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Federal Circuit Patent Watch

DECEMBER 26, 2006

Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.

Nos. 05-1396, -1429, -1430, Federal Circuit (*Rader*, Schall, Gajarsa)

[P]atentability for a chemical compound does not depend only on structural similarity. This court will not ignore a relevant property of a compound in the obviousness calculus. When claimed properties differ from the prior art, those differences, if unexpected and significant, may lead to nonobviousness.

On December 26, 2006, the Federal Circuit affirmed the district court's judgment that the Abbreviated New Drug Applications (ANDAs) for generic Zyprexa®, filed by Zenith (now known as IVAX), Teva, and Dr. Reddy's, infringed U.S. Patent No. 5,229,382, which related to olanzapine and its use to treat schizophrenia, and that the '382 patent was not invalid or unenforceable. The Federal Circuit stated:

> The trial court found that the defendants did not prove by clear and convincing evidence that claims 1, 2, 3, 7, 8, and 15 of the '382 patent were invalid as obvious under 35 U.S.C. § 103. On appeal, IVAX argues that the district court erred by erecting "a threshold requirement that defendants establish a teaching or incentive to treat the closest prior art (i.e., Compound '222) as a 'lead compound.'" IVAX also charges that the district court disregarded (1) the structural characteristic of olanzapine as the adjacent homolog of Compound '222, (2) the suggestions to delete fluorine from the prior art compound flumezapine, and (3) the observation that Compound '222 and flumezapine "bracket" olanzapine.
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> This court reviews obviousness without deference as a legal conclusion with underlying factual determinations which are reviewed for clear error. The factual underpinnings are: (1) the scope and content of the prior art, (2) the differences between the prior art and the claimed invention at the time of invention, (3) the level of ordinary skill in the art, and (4) the objective indicia of nonobviousness. For a chemical compound, a prima facie case of obviousness requires "structural similarity

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between claimed and prior art subject matter . . . where the prior art gives reason or motivation to make the claimed compositions." "[A] reasonable expectation of success, not absolute predictability" supports a conclusion of obviousness.

[T]he trial court found that a person of ordinary skill in the art would not have chosen Compound '222 as the beginning compound because it contained a hydrogen atom instead of a halogen atom, which again is not a preferred substituent. In addition, the prior art supplied no motivation to change the 2-ethyl in Compound '222 to a 2-methyl. The prior art would have instead suggested modification by adding a halogen atom to supply the neuroleptic substituent as a trigger for antipsychotic activity. The district court found that, at the relevant time, a person with ordinary skill in the art would not have expected any reasonable chance of success with other clozapine-like compounds.

And though olanzapine is also the adjacent homolog of Compound '222, patentability for a chemical compound does not depend only on structural similarity. This court will not ignore a relevant property of a compound in the obviousness calculus. When claimed properties differ from the prior art, those differences, if unexpected and significant, may lead to nonobviousness. In this case, the trial court noted some structural similarity of olanzapine and the prior art, but also accounted for the unexpected beneficial properties in olanzapine.

[Furthermore,] Lilly proved extensive secondary considerations to rebut obviousness. The trial court found the evidence clearly established four of the five proffered secondary considerations. Lilly established (1) a long-felt and unmet need; (2) failure of others; (3) industry acclaim; and (4) unexpected results. The record shows a long-felt need for a safer, less toxic, and more effective clozapine-like drug; a decade (or more) of failure to find a replacement for clozapine; a reasonable amount of commercial success for olanzapine; and a number of awards for olanzapine as indicators of industry acclaim. . . . In sum, these objective criteria buttressed the trial court's conclusion of nonobviousness.

For more information on these issues or other intellectual property law matters, please contact Lawrence M. Sung, Ph.D. at lsung@nixonpeabody.com or 202-585-8221.

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