No. 22-37

In the Supreme Court of the United States

TEVA PHARMACEUTICALS USA, INC., PETITIONER

v.

GLAXOSMITHKLINE LLC, ET AL.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

BRIEF FOR THE UNITED STATES AS AMICUS CURIAE

THOMAS W. KRAUSE
Solicitor
United States Patent and Trademark Office
Alexandria, VA 22314

SAMUEL R. BAGENSTOS
General Counsel
Department of Health and Human Services
Washington, D.C. 20201

MARK RAZA
Chief Counsel
Food and Drug Administration
Silver Spring, MD 20993

ELIZABETH B. PRELOGAR
Solicitor General
Counsel of Record
BRIAN M. BOYNTON
Principal Deputy Assistant Attorney General
MALCOLM L. STEWART
Deputy Solicitor General
MATTHEW GUARNIERI
Assistant to the Solicitor General
DANIEL TENNY
GERARD SINZDAK
Attorneys

Department of Justice
Washington, D.C. 20530-0001
SupremeCtBriefs@usdoj.gov
(202) 514-2217

QUESTION PRESENTED

By filing an abbreviated new drug application (ANDA), a manufacturer may seek approval from the Food and Drug Administration (FDA) to market a generic version of a previously approved brand-name drug. The ANDA must address, among other things, each patent that claims a method of using the drug, as identified by the brand-name manufacturer. Under the statutory scheme, one option available to a generic-drug manufacturer is to seek FDA approval to market a generic drug only for uses not claimed by an identified method-of-use patent. In those circumstances, the ANDA must propose generic-drug labeling that omits any portion of the brand-name drug's labeling that corresponds to a patented method of use.

Here, petitioner received FDA approval for a generic version of the brand-name drug Coreg, with labeling that omitted an indication on the Coreg labeling that the brand-name manufacturer had identified to FDA as claimed by a method-of-use patent. Respondents later sued petitioner for allegedly inducing doctors to infringe the patented method of use, based in part on the generic drug's FDA-approved labeling. The question presented is as follows:

Whether the court of appeals erred in holding that the FDA-approved labeling for petitioner's generic drug could provide evidence of intent to induce infringement of respondents' method-of-use patent, where that labeling carved out the portions of the brand-name reference drug's labeling that the brand-name manufacturer and FDA had identified as corresponding to the patented method.

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Statutes and regulations—Continued: Page

Miscellaneous: Page

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This brief is submitted in response to the Court's order inviting the Solicitor General to express the views of the United States. In the view of the United States, the petition for a writ of certiorari should be granted.

STATEMENT

1. Under the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 301 *et seq.*, new drugs may not be manufactured or sold in the United States without the prior approval of the Food and Drug Administration (FDA). 21 U.S.C. 355(a).[1] To obtain FDA's approval, a manufacturer generally must submit a new drug application (NDA). 21 U.S.C. 355(b). The NDA must contain proposed labeling for the drug, along with scientific

[1] Section 355 was amended during the pendency of this case. See Orange Book Transparency Act of 2020, Pub. L. No. 116-290, § 2, 134 Stat. 4889-4893. All citations in this brief to Section 355 are to the current version.

data and other information showing that the drug is safe and effective if used as instructed on the labeling. 21 U.S.C. 355(b)(1)(A)(i) and (vi); see 21 C.F.R. 201.57(c).[2]

To facilitate the introduction of lower-cost "generic version[s]" of approved "brand-name drug[s]," *Caraco Pharm. Labs., Ltd.* v. *Novo Nordisk, A/S*, 566 U.S. 399, 404 (2012), Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585, commonly known as the Hatch-Waxman Amendments. Under those amendments, a would-be generic competitor may file an abbreviated new drug application (ANDA) that "piggyback[s]" in key respects on an approved NDA. *Caraco*, 566 U.S. at 404. "Rather than providing independent evidence of safety and efficacy, the typical ANDA shows that the generic drug has the same active ingredients as, and is biologically equivalent to, the brand-name drug." *Id.* at 405 (citing 21 U.S.C. 355(j)(2)(A)(ii) and (iv)). Subject to specified exceptions, the labeling proposed for the generic drug must be "the same as the labeling approved" by FDA for the brand-name reference drug. 21 U.S.C. 355(j)(2)(A)(v).

To encourage generic competition "as soon as patents allow," *Caraco*, 566 U.S. at 405, the Hatch-Waxman Amendments establish mechanisms for identifying and resolving patent disputes. An NDA must contain "the patent number and expiration date of each patent for which a claim of patent infringement could reasonably

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[2] In the FDCA, the term "label" refers to the material printed on the immediate container of a drug, whereas the broader term "labeling" encompasses any printed material that accompanies a drug. See 21 U.S.C. 321(k) and (m). When the lower courts in this case referred to the "label[s]" for the drugs at issue, they were referring to the labeling. See, *e.g.*, Pet. App. 15a-16a.

be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug." 21 U.S.C. 355(b)(1)(A)(viii). That requirement applies when a patent claims either an active ingredient of the drug or a method of using it for which the NDA seeks FDA approval. 21 U.S.C. 355(b)(1)(A)(viii)(I) and (II). The applicant also must provide similar information about any such patent that is issued after the NDA has been approved and while it remains in effect. 21 U.S.C. 355(c)(2).

If FDA approves an NDA for an indication claimed in a method-of-use patent, the NDA holder must submit additional information. In 2008, when FDA was notified of the patent asserted in this case, an NDA holder was required to provide FDA with "a description of each approved method of use or indication and related patent claim," and an "[i]dentification of the specific section of the approved labeling for the drug product that corresponds to the method of use claimed by the patent." 21 C.F.R. 314.53(c)(2)(ii)(P)(1) and (2) (2008). The descriptions of patented uses that NDA holders are required to submit are called "use codes." *Caraco*, 566 U.S. at 405. FDA publishes those use codes in a compendium, known as the Orange Book, that lists approved drugs and notifies potential ANDA applicants of any patents that an NDA holder has identified as claiming either the listed drug itself or an approved method of using it. See *id.* at 405-406.

The Hatch-Waxman Amendments give an ANDA applicant several options for addressing unexpired patents listed in the Orange Book. First, the applicant may certify that it will market its generic drug only after the relevant patents expire. 21 U.S.C. 355(j)(2)(A)(vii)(III). Second, the applicant may certify its belief that the rel-

evant patents are invalid or would not be infringed by the manufacture or sale of the generic drug. 21 U.S.C. 355(j)(2)(A)(vii)(IV). Such a "paragraph IV certification" is deemed to be an act of patent infringement and may trigger litigation to determine the validity and scope of the disputed patents. *Caraco*, 566 U.S. at 407; see 35 U.S.C. 271(e)(2)(A). Third, the applicant may seek FDA approval to market a generic drug only for one or more indications *not* claimed by a method-of-use patent identified by the NDA holder. 21 U.S.C. 355(j)(2)(A)(viii).

This case concerns the third option, which is known as a "section viii statement." *Caraco*, 566 U.S. at 406. "A section viii statement is typically used when the brand's patent on the drug compound has expired and the brand holds patents on only some approved methods of using the drug." *Ibid.* As explained above, an ANDA generally must propose labeling that is the same as the labeling for the FDA-approved reference drug. An ANDA applicant that submits a section viii statement, however, must propose "labeling for the generic drug that 'carves out' from the brand's approved label the still-patented methods of use." *Ibid.*; see 21 C.F.R. 314.94(a)(8)(iv) and (12)(iii)(A). FDA may approve an ANDA with a section viii statement only if the proposed labeling omissions "do not render the proposed drug product less safe or effective than the listed drug for all remaining, non-protected conditions of use." 21 C.F.R. 314.127(a)(7).

FDA plays only a "ministerial" role in listing patents and use codes for these purposes. *Caraco*, 566 U.S. at 407 (citation omitted). FDA does not independently evaluate whether an NDA holder has accurately described the patented methods of use for an approved

drug. The agency instead takes the use codes submitted by the NDA holder "as a given," *id.* at 406, in assessing the modifications that must be made to the brand-name drug's labeling when an ANDA applicant invokes the section viii pathway. See, *e.g.*, 81 Fed. Reg. 69,580, 69,597-69,598 (Oct. 6, 2016).

2. In 1995, FDA approved an NDA submitted by respondent GlaxoSmithKline LLC (GSK) for carvedilol, which GSK markets under the brand name Coreg. Pet. App. 4a. FDA ultimately approved Coreg for three indications, listed separately on the drug's labeling: (1) "treatment of mild to severe heart failure of ischemic or cardiomyopathic origin, usually in addition to diuretics, ACE inhibitor, and digitalis, to increase survival"; (2) "reduc[ing] cardiovascular mortality in clinically stable patients who have survived the acute phase of a myocardial infarction and have a left ventricular ejection fraction of ≤40% (with or without symptomatic heart failure)"; and (3) "management of essential hypertension." C.A. App. 7992; see Pet. App. 4a-5a.

In 2002, petitioner submitted an ANDA seeking FDA approval to market a generic version of carvedilol. Pet. App. 6a. At that time, the Orange Book listed two relevant patents—one claiming the carvedilol compound and one ("the '069 patent") claiming a method of using carvedilol to treat congestive heart failure—that GSK had identified to FDA. *Ibid.*; see *id.* at 55a (Prost, J., dissenting). Petitioner certified that it would not market its generic drug until after the patent on the carvedilol compound expired in 2007. *Id.* at 6a (majority opinion). Petitioner also submitted a paragraph IV certification asserting that the '069 method-of-use patent was invalid. *Ibid.*

GSK did not file an infringement suit in response to petitioner's paragraph IV certification. Pet. App. 6a. GSK instead asked the U.S. Patent and Trademark Office (USPTO) to reissue the '069 patent with narrowing limitations. *Ibid.*; see 35 U.S.C. 251. In January 2008, the USPTO issued a reissued patent ("the '000 patent") that claimed "a method of decreasing mortality caused by [congestive heart failure] by administering carvedilol with at least one other therapeutic agent." Pet. App. 6a.

GSK notified FDA of the '000 patent and submitted a use code identical to the use code for the '069 patent: "Decreasing Mortality Caused By Congestive Heart Failure." C.A. App. 6882; see *id.* at 6176. The pertinent FDA form also instructed GSK to "identify the use" claimed in the '000 patent "with specific reference to the approved labeling" for Coreg. *Id.* at 6881. GSK responded: "treatment of mild-to-severe heart failure of ischemic or cardiomyopathic origin, usually in addition to diuretics, ACE inhibitor, and digitalis, to increase survival." *Ibid.* (capitalization altered). That description is essentially identical to the first indication in the FDA-approved labeling for Coreg. See *id.* at 7992.

In the interim, petitioner changed its approach in the ANDA process. Rather than proceeding with a paragraph IV certification, in 2007 petitioner submitted a section viii statement proposing to market generic carvedilol with labeling that would omit the method of use claimed in the '069 patent. Pet. App. 7a. Based on the use code and other patent-identification information that GSK had submitted to the agency, FDA gave petitioner redlined labeling designed to omit the portions of the Coreg labeling that corresponded to the method of use claimed in the '069 patent. See *id.* at 57a-58a (Prost,

J., dissenting). Specifically, the modified labeling omitted the first indication of use on the Coreg labeling, regarding "treatment of mild to severe heart failure," as well as related information such as dosage instructions for the omitted use. *Id.* at 58a (emphasis omitted); see C.A. App. 6908-6951.

In 2007, after FDA approved its ANDA, petitioner began to market its generic carvedilol with the carved-out or "skinny" labeling that omitted the first indication of use on the Coreg labeling. Pet. App. 7a, 15a. As noted above, GSK obtained the reissued '000 method-of-use patent in 2008. In 2011, FDA asked petitioner to revise its labeling in light of the de-listing of the '069 patent from the Orange Book; the agency also asked petitioner to state its position with respect to the reissued '000 patent. *Id.* at 8a. Petitioner took the position that, because its ANDA had already been approved, it was not required to address the '000 patent via a paragraph IV certification or otherwise, and petitioner did not seek to maintain any labeling carve outs. *Id.* at 8a-9a. In 2011, petitioner instead began to use labeling for its generic carvedilol that included all three indications of use on the Coreg labeling. *Id.* at 8a. The carved-out labeling therefore was in use from 2007-2011.

3. In 2014, GSK and an affiliate (collectively, respondents) brought this action in the District of Delaware, alleging that petitioner had induced third parties to infringe the '000 patent. Pet. App. 9a; see 35 U.S.C. 271(b). Direct infringement of a patent triggers a form of strict liability, for which the accused infringer's "knowledge or intent is irrelevant." *Global-Tech Appliances, Inc.* v. *SEB S.A.*, 563 U.S. 754, 761 n.2 (2011). A defendant can be held liable for induced infringement, by contrast, only if it actively induces a third party to

engage in conduct that the defendant knows constitutes direct infringement. *Id.* at 766. Here, the gravamen of respondents' complaint was that petitioner's marketing and distribution activities had induced doctors to prescribe petitioner's generic carvedilol to treat congestive heart failure, thereby infringing the method of use claimed in the '000 patent. Second Am. Compl. ¶¶ 52-67.

The case proceeded to a jury trial. The district court instructed the jury to consider liability during two distinct periods: the carved-out or "'partial label' period" from 2008 to 2011, "and the 'full label' period" from 2011 to 2015. Pet. App. 9a (citation omitted). The six-year statute of limitations prevented seeking damages for any alleged infringement before 2008, and the '000 patent expired in 2015. 35 U.S.C. 286; see Pet. App. 95a. The jury returned a verdict of infringement for both periods and awarded respondents $235 million in damages. Pet. App. 150a.

The district court granted petitioner's post-verdict motion for judgment as a matter of law. Pet. App. 149a-181a. The court held that no reasonable jury could find that petitioner's marketing of generic carvedilol had caused doctors to prescribe the generic drug to treat congestive heart failure. *Id.* at 160a-161a, 163a. With respect to the "skinny label period," *id.* at 165a, the court observed that the labeling for petitioner's generic carvedilol "did not instruct doctors to prescribe" the drug to treat congestive heart failure, making that use "an off-label use," *id.* at 166a.[3] The court viewed the trial evidence as insufficient to show that doctors had

[3] The FDCA does not prohibit doctors from prescribing an FDA-approved drug for "off-label" uses, *i.e.*, for indications other than those for which FDA has determined that the drug is safe and effective if used as instructed on the drug's labeling.

prescribed petitioner's generic carvedilol for that off-label use because of the drug's labeling or petitioner's conduct, rather than because of "other factors." *Id.* at 175a; see *id.* at 169a-176a.

4. A divided panel of the court of appeals reversed and remanded for further proceedings. The panel issued its first opinion in October 2020. Pet. App. 88a-146a. On rehearing, the panel vacated that opinion and issued a new opinion in August 2021. *Id.* at 1a-87a. Judge Prost dissented on both occasions.

a. As relevant here, the court of appeals' first opinion stated that "ample record evidence" supported the jury's finding that petitioner had caused physicians to directly infringe the '000 patent, including during the period when petitioner's generic carvedilol was marketed with carved-out labeling. Pet. App. 105a. The court stated that "the content of the product label" itself was "evidence of inducement to infringe." *Ibid.*

b. Petitioner sought rehearing en banc, supported by amici "concerned that [the panel's] decision could be read to upset the careful balance struck with section viii carve-outs." Pet. App. 11a. Petitioner and its amici contended that, under the panel's initial decision, an ANDA holder who receives FDA approval to market a generic drug with labeling that "omit[s] all patented indications" could be held liable for induced infringement "for merely marketing and selling under [the] 'skinny' label." *Ibid.* (citation omitted).

The court of appeals granted panel rehearing, vacated its initial decision, and issued a second decision. Pet. App. 1a-45a. In that decision, the court held that the jury was entitled to conclude that petitioner's carved-out labeling had "failed to carve out all patented indications." *Id.* at 12a. The court stated that the jury

could reasonably have determined that portions of that labeling—primarily those that described the use of carvedilol to reduce mortality in patients who have survived the acute phase of a heart attack (myocardial infarction), which is the second indication on the Coreg labeling—taught the patented method of using carvedilol to treat congestive heart failure. See *id.* at 15a-22a. The court acknowledged that GSK was required to identify to FDA those portions of the Coreg labeling that instructed a method of use claimed by a patent, and that GSK had identified only the first indication, not the second. *Id.* at 22a. In the court's view, however, whether the second indication on the Coreg labeling and other non-carved-out portions actually taught the patented method was a question of fact that the jury had "decided against [petitioner]." *Id.* at 23a.

The court of appeals further held that the jury was entitled to infer, based on the contents of the carved-out labeling, that petitioner had the requisite intent to induce infringement. The court explained that Federal Circuit "precedent has consistently held that, when a product is sold with an infringing label or an infringing instruction manual, such a label is evidence of intent to induce infringement." Pet. App. 28a; see *id.* at 29a n.6 (noting the general rule that, "when a label instructs or teaches a patented use, it can be evidence of intent to encourage that use"). The court additionally concluded, contrary to the district court, that the record contained substantial evidence of causation. *Id.* at 39a-42a. The court of appeals therefore reinstated the jury's verdict but remanded to the district court to address whether, in light of respondents' conduct, petitioner can establish

an affirmative defense to infringement under principles of equitable estoppel. *Id.* at 25a-26a, 45a.[4]

c. Judge Prost dissented. Pet. App. 46a-87a. She emphasized that, during the period from 2007-2011, petitioner's "skinny label carved out the very use—indeed, the *only* use—that [respondents] said was patented." *Id.* at 47a. Based on the trial evidence concerning petitioner's use of the carved-out label from 2007-2011, Judge Prost concluded that "no reasonable jury could have found * * * culpable intent to encourage infringement." *Id.* at 62a.

Judge Prost warned that the panel decision would "'throw[] a wrench' into Congress's skinny-label design." Pet. App. 86a-87a (citation omitted). She observed that the statutory scheme is "predicated" on the understanding that generic competitors, in seeking FDA approval of their ANDAs, may "rely on what brands [say] about what their patents cover[]." *Id.* at 85a. Judge Prost viewed the panel decision as leaving unclear what future generic manufacturers "should do differently" to avoid liability in similar circumstances. *Id.* at 84a.

d. The court of appeals declined to rehear the case en banc, Pet. App. 182a-185a, with Judges Prost, Dyk, and Reyna dissenting, see *id.* at 194a-204a, 205a-208a, 209a-210a.

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[4] The court of appeals also held that substantial evidence supports the jury's verdict of infringement during the period from 2011-2015, when petitioner marketed its generic carvedilol with labeling that included all three indications on the Coreg labeling. Pet. App. 37a-39a. Petitioner does not seek review of that holding. See Pet. i; cf. Cert. Reply Br. 11-12.

DISCUSSION

To foster greater competition and thereby reduce drug prices, the Hatch-Waxman Amendments authorize FDA "to approve the marketing of a generic drug for particular unpatented uses," even when the brand-name reference drug has received FDA approval for additional uses that remain patented. *Caraco Pharm. Labs., Ltd.* v. *Novo Nordisk A/S*, 566 U.S. 399, 415 (2012). A generic competitor seeking such FDA approval must file a section viii statement and propose labeling that carves out, from the FDA-approved labeling for the brand-name reference drug, those portions that correspond to the patented method of use. In general, when a generic competitor "play[s] by the rules" of the section viii pathway, Pet. App. 47a (Prost, J. dissenting) —that is, when it seeks and obtains FDA approval to market a generic drug with carved-out labeling designed to omit any instructions for using the drug in a patent-protected manner—its use of that labeling may not later be treated as evidence of intent to induce infringement.

After the Federal Circuit's initial decision in this case prompted an outcry from amici, the court issued a second decision holding that the jury could reasonably have found that petitioner's carved-out labeling continued to teach the patented method of use in portions of GSK's labeling that had not been carved out. See Pet. App. 15a-22a. The court further held that a reasonable jury could view petitioner's carved-out labeling as evidence of intent to induce infringement of respondents' method-of-use patent. See *id.* at 28a, 29a n.6. That purported clarification in fact "exacerbate[d]" the practical concerns raised by the court of appeals' initial opinion. *Id.* at 87a (Prost, J., dissenting). Under the decision be-

low, a jury may conclude that a generic manufacturer's engagement in the precise conduct that the Hatch-Waxman Amendments contemplate—namely, marketing an FDA-approved generic version of a brand-name drug with labeling that carves out those indications that the brand-name manufacturer has identified to FDA as claimed by a method-of-use patent—is itself evidence of intent to induce infringement of the patented method.

The court of appeals' holding that respondents presented sufficient evidence of petitioner's intent to induce infringement is erroneous and warrants this Court's review. The section viii pathway cannot function properly if FDA and generic manufacturers cannot rely on an NDA holder's representations to the agency regarding which portions of the brand-name drug's labeling teach patented methods of use. Uncertainty about the section viii pathway is likely to deter generic manufacturers from invoking that mechanism, thereby threatening the availability of lower-cost generic drugs, in contravention of the statutory design. This Court should grant the petition for a writ of certiorari and reverse the judgment of the court of appeals.

1. The decision below is incorrect. No reasonable jury could have concluded that the carved-out labeling for petitioner's generic carvedilol from 2007-2011 was itself evidence of intent to induce infringement.

a. Section 271(b) of the Patent Act of 1952, 35 U.S.C. 1 *et seq.*, provides that "[w]hoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. 271(b). To "actively induce[] infringement," *ibid.*, the accused infringer must act with the "intent to 'bring about the desired result,' which is infringement," *Commil USA, LLC* v. *Cisco Sys., Inc.*, 575 U.S. 632, 642 (2015) (citation omitted). Evidence of "'active steps . . .

taken to encourage direct infringement,'" such as "instructing how to engage in an infringing use," may show the requisite "affirmative intent." *Metro-Goldwyn-Mayer Studios Inc.* v. *Grokster, Ltd.*, 545 U.S. 913, 936 (2005) (citation omitted) (discussing patent law while adopting a rule for induced copyright infringement). But the inducement cannot be inadvertent or merely a foreseeable consequence of actions undertaken for other reasons. The accused infringer must have the specific intent to induce a third party to engage in conduct that the accused infringer knows to constitute infringement. *Commil*, 575 U.S. at 642; see *Global-Tech Appliances, Inc.* v. *SEB S.A.*, 563 U.S. 754, 766 (2011) (holding that proof of willful blindness is sufficient to establish knowledge under Section 271(b)); cf. Pet. App. 13a (citing circuit precedent).

A generic manufacturer's labeling cannot provide the requisite evidence of specific intent to induce infringement in a case like this one, where the generic manufacturer has carved out the specific indication identified by the brand-name manufacturer as corresponding to the patented method of use that is alleged to be infringed. The section viii pathway enables manufacturers to market generic versions of a brand-name drug where the drug itself is not patented and only some of its FDA-approved uses are claimed by a method-of-use patent. See 21 U.S.C. 355(j)(2)(A)(viii); pp. 3-4, *supra*. By authorizing FDA to approve an ANDA in those circumstances, Congress necessarily contemplated that "one patented use will not foreclose marketing a generic drug for other unpatented ones." *Caraco,* 566 U.S. at 406. If the generic manufacturer's use of FDA-approved carved-out labeling could support a finding of intent to induce infringement of the pa-

tented method of use that the carved-out labeling is intended to omit, generic manufacturers' invocation of the section viii pathway would be substantially deterred.

To be sure, FDA approval via the section viii pathway does not authorize a generic manufacturer to infringe any patent, or to induce others to do so. If a generic manufacturer actively promotes direct infringement of a brand-name manufacturer's method-of-use patent through communications *other than* the carved-out labeling, it may be held liable under Section 271(b). Or if the brand-name manufacturer timely objects to the generic drug's labeling as failing to carve out a still-patented method of use and puts the generic manufacturer on notice that the labeling teaches the method, a factfinder might reasonably infer intent to induce infringement if the generic manufacturer nonetheless proceeds. See pp. 19-20, *infra* (discussing mechanisms for objecting to proposed labeling and for correcting inaccurate patent information submitted to FDA). But where the generic manufacturer has carved out from the reference drug's labeling the indication that the brand-name manufacturer has identified as corresponding to the patented method of use, a jury may not properly infer intent to induce infringement from the carved-out labeling itself. To the contrary, the carved-out labeling is more naturally viewed as evidence of the generic manufacturer's "inten[t] *not* to encourage infringement." Pet. App. 62a-63a (Prost, J., dissenting).

b. In rejecting the foregoing line of argument, the court of appeals held that, despite GSK's representation that it had identified the indication on its own labeling that corresponded to the patented method of use, the jury could reasonably find that additional (*i.e.*, non-carved-out) language on petitioner's skinny labeling

also taught the patented method. See, *e.g.*, Pet. App. 12a, 21a. The court then invoked the general rule that, "when a label instructs or teaches a patented use, it can be considered evidence of intent to encourage that use." *Id.* at 29a n.6; see *id.* at 28a. That inference of intent is inappropriate here. The carved-out labeling did not reflect petitioner's unencumbered choice, but instead was driven by FDA regulatory requirements and GSK's own identification of the indication that should be excised. See *id.* at 64a (Prost, J., dissenting) (explaining that petitioner "asked to carve out GSK's patented uses, and the FDA in return used GSK's representations to provide [petitioner] with a carved-out label"). Whatever inferences might be drawn from a manufacturer's unilateral choice of labeling that is found to encourage infringing uses, "[t]he law simply does not permit an inference of culpable, intentional encouragement from [petitioner's] label on this record." *Id.* at 66a (footnote omitted).

To be sure, it is *possible* that a particular brand-name manufacturer could fail to identify all the language in its labeling that corresponds to a patented method of use, and even possible that a particular generic manufacturer could recognize that fact and seek to exploit it to induce doctors to practice the patented method. But the court of appeals identified no evidence that petitioner had actually engaged in any such manipulation. In these circumstances, even accepting the jury's (presumed) finding that petitioner's carved-out labeling taught GSK's patented method, no reasonable jury could have viewed petitioner's use of that labeling as evidence of intent to induce infringement.

Pointing to various "marketing efforts, catalogs, [and] press releases," the court of appeals stated that

the carved-out labeling was "not the only evidence" of intent to induce infringement here. Pet. App. 31a. But most of the evidence the court cited showed only that "the literature [petitioner] provided to doctors told them to read labels and to prescribe according to them." *Id.* at 30a. Absent independent evidence that petitioner understood its carved-out labeling to encompass patented uses, proof that petitioner expected and encouraged doctors to rely on the labeling cannot support an inference of intent to induce infringement.[5]

c. The decision below subverts the balance struck by Congress, creates significant uncertainty for FDA and generic manufacturers, and invites gamesmanship by brand-name manufacturers. Under the governing statutory scheme, FDA "cannot authorize a generic drug that would infringe a patent," but the agency "lacks 'both the expertise and the authority' to review patent claims." *Caraco*, 566 U.S. at 405-407 (brackets and citation omitted). Accordingly, the Hatch-Waxman Amendments place the onus on a brand-name manufacturer to describe any patented uses for which it seeks or has obtained FDA approval. 21 U.S.C. 355(b)(1)(A)(viii) and (c)(2). FDA's implementing regulations require the brand-name manufacturer to submit use codes—short descriptions of the methods of using the brand-name

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[5] The court of appeals also viewed press releases that petitioner had issued in 2004 and 2007 as evidence of intent to induce infringement. See Pet. App. 32a-36a. For the reasons set forth in Judge Prost's dissent, those releases are entitled to no meaningful evidentiary weight. See *id.* at 69a-74a. In particular, statements describing petitioner's carvedilol as the "AB-rated generic equivalent of" Coreg, *id.* at 32a (majority opinion) (citation omitted), simply reflect the truism that a generic drug is required to be therapeutically equivalent to its brand-name reference drug if used as directed on the labeling, see 21 U.S.C. 355(j)(2)(A)(iv) and (4)(F).

drug claimed by a patent—and to identify the portions of the approved labeling for the brand-name drug that "correspond[] to the method of use claimed by the patent." 21 C.F.R. 314.53(c)(2)(ii)(P)(2) (2008).

FDA does not independently vet those use codes or otherwise evaluate the validity or scope of the patents that the brand-name manufacturer identifies. FDA instead publishes the use codes and other patent information in the Orange Book, in part so that would-be generic competitors are on notice of the patents that the brand-name manufacturer has identified to the agency. Generic manufacturers may then evaluate those patents and make an informed choice among the statutory routes to market entry: awaiting expiration of all listed patents; submitting a paragraph IV certification with respect to one or more of the listed patents, thus inviting litigation over their scope or validity; or submitting a section viii statement with proposed carved-out labeling that excises language corresponding to any methods of use claimed by an unexpired patent. See 21 U.S.C. 355(j)(2)(A)(vii)(III)-(IV) and (viii).

The section viii pathway cannot function as designed unless FDA and generic manufacturers can rely on brand-name manufacturers' representations to the agency. FDA relies on the information submitted by brand-name manufacturers—such as use codes and identified sections of the brand-name drug's labeling—to determine which portions of the brand-name labeling must be carved out. Those carve-outs are one of the narrow exceptions to the general requirement that generic drugs must be labeled in the same manner as their brand-name equivalents. See 21 C.F.R. 314.94(a)(8)(iv), 314.127(a)(7); *Caraco*, 566 U.S. at 406. A generic manufacturer therefore is not free to omit additional portions

of the brand-name labeling beyond the omissions approved by FDA. And a generic manufacturer that obtains FDA approval for carved-out labeling generally does so on the understanding that the omissions on the labeling reflect the brand-name manufacturer's own views as to the scope of its patents. See Pet. App. 64a (Prost, J., dissenting) ("[B]y accepting the FDA-provided skinny label, which hewed to GSK's patented declarations, [petitioner] relied on GSK's representations of patent scope.").

Disputes may arise about the accuracy or completeness of the patent information submitted to FDA, but those disputes are not properly resolved through inducement litigation. If an NDA holder fears that FDA will mistakenly approve carved-out labeling that teaches a still-patented method of use, the NDA holder may file more complete and specific patent information with its application or may file a citizen petition seeking to halt the approval of the relevant ANDA. See 21 C.F.R. 10.30; 77 Fed. Reg. 25, 25 (Jan. 3, 2012). If FDA has already approved the ANDA, an aggrieved NDA holder may seek to stay the approval for further administrative review. See 21 C.F.R. 10.30, 10.35. On the other hand, if a generic manufacturer believes that patent information submitted by an NDA holder is inaccurate, it may notify FDA, which will bring the alleged errors to the NDA holder's attention. 21 C.F.R. 314.53(f). And if the NDA holder sues the generic manufacturer for infringement, the generic manufacturer may assert a counterclaim "seeking an order requiring the [NDA] holder to correct or delete" any inaccurate patent information, including use codes, that it has submitted to FDA. 21 U.S.C. 355(j)(5)(C)(ii)(I); see *Caraco*, 566 U.S. at 417-421.

Respondents, however, did not invoke any of the mechanisms for supplementing the patent information they had submitted to FDA or for challenging FDA's approval of the carved-out labeling for petitioner's generic carvedilol. Cf. *AstraZeneca LP* v. *Apotex, Inc.*, 633 F.3d 1042, 1057-1060 (Fed. Cir. 2010) (upholding a judgment of inducement liability that was premised on evidence that a generic manufacturer knew that its FDA-approved carved-out labeling had an "infringement problem," based in part on a citizen petition filed by the brand-name manufacturer objecting to another generic's ANDA). Respondents instead waited for years before alleging that petitioner's carved-out labeling had taught the patented method that the labeling was designed to omit. In those circumstances, the court of appeals erred in treating the labeling itself as evidence of intent to induce infringement.

2. The question presented warrants further review. If allowed to stand, the decision below threatens significant harm to competition and to consumers.

The section viii pathway is an integral component of a complex statutory scheme designed to encourage market entry by generic-drug manufacturers "as soon as patents allow." *Caraco*, 566 U.S. at 405. Generic drugs approved between 2018 and 2020 are estimated to have saved consumers more than $50 billion in the first 12 months of generic sales. Ryan Conrad et al., FDA, *Estimating Cost Savings from New Generic Drug Approvals in 2018, 2019, and 2020*, at 3 (2022). In many cases, FDA's approval of the first generic version of a brand-name drug reduced the price of the drug by more than 75%. *Id.* at 4. Such "first generic" approvals often involve carved-out labeling. See, *e.g.*, Bryan S. Walsh et al., *Frequency of First Generic Drug Approvals With*

'Skinny Labels' in the United States, 181 JAMA Internal Med. 995, 995-997 (2021). According to one recent study, the section viii pathway permitted generic drugs to be approved for sale an average of three years before the relevant method-of-use patents expired. See *id.* at 995.

Under the decision below, however, a generic manufacturer whose carved-out labeling conforms to FDA's instructions may still face liability, based on the content of the approved labeling itself, for inducing infringement of a patented method. That prospect may discourage manufacturers from invoking the section viii pathway, thereby decreasing the availability of lower-cost generic drugs. As Judge Prost observed, "if playing by the skinny-label rules doesn't give generics some security from label-based liability," there is a significant risk that "generics simply won't play." Pet. App. 198a (opinion dissenting from the denial of rehearing en banc).

3. This case is a suitable vehicle in which to address the question presented. To be sure, the case comes to this Court in an interlocutory posture; the Federal Circuit remanded for additional proceedings to determine whether petitioner can establish a meritorious equitable-estoppel defense. Pet. App. 25a-27a, 45a. But the possible availability of that affirmative defense in particular cases—based on legal standards that the court of appeals did not meaningfully clarify, and in a procedural posture where petitioner's intent to induce infringement will be taken as given—does not significantly reduce the potential deterrent effect on generic-drug manufacturers' invocation of the section viii pathway. Cf. *id.* at 66a n.14 (Prost, J., dissenting) (distinguishing the issue of estoppel from the question of "what *intent*

could be reasonably gleaned from the skinny label, given the way that label came about and the absence of other evidence of intent"). Given the uncertainty engendered by the decision below, regulated parties and consumers would benefit from prompt resolution of the question presented.

Respondents contend (Br. in Opp. 30-32) that further review is unwarranted because the regulatory landscape has changed in material ways since the events at issue here. In 2016, FDA amended its regulation addressing a brand-name manufacturer's duty to identify the sections or subsections of its labeling that describe a method of use claimed by a patent. See 21 C.F.R. 314.53(c)(2)(i)(O)(2) and (ii)(P)(2). But those "clarifying revisions," 81 Fed. Reg. at 69,597, did not fundamentally alter the regulatory scheme, which has always placed the onus on the brand-name manufacturer—not FDA or generic competitors—to identify accurately any methods of use claimed by a patent. More broadly, respondents do not show that any regulatory changes "moot[]" (Br. in Opp. 30) the question presented, lessen its prospective importance, or alter the evidentiary significance of a generic-drug manufacturer's use of FDA-approved carved-out labeling.

Respondents further contend (Br. in Opp. 33) that this case is "fact-bound" and involves unusual carved-out labeling that did not excise all references to a patented method of use. But the *potential* for inducement liability in these circumstances may significantly deter use of the section viii pathway, even if such liability is rarely imposed. And for the reasons Judge Prost identified in dissent, many of the "background facts here" will likely be present "in most skinny-label cases." Pet. App. 84a. If petitioner's carved-out labeling supports a

finding of intent to induce infringement, the section viii pathway will be seriously jeopardized.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted.

THOMAS W. KRAUSE
Solicitor
United States Patent and Trademark Office

SAMUEL R. BAGENSTOS
General Counsel
Department of Health and Human Services

MARK RAZA
Chief Counsel
Food and Drug Administration

ELIZABETH B. PRELOGAR
Solicitor General
BRIAN M. BOYNTON
Principal Deputy Assistant Attorney General
MALCOLM L. STEWART
Deputy Solicitor General
MATTHEW GUARNIERI
Assistant to the Solicitor General
DANIEL TENNY
GERARD SINZDAK
Attorneys

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