No. 22-37

In the Supreme Court of the United States

TEVA PHARMACEUTICALS USA, INC.,

Petitioner,

v.

GLAXOSMITHKLINE LLC,
SMITHKLINE BEECHAM (CORK) LIMITED,

Respondents.

On Petition For a Writ of Certiorari to The United States Court of Appeals for the Federal Circuit

SUPPLEMENTAL BRIEF FOR RESPONDENTS

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QUESTION PRESENTED

When a generic drug is doubly indicated for a patented use, and there is strong record evidence of intent and inducing conduct, can the generic manufacturer evade liability for induced patent infringement merely because it did not include on its label (i.e. "carved out") one of the two indications corresponding to the patented use?

RULES 24(B) AND 29.6 STATEMENT

All parties are identified in the caption of this brief. Respondent GlaxoSmithKline LLC, is a for-profit Delaware company. Respondent SmithKline-Beecham (Cork) Limited is a for-profit organization. GSK plc owns 10% or more of the stock in respondents.

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Rather than address the actual facts of this case and the documented history of the section viii "carve-out" process, the government rewrites both to reach the result it wants. Certiorari should not be granted based on such false premises, which will lead to messy merits proceedings dominated by factual disputes, making this case a poor vehicle for addressing the issues raised by the government.

A properly-instructed jury found Teva willfully intended to cause infringement with its "skinny label" generic carvedilol that carved out indication 1.1 of GSK's Coreg® label, but left on indication 1.2. There is no doubt substantial evidence supports this finding. The government focuses on one piece of that evidence – the label itself – to the exclusion of everything else, as if the issue of intent boils down only to that.

At trial, however, the jury heard voluminous additional evidence of Teva's intent, including testimony from Teva's commercial witness (admitting Teva intended to capture the entire heart failure market), statements in Teva's product brochures calling Teva's product a "Generic of COREG® Tablets," and 2004 and 2007 press releases publicizing that Teva's generic carvedilol should be used to treat heart failure. C.A.Appx10488, 4245, 6347, 6342. Those press releases remained on Teva's website for years, with the former explicitly lumping indications 1.1 and 1.2 together as "heart failure" and the latter deliberately describing Teva's product as a "generic version of GSK's cardiovascular agent COREG® (Carvedilol) Tablets" without any hint Teva's product had a skinny label. C.A.Appx11857, 10542; Pet.App.35a. GSK's physician expert testified unrebutted he read the releases and understood them to mean Teva's generic carvedilol should be used in accordance with the

method of use claimed in GSK's '000 patent. C.A.Appx11656, 11659. The jury also heard evidence Teva later switched to a full label with no carve out and without the required notice to GSK – a brazen move from which the jury could draw inferences regarding what Teva's intent was all along. C.A.Appx10569-10572, 11044, 11049-50; Pet.App.8a-9a.

Although no additional support was needed, the label itself was also evidence of Teva's intent. The government's contrary assertions rest on a clear misunderstanding about how the carved-out label arose. As demonstrated, neither FDA nor Teva could possibly have relied on GSK's 2008 Form 3542 in crafting Teva's "skinny label." Opp. 12-13. GSK submitted the form in February 2008, six months ***after*** Teva launched its "skinny label" generic carvedilol in September 2007. C.A.Appx6880-6882. The form had nothing to do with FDA's or Teva's conduct, so it cannot serve as the basis for overturning the jury's willful infringement finding.

But even if the form were probative of any issue on appeal, the government's statements about it are unmoored from the record. First, the government fails to even mention the use code identified by GSK, U-233, let alone argue choosing that use code was improper. U-233, "Decreasing Mortality Caused by Congestive Heart Failure," reads directly on Claim 1 of the asserted patent ("A method of decreasing mortality caused by congestive heart failure…") and is strikingly similar to indication 1.2 that Teva retained on its label ("Carvedilol is indicated to reduce cardiovascular mortality…"). C.A.Appx45, 7665. Second, contrary to the government's assertion, GSK did ***not*** "represent" on that form that the '000 patent was limited

to indication 1.1. U.S. Br. 15. The description GSK provided on the form applies equally to indication 1.1 *and* indication 1.2. C.A.Appx6881. Simply put, GSK made no misrepresentations to FDA or Teva about what approved uses were patented.

Just as puzzling is the government's unsupported assertion FDA purportedly "gave" the carve-out label to Teva "based on" GSK's submissions. U.S. Br. 6. For nearly two decades, the process has been the opposite, with generic applicants required by regulation to propose carve-outs based on their review of the use code, patent, and brand label, and FDA conducting a review of those carve-outs for safety and efficacy. 21 CFR 314.94(a)(8)(iv). That Teva apparently decided not to follow this process does not demonstrate an "intent not to infringe," but rather recklessness with respect to its statutory and regulatory responsibilities.

But this Court need not rely on GSK's, Teva's or the government's word on any of these factual matters. A supplemental proceeding on remand is already slated to address these questions in the context of Teva's equitable estoppel defense. The government attempts to short-circuit this process by resolving contested issues against GSK and dispensing with evidence and law that does not fit its policy objectives. This is no basis for recommending a grant of certiorari. The petition should be denied.

I. The Factual Underpinnings of the Government's Argument for Certiorari Are Unsupported by the Record and Will Be the Subject of Further Proceedings

At the heart of the government's brief are two erroneous factual assertions: 1) GSK "represented" on its 2008 Form 3542 that its patented use was limited to indication 1.1 on Coreg's label through the use of language "essentially identical" to indication 1.1 (U.S. Br. 6); and 2) "based on" information provided by GSK, FDA "gave" to Teva the redlined document that ultimately became its skinny label (*id.*). Neither assertion is supported by the record.

With respect to the former, the form at issue allowed NDA holders to identify the approved use covered by their patents by "indication ***or*** method of use information." C.A.Appx6881 (emphasis added). GSK chose the latter. *Id.* Indeed, GSK's 2008 Form 3542 neither states "indication 1.1" in the one-inch high by five-inch wide box provided on the form, nor cites indication 1.1.

Instead, GSK used language describing its approved (and patented) "method of use" in language from the approved label, the other option on the form. The language used contains a portion of the wording of indication 1.1, specifically, a portion that also covers the patented aspect of indication 1.2 – namely, treatment of those patients with MI/LVD who have symptomatic heart failure. As both parties' experts agreed, these patients by definition have congestive heart failure, one of the conditions listed by GSK in the box on the form. C.A.Appx10602-10606 (McCullough); C.A.Appx11132; 11226 (Zusman). Significantly, the language used on the form also ***omits*** language from indication 1.1 – reducing the risk of

hospitalization – that had not been shown in the clinical trial supporting indication 1.2 and thus would not cover that indication. C.A.Appx5545-5549.

At trial, the jury heard testimony explaining these distinctions from a scientific point of view, primarily from Mary Anne Lucas, a listed inventor on the '000 patent. Dr. Lucas explained to the jury the different stages of heart failure, and that patients who have recently suffered a heart attack and are symptomatic have "mild" heart failure. C.A.Appx10359-10360, 10381-10382. They heard her describe the clinical trial supporting indication 1.2 (CAPRICORN), which showed a decrease in cardiovascular mortality but *not* a reduction in the risk of hospitalization, while the clinical trials supporting indication 1.1 (COPERNICUS AND COMET) showed both. C.A.Appx10359-10360, 10378-10383, 5545-5549. And they heard both experts agree that symptomatic patients under indication 1.2 have congestive heart failure. C.A.Appx10602-10606, 11132, 11226.

Accordingly, if any generic applicant were to utilize GSK's Form 3542 in the "carve-out" process, the form's description of the method of use would have signaled the need to carve out both indication 1.1 *and* indication 1.2 to avoid patent infringement.

But regardless of how one reads Form 3542, its discussion of the label was irrelevant to Teva, as GSK did not submit the form until February 2008, six months ***after*** Teva launched its skinny-labeled product.[1] What was available to Teva to inspect, at the relevant time, was the '069 patent, e.g., Claim 1 "A method of decreasing mortality caused by congestive

[1] The record is silent as to when the form ultimately became public.

heart failure. . .," and the corresponding "use code," "Decreasing Mortality Caused by Congestive Heart Failure," which GSK later repeated on its 2008 Form 3542. In fact, the use code contains language that is closer to indication 1.2 than to indication 1.1.

> COREG is indicated ***to reduce cardiovascular mortality in*** clinically stable ***patients*** who have survived the acute phase of a myocardial infarction and have a left ventricular ejection fraction of less than or equal to 40% (***with*** or without **symptomatic *heart failure***) [see Clinical Studies (14.2)].

C.A.App.7665 (emphases added).

The government gives no weight to any of this, instead preferring to emphasize that the small box on the 2008 Form 3542 does not contain specific excerpts of language from indication 1.2, like the words "Left Ventricular Dysfunction." But that incorrectly presumes physicians would not understand "mild" congestive heart failure to be what indication 1.2 is describing in symptomatic patients. The physician experts at trial agreed to the opposite of that presumption, both testifying indication 1.2 does, in fact, describe patients suffering from congestive heart failure. C.A.Appx10602-10603, 11132.

All of this is to say what the government asserts about GSK's 2008 Form 3542 is inaccurate or, at minimum, the subject of dispute. If certiorari is denied, a bench trial on equitable estoppel will address the very issues raised by the government in its brief, as the majority at the Federal Circuit understood. Pet.App.25a. This Court should not grant review at this stage based on faulty factual assumptions by the government that

contradict the jury's implied fact finding and will be further refuted at the equitable estoppel trial.

At that bench trial, GSK will present evidence that, at all relevant times, FDA was well aware GSK and heart failure practitioners understood symptomatic patients under indication 1.2 were suffering from "mild" heart failure, and use of carvedilol could increase survival, one of the "methods of use" described in the box on GSK's 2008 Form 3542. For example, at the FDA advisory committee meeting regarding approval of indication 1.2 in 2002, GSK provided extensive testimony and documentation explicitly telling FDA that indication 1.2 covered patients with "mild" heart failure. C.A.Appx11968, 1193-65. GSK will also present information currently classified as confidential that bears on the issue of what, on GSK's label, other generic companies believed was and wasn't patented.

Also at issue in that bench trial will be the government's second critical and flawed assertion – that FDA prepared Teva's skinny label "based on" submissions from GSK. The present record contains not a shred of evidence to support this notion. Teva shielded most discovery into the origins of its skinny label through assertions of privilege, allowing the jury to see only emails describing Teva learning another generic applicant was intending to pursue a skinny label, deciding to go that same route, looking for a skinny label prepared by a generic company Teva had acquired, and at the last minute receiving a red-lined "skinny label" from FDA, with no further identification as to how that label came to be. C.A.Appx7993, 6908-6951.

The origins of this skinny label thus remain a mystery on the present record, despite the government's claim. And this is not merely a theoretical problem, but one with real impact on the merits. For example, the "redline" version of the skinny label provided by FDA to Teva in September 2007 has a different indication 1.1 than GSK's label for Coreg® approved in February of 2007, with GSK's label having the word "chronic" in indication 1.1, while the red-line "skinny label" version does not. GlaxoSmithKline, Coreg (carvedilol) package insert, revised 02/2007, U.S. Food and Drug Administration website, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2007/020297s022lbl.pdf; C.A.Appx6913.

Accordingly, granting certiorari here would result in only one thing for certain – a dispute over the facts that would impede consideration of any legal issues. Certiorari should not be granted when the factual record is in such dispute and a trial designed to address Teva's and the government's unsupported assertions will be held on remand.

II. The Government's View of the Carve-Out Process Contradicts Decades of FDA Published Practice, Policy and Guidance

In addition to relying on faulty factual assertions, the government's brief misstates the law and makes flawed policy arguments more appropriately addressed to Congress.

The government acts as if GSK should have submitted a redline label on its 2008 Form 3542. Not so. There was no requirement – nor room on the form – for the NDA holder to identify everything on its label related to the listed patent. 68 Fed. Reg. 36,686; 36,710-712 (June 18, 2003). And while FDA has never

required NDA holders to identify all the specific language on the label relating to the patented method of use, it did not even impose an obligation to identify sections and subsections of the labeling describing the claimed method of use until 2016, almost a decade after the events in question. 81 Fed. Reg. 69,599 (Oct. 6, 2016).

Rather, the focus of the regulatory process for two decades has been on use codes, which the Court recognized are "pivotal to FDA's implementation of the Hatch-Waxman Amendments." *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 419 (2012). In this process, FDA has consistently stated that its role in patent listing is ministerial and does not involve substantive review of patents. *Id.* at 406-07. FDA's guidance available at the time relevant to this case stated that FDA's regulations and practices surrounding use codes serve a notice function, but even use codes were "not meant to substitute for the applicant's review of the patent and the approved labeling." 68 Fed. Reg. 36,683 (June 18, 2003).

Here, the use code reads plainly on the '000 patent and indications 1.1 ***and*** 1.2. U-233, "Decreasing Mortality Caused by Congestive Heart Failure," is almost identical to the preamble of Claim 1: "A method of decreasing mortality caused by congestive heart failure . . . ." The story is the same as to the contested indication 1.2: "Carvedilol is indicated to reduce cardiovascular mortality…in patients … with … symptomatic heart failure."

After conducting a review of the patent in light of the use code, the applicant, ***not*** FDA, is supposed to "propose labeling for the generic drug that 'carves out' from the brand's label the still-patented methods of use." *Caraco*, 566 U.S. at 406. Even in proposing the

expanded 2015 regulatory requirements, FDA made clear it would defer to a generic applicant seeking a carve-out because the applicant has "a strong incentive to interpret the scope of the patent correctly to avoid being subject to patent infringement litigation following ANDA approval and potentially enjoined from marketing its product." 80 Fed. Reg. 6828 (February 6, 2015).

Teva's failure to follow this process is the cause of its current predicament. Contrary to the government's implications, generics are not bound to slavish copying of the innovator's label in the "skinny label" context. C.A.Appx10548-10550 (GSK's regulatory expert explaining changes Teva could have requested). For example, in *Takeda Pharmaceuticals U.S.A., Inc. v. West-Ward Pharmaceutical Corporation*, 785 F.3d 625, 630 (Fed. Cir. 2015), the generic label included statements not on the innovator's label that disclaimed the patented use. *See also AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1058-59 (Fed. Cir. 2010) (generic negotiated with FDA regarding wording of its label). But Teva failed to take basic steps to avoid an infringing label and, as the jury heard, actively encouraged infringement through multiple channels.

The government's proposed rewriting of the statutes to relieve Teva of the consequences of its actions flies in the face of long-standing precedent, practice and guidance. When Congress wanted to create a safe-harbor for generics, it did so expressly. *See* 35 U.S.C. § 271(e)(1).

Likewise, the government's position finds no support in this Court's inducement precedent. As GSK detailed and the government does not dispute, the uncontested jury instructions were in complete agree-

ment with *Grokster* and *Global-Tech*. Opp. 24-26 (citing *Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd.*, 545 U.S. 913, 935-37 (2005) and *Global-Tech Appliances, Inc. v. SEB S.A.*, 563 U.S. 754, 760 (2011)).

Moreover, "[i]nfringement is a question of fact." *Stilz v. United States*, 269 U.S. 144, 147 (1925). And the Federal Circuit majority held substantial evidence supported the jury verdict of willful infringement and did not upset the careful balance Congress struck in Hatch-Waxman. Pet.App.11a-12a, 14a-15a, 27a. The government's argument that a skinny label "cannot provide" evidence of specific intent, U.S. Br. 14, does not justify taking this factual question away from the jury.

As noted, the jury had sufficient evidence outside the label to find intent. *See supra* p. 1-2. Moreover, even the government retreats from its per se rule by acknowledging a generic manufacturer could be liable for exploiting its skinny label to induce doctors to practice the patented method. U.S. Br. 16. The dispute here – and in all the relevant cases – is thus factual, not legal.

And while the unique events at issue here occurred long ago and under a very different regulatory scheme, Opp. 30-31, the government fails to substantiate its claim that even under the current regulations, the section viii carve-out process is under threat. The government admits liability for inducement by a skinny label is "rarely imposed," U.S. Br. 22, and does not cite a single example of any change in practice since the verdict in this case was first affirmed in 2020.

To the extent any adjustment to Hatch-Waxman is needed, Congress is the proper forum for the government's policy-driven argument. Consistent with this, FDA announced it will be asking Congress to do just that. U.S. Food and Drug Administration, *Summary of FDA's FY2024 Legislative Proposals* at 3, available at https://www.fda.gov/media/166049/download. In that request, FDA conceded that the Federal Circuit majority indicated its decision was narrow, fact dependent, and does not upset the careful balance struck by Hatch-Waxman. *Id.* And while the record contains no evidence that the decision has discouraged section viii carve-outs, Congress can hear from all stakeholders – pharmaceutical innovators, generic manufacturers, insurance providers, doctors and patients – and make a public policy decision about whether any adjustment to the careful balance of Hatch-Waxman is needed. This Court should not preempt that process by accepting the government's policy-driven invitation to rewrite the statute and ignore all the evidence that supported the jury's verdict.

The petition for writ of certiorari should be denied.

Respectfully submitted,

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