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GENERICSWEB
THE SEARCH IS OVER

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Two Big Wins for Generics Clarify Non-infringement Strategies for Method of Use Patents

Two recent decisions, one by the U.S. Supreme Court and one by the U.S. Court of Appeals for the Federal Circuit, both issued in April, clarified the law regarding defenses to law suits involving "method-of-use" patents in Hatch-Waxman cases, and provide generics with more certainty in planning their paragraph IV challenges. On April 16, 2012, in *Bayer Schering Pharma AG v. Sandoz Inc.*, a case involving the drug Yasmin®, the U.S. Court of Appeals for the Federal Circuit ruled that generic drug makers could not infringe patent claims reciting a method of use of a U.S. Food and Drug Administration (FDA)-approved drug where the FDA had not approved the drug for the claimed uses, and where the FDA-approved labeling did not indicate instructions or any intent to encourage the claimed use

On April 17, 2012, in *Caraco Pharmaceutical Laboratories, Ltd. v. Novo Nordisk A/S*, a case involving the drug Prandin®, the U.S. Supreme Court unanimously ruled that a generic drug manufacturer may use the counterclaim provision of 21 U.S.C. § 355(j)(C)(ii)(I) to force correction of an Orange Book use code that inaccurately described the brand's patent as covering a particular method of using the drug.

Although these cases impact different aspects of noninfringement defenses, they were big wins for generics because they helped clarify two very common, but long-standing grey areas faced by generics asserting noninfringement of method-of-use patents in Hatch-Waxman cases.

The Yasmin® Case: Relevance of "Indications and Usage" in Infringement Litigation

Yasmin® is an oral contraceptive marketed by Bayer. Sandoz, Watson and Lupin filed abbreviated new drug applications ("ANDAs") in which they certified that the three patents that Bayer listed in the Orange Book in connection with Yasmin® were either invalid, unenforceable or would not be infringed by their generic versions of Yasmin®. Bayer sued all three generic manufacturers, alleging infringement of one of the three listed patents, U.S. Patent No. 5,569,652 ("the '652

patent"). The '652 patent does not claim the active ingredient in Yasmin® or the use of Yasmin® solely as a contraceptive, but instead covers a method of use narrowly focused on simultaneously achieving three effects in patients: an anti-androgenic effect (anti-acne), an anti-aldosterone effect (diuretic) and a contraceptive effect.

The FDA-approved label for Yasmin® undisputedly indicated that the product was approved as an oral contraceptive. However, the parties disagreed whether the label could also be interpreted to indicate that Yasmin® should be used as claimed in the '652 patent, *i.e.*, as an anti-acne and diuretic drug in addition to a contraceptive. Watson and Sandoz argued that Yasmin® was approved only for contraceptive use, that their ANDAs necessarily included an "indications and usage" section which provided instructions only for contraceptive use and that such contraceptive-only indications were not covered by the '652 patent. The trial court concluded that there was nothing in the generic labels to indicate that the defendants sought to promote their generic products based on the anti-androgenic or anti-aldosterone properties claimed in the '652 patent, and entered judgment of noninfringement in favor of the defendants. Bayer appealed to the Federal Circuit, which has exclusive jurisdiction over patent disputes.

The primary issue on appeal was whether the FDA had affirmatively approved Yasmin® (found it safe and effective for) the unindicated uses of inducing anti-acne and diuretic effects in patients with a specific, simultaneous need for all three claimed effects. The Federal Circuit ruled that the generic products would not infringe the '652 patent. The court focused primarily on the "Indications and Usage" portion of the approved drug label because this portion of the label details the specific conditions that the FDA approved the drug to treat, despite the fact that (a) the FDA was aware that Yasmin® could therapeutically address all three patented effects, and (b) it had even approved marketing materials promoting the use of Yasmin® to achieve those effects. Although additional potential effects of the drug may be described in other sections of the label, the court found that information in those sections failed to establish that the FDA *affirmatively approved* the drug for producing those effects in a patient who needs them. The majority also noted that under FDA labeling regulations, *only* the indications and usage portion of the label reflects the FDA's approval. Importantly, the court held that because the FDA had not formally approved Yasmin® for all three purposes claimed in the '652 patent, as a matter of law Bayer could not state a valid claim for patent infringement.

This decision is favorable for the generic industry because method-of-use patents covering different aspects of therapy with a drug are extremely common in the Orange Book. Often such patents will contain method of use claims that are not specifically FDA-approved indications. Knowing the importance of specific sections of the FDA-approved label, especially a drug's approved indicated uses, will provide guidance to generics who are attempting to avoid infringement of such patents.

The Prandin® Case: Generics May Challenge Incorrect Use Code Information

The drug at issue in this case was Prandin®, the active ingredient of which is repaglinide, a drug that is used for the treatment of type 2 diabetes (non-insulin dependent diabetes mellitus). There are three FDA-approved indications for Prandin®: (1) treatment with repaglinide alone; (2) treatment with repaglinide in combination with metformin; and (3)

treatment with repaglinide in combination with thiazolidinediones (TZDs). When Caraco filed its ANDA in 2005 seeking approval to market generic repaglinide, the Orange Book included U.S. Patent No. 6,677,358 ("the '358 patent"), which claims only the second FDA-approved use: repaglinide-metformin combination therapy. At the time Caraco filed its ANDA, the Orange Book use code for the '358 patent was "[u]se of repaglinide in combination with metformin to lower blood glucose."

Caraco's ANDA certified to the FDA that the '358 method-of-use patent was invalid, unenforceable and/or would not be infringed by Caraco's proposed generic repaglinide product, prompting Novo to sue Caraco for infringement of the '358 patent. Upon review of Caraco's ANDA, the FDA advised Caraco that if it was not seeking to market repaglinide with metformin, it could revise its label to "carve out" or omit Novo's patented metformin-repaglinide combination therapy, which would clear the way for approval of Caraco's product upon expiration of the '035 compound patent.
When Novo learned of Caraco's carve-out request, it revised the '358 patent use code to broadly state that the patent covers "[a] method for improving glycemic control in adults with type 2 diabetes," which was sufficiently broad to encompass all three FDA-approved uses. Because the FDA does not to attempt to confirm the accuracy of use codes, it accepted Novo's revised use code for the '358 patent as correct. Based on the fact that the revised patent use code overlapped with all three approved indications, the FDA then rejected Caraco's pending label carve-out request. Caraco responded by filing a counter-claim under 21 U.S.C. § 355(j)(5)(C)(ii)(I), requesting that Novo restore the original, narrow use code description for the '358 patent, which would allow the FDA to accept the carve-out request and theoretically proceed to approval of Caraco's generic product.

The trial court ordered Novo to restore the old use code within 20 days, sparking Novo to seek immediate appellate review. The main issue on appeal before the Federal Circuit was whether the counterclaim statute only allowed for generics to correct typographical errors in patent number or expiration date, or remove a patent if it does not cover any FDA approved methods of using the drug, or whether the statute was also available to correct a listing that did not accurately describe the true scope of the Orange Book listed patent, as was the case here. A divided Federal Circuit panel reversed the district court and found for Novo, holding that the counterclaim provision did not create a tool to compel "the patent holder to change its use code narrative." The case was then appealed to the United States Supreme Court.

In a unanimous decision for Caraco, the Supreme Court wholly disagreed with the Federal Circuit and Novo, holding that the text, context and legislative history of the statute supported an interpretation that allowed for *both* deletion of a patent from the Orange Book, and correction of a listing when the brand has misdescribed the patent's scope, or has made a typographical error. The Court reasoned that part of Congress' intent in passing the counterclaim provision was to prevent exploitation of FDA's determination that it cannot police accurate submission of patent information to the FDA for listing in the Orange Book. In its opinion, the Court discussed the crippling effect incorrect use codes can have on ability of the Hatch-Waxman scheme to function properly. Due to the lack of FDA review regarding scope of use codes, and the previous inability for generics to request corrections, creative drafting of use codes had become a strategy for brand pharmaceutical manufacturers to delay generic approvals. A brand's improper listing and characterization of

patents in the Orange Book, as was the situation here, ultimately prevents approvable, non-infringing generic products from obtaining FDA approval, which directly contravenes one of the primary goals of the Hatch-Waxman Act.

The Court's broad holding and restoration of the full scope of the counterclaim provision in this case is consistent with the intention behind the counterclaim provision and restores a key defense for generic manufacturers facing method-of-use patents with incorrect use codes. It also discourages brand-name drug manufacturers, as Novo did in this case, from "correcting" use codes when faced with generic competition in an attempt to bolster their infringement claims.

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