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Patents

Standards of Review: Implications for Patent Challengers

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The standard of review is frequently cited but often overlooked as being outcome-determinative in patent cases. A recent trio of decisions by the Federal Circuit illustrates the differences in outcome that result from the standard of review for issued patents, challenged for validity in the Federal Courts, versus that for patent applications examined for patentability by the U.S. Patent and Trademark Office. A renewed consideration of these differences may motivate a patent challenger to proceed proactively under one of the post-grant reexamination procedures within the U.S. Patent Office (i.e., post-grant review (PGR) and inter partes review (IPR)) rather than reactively in the context of an invalidity defense or declaratory judgment action.

Patent applications are examined for patentability using a preponderance of the evidence standard. That is, claims will be allowed if the evidence in favor of patentability is more convincing than the evidence in opposition to it.[1,2] In contrast, an issued patent enjoys a statutory presumption of validity,[3] under which a challenger must establish invalidity by clear and convincing evidence in the federal courts. The new America Invents Act post-grant reexamination procedures, conducted within the U.S. Patent Office, do not afford the patentee with the same presumption of validity it enjoys within the federal court system. PGR and IPR are conducted under a lower preponderance of the evidence standard, although, unlike initial examination of a patent application, it is the challenger's burden to prove invalidity.[4] A spate of recent decisions indicates that the U.S. Court of Appeals for the Federal Circuit has its eye firmly on the standard of review issue, which may result in different outcomes based on similar facts.

In re Droge

On Sept. 21, 2012, a panel of the Federal Circuit in *In re Droge* (2011-1600) held that the claims in U.S. patent application serial No. 10/082,772 were unpatentable as obvious over the prior art. The claims were directed to a method for sequence-specific recombination of DNA in eukaryotic cells[5] by expressing in those cells either one of two mutant recombinase enzymes. The rejection initially asserted by the examiner, and subsequently affirmed by the Board of Patent Appeals and Interferences (BPAI) and the Federal Circuit, relied on three prior art references. Crouzet disclosed that the wildtype (non-mutant) enzymes were capable of catalyzing recombination in prokaryotic cells[6] and eukaryotic cells, while Christ and Droge disclosed that the mutant enzymes worked in prokaryotic cells. Finally, the examiner relied on Lange-Gustafson as evidence that the skilled artisan had a reasonable expectation of success

[1] *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992).

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[2] *Manual of Patent Examining Procedure 2142.*
[3] *35 U.S.C. § 282.*
[4] *35 U.S.C. §§ 316(e) and 326(e).*
[5] Eukaryotic cells (e.g., mammalian cells) are characterized by the presence of a nucleus that contains the DNA in a non-supercoiled conformation, and the absence of recombinase co-factors (e.g., integration host factor).
[6] Prokaryotic cells (e.g., bacteria) are characterized by the absence of a nucleus, DNA in a supercoiled conformation, and the presence of recombinase co-factors.

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in combining the mutant enzymes of Crist & Droge with the eukaryotic cells of Crouzet. Specifically, Lange-Gustafson disclosed that the enzyme worked equivalently on supercoiled (prokaryotic) and non-supercoiled (eukaryotic) DNA in the absence of particular enzyme co-factors which were known to be absent in eukaryotic cells.

Droge attempted to rebut the examiner's prima facie case of obviousness with an expert declaration by the inventor. The declaration alleged that the skilled artisan had no expectation of success in the combination because of differences in the co-factor status (absent in eukaryotic cells) and the topology of the DNA (non-supercoiled in eukaryotic cells). Under a preponderance of the evidence standard, the examiner found this declaration insufficient to overcome the rejection because it was unsupported by data and contained only mere allegations of unpredictability. Ultimately, the Federal Circuit, under a deferential standard of review, held that the BPAI's affirmation of the examiner's rejection was supported by substantial evidence. Thus, the Droge examiner, challenging the patentability of the claims, was able to establish that the claims were more likely to be unpatentable than not, under the relatively less stringent preponderance of the evidence standard.

Pozen Inc. v. Par Pharmaceutical Inc.

On Sept. 28, 2012, a panel of the Federal Circuit in *Pozen Inc. v. Par Pharmaceutical Inc.* (2011-1584, -1585, -1586) held the claims of three Pozen patents[7] not invalid for obviousness. The patented claims are directed to compositions and methods for treating migraine by the simultaneous administration of a serotonin (5-HT) receptor agonist and a long-acting nonsteroidal anti-inflammatory drug (NSAID). Pozen brought this suit in response to the defendants' abbreviated new drug application (ANDA) filings relating to Pozen's approved product, Treximet, which is a combination of sumatriptan (a 5-HT receptor agonist) and naproxen (an NSAID).

As an initial matter, it was undisputed that both sumatriptan and naproxen were individually known in the art prior to Pozen's patents and that sumatriptan was used for the treatment of migraine. However, Pozen also had discovered that the combination of these drugs produces a longer lasting efficacy and reduces migraine relapse compared to the administration of naproxen or sumatriptan alone.

The defendants' challenge to the '499 and '458 patents as being invalid for obviousness was based on four prior art references. First, the defendants alleged that Parma discloses the simultaneous, or at least concomitant, administration of sumatriptan and NSAIDs, which renders obvious the asserted claims. In sustaining validity, the court found that Parma did not specifically suggest simultaneous administration of the two drugs, disclosed that treatment with sumatriptan alone was unsatisfactory for treating migraine, and made no mention of any relative success in the use of the sumatriptan/NSAID combination, let alone that the combination would have improved therapeutic benefits over those expected following administration of the drugs individually.

The court followed similar reasoning in reviewing defendants' arguments based on two patient records from the Henry Ford Hospital and a single patient report in the Catarci reference. Each of these references indicated that patients were concomitantly (but not simultaneously) administered an NSAID for migraine prophylaxis and sumatriptan for migraine treatment. Two of the patients were shortly switched to different treatment regimens, indicating to the court that the sumatriptan/NSAID was ineffective. Further, the court found that the Catarci reference, in fact, provided a teaching away from the use of a sumatriptan/naproxen combination.

Finally, the court reviewed defendants' allegation of obviousness over Saadah and a secondary reference, Raskin. Saadah discloses the simultaneous delivery of ergotamine (a 5-HT receptor agonist that was widely used to treat migraine), naproxen, metoclopramide, and caffeine wherein each of the component drugs was used for a different physiological purpose. The defendants alleged that it would have been obvious to the skilled artisan to merely substitute sumatriptan for ergotamine in Saadah to arrive at the claimed invention. In affirming the district court's holding of non-obviousness, the Federal Circuit adopted Pozen's reasoning that sumatriptan, unlike ergotamine, was known to have the same physiological effects as the three other drugs so an artisan motivated to substitute sumatriptan for ergotamine also would be motivated to eliminate the other medications, thereby resulting in sumatriptan monotherapy. Furthermore, the court found that nothing in either Saadah or Raskin teach or suggest the improved efficacy of the claimed combinations.

The Federal Circuit therefore sustained the district court's conclusion of no invalidity for obviousness. In other words, the patent challenger, in court, failed to establish invalidity under the heightened requirement for clear and convincing evidence required to rebut the presumption of patent validity.

Admittedly, Pozen's argument for non-obviousness is stronger than that of Droge. Pozen's case was bolstered by a finding that the claimed drug combination had improved efficacy parameters compared to Droge's unsupported allegations of unpredictability in the prior art. However, these decisions leave one to wonder whether a rejection of Pozen's claims made by the U.S. Patent Office, measured by a preponderance of the evidence standard, would have been sustained on appeal because each of the claimed drugs is being used in its intended way for its intended purpose and some level of additive improvement would be expected from the combination. Alternatively, it is possible that Droge's claims may have withstood a similar obviousness challenge had those claims enjoyed the presumption of validity afforded to issued patents.

In re Baxter International Inc.

The issue of the differing standards of review based on the procedural posture of the patentability/validity challenge was crystalized in the 10-1 per curiam decision of the Federal Circuit to deny an en banc rehearing in *In re Baxter Inc.* (2011-1073). The decision was published on Oct. 26, 2012.

The Baxter patent at issue has taken two tortuous and divergent paths. Fresenius USA Inc. subjected the patent to simultaneous invalidity challenges in a declaratory judgment action and a reexamination at the U.S. Patent Office with different outcomes. In 2003, Fresenius initiated a declaratory judgment action in

[7] U.S. Patent Nos. 6,060,499, 6,586,458, and 7,332,183.

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which it admitted infringement but argued that the patent was invalid for obviousness. The district court entered judgment as a matter of law in favor of the patentee, Baxter, on the question of obviousness, and this holding eventually was affirmed by the Federal Circuit.[8] Thus, Fresenius failed in its declaratory judgment action to prove that the patent claims are obvious by the heightened clear and convincing evidence sufficient to rebut the Baxter patent's presumption of validity.

In 2006, Fresenius also requested, and was granted, reexamination of the Baxter patent by the U.S. Patent Office. Relying on some of the same prior art as the courts had in the declaratory judgment action, but being bound only by the lower preponderance of the evidence standard, the BPAI sustained the examiner's rejection for obviousness. This BPAI decision on the reexamined claims was made in full view of the earlier Federal Circuit ruling in the declaratory judgment action. Baxter subsequently appealed the BPAI decision, which subsequently was affirmed by a panel of the Federal Circuit.[9] Thus, the Baxter patent was strong enough to withstand a validity challenge when it enjoyed a presumption of validity in a declaratory judgment action, but was unable to withstand a similar challenge without that presumption during reexamination.

Baxter petitioned for rehearing *en banc* in an attempt to overturn the later Federal Circuit decision affirming unpatentability. On Oct. 26, Justice Kathleen M. O'Malley wrote the sole concurring opinion to the *per curiam* decision denying Baxter's petition. Chief Justice Randall R. Rader and Justice Richard Linn joined. In explicating the seemingly disparate results in which the Federal Circuit itself had denied Fresenius' invalidity challenge during the declaratory judgment action only to have the U.S. Patent Office find the claims unpatentable on similar grounds, Justice O'Malley stated:

> A judgment in favor of a patent holder in the face of an invalidity defense or counterclaim merely means that the patent challenger has *failed to carry its burden of establishing invalidity by clear and convincing evidence* in that particular case. . . If the PTO later considers the validity of that same patent, it does so. . . *under the lesser burden of proof that applies in reexamination proceedings* (emphasis added).

Thus, the Federal Circuit does not see as inconsistent a result in which a patent challenger prevails at the U.S. Patent Office in a reexamination proceeding on grounds that were unsuccessful in cases initiated in the federal courts. The justification for these seemingly disparate results is placed squarely on the differences in the standard of review in each proceeding.

Strategic Implications for Patent Challengers

The recent implementation of the America Invents Act has brought with it new procedures for post-grant reexamination. These new procedures may have some attendant disadvantages for patent challengers in certain cases, including the limitations on discovery and the estoppel provisions that attach to unsuccessful challenges. Notwithstanding these disadvantages, potentially proactive patent challengers should consider that the different (lower) standard of review afforded by post-grant reexamination at the U.S. Patent Office may result in a rapid and more favorable outcome than for reactive patent challengers who wait in the hope of asserting a similar invalidity defense to an infringement allegation in the federal courts.

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[8] *Fresenius USA Inc. v. Baxter International Inc.*, 582 F.3d 1288, 92 USPQ2d 1163 (Fed. Cir. 2009).

[9] *In re Baxter International Inc.*, 678 F3d 1357, 102 USPQ2d 1925 (Fed. Cir. 2012).