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GSK v. Teva – Induced Infringement Liability Despite Skinny Label

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In *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA, Inc.*, the Federal Circuit reinstated a jury's verdict that Teva infringed GSK's patented method of using its Coreg® drug product, even though Teva's product was initially launched with a skinny label that carved-out the infringing method. *See* No. 2018-1976 (Fed. Cir. Oct. 2, 2020) ("*GSK*"). The precedential decision has potentially far-reaching impacts in generic pharmaceutical and biosimilar cases. The 2-1 opinion included a lengthy dissent from Chief Judge Sharon Prost, and Teva has already indicated they will pursue further appeals, likely keeping the law of induced infringement in skinny label cases unsettled for months to come.

35 U.S.C. § 271(b): Induced infringement and new uses for old drugs

Section 271(b) defines liability for inducing the direct infringement of another party: "whoever actively induces infringement of a patent shall be liable as an infringer."

To prove inducement, a plaintiff must present evidence of active steps taken to encourage direct infringement; mere knowledge about a product's characteristics or that it may be put to infringing uses is not enough.[1] A generic or biosimilar manufacturer may induce infringement of a method of treatment patent under § 271(b) by proposing drug labeling with knowledge and specific intent to actively induce direct infringement by physicians.[2] When a plaintiff relies on a generic or biosimilar drug label for evidence of intent, courts examine whether the proposed label "encourage[s], recommend[s], or promote[s] infringement."[3] "Merely describing the infringing use, or knowing of the possibility of infringement, will not suffice; specific intent and action to induce infringement must be shown."[4]

It is also important to consider whether allegations of indirect infringement are made pre- or post-launch of the generic or biosimilar product. When a generic or biosimilar drug is not yet on the market, patentees can pursue actions for induced infringement against manufacturers through the artificial act of infringement created by Section 271(e). In this context, the inducement analysis is limited to intent that may be inferred from the generic or biosimilar manufacturer's proposed drug label, since pre-launch marketing, advertisement or other possible means of communication with direct infringers generally will not exist before launch.[5] In contrast, in a post-launch scenario, such as existed in this case, plaintiffs seeking money damages for inducement claims premised on actual acts of direct infringement must support them with sufficient evidence of active steps taken by the manufacturer to induce that direct infringement.[6]

Jury found Teva induced infringement, but trial judge overruled them

The case involved GSK's blood pressure drug, Coreg®, which is used to treat patients with congestive heart failure ("CHF") and other cardiovascular disorders. Teva filed an Abbreviated New Drug Application ("ANDA") with the FDA to manufacture a generic version of Coreg®, and sought approval for a label that carved out GSK's patented indication for treatment of CHF. By this time, composition of matter patents for Coreg® had expired and no patents remained for the indications listed on Teva's skinny label. Teva launched with this skinny label in 2007, but was required by the FDA to amend its label in 2011 to add back the patented CHF indication. Although GSK's patent for the CHF indication had been reissued in 2008, GSK only brought suit for patent infringement in Delaware after the 2011 full label expansion. GSK alleged that Teva had induced infringement during the period

when Teva's label included the CHF indication (full label period), as well as the period when Teva's label did not include the CHF indication (skinny label period). A jury agreed with GSK, awarding it $235 million in damages.[7]

After trial, Teva moved for judgment as a matter of law ("JMOL") to reverse the jury verdict. Teva's JMOL motion centered on the standard for inducement-causation, which had been disputed during the litigation in the fight over proposed jury instructions.[8] Teva argued that proof of liability for inducement required GSK to prove that "Teva's alleged inducement, *as opposed to other factors*, actually caused the physicians to directly infringe."[9] GSK meanwhile argued that the Federal Circuit's acceptance of circumstantial evidence to support a showing of inducement meant that "[p]roduct labels, advertisements, or user manuals directed to a class of direct infringers can be sufficient to prove inducement without hard proof that any direct infringer physician stated that she read Teva's labels and that caused her to prescribe Teva's generic [] in an infringing manner"[10]

In siding with Teva's theory on causation, Judge Leonard P. Stark found that GSK had not presented any evidence "that any doctor was ever induced to infringe the [] patent by Teva's label (either skinny or full)," while Teva had presented "uncontroverted evidence of alternative factors that caused physicians to prescribe [its generic] in an infringing manner."[11] Such "uncontroverted evidence" included: 1) proof that doctors had access to various resources, such as the American Heart Association and American College of Cardiology guidelines, which they relied on in making treatment decisions; 2) proof of GSK's own Coreg® label/product insert, and its promotional activity, which instructed physicians on how to use carvedilol; and 3) expert testimony from doctors that they relied on "guidelines and research, as well as their own experience [and] GSK marketing" when deciding how to prescribe Teva's generic.[12] Notably, none of these doctors testified that they viewed Teva's label as impacting prescribing behavior. GSK's expert admitted that he had not read Teva's generic label before he started writing prescriptions for carvedilol, and that prescriptions for Coreg® were automatically switched to generic without any knowledge on the physicians' part.[13]

Judge Stark distinguished the pre-launch case law on induced infringement cited by GSK, explaining that "[t]his Court has decided that reliance on a label and speculation about what may occur in the future cannot substitute for actual evidence about what has actually occurred in the past when, as in this case, there has been a period of actual, past conduct that is pertinent to infringement."[14] Based on that post-launch record, Judge Stark found that a reasonable jury could only have found that alternative "non-Teva" sources of information are what actually caused physicians to infringe. Without sufficient evidence of causation, Judge Stark held that GSK had failed to meet its burden of proof for induced infringement.

Federal Circuit reverses, reinstating GSK's $235 million jury verdict

GSK appealed, arguing that the district court erred by discrediting its evidence of Teva's press releases and promotional materials and by "analyzing causation in a manner inconsistent with the statute, precedent, and common law."[15] In its opening brief, GSK acknowledged that causation is an element of inducement, but contended that "a jury may infer that a defendant has actually induced infringement – *i.e.*, that its actions have "led to direct infringement" by third parties – where the defendant has intentionally promoted infringement.[16] Pointing to decisions such as *Power Integrations*, GSK renewed its argument that hard proof of actual infringement by an individual third party is not required where there is circumstantial evidence of inducement directed to a class of direct infringers.[17] GSK also relied on the common law principles of aiding and abetting liability to argue that "[a] person is liable as an aider and abettor so long as they provide any successful assistance to the wrongful act, regardless of how exactly they provide that assistance."[18]

Teva responded that GSK's causation standard is not appropriate for the context where physicians are already practicing the patented method prior to the generic's launch because their prescribing behavior is not impacted by the generic's label,[19] and that decisions such as *Power Integrations* merely reinforce the "unremarkable" proposition that an element such as causation may be proven with circumstantial rather than direct evidence.[20] Responding to GSK's arguments based on criminal aiding and abetting law, Teva pointed out that "[t]he Restatement makes clear that giving 'encouragement or assistance' is tortious *only* '[i]f the encouragement or assistance is a substantial factor in causing the resulting tort.'"[21]

In its 2-1 decision, the Federal Circuit sided with GSK: "[P]recedent makes clear that when the provider of an identical product knows of and markets the same product for intended direct infringing activity, the criteria of induced infringement are met."[22]

Relying heavily on the substantial evidence standard of review, the majority held that Judge Stark erred by re-weighing the evidence to overturn the jury's verdict. The court emphasized that jury verdicts should only be reversed "sparingly" and, "viewing the evidence in the light most favorable to the nonmovant … there is insufficient evidence from which a jury reasonably could find liability."[23] The majority opinion pointed to Teva's press releases and marketing communications as sufficient circumstantial evidence to show that Teva took active steps to encourage the off-label infringing use. In the majority's view, these communications stated that Teva's generic was equivalent to Coreg® and thus implied that it could be prescribed for all the same uses – including the infringing one. In particular, the court focused on Teva's advertisement of its "AB rating" for its generic: GSK, supported by physician and FDA expert testimony, argued that doctors would infer from the AB rating that Teva's generic was approved for all the same uses as Coreg®, including CHF – Teva's skinny label notwithstanding. Owing to the enormous difference in price between Teva's generic and GSK's drug (4 cents versus $1.50 per pill), Teva now owes $234 million in lost profits damages to GSK, even though it only sold $74 million worth of its drug (for all uses) and ultimately operated its generic carvedilol franchise at a net loss.[24]

In a 30-page dissent, Chief Judge Prost argued that the holding nullifies the practice of skinny label launches, despite express Congressional approval for the practice.[25] Chief Judge Prost contended that the case effectively extends patent life far beyond the expiration of composition patents, allowing brands to maintain monopolies where any new use for the old drug remains on patent – even if the generic or biosimilar does not seek FDA approval for that use. In Chief Judge Prost's words: "Contrary to Congress's intent, the Majority … allows one patented method to discourage generics from marketing skinny labels—thus, slowing, rather than speeding, the introduction of low-cost generics."[26]

Consequences for generic drug and biosimilar cases going forward

Brand manufactures in post-launch cases now have a roadmap to seek damages for induced infringement even when the generic has expressly carved-out the infringing use from its FDA-approved label. Applying the majority's reasoning, brands can build a circumstantial case to demonstrate inducement by pointing to evidence beyond the label, including external communications that generally announce equivalence between the generic and brand drugs; testimony that physicians know of and rely on such communications; and the generic's knowledge of possible revenue from off-label infringing uses. In light of the GSK decision, brands will seek to develop evidence to prove that generics know they will profit from infringing sales even if they don't include them on their skinny label.

Generics and biosimilars pursuing a skinny label strategy to carve out patented treatment methods of an otherwise unpatented drug should carefully evaluate all external communications, promotional materials and market predictions for evidence implying the generic can or will be used for the infringing method of use. This evaluation is further complicated in situations where the FDA requires the inclusion of certain information on the drug label that could serve as additional evidence of inducement. Several existing cases may inform the steps a generic or biosimilar manufacturer could consider to avoid induced infringement liability, such as express negative statements in their label and/or marketing stating that the product is not approved for the infringing method of use.[27]

Teva has already stated it will appeal the decision and may seek *en banc* review by the full Federal Circuit. Either party might seek Supreme Court review of any future appellate ruling, giving the high court the opportunity to revisit induced infringement liability for the first time since their 2011 *Global-Tech* decision. Due to the timeline remaining for appeals and the importance of clear standards on this issue for the industry, expect stakeholders to utilize the majority and dissenting opinions for months if not years to come.

Take home lessons for the biopharmaceutical industry

- Brand manufactures and reference sponsors may more aggressively pursue induced infringement claims in skinny label

cases. Proposed jury instructions that would require proof of direct, proximate causation between the defendant and the infringing physician's conduct will be challengable under *GSK*.

- Generic drug and biosimilar manufacturers pursuing skinny label strategies should scrutinize all aspects of their promotional materials, market predictions, other content of labels and any other external communications, to ensure they will not trigger liability under *GSK's* view of acceptable evidence for induced infringement.
- As further appeals continue, the standards for induced infringement liability in post-launch cases will likely remain unsettled for months to come.

Notes

1. *Takeda Pharm. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 630–31 (Fed. Cir. 2015); *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003).
2. 35 U.S.C. § 271(b); *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1364 (Fed. Cir. 2003) ("[M]ere knowledge of possible infringement by others does not amount to inducement; specific intent and action to induce infringement must be proven.").
3. *Takeda Pharm. U.S.A.*, 785 F.3d at 631.
4. *HZNP Medicines LLC v. Actavis Labs. UT, Inc.*, 940 F.3d 680, 702 (Fed. Cir. 2019).
5. *See GlaxoSmithKline LLC v. Glenmark Pharms. Inc.*, 2017 WL 2536431 at *2 (D. Del. June 9, 2017).
6. *Id.*; *see also Andrulis Pharms. Corp. v. Celgene Corp.*, 2014 WL 1572906, at *2 (D. Del. Apr. 10, 2014).
7. *GSK*, No. 2018-1976 (Fed. Cir. Oct. 2, 2020), slip op. at 3-7.
8. *Id.* at 8-9.
9. *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA Inc.* (C.A. No. 1:18-cv-878) (D.I. 431 at p. 30) (emphasis added).
10. *Id.* at pp. 28-29.
11. *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA Inc.*, 313 F.Supp.3d at 595.
12. *Id.* at 594.
13. *Id.*
14. *Id.* at n.14.
15. *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA Inc.* (C.A. No. 18-1976) (D.I. 26 at p.22).
16. *Id.* at p.24.
17. *Id.* at p.26.
18. *Id.* at p.46 *citing* Restatement (Second) of Torts § 876, Comment on Clause (b)
19. *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA Inc.* (C.A. No. 18-1976) (D.I. 56 at p.32).
20. *Id.* at p.33.
21. *Id.* at p.36 *citing* Restatement (Second) of Torts § 876, Comment on Clause (b).
22. *GSK,* No. 2018-1976 (Fed. Cir. Oct. 2, 2020), slip op. at 16 (citing *Global-Tech Appliances, Inc. v. SEB S.A.*, 563 U.S. 754 (2011)).
23. *Id.*, slip op. at 9.
24. *Id.*, slip op. at 33. (Prost, C.J., dissenting).
25. *Id.* (Prost, C.J., dissenting).
26. *Id.*, slip op. at 23. (Prost, C.J., dissenting).
27. *See, e.g., Otsuka Pharm. Co. v. Torrent Pharm. Ltd., Inc.*, 99 F. Supp. 3d 461, 490 (D.N.J. 2015); *Takeda Pharm. USA, Inc. v. W.-Ward Pharm. Corp.*, 72 F. Supp. 3d 539, 547 (D. Del. 2014), aff'd (Jan. 9, 2015), *aff'd in part, appeal dismissed in part sub nom. Takeda Pharm. U.S.A., Inc. v. W.-Ward Pharm. Corp.*, 785 F.3d 625 (Fed. Cir. 2015).

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