

Reversing USPTO Appellate Board Ruling: Not An Easy Task

Law360, New York (November 01, 2012, 12:48 PM ET) -- In *In re Droge*, the federal circuit upheld the decision of the U.S. Patent and Trademark Office Board of Patent Appeals and Interferences that found that claims directed to recombinant biotechnology methods were obvious. At eight pages, the decision is one of the shortest precedential opinions that I've read, and illustrates the difficulty of overturning a board decision of obviousness.

The Patent Application at Issue

The patent application at issue was published as US 2003/0027337. Claim 29 was deemed to be representative, and is set forth below as presented in the Federal Circuit decision:

29. A method of sequence specific recombination of DNA in a eukaryotic cell, comprising:
(a) providing said eukaryotic cell, said cell comprising a first DNA segment integrated into the genome of said cell, said first DNA segment comprising an [attB, attP, attL, or attR sequence or derivative thereof] ...
(b) introducing a second DNA segment into said cell ...
(c) further comprising providing to said cell a modified bacteriophage lambda integrase Int, wherein said modified Int is Int-h or Int-h/218, which induces sequence specific recombination through said attB and attP or attR and attL sequences.

The Obviousness Rejection

The claims were rejected as obvious over the combination of U.S. Patent 6,143,530 (Crouzet) and an article by Christ and Droge (two of the three inventors of the application at issue).

As summarized by the federal circuit, Crouzet discloses "methods of making therapeutic DNA molecules using sequence-specific recombination either in a host cell or in vitro ... [using] bacteriophage λ and wild-type Int protein to insert a foreign DNA sequence into a host cell using the attB and attP recognition sites." Crouzet further states that the method "may be carried out in any type of cell host," such as "bacteria or eukaryotic cells (yeasts, animal cells, plant cells)." However, "Crouzet does not disclose use of modified integrases."

As summarized by the federal circuit, Christ & Droge "discloses that the modified integrase proteins Int-h and Int-h/218 mediate sequence-specific recombination in prokaryotic cells," and that "compared to wild-type Int, the modified proteins Int-h and Int-h/218 have the advantage of an increased binding affinity for core binding sites present in the att regions." The reference "also discloses that Int-h and Int-h/218 can perform recombination ... in the absence of certain protein co-factors that assist with recombination, such as the integration host factor (IHF)." As noted by the federal circuit, "IHF is present in prokaryotic cells but not in eukaryotic cells."

In support of its obviousness determination, the board found that "because 'the wild-type integrase works in eukaryotic cells, the ordinary artisan would have had a reasonable expectation of success that [Int-h and Int-h/218] would also function at some level in eukaryotic cells.'"

The applicant had submitted a declaration by inventor and author Droge, attesting that "a person of ordinary skill in the art would not have had a reasonable expectation of success in using Int-h and Int-h/218 to induce recombination in eukaryotic cells." However, the board concluded that another scientific article "refuted the assertions in the Droge Declaration."

The Federal Circuit Decision

The applicant's main argument on appeal was that "a person of ordinary skill in the art would not have had a reasonable expectation of success in combining the teachings of [the cited] references."

Droge argues that Christ and Droge's disclosure of using the modified integrase proteins Int-h and Int-h/218 to facilitate recombination in prokaryotic cells would not lead a skilled artisan to expect that these integrases would also work in eukaryotic cells.

However, the federal circuit found that "substantial evidence supports the Board's determination." In particular, the court noted that the scientific article "directly contradicts the assertion in the Droge Declaration that a skilled artisan would not expect the modified integrases Int-h and Int-h/218 to work in eukaryotic cells" In explaining its decision, the court cited *In re Kubin* for the proposition that "[o]bviousness does not require absolute predictability of success . . . all that is required is a reasonable expectation of success."

Substantial Evidence

This case highlights how difficult it can be to overturn a board decision of obviousness. The federal circuit reviews the board's factual findings for "substantial evidence," and will uphold them if it finds "such relevant evidence as a reasonable mind might accept as adequate to support a conclusion." Thus, the court does not make an independent determination but rather considers whether the board's decision is supported by the record.

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