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Federal Circuit Reaffirms That There Is No 'Reasonable Expectation Of Success' In Trying To Invalidate A Chemical Compound Claim As Obvious

The Federal Circuit (in an unpublished opinion) recently reaffirmed the difficulty generic challengers face when trying to establish chemical structural obviousness to invalidate a drug compound patent claim.[1]

This recent ruling involved Takeda's U.S. Patent No. 7,807,689 ("the '689 Patent"), which claims alogliptin, a uracil-containing dipeptidyl peptidase IV ("DPP-IV") inhibitor used to treat Type II diabetes. The '689 Patent is listed in the Orange Book for Takeda's anti-diabetes drug products, Nesina ®, Kazano®, and Oseni®, each of which contains alogliptin benzoate as an active ingredient. Two ANDA applicants, Torrent and Indoco, challenged the validity of claims 4 and 12 of the '689 Patent as obvious under 35 U.S.C. § 103 and for non-statutory obviousness-type double patenting ("OTDP"). [2]

Obviousness and OTDP are separate bases for patent invalidity. Both arguments, as applied to chemical compound claims, require that a person of ordinary skill in the art ("POSA"), as of the priority date of the patent claim, would have been motivated to make the specific molecular modifications and have a reasonable expectation that those modifications would result in the claimed compound.[3]

After a two-day bench trial and extensive expert testimony, Judge Stanley Chesler (D.N.J.) found that a POSA would have had no motivation to make the specific molecular modifications to arrive at alogliptin and no reasonable expectation that such modifications would successfully result in a molecule having alogliptin's structure and biological properties. Judge Chesler therefore concluded that the ANDA applicants failed to prove by clear and convincing evidence that the challenged claims are invalid for either obviousness or OTDP.[4] The Federal Circuit, finding no clear error in Judge Chesler's findings, affirmed. [5]

The specificity with which the prior art must teach the modifications to arrive at the claimed compound is one of the challenges of establishing an obviousness or OTDP argument. As Judge Chesler states, "[T]he general commercial motivation to develop novel compounds does not suffice 'to show that the prior art would have suggested making the *specific molecular modifications* necessary to achieve the claimed invention'." [6] Indeed, where the starting point is a "complicated compound" with "many possibilities for modification" (as most drug compounds are), ANDA challengers must clearly and convincingly prove that each modification leading to the claimed compound is "the one, among all the possibilities, that would have been successfully pursued." [7]

Even more challenging is establishing that said POSA would have had a reasonable expectation of success that those modifications would result in the claimed compound and its properties. As the Federal Circuit stated at the start of its discussion, "Relevant to 'the assessment of [reasonable] expectation of success' . . . is the

undisputed factual finding that 'in the relevant art of pharmaceutical development, very small changes in molecular structure can have dramatic effects on the properties of the molecule'." [8] Reasonable expectation of success in the context of chemical compounds encompasses both success in achieving the desired chemical structural modification and success in predicting the effects of that modification on the compound's properties.[9]

For at least these reasons, the bar for invalidating a chemical compound claim as obvious remains high.

Footnotes

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[1] *Takeda Pharm. Co. Ltd. v. Torrent Pharms. Ltd.*, Nos. 2020-1552, 2020-1598, 2021 WL 560763 (Fed. Cir. Feb. 16, 2021).

[2] *Takeda Pharm. Co. Ltd. v. Torrent Pharms. Ltd.*, Nos. 17-3186 (SRC)(CLW), 17-7301 (SRC)(CLW), 2020 WL 549594 (D.N.J. Feb. 4, 2020), aff'd, Nos. 2020-1552, 2020-1598, 2021 WL 560763 (Fed. Cir. Feb. 16, 2021).

[3] Otsuka Pharm. Co., Ltd. v. Sandoz, Inc., 678 F.3d 1280, 1298 (Fed. Cir. 2012); *see also Takeda*, 2020 WL 549594, at *10; *Takeda*, 2021 WL 560763, at *1. The main difference between obviousness and OTDP is that obviousness requires that the prior art would have led a POSA to select a lead compound over other prior art compounds as a starting point for making modifications. See, *e.g., Novartis Pharms. Corp. v. W.-Ward Pharms. Int'l Ltd.* , 923 F.3d 1051, 1060 (Fed. Cir. 2019), *ruled patentable*, No. IPR2016-01479, 2020 WL 5900605 (P.T.A.B. Oct. 5, 2020), whereas OTDP requires a POSA to start with an earlier claimed compound in a co-owned patent, *e.g., Otsuka*, 678 F.3d at 1297-98.

[4] *Takeda*, 2020 WL 549594, at *26.

[5] *Takeda*, 2021 WL 560763, at *1.

[6] *Takeda*, 2020 WL 549594, at *15 (emphasis added) (quoting *Amerigen Pharms. Ltd. v. UCB Pharma GmBH*, 913 F.3d 1079, 1089 (Fed. Cir. 2019)); *see also Takeda*, 2021 WL 560763 at *1-2 (reviewing the specific modifications needed to arrive at alogliptan and the lack of prior art teachings that would have motivated a POSA to make those specific modifications).

[7] *Takeda*, 2020 WL 549594, at *19-20 (quoting *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 689 F.3d 1368, 1378 (Fed. Cir. 2012)); *see also Takeda*, 2021 WL 560763, at *2 (stating that nothing in the prior art that would have motivated a POSA to make a specific argued for modification "given myriad more conservative and predictable modifications that were available").

[8] *Takeda*, 2021 WL 560763, at *1 (quoting J. Chesler's opinion, *Takeda*, 2020 WL 549594, at *10, *11).

[9] *See, e.g., Takeda*, 2020 WL 549594, at *11, *25 (J. Chesler finding as matters of fact, *inter alia*, that prior art

"did not have available the structural information needed to perform scaffold hopping on a non-peptidic DPP-IV inhibitor with a reasonable expectation of success" and that "a POSA replacing a xanthine scaffold with a uracil would not be able to predict the resulting properties of the compound").