NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

2008-1427, -1428
(Interference No. 105,553)

ROBERT CHAPMAN, LONN S. RIDER, QI HONG,
DONALD KYLE, and ROBERT KUPPER,

Appellants,

v.

MICHAEL LAWRENCE CASNER, JEN-SEN DUNG,
ERNO M. KESKENY, and JIN LUO,

Cross Appellants.

Joseph R. Robinson, Darby & Darby P.C., of New York, New York, argued for appellants. With him on the brief were Samuel S. Woodley, and Martin S. Sulsky, of Washington, DC.

Douglas R. Nemec, Skadden, Arps, Slate, Meagher & Flom LLP, of New York, New York, argued for cross-appellants. With him on the brief were Edward V. Filardi and Stacey L. Cohen. Of counsel was Jeffrey A. Pade, of Washington, DC.

Appealed from: United States Patent and Trademark Office
Board of Patent Appeals and Interferences

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DECIDED: March 11, 2009

Before LOURIE, RADER, and PROST, Circuit Judges.

Opinion for the court filed by Circuit Judge PROST. Dissenting opinion filed by Circuit Judge RADER.

PROST, Circuit Judge.

Robert Chapman, Lonn Rider, Qi Hong, Donald Kyle, and Robert Kupper's ("Chapman's") U.S. Patent Application No. 11/391,897 ("the '897 application") and Michael Casner, Jen-Sen Dung, Erno Keskeny, and Jin Luo's ("Casner's") U.S. Patent No. 7,153,966 ("the '966 patent") both claim methods of preparing oxycodone that

reduce the levels of a potentially toxic intermediate, 14-hydroxycodeinone. In Interference No. 105,553, the Board of Patent Appeals and Interferences ("the Board") granted Casner's motion seeking judgment that Chapman claims 96–118 were unpatentable under 35 U.S.C. § 103(a). Chapman appeals, asking us to hold claims 96–118 of the '897 application nonobvious. Casner maintains that those claims were obvious, but has also lodged a cross-appeal, arguing that if we reverse the Board's holdings as to the '897 application, we should reverse its holdings on the '966 patent and remand for a priority determination. For the reasons set forth below, we affirm the Board's obviousness determination.

I. BACKGROUND

The '897 application is entitled "Process for Preparing Oxycodone Hydrochloride Having Less Than 25 ppm 14-Hydroxycodeinone." The only independent claim at issue is claim 96, which recites:

> A process for preparing oxycodone or an oxycodone salt, which process comprises steps of:
> (a) preparing a mixture of oxycodone, solvent and an acid;
> (b) incubating the mixture under conditions suitable to promote reaction of 8,14-dihydroxy-7,8-dihydrocodeinone to 14-hydroxycodeinone; and subsequently
> (c) exposing the mixture to hydrogenation reagents under conditions sufficient for conversion of 14-hydroxycodeinone to oxycodone.

J.A. 77 (emphases added).

Oxycodone is a synthetic analgesic opioid used to relieve pain. Typically, one prepares oxycodone by first oxidizing thebaine. This step converts thebaine into two types of compounds: 14-hydroxycodeinone ("14-hydroxy") and the 8,14-dihydroxy-7,8-dihydrocodeinones (collectively, "8,14-dihydroxys"). The 14-hydroxy is converted via hydrogenation into oxycodone, which is then treated with acid during a final "salting"

step to yield pharmaceutical grade oxycodone. Any 14-hydroxy remaining at the end of the reaction is problematic, as the compound is potentially toxic.

The 8,14-dihydroxys created during the initial oxidation step are stereoisomers—there are two forms, designated "8α" and an "8β," that differ only by the relative orientation of a hydroxyl group. Chapman claims that prior to the '897 application, persons of ordinary skill in the art did not know that 8α formed during the reaction. Instead, they believed that thebaine oxidized to form 14-hydroxy and 8β, and that any 14-hydroxy remaining at the end of the reaction was leftover, unreacted 14-hydroxy. In fact, during the salting step at least one of the 8,14-dihydroxys reacts with acid to form "new" 14-hydroxy; this 14-hydroxy can then, of course, undergo hydrogenation to become additional oxycodone.

Chapman argues that he was the first to recognize that additional 14-hydroxy is created from 8α during the reaction's salting step, and that the "new" 14-hydroxy can therefore yield additional oxycodone. Chapman purports to claim this method of eliminating the "new" 14-hydroxy in claim 96. The claim does not, however, differentiate between the 8α and 8β forms of 8,14-dihydroxy, nor does the claim language specifically disclose which conditions are "suitable" for promoting the desired reaction from 8,14-dihydroxy to 14-hydroxy.

We have jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

II. DISCUSSION

Obviousness is a legal conclusion based on underlying findings of fact. In re DBC, 545 F.3d 1373, 1377 (Fed. Cir. 2008). We review the Board's ultimate

determination of obviousness de novo, while we review the Board's underlying factual findings for substantial evidence. Id.

We first turn to Chapman's arguments. Chapman claims that prior to the '897 application, no one knew that 8α was formed during thebaine oxidation. Nor, according to Chapman, was it known that 8α could react with acid under certain "commercial conditions" to form additional 14-hydroxy. Chapman admits that the prior art disclosed 8β, but claims that "under commercial oxycodone production conditions," 8β converts into a benign salt, not into 14-hydroxy. In his view, the prior art would lead a person of ordinary skill in the art to believe that 8β must be treated with "stronger than commercially used" amounts of hydrochloric acid before it converts to 14-hydroxy.

Casner states that Chapman never claimed 8α as crucial to the invention before the Board; in other words, Chapman never tried to distinguish the prior art based on stereochemistry. Casner likewise argues that Chapman waived any "commercial conditions" limitation. Chapman responds that both issues were raised, although the stereochemistry argument is emphasized on appeal because Casner did not produce the "Proksa" reference (upon which the Board relied) until its response, leaving Chapman little opportunity to analyze and respond to the specific issues raised by that reference. Chapman also argues that since the Board identified a "commercial need" for reduced levels of 14-hydroxy, and found that a person of skill in the art would work in the "highly competitive pharmaceutical industry," the Board understood that commercial conditions were at issue.

Chapman does not direct us to specific arguments in submissions to the Board where counsel pursued the claim that commercial conditions were necessary; nor has

Chapman clarified which conditions would qualify as "commercial conditions." Similarly, although 8α is identified in some of the '897 application's figures, and Chapman's expert made references to stereoisomers in reviewing the prior art, Chapman has not identified any statement before the Board that explicitly differentiated between the invention and the prior art based on stereochemistry.

Regardless, we need not resolve the waiver issue definitively. Chapman maintains, and we agree, that "[t]he term '8,14-dihydroxy' properly includes 8α, but there is no reason for that term to be limited to that isomer in Chapman's claims. The term 'conditions' properly includes commercial conditions, but there is no reason to limit that term to commercial conditions in Chapman's claims." Appellant's Reply Br. 27. Further, the '897 application states: "The term 8,14-dihydroxy-7,8-dihydrocodeinone includes either 8α,14-dihydroxy-7,8-dihydrocodeinone; or 8β,14-dihydroxy-7,8-dihydrocodeinone or can include a mixture of both compounds." '897 application ¶ 0043.

Thus, claim 96 merely requires one to incubate the mixture "under conditions suitable to promote reaction" of 8,14-dihydroxy to 14-hydroxy. Therefore, prior art references that disclose either the 8α or 8β form of 8,14-dihydroxy converting to 14-hydroxy, or disclose any reaction condition (whether "commercial" or not) that promotes the conversion of 8α or 8β to 14-hydroxy, may render the claim obvious. See In re May, 574 F.2d 1082, 1088–89 (C.C.P.A. 1978) ("[The reference] expressly discloses . . . a species within the genus of claim 1. Therefore, [the reference] is a technical anticipation of claim 1. Appellants' assertions to the contrary notwithstanding, this finding does not constitute a new ground of rejection; lack of novelty is the epitome of obviousness."); cf. Medichem, S.A. v. Rolabo, S.L., 353 F.3d 928, 934–35 (Fed. Cir.

2003) (concluding that first step of an interference-in-fact inquiry was satisfied where two method claims had a genus/species relationship, since "'[i]t is . . . an elementary principle of patent law that when, as by a recitation of ranges or otherwise, a claim covers several compositions, the claim is "anticipated" if one of them is in the prior art.'" (quoting Titanium Metals Corp. v. Banner, 778 F.2d 775, 782 (Fed. Cir. 1985)); Eli Lilly & Co. v. Barr Labs., Inc., 251 F.3d 955, 971 (Fed. Cir. 2001) (in context of an obviousness-type double patenting analysis, noting that "[t]he only other difference between [the two method claims] is that the former is directed to humans while the latter is directed to animals," and "[o]ur case law firmly establishes that a later genus claim limitation is anticipated by, and therefore not patentably distinct from, an earlier species claim.").

The Board found that the prior art discloses methods under which at least one 8,14-dihydroxy reacts to yield 14-hydroxy under certain conditions. Specifically, the Board noted that the FDA "recognized that there was a need to eliminate impurities in oxycodone," and then proceeded to walk through the prior art, which disclosed: that both 14-hydroxy and 8,14-dihydroxy were known impurities during the thebaine oxidation reaction; that treatment of 8,14-dihydroxy with hydrochloric acid converts 8,14-dihydroxy into 14-hydroxy under certain reaction conditions; that one of skill in the art would be able to identify those conditions; and that 14-hydroxy may be removed from oxycodone via hydrogenation.

As mentioned, claim 96 would have been obvious if properly-combinable references disclosed conditions suitable to promote reaction of 8,14-dihydroxy to 14-hydroxy. The prior art references here do just that: they indicate that 8β, at least, will

under certain reaction conditions form 14-hydroxy. Given that claims directed to the genus (methods for eliminating 8,14-dihydroxys) can be anticipated or rendered obvious by references disclosing the species (methods for eliminating either the 8α or 8β form of 8,14-dihydroxy), we agree with the Board that the method described in claim 96 would have been obvious. As a result, we need not address Casner's cross appeal.

III. CONCLUSION

For the reasons detailed above, we affirm the Board's decision to reject claims 96–118 of the '897 application under 35 U.S.C. § 103(a).

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RADER, Circuit Judge, dissenting.

The Food and Drug Administration seeks the removal of impurities such as 14-hydroxy from the pain medicine oxycodone salt. During research on oxycodone, Chapman discovered that oxidation of thebaine creates the stereoisomer 8α, which in turn creates additional 14-hydroxy during formulation of this important pharmaceutical. Until this discovery, this field of art believed that the original oxidation step created the additional 14-hydroxy impurity. After discovering 8α, Chapman learned to isolate and hydrogenate the additional 14-hydroxy to eliminate most of these impurities. Chapman, thus, was the first person to identify the true nature of the "leftover" 14-hydroxy problem

and the first to solve it. Because this important and innovative solution deserves a patent over the prior art, I would reverse the Board.

Chapman's invention calls to mind the Supreme Court's resolution of Eibel Process Co. v. Minnesota & Ontario Paper Co., 261 U.S. 45 (1923). In Eibel, the primary distinction of the invention over the prior art was discovery of the problem in that discipline. Id. at 67-68. Eibel discovered that unequal speeds of stock and wire produced a defective paper product under high machine speeds. Id. The variance in paper speed created disturbances and ripples some ten feet from the discharge. Id. With the problem defined, Eibel easily prescribed the solution by elevating one end of the paper feed to equalize the speeds of the wire and the paper stock by gravity. Id. at 64.

In this case, Chapman discovered that the salting of stereoisomer 8α, not the oxidation of thebaine, created the additional 14-hydroxy impurity in oxycodone salt. He solved this problem by isolating and hydrogenating the 14-hyrdroxy to form additional oxycodone. Chapman's invention was not the mere use of a known technique to remedy a known source of trouble, but was, as Chief Justice Taft stated, "the discovery of the source not before known and the application of the remedy" for which he seeks reward of the grant of a patent. Id. at 68.

Similarly, in In re Conover, Conover discovered a solution to the problem of connecting a rod to an outboard motor engine containing compact, anti-friction roller bearings. 304 F.2d 680, 681 (C.C.P.A. 1962). A phenomenon known as "galling" could destroy the bearings at unpredictable times by heating of the roller elements. Id. at 681-82. To overcome this "galling," Conover put a non-galling material, such as silver, on

the end faces of the connecting rod bearings. Id. at 682. Citing the rationale of Eibel, the Court of Customs and Patent Appeals ("CCPA") found that the differences between Conover's patent application and the prior art were such that "the subject matter as a whole," i.e., (a) "the discovery of the cause of the bearing failures" and (b) "its elimination by the claimed plating of . . . the contacting areas of the face portions of the connecting rods and the crank cheeks, were not obvious from the prior art at the time the invention was made to a person having ordinary skill in this art." Id. at 684.

In In re Sponnoble, the pharmaceutical industry faced the problem of unwanted moisture leakage between liquid and solid compartments in vials. 405 F.2d 578, 586 (C.C.P.A. 1969). Sponnoble discovered that the cause of this leakage was the passage of moisture through, rather than around, the center plug of the vial. Id. He solved the problem by fabricating a center seal plug of butyl rubber with a silicone coating. Id. The CCPA found, "a patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified. This is part of the 'subject matter as a whole' which should always be considered in determining the obviousness of an invention under 35 USC 103." Id. at 585. In resolving the issue of obviousness, the court stated, "The crux of the matter . . . is the discovery by appellant that passage through the center plug was a major cause of moisture transmission." Id. at 586. The court reasoned that "[t]he question here is whether the prior art recognized the cause of the problem," which it did not. Id.

The CCPA in In re Peehs found that Peehs had represented to the Patent and Trademark Office that up until the time of the claimed invention, "the nuclear [power] industry faced the problem of undesirable stressing of fuel rod claddings in gas-cooled

nuclear reactors." 612 F.2d 1287, 1290 (C.C.P.A 1980). Peehs discovered that "the cause of this stressing was sticking between the metal surfaces of the claddings and the contact elements of the spacer grids." Id. He solved this problem by "roughening one of the contact surfaces." Id. Thus, as in Eibel, Conover, and Sponnoble, "the crux of the matter is the discovery by appellants of the cause of a problem, and the determinative question is whether that cause would have been recognized by one of ordinary skill in the art at the time the invention was made." Id.

In reversing the Board's holding of obviousness, the CCPA found "no support for the conclusion that those of ordinary skill in the art would have recognized that sticking between the fuel rod claddings and the spacer grid contact elements caused the stressing of the claddings." Id. The court also found that "'[where] there is no evidence of record that a person of ordinary skill in the art at the time of [an applicant's] invention would have expected [a problem]', e.g., sticking, 'to exist at all, it is not proper to conclude that [an invention]', e.g., roughening one of the contact surfaces, 'which solves this problem, . . . would have been obvious to that hypothetical person of ordinary skill in the art.'" Id. (citing In re Nomiya, 509 F.2d 566, 572 (C.C.P.A. 1975)).

The Supreme Court in KSR International Co. v. Teleflex Inc. recently held that "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." 127 S.Ct. 1727, 1742 (2007). This case, as are Eibel, Conover, Sponnoble, and Peehs, is distinguished from KSR because there were no "finite number

of identified, predictable solutions" that were used to discover the source of and solution to the problems. Id. No persons of ordinary skill in the art knew of the existence of 8α before Chapman and, in fact, were trying to solve the problem of removing excess 14-hydroxy impurities from oxycodone salt by other means. Because no other persons had discovered and solved this problem as Chapman did, his invention is the product of innovation and not of "ordinary skill and common sense." Id.

Following KSR, this court in 2008 in Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc., found an invention worthy of a patent when a researcher in his search for a new antidiabetic drug, accidentally discovered topiramate. 520 F.3d 1358 (Fed. Cir. 2008). Topiramate is a reaction intermediate that has powerful anticonvulsant properties marketed by Ortho-McNeil as TOPOMAX® for the treatment of epilepsy. Id. at 1360. This court attached particular importance to the objective criteria of nonobviousness, including the powerful, unexpected results of topiramate (i.e., anticonvulsive activity), skepticism of experts, copying, and commercial success. Id. at 1365. "As this court has repeatedly explained, this evidence is not just a cumulative or confirmatory part of the obviousness calculus but constitutes independent evidence of nonobviousness." Id. (citing Catalina Lighting, Inc. v. Lamps Plus, Inc., 295 F.3d 1277, 1288 (Fed. Cir. 2002) ("Objective indicia may often be the most probative and cogent evidence of nonobviousness in the record.")).

Chapman unexpectedly discovered that the stereoisomer 8α, when salted, creates additional 14-hydroxy. This additional 14-hydroxy can be isolated and hydrogenated to create additional oxycodone, containing much less of the 14-hydroxy impurities that the FDA desired removed from oxycodone salt. Persons of ordinary skill

in the art never discovered or appreciated the presence of 8α as the source of the additional 14-hydroxy. The prior art disclosed that 14-hydroxy was a carry-over from the oxidation of thebaine, resulting in leftover, unreacted 14-hydroxy in the oxycodone salt. "[T]he challenges of this inventive process would have prevented one of ordinary skill in this art from traversing the multiple obstacles to easily produce the invention in light of the evidence available at the time of invention." Ortho-McNeil, 520 F.3d at 1365. Chapman, therefore, unexpectedly discovered the true source of the additional 14-hydroxy and solved the problem by removing the impurity from oxycodone salt. Because the prior art could not have intended or appreciated Chapman's discovery or solution, this invention deserves patent protection.

For the foregoing reasons, I respectfully dissent.