Ex Parte Kubin: Board of Patent Appeals and Interferences Applies "Obvious to Try" in Post-KSR Biotechnology Appeal

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For the past fifteen years, the PTO has been issuing patents based on its interpretation of Federal Circuit precedent that a previously unknown DNA sequence that encodes a known polypeptide is non-obvious. This precedent, established by the Court of Appeals for the Federal Circuit in *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993), and later reaffirmed in *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995), is now being challenged by the Patent Office Board of Patent Appeals and Interferences (Board). In *Ex Parte Kubin*, 2007 WL 2070495 (B.P.A.I. May 31, 2007), the Board determined that a DNA sequence encoding a functionally characterized but un-isolated receptor protein was "the product not of innovation but of ordinary skill and common sense," leading it to conclude that the DNA sequence was obvious under 35 U.S.C. § 103(a) and therefore not patentable.

In *Bell* and *Deuel*, the Federal Circuit established a per se rule affirming the patentability of a specific DNA sequence encoding a completely or partially structurally characterized protein, even given that generally applicable methods were available that could be used to isolate DNA sequences using the amino acid sequence of the protein encoded thereby as a starting point. In *Bell*, the Federal Circuit reversed a PTO rejection of the applicant's claimed nucleic acid sequence based upon the combination of a primary reference disclosing the complete amino acid sequence of the protein encoded by the claimed DNA with a secondary reference describing a general method of gene cloning. The Federal Circuit held that the combination of these prior art references did

not render the claimed nucleic acid sequence obvious because the structure of the DNA (as opposed to the method of obtaining it) was not obvious. In *Deuel*, the Federal Circuit reversed the Board's rejection of the applicant's claimed DNA sequence based upon the combination of a primary reference disclosing the partial amino acid sequence of protein encoded by the claimed DNA with a secondary reference describing a general method of gene cloning. Again, the Federal Circuit held that the prior art did not render the claimed DNA obvious because of the lack of structural obviousness. In dicta, however, the *Deuel* court noted that if the complete amino acid sequence of a protein were known, the genus of all DNA sequences encoding the protein might be obvious, because one skilled in the art could use knowledge of the genetic code, with the aid of a computer, to generate the genus of all possible DNA sequences encoding the protein. Thus, *Bell* and *Deuel* created a requirement of a structural relationship between a prior art amino acid sequence and the particular DNA sequence being claimed in order to find the claimed DNA sequence obvious over the prior art. In *ex Parte Kubin*, however, the Board completely discarded the reasoning that led to the *Bell/Deuel* holdings.

The *Kubin* appeal involved claims directed to any one of the group or "genus" of DNA sequences encoding a polypeptide at least 80% identical to a particular surface marker protein (NAIL or p38) on natural killer (NK) immune cells. The NAIL protein is a cell surface marker, or receptor, on the surface of NK cells that modulates the activity of NK cells. The patent examiner found Kubin's claims obvious over a combination of prior art teachings of general cloning methods with the disclosure, in the Valiante et al. patent, of the functional characteristics of the NAIL protein on cultured cells, a monoclonal antibody that binds to a portion of the NAIL protein, and a prophetic

example of how to isolate NAIL DNA and the protein using conventional cloning and sequencing methodologies. The prior art did not disclose the amino acid sequence (partial or complete) of the NAIL protein. In fact, the NAIL protein had not even been isolated, and the prophetic example did not even provide a specific method by which to obtain it. On appeal to the Board, Kubin argued that, based on *Bell* and *Deuel*, the claimed DNA sequence cannot be rendered obvious by the mere knowledge of the protein's functional characteristics and hypothetical methods for generating the DNA sequence. Yet, the Board affirmed the Examiner's rejection, finding that the claims were unpatentable because the isolation of the NAIL DNA sequence would have been "obvious to try," and upon "trying" there would have been a reasonable expectation of success.

The Board's decision in *Kubin* is a huge leap over the principles set down in *Bell* and *Deuel*. *Bell* and *Deuel* established that there must be some structural relationship between an amino acid sequence characterized in the prior art and a claimed DNA sequence in order for the DNA sequence to be rendered obvious. In *Kubin*, neither the "purified and isolated protein," nor its amino acid sequence existed in the prior art. The Valiante patent merely disclosed an antibody that binds to the NAIL protein as expressed on cultured cells. In the Valiante patent, a 38kd species identified as "p38" was detected by Western blotting, but the "p38" was not further isolated or purified. Nevertheless, the Board held that the claimed DNA sequences encoding for NAIL were obvious, despite the lack of any prior art that would permit derivation of the NAIL-encoding DNA sequences from the sequence of the NAIL protein.

The Board relied on the Supreme Court's 2007 decision in *KSR v. Teleflex*, 127 S. Ct. 1727, 82 U.S.P.Q.2d 1385. In *Kubin*, the Board noted that "under *KSR*, it's now apparent 'obvious to try' may be an appropriate test in more situations than we previously contemplated." Thus, the Board concluded that because a person skilled in the art would have had reason to try the disclosed hypothetical method for isolating NAIL DNA, and such a person would have had a reasonable expectation of success, the "obvious to try" test applied to render the NAIL DNA sequence obvious under § 103(a). In its attempt to follow *KSR*, however, the Board disregarded the precedent set down in *Bell* and *Deuel*.

The Board also found that the specification enabled the preparation of the claimed DNA but that it did not contain an adequate written description requirement of DNA molecules that would encode a polypeptide 80% identical to the NAIL sequence that would still bind to CD48.

In some ways, the *Kubin* decision mirrors *Reagents of the University of California v. Eli Lilly*, in which the court invalidated claims to cells expressing cloned DNA encoding human insulin. Even though the sequence of human insulin was known, and methods were available to isolate the DNA encoding it, the court held that the specification, which described only the functional properties of the DNA, did not contain an adequate characterization of the DNA, and so invalidated the claim based on the failure of the specification to meet the written description requirement of § 112. While a prior art reference need not meet the written description requirement in order to support an obviousness rejection, a reference containing a prophetic example that does not even purport to result in isolation of the DNA or the target protein it encodes would seem to be

a shaky foundation on which to support an obviousness rejection of a DNA molecule that encodes a protein that has been fully characterized by applicants.

If *Kubin* is reviewed, the Federal Circuit will have to decide whether to overturn *Bell* and *Deuel* in favor of the Supreme Court's recent interpretation of obviousness in *KSR*. A decision to overturn these key biotechnology decisions would make it more challenging for patent practitioners and their clients to obtain and defend patents containing "gene claims." While the "golden age" of patenting every new gene that is isolated may be over, the consequences for pharmaceutical and biotechnology patenting of replacing the requirement for structural unobviousness with some version of the qualitative "obvious to try" standard should be considered in depth before *Kubin* is affirmed or reversed.