



# LIFE SCIENCES LAW & INDUSTRY



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**REPORT**

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**Patents**

*The U.S. Court of Appeals for the Federal Circuit April 3 in *In re Kubin* affirmed the Patent Office's rejection of an attempt to patent a gene sequence, stating that well-known cloning techniques could derive the "readily knowable and obtainable structure of an identified protein" coded by that gene. In ruling, the court said that its *In re Deuel* precedent had been discredited by the U.S. Supreme Court decision on obviousness in *KSR International Co.* The initial reaction from the life sciences community was that the *Kubin* decision will be detrimental to patent prosecution. BNA asked attorneys working with life sciences-related patents to discuss the effect of the decision on biotechnology patents, life sciences law, and the life sciences industry..*

## ***In re Kubin* Decision Raises Troubling Issues for Life Sciences**

**T**he Federal Circuit's *In re Kubin* decision raises troubling issues for life sciences patent prosecution and litigation and could even delay pending legislation on follow-on biologics, life sciences attorneys told BNA, although some attorneys took a different view.

Janet M. MacLeod of Crowell & Morning LLP, New York, said that *Kubin* is likely to significantly affect the industry.

"*Kubin* discredits the court's repudiation of the 'obvious to try' doctrine it articulated in *Deuel*, but it does not preclude patent prosecution for nucleic acid molecules that encode a protein that was known in the prior art. Rather, in prosecution of claims directed to isolated nucleic acids, the obviousness inquiry will now follow on the predictability of a method of cloning a nucleic acid rather than the predictability of the sequence," MacLeod said.

"Rebuttal of a prima facie case of obviousness may consequently require evidence of unpredictability in the method of cloning or evidence of unexpected properties of the resulting nucleic acid molecule," she explained.

William Gaede of McDermott Will & Emery LLP, Menlo Park, Calif., told BNA that it is difficult to assess

the reach of *Kubin*'s holding because "many biological and chemical process techniques are known and basic DNA sequences and other chemical compounds are in the art. Will *Kubin* be applied to claims directed to antibodies?" Gaede asked.

Hans Sauer, associate general counsel for intellectual property at the Biotechnology Industry Organization, told BNA he was disappointed with the way the court analyzed and discredited the Federal Circuit's *Deuel* precedent, which has been key to classic biotechnology patents.

**Case History.** Marek Kubin and Raymond Goodwin submitted a patent application (No. 09/667,859) for polynucleotides encoding natural killer (NK) cell activation inducing ligand polypeptides (NAIL). NK cells have been implicated as mediators of host defenses against infection in humans with a variety of illnesses, such as varicella zoster, herpes simplex, hepatitis B, and hepatitis C. They also are involved with both resistance to and control of the spread of cancer. NAIL is a cell surface marker, or receptor, on the surface of NK cells. Claim 73 of the patent application cites the discovery of a binding relationship between NAIL and a protein

known as CD48. The NAIL-CD48 interaction has important biological consequences for NK cells, including an increase in cell cytotoxicity and in production of interferon.

A Patent and Trademark Office examiner rejected this and other claims as obvious under 35 U.S.C. § 103, and for lack of enablement and written description under 35 U.S.C. § 112. On appeal to the Board of Patent Appeals and Interferences, Kubin argued that the examiner's obviousness rejection conflicted with Federal Circuit precedent in *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995). In *Deuel*, the Federal Circuit made two related holdings key to biotechnology patenting: "knowledge of a protein does not give one a conception of a particular DNA encoding it," and "obvious to try" is an inappropriate test for obviousness. However, in affirming the examiner's rejection, the BPAI, in a 5-0 opinion written by Administrative Patent Judge Nancy Linck, distinguished *Deuel* and concluded that "at least one of appellants' claimed polynucleotides would have been obvious to one of ordinary skill in the art at the time Appellants' invention was made" (1 LSLR 345, 7/20/07). The board also said the holding in *Deuel* was in doubt because of the Supreme Court's decision in *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007) (see 1 LSLR 153, 5/11/07). Kubin appealed to the Federal Circuit (3 LSLR 6, 1/16/09).

**Deuel Discredited, O'Farrell Resurrected.** In the Federal Circuit's April 3 decision, Judge Randall R. Rader addressed obviousness only and affirmed the BPAI's decision, and in doing so issued a stronger statement that *Deuel* likely no longer is binding precedent (*In re Kubin*, Fed. Cir., No. 2008-1184, 4/3/09) (3 LSLR 318, 4/10/09).

Rader agreed with the board that the Supreme Court's ruling in *KSR* cast doubt on the Federal Circuit's repudiation in *Deuel* of the "obvious to try" doctrine. "Insofar as *Deuel* implies the obviousness inquiry cannot consider that the combination of the claim's constituent elements was 'obvious to try,' the Supreme Court in *KSR* unambiguously discredited that holding," Rader said.

Rader noted that the Supreme Court's admonition against such a formalist approach to obviousness "actually resurrects this court's own wisdom in" *In re O'Farrell*, 853 F.2d 894, 895-99 (Fed. Cir. 1988). *O'Farrell* acknowledged that the "obvious to try" incantation can be misunderstood, Rader said, adding that the court in that case outlined two situations where "obvious to try" can be erroneously equated with obviousness:

- Rejecting an invention as obvious to try is not warranted, according to *O'Farrell*, "where a defendant merely throws metaphorical darts at a board filled with combinatorial prior art possibilities," Rader said. At the opposite end of the spectrum, Rader noted, as encapsulated in *KSR*, obviousness arises "where a skilled artisan merely pursues 'known options' from a 'finite number of identified, predictable solutions.'"

- *O'Farrell* also found impermissible obviousness rejections where what was "obvious to try" was "to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." Again, Rader said in contrasting the inverse

proposition in *KSR*, patentability is barred for obviousness when "the improvement is [no] more than the predictable use of prior art elements according to their established functions."

"Obviousness does not require absolute predictability of success—all that is required is a reasonable expectation of success," Rader stressed, quoting from *O'Farrell*.

He found that the neither of the two "obvious to try pitfalls" applied in the instant case, concluding that "the record shows that a skilled artisan would have had a resoundingly 'reasonable expectation of success' in deriving the claimed invention in light of the teachings of the prior art."

**Troubling Implications.** Gaede told BNA that the decision overemphasizes the "obvious to try" inquiry addressed in *Deuel*, and raises "troubling implications for the future."

Gaede explained, "First, the decision appears not to have paid proper deference to the Federal Circuit's en banc decision *In re Dillon*, 919 F.2d 688 (Fed. Cir. 1990) and its panel decisions of *In re Bell*, 991 F.2d 781 (Fed. Cir. 1993) and *In re Deuel*. These decisions stand for the proposition that the fundamental obviousness inquiry of a chemical compound, such as DNA, is whether there is an established structural relationship between a prior art compound and the claimed compound. This was reaffirmed in *Takeda v. Alpharma* [see 2 LSLR 276, 4/11/08], which was post-*KSR*. *Kubin's* reliance on methods for isolating the claimed compounds, even if known, rather than on structural similarity of the claimed compound with the prior art, does not address the fundamental structural similarity issue and appears to resort to hindsight."

Gaede continued, "Second, it is difficult to assess where *Kubin's* reasoning stops because many biological and chemical process techniques are known and basic DNA sequences and other chemical compounds are in the art. Will *Kubin* be applied to claims directed to antibodies? In light of the human genome project putting human DNA sequences into the prior art, are claims directed to a human DNA sequence composition arguably obvious even if the utility of the prior art sequence is not known? In short, *Kubin* potentially raises a number of troubling issues for the ability of biotechnology companies to protect key DNA and small molecule compositions," Gaede said.

**FOB Bills May Be Delayed.** Jane Love of Wilmer Hale, New York, told BNA, "The effect of *In re Kubin* on the life sciences industry will likely include a focus on the discussion of *In re O'Farrell*. The scientific facts are important to develop insofar as they support a situation where there are combinations of prior art possibilities and the art teaches no more—here, the life sciences patentee would be throwing 'metaphorical darts' at this board of prior art. The development of the state of the art will be key in determining whether or not there would have been a reasonable expectation of success and to guard against impermissible hindsight. The language of *KSR* calls for a 'finite number of identified, predictable solutions' and the life sciences patentee can seek to develop the case of unpredictability when facing an obviousness challenge."

Crowell & Morning's MacLeod said that the decision will affect litigation of biotechnology patents, particularly if an abbreviated process for FDA approval of

follow-on biologic (FOB) or biogeneric drugs is approved by Congress and implemented. She wondered, however, if *Kubin* could actually frustrate approval of pending legislation that would create the abbreviated process.

Competing bills recently introduced in Congress (3 LSLR 348, 4/10/09; 3 LSLR 291, 3/27/09; 3 LSLR 240, 3/13/09) differ significantly in the length of the data exclusivity period—the period during which a follow-on applicant is precluded from using the innovator’s data to obtain FDA approval. MacLeod said, “The length of the data exclusivity period affects the timing of and incentive for challenges to the innovator’s patents and is the most contested aspect of the proposed legislation. Perceived vulnerability of biotechnology patents to an obviousness challenge based on *Kubin* will make a longer data exclusivity period and a longer time for return on investment even more critical for innovator companies and a shorter exclusivity period and earlier opportunity for patent challenge far more desirable to follow-on applicants.”

**Unclear, Disconcerting.** In its amicus brief urging the Federal Circuit to reverse the BPAI’s obviousness finding, the Biotechnology Industry Organization said, “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.”

Asked at a BIO conference in June 2008 to predict the outcome of the Federal Circuit’s review of *Kubin*, BIO’s Sauer said, “*Deuel* is the law. I think it would be hard for the Federal Circuit to confirm the board’s decision, especially since *KSR* was about mechanical inventions” (2 LSLR 562, 7/4/08).

After the CAFC’s decision was announced, Sauer told BNA he was disappointed with the way the court analyzed *Deuel*. He said that the court in *KSR* was talking about combination inventions and the “many ways of putting pieces of prior art together.” In contrast, *Deuel* involved the method of getting from “A to point B” when B is undiscovered. In *Kubin*, he said, “we have a protein in the prior art that wasn’t sequenced, and a reliable method to get from the protein to the nucleotide sequence,” but the structure was still unknown.

Also disappointing to Sauer was that nothing in the opinion showed where the Federal Circuit’s obviousness analysis would end in the chain of developments after discovering the structure. In *Kubin*, Sauer said, a protein blot on a gel made the later-discovered gene unpatentable because it would have been obvious to any scientist to try routine cloning methods to get to the same result. But while it was “obvious” that many scientists would have wanted to discover that gene and

that the tools for doing so existed, the simple fact is that Kubin discovered it first, Sauer said. Would the Patent Office rather that Kubin had not even tried? Sauer asked.

**Decision’s Significance Questioned.** Two noted attorneys writing for patent blogs took a more pragmatic view of the decision.

In an April 5 posting on the Patent Docs blog, Kevin E. Noonan of McDonnell Boehnen Hulbert & Berghoff, Chicago, acknowledged that patent applications filed after *Deuel* and prior to the Human Genome Project (HGP) could be made more open to an obviousness challenge because of the court’s decision. But cases involving many of these genes will be lacking some if not several of the factual underpinnings of the *Kubin* decision, Noonan wrote.

And for applications filed after the HGP, *Kubin* will have little effect since a fundamental pillar of the court’s decision in *Kubin* was that p38 was known, Noonan said. After the HGP, “many (if not most) of the genes patented or that have been attempted to be patented were not known prior to their discovery.”

Consequently, according to Noonan, “the sky will not be falling on biotechnology patenting” because of this decision. The court’s ruling “is sufficiently narrow that it should not provoke a sea change in the fortunes of such gene claims,” he concluded. (*For additional comments on the decision by Noonan, see related item in the Industry News section.*)

In his April 6 patent blog, Christopher Holman of the University of Missouri, Kansas City, School of Law, agreed with Noonan and added, “I am not so sure [the decision] will be that significant, unless investors perceive that it does have serious negative implications for biotechnology. I think we should try to counter that. A perception among investors that biotechnology has been harmed by *Kubin* could cause more damage to biotechnology than the decision itself.”

An attorney associated with one of the amicus briefs filed on behalf of the plaintiffs who asked not to be identified told BNA that the decision was on balance better than the BPAI decision in that it laid out a research pathway that suggested that the “obvious to try” concept can go both ways. The attorney added that the decision left plaintiffs a few unpredictability variables.

However, BIO’s Sauer seemed to voice the concerns of most of the attorneys interviewed when he told BNA that the opinion was “unclear but disconcerting enough to give us pause and consider its implications.”

BY JOHN T. AQUINO

Full text of the opinion is available at <http://pub.bna.com/ptcj/081184Apr3.pdf>.