

NEWSSTAND

"Obvious to Try": A New Standard for Biotechnology Inventions?

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This Spring, the United States Court of Appeals for the Federal Circuit ("Federal Circuit") handed down a widely anticipated decision pertaining to the biotechnology arts in *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009), which affirmed the finding by the Board of Patent Appeals and Interferences (BPAI) that Kubin et al.'s invention was obvious under 35 U.S.C. § 103.

With this decision, the court addressed the obviousness standard of DNA-based inventions in view of the landmark decision in *KSR Int'l v. Teleflex, Inc.* and the extension of KSR to the "unpredictable" arts making up biotechnology.

In doing so, the Federal Circuit in *In re Kubin* effectively overturned its long-time precedent reflected in *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995) by now holding that it would have been "obvious to try" under KSR to obtain a nucleic acid molecule encoding a known protein coupled with the availability of conventional techniques for obtaining nucleotide sequences. Thus, *In re Kubin* establishes the applicability of the "obvious to try" standard as a proper basis for obviousness of DNA-based inventions.

The main issue considered by the Federal Circuit in *In re Kubin* was whether the BPAI was correct in upholding the Examiner's rejection of obviousness on the grounds that it would have been "obvious to try" to obtain specific DNA sequences of a *known* protein using known methodologies. In the past, this standard usually was not applied to biotechnology cases in view of at least *In re Deuel*.

Not surprisingly, the Federal Circuit's decision was not embraced by the biotechnology industry as it renders it more difficult to obtain patents for DNA-based inventions. In addition, the decision illuminates the Federal Circuit's apparent view that biotechnology is quickly becoming a less unpredictable art. As such, the securing and protection of patents in this technology area may grow to be more difficult where subject matter, otherwise patentable, will be increasingly viewed as "obvious to try."

The Kubin Application and the Obviousness Rejection

On September 20, 2000, Marek Z. Kubin and Raymond G. Goodman, filed a patent application entitled "NK Cell Activation Inducing Ligand (NAIL) DNA and Polypeptides, and Use Thereof" ("the Kubin application"). The inventors sought patent protection of isolated nucleic acid molecules encoding NAIL polypeptides, the NAIL polypeptides themselves, and methods for

modulating the activity of NK (“natural killer”) cells using the NAIL polypeptides and nucleotide sequences.

According to the inventors, NK cells are a major type of immune system component which are involved in killing certain tumors and virus-infected cells and which are also thought to bear an important overall role as regulators of immune responses—mediated through cytokine-releasing activities. The application teaches that human NK cells were previously known to comprise a specific cell surface protein (“p38” or NAIL) that, once activated, provide the NK cells with their cytotoxic and cytokine-releasing properties.

However, neither the amino acid nor the nucleotide sequence of NAIL (or p38) were previously described in the art before Kubin et al.’s invention. The Kubin application specifically describes the isolation and cloning of the cDNA sequence encoding human p38 (NAIL) protein, provides the NAIL sequences and shows that the NAIL protein binds the immune system cell marker CD48, the interaction of which is shown to have potential therapeutic benefits. The Applicants claimed a genus of nucleic acid molecules that encode CD48-binding proteins having 80% sequence identity with amino acids 22-221 of NAIL.

The Examiner rejected the claims as being obvious over the prior art. According to the Examiner, one reference discloses the p38 protein (NAIL), its role in signal transduction and NK cell cytotoxicity, and a monoclonal antibody (C1.7) that specifically binds to p38. The reference does not disclose the DNA or amino acid sequences of p38 (NAIL). Nevertheless, the Examiner argued that conventional methodologies provided both in the specification and in the art could have easily been used to obtain the corresponding p38 (NAIL) cDNA and amino acid sequences using the C1.7 antibody.

The Applicants appealed the Examiner’s final rejection to the Board of Patent Appeals and Interferences (BPAI), which upheld the Examiner’s rejection of obviousness. The Applicants then appealed to the Federal Circuit, which affirmed the obviousness determination of the BPAI.

The Federal Circuit Decision

The Federal Circuit first addressed and upheld the factual findings made by the BPAI. In particular, the court agreed with the BPAI’s finding that Kubin used the same basic conventional methodologies as the prior art to isolate the NAIL cDNA. In addition, the court also agreed with the BPAI’s finding that “one of ordinary skill in the art would have recognized the value of isolating NAIL cDNA, and would have been motivated to apply conventional methodologies, such as those disclosed and utilized in in the prior art, to do so.

The court then addressed the BPAI’s conclusions on the merits and Kubin’s arguments.

In doing so, the Federal Circuit considered the effect of its prior obviousness jurisprudence on the BPAI’s conclusion of obviousness, holding that its previous rejection of the “obvious to try” doctrine for certain biotechnological inventions no longer applied in view of KSR’s discrediting of *Deuel*.

For over 10 years, Applicants and patentees alike have relied on the Federal Circuit's holding in *In re Deuel* to thwart obviousness challenges to DNA-based claims as "obvious to try." However, this may no longer be a feasible argument or defense. The Federal Circuit, agreeing with the BPAI, points out that the Supreme Court in *KSR* has effectively overruled *In re Deuel*'s "obvious to try" doctrine. In particular, the Federal Circuit, held that "[i]nsofar 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. In fact, the Supreme Court expressly invoked *Deuel* as a source of the discredited "obvious to try" doctrine."

The court then observes that the Supreme Court's analysis in overruling *In re Deuel* was in line with its own prior obviousness jurisprudence expressed in its pre-*Deuel* decision in *In re O'Farrell*, 853 F.2d 894 (Fed. Cir. 1988), which held that for there to be obviousness, all that is required is a "reasonable expectation of success." One issue the court focused on was the meaning of "obvious to try," which the court noted was often misapplied in two different impermissible situations. First, "obvious to try" should not equate to obviousness where the thing that would have been "obvious to try" would involve trying various adjustable parameters without clear direction as to their significance or effect. Second, "obvious to try" should not equate to obviousness where what was "obvious to try" was a new technology or approach with nothing more than general guidelines for its use or application.

With respect to this earlier decision, the *Kubin* court states that *O'Farrell*'s first impermissible "obvious to try" situation is actually stated in the inverse by the Supreme Court in *KSR* by its holding that "where a skilled artisan merely pursues "known options" from a "finite number of identified, predictable solutions," obviousness under 103 arises." Thus, on the bases that the prior art teaches the protein of interest (p38), includes a motivation to isolate the gene coding for that protein (p38 is a marker on all NK cells), and provides illustrative instructions for cloning cognate genes, the Federal Circuit held under *KSR* that the claimed invention is "the product not of innovation but of ordinary skill and common sense." Or, as the court states under its earlier *In re O'Farrell* analysis, the invention was obvious because "a skilled artisan should have had a resoundingly 'reasonable expectation of success' in deriving the claimed invention" without being impermissibly "obvious to try."

Conclusion

After *In re Kubin*, some things are clearer than others. For instance, on the one hand, *In re Kubin* does not change the fact that, under *KSR* and earlier jurisprudence, the determination of obviousness is still highly fact specific. On the other hand, while *In re Kubin* makes it clear that the "obvious to try" standard can now be applied in the "unpredictable" art of biotechnology under certain circumstances, i.e., known protein and known methods for obtaining nucleic acid and amino acid sequences, the extent that the "obvious to try" standard will be applied to situations outside of the facts of *In re Kubin* remains to be seen.

At a minimum, it would appear that *In re Kubin* will make it more difficult to secure patents covering DNA sequences if the corresponding protein is known or has been previously identified (with or without an amino acid or partial amino acid sequence thereof) and general methods for

DNA cloning and sequencing are available that can be used to obtain the claimed DNA sequence.

At least for now, the impact of the *Kubin* decision on biotechnology inventions may likely be limited to claims directed to DNA sequences. However, given the court's view that *KSR* should not be restricted to the "predictable arts" on the basis that the "unpredictable art" of biotechnology can be, in certain instances, "profoundly 'predictable,'" there exists a justifiable concern that as the art of biotechnology continues to mature and progress, the Federal Circuit may possibly expand the reach of *In re Kubin* into other areas of biotechnology, possibly rendering a wider-array of inventions "obvious to try." Only time will tell as to *Kubin*'s ultimate effect on biotechnology inventions as additional factual scenarios are brought before the courts.