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Pharmaceutical Formulations: Ready For Patenting?

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Law360, New York (December 20, 2016, 5:35 PM EST) --
Pharmaceutical companies are increasingly combining forces through research and collaboration agreements. It is critical to ensure that as companies negotiate and enter into these agreements, they do not inadvertently create an on-sale bar. The on-sale bar doctrine may be triggered if an invention was "on sale" and "ready for patenting" one year before the effective filing date. To minimize the risk of an on-sale bar or a public use bar, a patent application should also be filed — at the latest — within one year of the date that an invention is ready for patenting, i.e., the critical date. But when an invention is ready for patenting is not always clear.


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The Federal Circuit provides some guidance as to when a particular invention is ready for patenting, but the issue is highly fact-dependent and there are no hard-and-fast rules. This is particularly true for pharmaceutical formulations. The good news is that there is no indication that the analysis has changed before and after the America Invents Act. Therefore, the Federal Circuit's history of jurisprudence provides guidance that can help determine whether a formulation invention is ready for patenting. In this article, we review cases, including the Helsinn v. Teva on-sale bar case, concerning reduction to practice for pharmaceutical formulations in the context of the burdens placed on patent challengers.

In Pfaff v. Wells Electronics Inc., the U.S. Supreme Court articulated a two part standard for the application of the on-sale bar.[1] It held that a patent is invalid under the on-sale bar if the invention was (1) the subject of a commercial offer for sale, and (2) ready for patenting prior to the critical date.[2] Although it's debatable whether the AIA changed the requirement for a commercial offer for sale from covering both secret and public sales to covering only public sales, the ready for patenting prong under Pfaff appears to remain unchanged. In Pfaff, the Supreme Court described two ways for a party to establish that an invention is ready for patenting: (1) by proof of reduction to practice before the critical date; or (2) by proof that prior to the critical date the inventor had prepared drawings or other descriptions of the invention that were sufficiently specific to enable a person skilled in the art to practice the invention.[3] Although on its face it would seem that this Supreme Court test would be straightforward, its application is not so simple when determining whether a pharmaceutical formulation is ready for patenting.

Reduction to Practice

For pharmaceutical formulation claims, especially claims covering FDA-approved formulations, courts primarily focus on reduction to practice to fulfill the "ready for patenting" prong of the on-sale or public use analysis.[4] To demonstrate reduction to practice, courts impose a burden on a patent challenger to prove that the inventor (1) constructed an embodiment or performed a process that met all the limitations; and (2) determined that the invention would work for its intended purpose.[5] Beyond that, testing is required to demonstrate reduction to practice in some instances because without such testing there cannot be "sufficient certainty" that the invention will work for its intended purpose(s).[6]

Failure to establish with "sufficient certainty" that a pharmaceutical formulation will work for its intended purpose might doom a formulation patent challenge predicated on a reduction to practice and public use before the critical date. In In re Omeprazole Patent Litig. v. Apotex Corp., the Court of Appeals for the Federal Circuit affirmed the district court's finding that a pharmaceutical formulation was not ready for patenting until the completion of clinical trials showing that the formulation was both safe and effective — the intended purpose for the formulation.[7] The patent claims in In re Omeprazole encompassed a pharmaceutical preparation containing omeprazole having an inert subcoating.[8] Before the critical date, the patent owner commissioned Phase III clinical trials to determine the safety and efficacy of the claimed formulation in order to obtain U.S. Food and Drug Administration approval.[9] Despite the fact that the claimed formulation was completed well before the Phase III trials, used in the Phase III trials, and in the marketed drug, the district court found that at the time of Phase III trials, the inventors believed only that the formulation "might solve the twin problems of in vivo stability and long-term storage" and that "the Phase III formulation still required extensive clinical testing and real-time stability testing to determine whether it could treat gastric acid disease safely and effectively."[10] Addressing evidence that the Phase III formulation had been produced before the Phase III trials began, the CAFC stated that "[t]he existence of the formulations, however, does not establish that the [inventors] had determined that the invention would work for its intended purpose."[11] This effectively places heavy burdens of proof on challengers of formulation patents and is beneficial to owners of formulation patents.

Courts consider In re Omeprazole good law today. In the recent on-sale bar case Helsinn Healthcare SA v. Reddy's Labs. Ltd., the district court focused exclusively on reduction to practice and relied heavily on In re Omeprazole, holding in favor of the patentee that Helsinn's formulation was not ready for patenting before the critical date because the inventor had not determined that the claimed formulation would work for its intended purpose (i.e., effectiveness in reducing cancer chemotherapy-induced nausea and vomiting (CINV)) and therefore was not reduced to practice.[12] The asserted claims in the Helsinn patent covered a pharmaceutical formulation for intravenous administration to a human to reduce the likelihood of CINV, where the formulation comprised 0.25 mg palonosetron hydrochloride.[13] Before the critical date, Helsinn tested the 0.25 mg formulation in a Phase II trial in which efficacy was not statistically significant; and in a Phase III trial that generated preliminary unblinded data for the trial.[14] The complete efficacy data analysis for the Phase III trial was not completed until six months after the critical date.[15] Therefore, the district court found that Teva, the patent challenger, had not shown by clear and convincing evidence that as of the critical date, the inventor had determined that the invention would work for its intended purpose.[16] This finding alone would have immunized the claims from an effective on-sale bar challenge regardless of whether the sale was private or public.

Enabling Descriptions

On appeal and during oral argument before the CAFC on Oct. 4, 2016,[17] Teva additionally argued that the claimed formulation was ready for patenting before the critical date because no reduction to practice was required as long as the patentee provided an enabling disclosure sufficient for a POSA to make and use the invention.[18]

The enablement requirement ensures that the specification describe the invention in such terms that one skilled in the art can make and use the claimed invention.[19] However, to comply with the enablement requirement, it is not necessary to "enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim limitation to that effect."[20] Although the statute does not use the term "undue experimentation," courts require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation.[21]

In the Helsinn appeal, Teva argued that before the critical date, the invention could be practiced by a POSA because the claimed dosage of 0.25 "was showing some efficacy" in the Phase II trial and this efficacy was confirmed by the Phase III trial, and thus the formulation was ready for patenting before the critical date.[22] Teva also argued that the district court erred, arguing that showing statistical significance in efficacy concerns "FDA standards, not the patent law" and "FDA standards do not control in patent cases."[23] Teva argued that some showing of efficacy at the claimed dosage of 0.25 mg satisfied the enablement requirement and established that the invention was ready for patenting before the critical date.[24] Teva thus argued on appeal that the claimed formulation was enabled before the critical date and thus was ready for patenting.

It will be interesting to see if and how the CAFC decides on the ready for patenting issue in the hotly anticipated Helsinn decision. Under current case law, a challenger bears the burden of establishing — by clear and convincing evidence — that a claimed pharmaceutical formulation would work for its intended purpose with "sufficient certainty." Currently, such certainty would mostly likely require actual clinical testing data. Thus, establishing reduction to practice during litigation may present a much higher threshold (a sufficient certainty) than proving enablement (satisfying the Wands factors), which would only require a disclosure sufficient for a POSA to make and use the claimed formulation without undue experimentation. But it's not possible to predict what showing of efficacy would be required to support enablement of a pharmaceutical formulation — in particular an FDA approved formulation. It is also possible that the Federal Circuit might revisit the "sufficient certainty" standard and conform it more closely to the Wands factors — an outcome that will likely affect validity challenges to formulation patents for years to come.

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[1] Pfaff v. Wells Electronics Inc., 525 U.S. 55, 67 (1998).

[2] Id.

[3] Id. at 67-68.

[4] See, e.g., In re Omeprazole Patent Litig. v. Apotex Corp., 536 F.3d 1361 (Fed. Cir. 2008).

[5] Z4Techs. Inc. v Microsoft Corp., 570 F.3d 1340, 1352 (Fed. Cir. 2007)(citing Cooper v. Goldfarb, 154 F. 3d 1321, 1327 (Fed. Cir. 1998).

[6] Id. at 1352 (citing Slip Tracks Sys. Inc. v. Metal-Lite Inc., 304 F.3d 1256, 1267 (Fed. Cir. 2002).

[7] In re Omeprazole, 536 F.3d at 1372-75.

[8] Id.at 1365 (holding that the addition of the inert subcoating increases storage stability and improves efficacy by preventing omeprazole from degrading in the stomach so that it can reach small intestine where it is absorbed).

[9] Id. at 1371-72.

[10] Id.at 1373-74.

[11] Id. at 1374.

[12] Helsinn Healthcare S.A. v. Reddy's Labs. Ltd., No. 11-3962, 2016 U.S. Dist. LEXIS 27477, at *203-04 (D.N.J. Mar. 3, 2016).

[13]Id. at *13-14.

[14] Id. at *197, 200.

[15] Id. at *201 (finding the completed Phase III date as July 19, 2002 despite the final Clinical Study Report data results being identical to the preliminary unblinded data dated Jan. 7, 2002).

[16] Id. At *204.

[17]Oral Argument at 22:13-22:58, Helsinn Healthcare S.A. v.Teva Pharmaceuticals USA Inc., No. 16-1284 (Fed. Cir. Oct. 4, 2016), available at http://www.cafc.uscourts.gov/oral-argument-recordings/search/audio.html?title=&field_case_number_value=16-1284&field_date_value2%5Bvalue%5D%5Bdate%5D=&=Search.

[18] See also Corrected Brief for Defendants-Appellants Teva Pharmaceuticals USA Inc., Teva Pharmaceutical Industries Ltd. at 23-25, Helsinn Healthcare S.A. v.Teva Pharmaceuticals USA Inc., No. 16-1284 (Fed. Cir. Mar. 8, 2016)("Defendant-Appellant Opening Brief").; Principal Brief of Plaintiffs-Appellees Helsinn Healthcare S.A. and Roche Palo Alto LLC at 24-29, Helsinn Healthcare S.A. v.Teva Pharmaceuticals USA Inc., No. 16-1284 (Fed. Cir. Apr. 25, 2016) (urging the Federal Circuit to reject the enablement argument on the grounds that Teva never raised the ready for patenting issue based on enablement at trial and, thus waived this argument).

[19] 35 U.S.C. § 112(a) (2015).

[20] CFMT, Inc. v. Yieldup Int'l Corp., 349 F.3d 1333, 1338 (Fed. Cir. 2003).

[21] In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

[22] Defendant-Appellant Opening Brief, supra note 17, at 28-36.

[23] Id. at 30.

[24] Id. at 28-36.
