *Deuel* and the presently claimed invention relate to compounds clearly not predictable by comparison to any other compounds in the prior art, and whose structure cannot be described as an obvious combination of known components. As in *Deuel*, the prior art in the present case discloses no similar structures, and does not provide a "finite number of identified, predictable solutions" representing such structures. *See KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1742 (2007). In *KSR* the Court repeatedly emphasized its focus on obviousness of combinations of known components:

> The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.

Id. at 1739.

> [W]hen a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result.

Id. at 1740.

> [W]hen a patent "simply arranges old elements with each performing the same function it had been known to perform" and yields no more than one would expect from such an arrangement, the combination is obvious.

Id. (quoting *Sakraida v. AG Pro, Inc.*, 425 U. S. 273, 282 (1976)).

> [A] court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.

Id.

> [A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.

Id. at 1741.

> [C]ommon sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established function.

Id.

The Supreme Court in *KSR* stated in dicta that "obvious to try" could serve as basis for obviousness. The Supreme Court's comments, however, were directed

to the obviousness of combining *known* prior art elements to yield a predictable structure:

> The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the *combination of elements* was "obvious to try." *Id.*, at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a *combination* was obvious to try might show that it was obvious under § 103.

Id. at 1742 (emphases added).

Unlike in the present case, the above comments are directed to when there is a design need or market pressure to solve a problem and a skilled artisan could arrive at the claimed invention by predictably combining structural elements from the prior art. *KSR* does not support the Board's position that an "obvious to try" analysis could apply to an invention or discovery—such as a genus of nucleic acid compounds—that is not a predictable combination of known structural elements. Nor does *KSR* stand for the proposition that an unpredictable nucleic acid sequence could be rendered unpatentable by using a known method for discovering it.

This is not a case where the Supreme Court has specifically criticized a Federal Circuit doctrine as conflicting with Supreme Court precedent, such that this court would be compelled to follow. *Cf. SanDisk Corp. v. STMicroelectronics, Inc.*, 480 F.3d 1372, 1380 (Fed. Cir. 2007) (noting that "the Court specifically addressed and rejected our reasonable apprehension test" in *MedImmune, Inc. v. Genentech, Inc.*, ---U.S. ----, 127 S.Ct. 764, 166 L.Ed.2d 604 (2007)).

The Supreme Court in *KSR* never cited *Deuel* in its own analysis and discussion of "obvious to try." Instead, the Court cited *Deuel* just once in summarizing this court's reasoning. Specifically, *Deuel* appears in a parenthetical of the Supreme Court citation to this court's rejection of "obvious to try" as basis for considering it obvious to combine components disclosed in separate references:

> That it might have been obvious to try the combination of Asano and a sensor was likewise irrelevant, in the court's view, because "'"[o]bvious to try" has long been held not to constitute obviousness.'" *Id.*, at 289 (quoting *In re Deuel*, 51 F. 3d 1552, 1559 (CA Fed. 1995)).

KSR, 127 S. Ct. at 1739.

Deuel appears nowhere else in *KSR*. The Supreme Court could have discussed *Deuel* but did not. In particular, *KSR* nowhere mentions the legal principles expressed in *Deuel*. *KSR* nowhere mentions obviousness based on the

method of arriving at the claimed invention. *KSR* nowhere mentions obviousness of new chemical entities, and nowhere conflicts with *Deuel* as good patent law.

This court's statements in *Deuel* about "obvious to try" are peripheral to the core legal principle expressed in *Deuel* that:

> What cannot be contemplated or conceived cannot be obvious. . . . [T]he existence of a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious, in the absence of other prior art that suggests the claimed DNAs.

Deuel, 51 F.3d at 1558-59.

Taken in context, the comments in *Deuel* regarding "obvious to try" relate to general incentive to solve a problem absent a recognizable solution—not motivation to try combinations of known components:

> "Obvious to try" has long been held not to constitute obviousness. *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680-81 (Fed. Cir. 1988). A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out.

Deuel, 51 F.3d at 1559. *KSR* did not overturn, or even weaken, *Deuel*'s precedential authority. Nor did the Supreme Court in *KSR* intend to replace one rigid obviousness test (the "TSM test") with another ("obviousness to try").

Deuel is controlling legal authority on the obviousness of nucleotide sequence claims.[1] This court must sit *en banc* to overturn *Deuel*. A panel has no authority to overturn or ignore *Deuel*, in light of the barely relevant dicta in *KSR*.[2] Neither does the Board.

C. *DEUEL* IS WELL-GROUNDED IN PATENT LAW

The legal principles underpinning *Deuel* are too well grounded in this court's jurisprudence to be casually disregarded by the PTO.

Deuel does not stand alone. Before *Deuel*, this court held that prior art disclosure of the complete amino acid sequence of a protein does not render obvious the natural, or human, gene that codes for the protein. *In re Bell*, 991 F.2d 781, 784 (Fed. Cir. 1993) (holding that due to the genetic code's degeneracy, the "amino acid sequences could be coded for by more than 10^{36} different nucleotide

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[1] In a recent pre-*KSR* case on utility of nucleotide sequence claims, a dissenting opinion argued that the utility requirement of 35 U.S.C. § 101 was less well suited than obviousness establish unpatentability of such claims, and criticized Deuel as making obviousness too difficult to establish. *In re Fisher*, 421 F.3d 1365, 1367 (Fed. Cir. 2005) (Rader, J., dissenting). The dissent nevertheless recognized Deuel as controlling precedent.

[2] This court has recently, post-*KSR*, spoken approvingly of *Deuel* and its approach to obviousness. *See Takeda Chem. Indus., Ltd. v. Alphapharm Pty.*, 492 F.3d 1350, 1356 (Fed. Cir. 2007) ("a *prima facie* case of unpatentability [requires] a showing that the 'prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention'" (quoting *Deuel*, 51 F.3d at 1558)).

sequences, only a few of which are the human sequences that Bell now claims"). In *Bell*, the claims at issue were drawn to nucleic acid molecules containing a human sequence encoding a growth factor. The prior art disclosed the amino acid sequence for the growth factor. This court rejected the proposition that "the established relationship in the genetic code between a nucleic acid and the protein it encodes also makes a gene prima facie obvious over its correspondent protein" in the context of a claimed human gene. *Bell*, 991 F.2d at 784. This court emphasized in *Bell* that "the issue is the obviousness of the claimed compositions, not of the method by which they are made." *Bell*, 991 F.2d at 785.

Deuel followed *Bell*, in holding that a partial amino acid sequence of a desirable protein would not render obvious claims broadly covering any DNA sequence coding for the protein's complete amino acid sequence, as recited in the claim, or a claim to a cDNA having a recited nucleotide sequence that codes for the protein. *Deuel*, 51 F.3d at 1555. *Deuel* emphasized that the patent claims at issue defined "new chemical entities in structural terms" and that for such new chemical entities, "[n]ormally a prima facie case of obviousness is based upon structural similarity, *i.e.*, an established structural relationship between a prior art compound and the claimed compound." *Deuel*, at 1557-58.

In *Bell* and *Deuel*, the prior art disclosed general methods for isolating cDNA or DNA molecules. Nevertheless, this court held as follows:

> We today reaffirm the principle, stated in *Bell*, that the existence of a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious, in the absence of other prior art that suggests the claimed DNAs.

Id. at 1559.

Deuel's reliance on conventional tests of obviousness for chemical compounds is appropriate, because its characterization of the claimed genes as new chemical entities is accurate. "A gene is a chemical compound." *In re Wallach*, 378 F.3d 1330, 1335 (Fed. Cir. 2004) (quoting *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991)).

D. PATENTABILITY SHALL NOT BE NEGATIVED BY THE MANNER IN WHICH THE INVENTION WAS MADE

The Board's line of reasoning would require evaluating how the inventors arrived at the claimed invention, a dangerously subjective test that would contribute no predictability or clarity to the law of obviousness. This approach also violates the plain prohibition in the final sentence of 35 U.S.C. § 103(a) not to consider the inventor's method of discovery: "Patentability shall not be negatived by the manner in which the invention was made." § 103(a).

This second sentence of § 103(a) was meant to exclude from an obviousness analysis the method used to arrive at an invention. The legislative history of the 1952 Patent Act introducing § 103(a) contains the following statement: "The second sentence [of § 103(a)] states that patentability as to this requirement is not to be negatived by the manner in which the invention was made, that is, it is immaterial whether it resulted from long toil and experimentation or from a flash of genius." S. Rep. No. 82-1979 (1978), *as reprinted in* 1952 U.S.C.C.A.N. 2394, 2411, 1952 WL 3180 (Leg. Hist.). *See also*, *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 16, 17 n.8 (1966) ("The second sentence [of § 103(a)] states that . . . it is immaterial whether [the claimed invention] resulted from long toil and experimentation or from a flash of genius").

This court's predecessor court, the Court of Customs and Patent Appeals, whose decisions this court has adopted as binding precedent, *South Corp. v. U.S.*, 690 F.2d 1368 (Fed. Cir. 1982), has relied on this prohibition to strongly criticize reference to "routine testing" or "routine experimentation" as basis for obviousness. *See, e.g.*, *In re Yates*, 663 F.2d 1054, 1056 n.4 (C.C.P.A. 1981) ("[E]mphasis upon routine experimentation is contrary to the last sentence of section 103."); *Appl'n of Saether*, 492 F.2d 849, 854 (C.C.P.A. 1974) ("In his argument that 'mere routine experimentation' was involved in determining the optimized set of characteristics, the solicitor overlooks the last sentence of 35

U.S.C.A. § 103"); *Appl'n of Fay*, 347 F.2d 597, 602 (C.C.P.A. 1965) ("[W]e do not agree that 'routine experimentation' negatives patentability.").

This court has acknowledged those C.C.P.A. cases in emphasizing that routine experimentation might be appropriate to consider where the inventors simply verified the expected results of forming suggested addition salts of a known compound, but not where the inventors discovered a structurally nonobvious new compound:

> These type of experiments used by Pfizer's scientists to verify the physicochemical characteristics of each salt are not equivalent to the trial and error procedures often employed to discover a new compound where the prior art gave no motivation or suggestion to make the new compound nor a reasonable expectation of success.

Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1366-67 (Fed. Cir. 2007). *Amicus* urges this court to be mindful that "the pharmaceutical industry may be particularly adversely impacted by application of an 'obvious to try' analysis." *Pfizer v. Apotex*, at 1367 (citing the dissent in *In re Merck & Co.*, 800 F.2d 1091 (Fed. Cir. 1986). In particular, this court should be mindful of the tension between the "obvious to try" doctrine and the second sentence of § 103(a), as noted in dissent in *In re Merck*:

> Congress has also rejected [the obvious to try] approach by enacting the second sentence of 35 U.S.C. § 103, which states "[p]atentability shall not be negatived by the manner in which the invention was made." The reviser's note on this sentence states "it is immaterial whether it resulted from long toil and experimentation or from a flash of genius."
>
> The obvious-to-try analysis is an attack on the method of making an invention that specifically penalizes people in areas of endeavor where advances are won only by great effort and expense. The pharmaceutical field is particularly hard hit because there is an overabundance of structures that are obvious to try.

In re Merck, 800 F.2d at 1099-1100 (Baldwin, J., dissenting). To the extent that *KSR* breathed new life into the obvious to try approach to obviousness, this should not be extended to circumstances where the entire obviousness analysis rests on the particular method used to arrive at a new chemical entity, absent disclosure in the prior art of structurally similar compounds or combinable components yielding a predictable target structure.

E. THE BOARD'S ERRORS JEOPARDIZE BIOTECHNOLOGICAL INNOVATION AND EXISTING NUCLEIC ACID PATENTS

Amicus urges caution in setting precedent for establishing obviousness based on known methods for arriving at an invention, especially where the structure of the invention cannot be predicted from prior art structures or structural elements.

The Board's decision disturbs settled expectations regarding validity of existing nucleic acid patents. If this court affirms the Board in *Kubin*, the validity of numerous issued patents on genomic inventions would be in doubt.

The Board held that it would be obvious to isolate and identify the cDNA of a protein once the protein is recognized as useful, even absent any disclosure of the protein's amino acid sequence, because "there were a limited number of methodologies available" to determine a protein's cDNA. A9.

As a result, it would be nearly impossible to patent a claim covering cDNA coding for a protein if the protein has been identified as useful in the prior art. This would cast doubt on the validity of the many issued patents claiming such cDNA. The Board's reasoning could apply regardless of whether the claim is drawn to a genus of cDNAs that encode a specific amino acid sequence (as is the case here), or to a particular nucleotide sequence (as was the case in *Bell* and in claims 5 and 7 of *Deuel*).

But the Board's obviousness reasoning does not end with the cDNA that encodes such a protein. Scientists often use established molecular biology methods to insert newly-discovered nucleotide sequences into host cell lines, and the so-transformed host cell lines are grown in cell culture to produce the protein in

recombinant form. Under the Board's reasoning, the prior art disclosure of the protein could render obvious not only the cDNA, but also the recombinant host cell line into which that cDNA was inserted. The same "obvious to try" reasoning could apply to other lines of scientific inquiry that logically follow from the discovery of the cDNA and rely on established research methods. As available molecular biology methods increase in number and become more reliable, obviousness (under the Board's reasoning) would extend further and further along the chain of scientific inquiry, irrespective of the fact that the end result of this often time-consuming and expensive research effort results in an entirely unpredictable life-enhancing innovation.

Amicus posits that this reasoning inherently threatens future innovation in molecular biology and the development of new and valuable products made by modern biotechnology. Paradoxically, the growing sophistication and reliability of modern molecular biology techniques, which were created in the hope that they will enable untold discoveries and advances in biology and medical and agricultural science, would prevent universities, research institutions, and early-stage biotechnology businesses from obtaining patents on unpredictable nucleotide sequences and other valuable inventions based on them, and would discourage the investment in genomic research and development of therapeutic and agricultural products that so heavily depend on the availability of patent protection.

F. THE BOARD'S REASONING IF AFFIRMED WOULD THREATEN PATENTABILITY OF CHEMICAL ENTITIES IN GENERAL

After *KSR*, in a case involving obviousness of a combination of known components, a dissenting opinion cited § 103(a) in voicing concern about the dangers to the pharmaceutical industry of giving excessive weight to whether the inventors used methods considered to be routine:

> The panel also found that amlodipine besylate was not patentable since it was made by a routine testing or a "well known problem solving strategy." This clearly violates the statutory mandate that "patentability shall not be negatived by manner in which the invention was made." 35 U.S.C. 103(a). Many if not most pharmaceutical inventions are discovered through a routine screening protocol or through an established trial and error process. Pharmaceutical inventions discovered by these routine screening methods include not only new formulations and salt forms, but also include the active pharmaceutical compounds themselves. Thus, this decision calls into question countless pharmaceutical patents, which in turn could have a profoundly negative effect on investments into the design and development of new life-saving pharmaceuticals.

Pfizer, Inc. v. Apotex, Inc., 488 F.3d 1377, 1384 (Fed. Cir. 2007) (denial of reh'g en banc) (Rader, J., dissenting). Such a negative effect would be fueled by the Board's decision here, which *Amicus* asks the court to reverse by following its precedent.

The Board's decision opens the door to a new and potentially dangerous basis for rejecting claims to new chemical and biochemical compounds. This would threaten the development of new drugs, diagnostic tests, and other biotechnology-derived products such as pest and herbicide resistant crops, which now rely more and more on biotechnology for their development. Under the Board's reasoning, a new chemical entity, created in the hope that it would have certain properties, could be obvious if it was arrived at by known methods, even if the new chemical entity was structurally dissimilar to, and completely unpredictable from, any prior art compound.

This new obviousness doctrine could render unpatentable new chemical entities developed using modern drug development techniques. One such technique is to identify compounds that inhibit an enzymatic protein known to play a role in a medical indication. Although the technique used to test and identify active compounds is known in the art, tens or hundreds of thousands of compounds of varying structures may be tested to identify the compounds with the desired properties. Presently, new compounds discovered by such a method would be nonobvious, provided the compounds are structurally dissimilar from prior art compounds. Under the Board's decision, however, such new compounds might be considered obvious. The methods used are routine (synthesizing a collection of compounds for testing, testing the compounds for *in vitro* activity against the

enzyme, and testing active compounds for *in vivo* activity in an animal model) and while the compounds' structures are dissimilar to those in the prior art, there would have been a reasonable expectation of success that the large-scale use of such routine methods would identify at least some compounds with the desired biological properties.

Similarly, if a plant is found to have certain useful properties (*e.g.*, a particular medicinal value or a resistance to certain insect pests), the active compound extracted from the plant might be considered obvious. Known methods would be used to extract the compound. And while the compound might be structurally dissimilar from prior art compounds, the compound could be expected to exhibit the medicinal or pesticidal properties of the plant, and would be expected to exist in the plant. Thus, there would have been a reasonable expectation of success in isolating an active compound (albeit unknown beforehand) using known methods.

The Board's reasoning, in addition to being contrary to this Court's precedent, could render obvious many such life sciences inventions resulting from using known research methods. BIO urges this Court not to adopt such a change in precedent because doing so would discourage investment in medical and

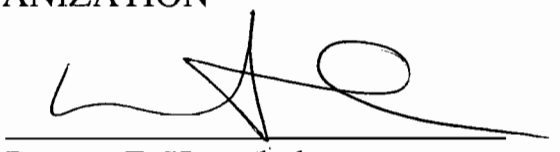
agricultural discovery and slow the pace at which new drugs, diagnostics, and crops are developed. Public policy cries out against such a result.

V. CONCLUSION

BIO requests reversal of the Board's decision. BIO further requests that this Court avoid disturbing the settled law of *Deuel*. The record and controlling precedent provide no basis for diluting the clear doctrinal pronouncements of *Deuel* and its line of case law.

Respectfully submitted,
BIOTECHNOLOGY INDUSTRY ORGANIZATION

June 10, 2008

By 

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UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

IN RE KUBIN, 2008-1184

I HEREBY CERTIFY that two (2) copies of the foregoing BRIEF OF AMICUS CURIAE BIOTECHNOLOGY INDUSTRY ORGANIZATION SUPPORTING APPELLANTS AND REVERSAL were sent by overnight courier this 10th day of June, 2008, to the following:

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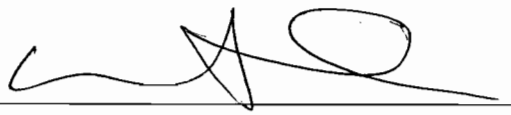
(s) 

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