No. 11-800

IN THE
Supreme Court of the United States

APOTEX INC. AND APOTEX CORP.,

Petitioners,

v.

ALLERGAN, INC., EXELA PHARMSCI INC., AND EXELA PHARMSCI PVT., LTD.,

Respondents.

On Petition For A Writ Of Certiorari To The United States Court Of Appeals For The Federal Circuit

REPLY BRIEF FOR PETITIONERS

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REPLY BRIEF FOR PETITIONERS

In rejecting the argument that it would have been "obvious to try" to combine two previously patented eyedrop solutions routinely used together, the Federal Circuit applied a flawed version of the "obvious to try" test that renders that test a nullity. Respondents argue that Apotex failed to establish several formal "pre-requisites" to the application of the "obvious to try" test. But that multi-step approach is precisely the type of rigid and formalistic test rejected in *KSR International Co.* v. *Teleflex Inc.*, 550 U.S. 398 (2007).

The Federal Circuit further erred in treating the obviousness determination as a factual one and therefore deferring to the trial court's "factual finding[]" that it would not have been obvious to try combining the two formulations. Pet. App. 19a. Respondents try to downplay that fundamental error by suggesting that the standard of review is irrelevant in this case and unimportant in all cases. This Court's review is necessary because the Federal Circuit's application of the wrong standard of review was case-dispositive here and engenders uncertainty in the administration of the Nation's patent laws.

I. THE FEDERAL CIRCUIT'S RIGID AND FORMALISTIC APPLICATION OF THE "OBVIOUS TO TRY" TEST CONFLICTS WITH *KSR*

It is undisputed that the patents-in-suit simply claim the combination of Alphagan® and Refresh Tears®—two commercially successful eyedrop formulations marketed by respondents. It is also undisputed that a person having ordinary skill in the art (PHOSITA) would have known that Alphagan® and Refresh Tears® were routinely prescribed together for glaucoma patients. The lower court nevertheless held that it would not have been "obvious to try" to combine the two because they "*might*" be "incompatible or ineffective when combined in a single solution." Pet. App. 14a (emphasis added). As we explained (Pet. 17-20), that is not an "obvious to try" standard; it is a "guaranteed to succeed" standard.

Respondents counter that the Federal Circuit "simply held the 'obvious to try' test does not come into play in this case because Apotex failed to establish the pre-requisites for applying the test—namely, that the combination in question be one of a finite number of predictable solutions, the pursuit of which leads to 'anticipated success.'" Opp. 24. But that argument only underscores how the Federal Circuit has ossified the "obvious to try" standard into a rigid test that conflicts with *KSR*.

In *KSR*, this Court rejected the use of "rigid and mandatory formulas" to determine obviousness. 550 U.S. at 419. "[F]ormalistic" tests, this Court explained, must give way to simple "[c]ommon sense." *Id.* at 419, 420. Adopting an "expansive and

flexible approach," this Court recognized that a particular combination of known elements could be "obvious to try." *Id.* at 415, 421. To be sure, this Court set forth reasonable limitations on the "obvious to try" standard. *Id.* at 421. But those limitations just serve to prevent the "obvious to try" standard from becoming an "obvious to grasp at straws" standard.

If "obvious to try" means anything, then surely it means that it would have been obvious to *try* to combine two commercially successful products routinely used together to treat the same medical condition—even if there was some chance that the two products "might" be incompatible. Pet. App. 14a. Under respondents' theory, however, courts cannot even *consider* obviousness to try unless the challenger first "establish[es]" several "pre-requisites"—including a threshold showing that the combination would be an "anticipated success." Opp. 24. That multi-part approach converts the flexible "obvious to try" standard into the type of "rigid" and "formalistic" test rejected in *KSR*.[1]

Respondents, moreover, misinterpret each element of the inquiry. First, they assert that the

[1] Respondents make much of the fact that, in a *subsequent* case in the Federal Circuit, Apotex stated that "[i]n *In re Brimonidine*, there was no such roadmap" to the invention. Opp. 18 (internal quotation marks omitted); Opp. 34-35. But that statement simply reflects the fact that, after the lower court rendered its decision in this case, that decision was binding precedent in the very court Apotex was addressing. Seeking to distinguish that precedent, Apotex characterized how the Federal Circuit must have seen the facts of this case in ruling as it did.

"obvious to try" test is inapplicable here because the prior art did not disclose a "finite number" of solutions. Opp. 19. They cite the "seemingly endless" number of possible variables that can be altered in an eyedrop formulation. *Ibid.* But respondents focus on the wrong question. The right question is not whether there are many *conceivable* ways to vary a known product, but whether the prior art identifies a more limited number of variables worthy of experimentation.

In some cases, the prior art may disclose too many possible solutions to constitute a suitable lead for experimentation under the "obvious to try" standard. *E.g.*, *Takeda Chem. Indus., Ltd.* v. *Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356-57 (Fed. Cir. 2007) (single patent disclosed "hundreds of millions" of compounds). That is not the case here. The knowledge that Alphagan® and Refresh Tears® were routinely prescribed together for glaucoma patients created a motivation to try a *single* set of ingredients: the combination of those two formulations. The only question is whether it would have been obvious to try *that* combination—not, as respondents allege, whether there existed other conceivable permutations.

Moreover, while bemoaning the "endless" number of options available, Opp. 19, respondents state that Alphagan® P's inventors tried "17 other formulations before investigating Apotex's suggested combination" of Alphagan® and Refresh Tears®, Opp. 20. But, aside from the need to avoid focusing on a specific experimenter's path, surely 17 is a "finite number." *KSR*, 550 U.S. at 421. Indeed, the Federal Circuit has recognized that "[i]t would be logical to try"

every option taught in the prior art when the number of such options "was small, i.e., *only 53*." *Pfizer, Inc.* v. *Apotex, Inc.*, 480 F.3d 1348, 1363 (Fed. Cir. 2007) (emphasis added and internal quotation marks omitted). If 53 is a "small" finite number, so is 17. Furthermore, the inconsistent results the Federal Circuit reaches in similar cases reflect a need for guidance from this Court.

Second, respondents assert that the "obvious to try" standard applies only if the pursuit of known options "leads to 'anticipated success.'" Opp. 18. As we explained (Pet. 19), however, *KSR* states that *if* the use of a finite number of options "leads to the anticipated success" *then* the solution that results from that use of known options "is likely the product not of innovation but of ordinary skill and common sense." *KSR*, 550 U.S. at 421. In other words, the "anticipated success" language does not, as respondents contend, require an "expectation of success." Opp. 18. Rather, it requires a relationship between the problem the experimenter was trying to solve and the "success" ultimately achieved.

Here, the Federal Circuit rejected Apotex's "obvious to try" argument because the combination claimed "would not have been an anticipated success." Pet. App. 19a (internal quotation marks omitted). That is the erroneous standard that the Federal Circuit has consistently applied since *KSR*. See *Rolls-Royce, PLC* v. *United Technologies Corp.*, 603 F.3d 1325, 1339 (Fed. Cir. 2010); *Abbott Laboratories* v. *Sandoz, Inc.*, 544 F.3d 1341, 1352 (Fed. Cir. 2008). As Judge Dyk recognized in his dissenting opinion in this case (which respondents do not mention), the standard embraced by the majority

requires an "absolute predictability of success." Pet. App. 25a (internal quotation marks omitted). This Court should take this opportunity to correct that flawed interpretation of the "obvious to try" standard.[2]

Finally, respondents fixate on what the *patentee* thought, rather than on what would have been obvious to a hypothetical PHOSITA. They refer to the inventors' "low expectations" for Refresh Tears®-based formulations, Opp. 7; the inventors' "surprise" that the Alphagan® P formulation worked, *ibid.*; and the "effort" that the inventors put into Alphagan® P's development, Opp. 35. But "[t]he question is not whether the combination was obvious to the patentee but whether the combination was obvious to a person with ordinary skill in the art." *KSR*, 550 U.S. at 420; see 35 U.S.C. § 103(a).[3]

Respondents argue (at 25) that, because the inventors themselves were "people of at least

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[2] Respondents also suggest that the "obvious to try" test "is especially susceptible to hindsight bias." Opp. 33 (internal quotation marks omitted). That argument is foreclosed by *KSR*, which expressly endorsed the "obvious to try" test and made clear that the Federal Circuit had drawn "the wrong conclusion from the risk of courts and patent examiners falling prey to hindsight bias." 550 U.S. at 421.

[3] Respondents' contention (at 35) that developing Alphagan® P took "significant . . . effort" is similarly beside the point. "Sweat of the brow" is not a criterion for patentability. See 35 U.S.C. § 103(a) ("Patentability shall not be negatived by the manner in which the invention was made."); *Compton* v. *Metal Prods., Inc.*, 453 F.2d 38, 42 (4th Cir. 1971) ("Neither is the amount of time spent by [the inventor] in devising the method a controlling factor.").

ordinary skill that were focused on the problem," their self-reported "surprise" at Alphagan® P's success is necessarily relevant to the obviousness inquiry. But that is like arguing that an alleged tortfeasor's views on whether he was negligent is relevant because he is a "reasonable person." Respondents cannot convert the objective obviousness test into a subjective one.

Imagine that a company manufactures a peanut-butter sandwich, and bottled grape jelly. Customers purchase and consume the products together without any deleterious consequences. The same manufacturer then decides to create a new product that simply combines the peanut-butter sandwich and the jelly into a single pre-packaged peanut-butter-and-jelly sandwich. Would it have been "obvious to try" that combination?

Under the "obvious to try" test applied by the Federal Circuit (and embraced by respondents), the answer would be "no," because even though the two products were compatible when consumed together, they "might" be "incompatible . . . when combined in a single [sandwich]." Pet. App. 14a. The peanut butter might "oxidize" the jelly when they are in continued contact. Or the jelly might soak through the bread. But a common-sense application of the "obvious to try" test would simply ask whether, given the prior-art products—and the fact that they were routinely consumed together—it would have been obvious to *try* combining the two products into a single sandwich.

Ten years before *KSR*, the Federal Circuit considered a similar question: whether it would have been obvious to combine the painkiller ibuprofen (the

active ingredient in Motrin®) with the decongestant pseudoephedrine into a single product for the relief of cold symptoms. *Richardson-Vicks Inc.* v. *Upjohn Co.*, 122 F.3d 1476 (Fed. Cir. 1997). As in this case, it was undisputed that "doctors had in fact prescribed ibuprofen in combination with pseudoephedrine, albeit not in a [single unit]." *Id.* at 1480. And, as in this case, the patentee had argued that, even though the products were routinely prescribed together, a PHOSITA would have thought it "illogical" or "impossible" to combine the two products into "a single tablet." *Id.* at 1482, 1483-84. Applying a common-sense approach to the obviousness inquiry, the court rejected that argument and held that it would have been obvious to combine the two products in a single unit. *Id.* at 1483-84.

The only explanation for the contrary result reached in this case is that in "obvious to try" cases the Federal Circuit now applies an even narrower and more rigid obviousness analysis than it did before *KSR*. Review by this Court is necessary.[4]

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[4] In keeping with their mantra that this case turns on purely "factual issues," Opp. 1, 14, 17, respondents question several factual statements made in the petition. But those statements were taken—nearly verbatim—from respondents' *own* briefing below. For example, respondents take issue with Apotex's statement that "formulating Alphagan® at the higher pH of Refresh Tears® was desirable because it is closer to the pH of the eye," Opp. 27, but they stated below that "[i]t is desirable to formulate ophthalmic formulations around a pH of 7.4, the pH of the eye," Resp. C.A. Br. 5. Similarly, respondents now dispute that "using Refresh Tears® would have been advantageous because Purite® is a gentler preservative on the

II. THE FEDERAL CIRCUIT APPLIED THE WRONG STANDARD OF REVIEW

Respondents cannot dispute that "[t]he ultimate judgment of obviousness is a legal determination." *KSR*, 550 U.S. at 427. But they remain agnostic on whether the existence of a motivation to combine prior-art references is a factual or legal determination. See Opp. 29 ("The result here is the same regardless of the standard of review.").

The Federal Circuit has expressed no such ambivalence. It has repeatedly asserted that "[t]he presence or absence of a motivation to combine references in an obviousness determination is a *pure question of fact*." *In re Gartside*, 203 F.3d 1305, 1316 (Fed. Cir. 2000) (emphasis added); *Alza Corp.* v. *Mylan Labs., Inc.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006); *Wyers* v. *Master Lock Co.*, 616 F.3d 1231, 1238-39 (Fed. Cir. 2010) ("*KSR* did not change this rule."). Consistent with that view, the court deferred to the district court's "factual finding[]" that a PHOSITA would not have been motivated to try to combine Alphagan® and Refresh Tears®. Pet. App. 19a.

As we explained (Pet. 29-31), that approach conflicts with *KSR*, which clarified that the *Graham* factors are the factual components of the obviousness inquiry, 550 U.S. at 427, and treated the question whether a PHOSITA would have been motivated to modify the prior art as a "legal" question, *id.* at 424-

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eye than BAK," Opp. 27, but they themselves characterized Purite® as "a gentle preservative proprietary to Allergan," Resp. C.A. Br. 8.

25. The question whether a PHOSITA would have been motivated to combine prior-art references *is* the question of obviousness *vel non*; if there was a motivation to combine references, then the resulting combination would by definition have been obvious. The Federal Circuit's contrary interpretation can be corrected only by this Court.

Respondents protest that "there are many cases in which the Federal Circuit has found obviousness as a matter of law in the wake of *KSR*, either on summary judgment or JMOL." Opp. 30. When reviewing a summary-judgment decision, however, a court of appeals has no factual findings to defer to; it therefore *has to* rule on obviousness as a matter of law. See generally *Griffin* v. *United States*, 502 U.S. 46, 59 (1991) ("In one sense 'legal error' includes inadequacy of evidence—namely, when the phrase is used as a term of art to designate those mistakes that it is the business of judges . . . and of appellate courts to identify and correct.").

The Federal Circuit "review[s] the jury's conclusions on obviousness, a question of law, without deference, and the underlying findings of fact, whether explicit or implicit within the verdict, for *substantial evidence*." *Boston Scientific Scimed, Inc.* v. *Cordis Corp.*, 554 F.3d 982, 990 (Fed. Cir. 2009) (emphasis added and internal quotation marks omitted). The question whether the existence of a motivation to combine references is a legal determination is therefore equally critical when reviewing JMOL decisions. The logical implication of the Federal Circuit's theory is that courts should defer to the jury's implicit "finding[] of fact" that a PHOSITA was motivated to try to combine prior-art

references—which of course means deferring to the jury's obviousness determination. That bizarre result only underscores the absurdity of treating the existence of a motivation to combine as a factual determination.

Respondents' contention that the standard of review is irrelevant in this case also falls flat. They state that, "[o]nce the district court *found"* that a PHOSITA would have "expected the combination to fail," the question whether it would have been "obvious to try" the combination was an "easy" one to answer under *any* standard of review. Opp. 29 (emphasis added). But that just begs the question whether an expectation of success is a factual determination. It's not. Respondents cannot save the decision below on the ground that it applied the wrong standard of review *multiple* times.

Finally, respondents argue that it is unnecessary to treat the "obvious to try" or "motivation to combine" issues as legal for the sake of "uniformity" because the specific questions at issue in this case "are hardly likely to recur in other cases." Opp. 32 (internal quotation marks omitted). But the question at issue in this case is not the narrow question whether "brimonidine would be sufficiently soluble at pH > 7." *Ibid.* The question is whether it would have been "obvious to try" combining two commercially successful products that were known to be used together. That is a recurring question in

patent law[5]—and one with profound consequences.

This Court, moreover, has repeatedly stressed the "importance of uniformity in the treatment of a given patent." *Markman* v. *Westview Instruments, Inc.*, 517 U.S. 370, 390 (1996). Indeed, "[i]t was just for the sake of such desirable uniformity that Congress created the Court of Appeals for the Federal Circuit as an exclusive appellate court for patent cases." *Ibid*; see S. Rep. No. 97-275, at 4-5 (1981). Treating the "obvious to try" and "motivation to combine" determinations as factual determinations undermines the very uniformity and predictability that a well-functioning patent system requires.

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[5] *E.g.*, *Richardson-Vicks*, 122 F.3d 1476 (combination of ibuprofen and decongestant that were known to be prescribed together); *Ortho-McNeil Pharm., Inc.* v. *Teva Pharms. Indus., Ltd.*, 344 F. App'x 595, 601 (Fed. Cir. 2009) (Mayer, J., dissenting) ("The claimed invention does nothing more than combine two well-known pain relievers . . . in a single tablet."); *McNeil-PPC, Inc.* v. *L. Perrigo Co.*, 337 F.3d 1362, 1369-70 (Fed. Cir. 2003) (combination of antidiarrheal and antiflatulent that were known to be used together); *Application of Diamond*, 360 F.2d 214, 217 (CCPA 1966) (combination of "commonly used drugs in the treatment of . . . collagen diseases").

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted.

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