United States Court of Appeals for the Federal Circuit

BAYER PHARMA AG, BAYER INTELLECTUAL PROPERTY GMBH, BAYER HEALTHCARE PHARMACEUTICALS, INC.,
Plaintiffs-Appellees

v.

WATSON LABORATORIES, INC., ACTAVIS PHARMA, INC.,
Defendants-Appellants

2016-2169

Appeal from the United States District Court for the District of Delaware in No. 1:12-cv-00517-GMS, Judge Gregory M. Sleet.

Decided: November 1, 2017

DAVID I. BERL, Williams & Connolly LLP, Washington, DC, argued for plaintiffs-appellees. Also represented by BRUCE GENDERSON, DOV PHILIP GROSSMAN, AARON P. MAURER, ADAM LAWRENCE PERLMAN, THOMAS S. FLETCHER, GALINA I. FOMENKOVA.

WILLIAM M. JAY, Goodwin Procter LLP, Washington, DC, argued for defendants-appellants. Also represented

by ELIZABETH HOLLAND, ROBERT V. CERWINSKI, BRIAN ROBINSON, New York, NY; DAVID ZIMMER, Boston, MA.

Before LOURIE, MOORE, and O'MALLEY, *Circuit Judges.*

MOORE, *Circuit Judge.*

Watson Laboratories, Inc. appeals the District of Delaware's final judgment holding Watson failed to prove by clear and convincing evidence that claims 9 and 11 of U.S. Patent No. 8,613,950 ("the '950 patent") would have been obvious. We hold the district court clearly erred in finding a skilled artisan would not have been motivated to use the claim elements. Considering the district court's clear error together with the remainder of its fact findings, we conclude that claims 9 and 11 of the '950 patent would have been obvious. We therefore reverse.

BACKGROUND

In 2003, the Food & Drug Administration ("FDA") granted Bayer[1] approval to market vardenafil hydrochloride trihydrate to treat erectile dysfunction ("ED") under the name Levitra. Vardenafil belongs to a class of ED drugs called phosphodiesterase inhibitors. When the FDA approved Levitra, two other phosphodiesterase inhibitors were already on the market: Pfizer launched sildenafil under the name Viagra in 1998, and Eli Lilly launched tadalafil under the name Cialis in 2003. Levitra, Viagra, and Cialis are each formulated as immediate-release tablets that are swallowed whole.

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[1] For purposes of this opinion, Bayer Pharma AG, Bayer Intellectual Property GmbH, and Bayer Healthcare Pharmaceuticals, Inc. are referred to as "Bayer" both collectively and individually.

The '950 patent issued on December 24, 2013. It claims priority to March 1, 2005 and lists Bayer as its assignee. It is directed to a formulation of vardenafil "in the form of an uncoated tablet which disintegrates rapidly in the mouth," commonly referred to as an oral disintegrating tablet ("ODT"). *See* '950 patent at claim 8. Bayer markets a commercial embodiment of the '950 patent, vardenafil ODT, under the name Staxyn.

Watson filed an Abbreviated New Drug Application ("ANDA") with the FDA seeking approval to market a generic version of Staxyn. Bayer filed the instant case asserting infringement of the '950 patent. Claims 9 and 11, both of which depend from claim 8, are the only claims at issue:

> 8. A drug formulation in the form of an uncoated tablet which disintegrates rapidly in the mouth and releases the drug in the mouth without swallowing the tablet comprising vardenafil hydrochloride trihydrate, and at least two sugar alcohols.
>
> 9. The drug formulation according to claim 8, wherein said sugar alcohols are a mixture of sorbitol and mannitol.
>
> 11. The drug formulation of claim 8, wherein at least one sugar alcohol is sorbitol.

The parties agree that claim 8's requirement that the formulation "releases the drug in the mouth" means it is an immediate-release formulation.

The district court held a six-day bench trial to consider the validity of the '950 patent. Watson argued the claimed formulation of vardenafil would have been obvious to a person of ordinary skill in the art based on multiple exemplary references showing a motivation to:

(1) create an ODT formulation of vardenafil[2]; (2) select mannitol and sorbitol as sugar alcohols[3]; and (3) make the

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[2] The prior art relied on by Watson at trial and discussed herein are, for the vardenafil ODT limitation: (1) Chang et al., "Fast Dissolving Tablets," Pharmaceutical Technology, Vol. 24 No. 6 ("Chang"); (2) U.S. Patent Application Pub. No. 2002/0091129 ("Boolell"); (3) U.S. Patent No. 6,683,080 ("Fryburg"); (4) "Pfizer/Scherer deal on fast-acting Viagra," SCRIP World Pharmaceutical News, No. 2332/22 (May 6th/8th 1998) ("SCRIP"); (5) Habib et al., "Fast Dissolving Drug Delivery Systems," 17 Critical Reviews in Therapeutic Drug Carrier Systems 61 (2000) ("Habib"); (6) Ghosh et al., "Intraoral Delivery Systems: An Overview, Current Status, and Future Trends" in Drug Deliver to the Oral Cavity: Molecules to Market (Ghosh et al., eds., 2005) ("Ghosh"); (7) U.S. Patent Application Pub. No. 2002/0002172 ("Bell-Huff"); (8) European Patent Application Pub. No. EP1120120 ("Furitsu"); and (9) PCT Application Pub. No. WO 02/05820 ("Chen").

[3] The prior art relied on by Watson at trial and discussed herein are, for the sorbitol and mannitol limitation: (1) Fu et al., "Orally Fast Disintegrating Tablets: Developments, Technologies, Taste-Masking and Clinical Studies," 21 Critical Reviews in Therapeutic Drug Carrier Systems 443 (2004) ("Fu"); (2) Bauer et al., "Particle design by surface modifications: spray-dying and co-granulation of mannitol/sorbitol mixtures," 11 S.T.P. Pharma Sciences 203 (2001) ("Bauer"); (3) Joshi et al, "Added Functionality Excipients: An Answer to Challenging Formulations," Pharmaceutical Technology, June 2004 ("Joshi"); (4) U.S. Patent No. 6,544,552 ("Sparks"); (5) U.S. Patent Application Pub. No. 2003/0119642 ("Norman"); (6) SPI Pharma, "Quick-Dissolving Tablets Made Easy with Pharmaburst™," Special Delivery (Spring 2002) ("Pharmaburst"); (7) Ghosh.

ODT formulation immediate-release. The district court rejected each of Watson's arguments. It found a person of ordinary skill in the art would not have been motivated to create an ODT formulation of vardenafil and would not have used mannitol and sorbitol as excipients. It found the prior art taught away from formulating vardenafil ODT as immediate-release. The district court also addressed Bayer's objective evidence of nonobviousness and found it supported its conclusion that Watson failed to prove by clear and convincing evidence that claims 9 and 11 would have been obvious. Watson appeals. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

A patent may not issue "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103. Obviousness depends on the following factual determinations: "(1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art at the time the invention was made; and (4) objective evidence of nonobviousness, if any." *In re Kubin*, 561 F.3d 1351, 1356 (Fed. Cir. 2009) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966)). On appeal from a bench trial, we review the district court's findings of fact for clear error. *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1359 (Fed. Cir. 2007). "A finding is 'clearly erroneous' when[,] although there is evidence to support it, the reviewing court on the entire evidence is left with the definite and firm conviction that a mistake has been committed." *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 395 (1948). Based on the underlying factual findings, whether a claimed invention would have been obvious is a question of law reviewed de novo. *Pfizer*, 480 F.3d at 1359.

A. Vardenafil ODT Limitation

The district court determined that Watson failed to meet its burden of proving by clear and convincing evidence that there would have been a motivation to formulate vardenafil as an ODT formulation. This determination rested largely on the court's finding the testimony of Bayer's expert, Dr. Wicks, more persuasive than the testimony of Watson's expert, Dr. Jacobs. The district court found it important that, according to Dr. Wicks, no ED ODT drug was on the market as of the '950 patent's priority date. J.A. 9–10 (citing J.A. 676 at 855:15–19). It credited Dr. Wicks' testimony that a person of ordinary skill in the art would not have focused on an ODT formulation of vardenafil "because of the rarity of ODT formulations." J.A. 9 (citing J.A. 671 at 833:21–834:2). It cited Dr. Wicks' testimony in finding that a person of ordinary skill in the art "would not have considered vardenafil to be a good candidate for formulation as an ODT because vardenafil was known as an [ED] medication and ODTs were not considered particularly applicable to this area." J.A. 9 (citing J.A. 675–76 at 852:13–853:4, 853:25–854:4).

The district court cited the absence of any other ODT formulations of ED drugs on the market as of the '950 patent's priority date. It cited the Fu reference, which, like the SCRIP reference, showed Pfizer announced plans to launch an ODT version of Viagra (sildenafil) in May 1998, but noted Pfizer still had not brought the product to market by March 2005. J.A. 9 (citing J.A. 19103–04). Despite the fact that the 2005 Ghosh reference stated that Pfizer was continuing to develop an ODT formulation of sildenafil, the court found this not persuasive because it concluded that the reference's claim was based on a publication from 1998. J.A. 9 (citing J.A. 19196–97, 19210). It cited the Habib reference, which did not list ED drugs in its table titled "Various Therapeutic Areas in Which the Fast-Dissolve Dosage

Forms are Most Applicable," to support finding that ODTs were not particularly applicable to ED drugs. J.A. 9 (citing J.A. 19265).

The clear error in the district court fact finding that there was no motivation to formulate ED drugs in ODTs, is that it concluded that the record did not contain an indication that ED drugs would be good candidates for ODT formulations. *See, e.g.*, J.A. 9 (finding "vardenafil was known as an [ED] medication and ODTs were not considered particularly applicable to this area"). This is simply not accurate. Watson relied on nine prior art references to support its assertion that there would have been a motivation to create an ODT formulation of vardenafil. Dr. Jacobs testified that the Chang reference states "drugs for [ED] would be good candidates for ODT formulation." J.A. 448 at 310:20–311:11. He testified the Boolell and Fryburg references each disclose formulating vardenafil as an ODT. J.A. 448–49 at 3:11:17–312:6. He testified that numerous companies had already begun formulating ODT versions of ED drugs: Pfizer filed the Bell-Huff patent application directed to sildenafil ODT; Eisai filed the Furitsu patent application claiming an ODT formulation of phosphodiesterase inhibitors; and Lavipharm filed the Chen international patent application, identifying ODT versions of sildenafil. J.A. 449–50 at 314:3–319:1. Watson's post-trial briefing identifies the same set of references, all of which were produced as trial exhibits and filed with the court.

These six references—Chang, Boolell, Fryburg, Bell-Huff, Furitsu, and Chen—are absent from the district court's decision. While it is certainly not necessary for a district court to evaluate all references presented to it, nowhere here does it mention these key references in analyzing whether the prior art taught vardenafil ODT or whether a skilled artisan would have been motivated to formulate vardenafil ODT. These references are highly relevant to whether a person of ordinary skill in the art

would have been motivated to formulate ODT vardenafil. And their express disclosures cause the district court fact finding regarding motivation to combine to be clear error. *See Pfizer*, 480 F.3d at 1363 (holding the district court clearly erred when it failed to consider relevant prior art).

The district court's finding that "the [person of ordinary skill in the art] would not have considered vardenafil to be a good candidate for formulation as an ODT because vardenafil was known as an erectile dysfunction medication and ODTs were not considered particularly applicable to this area" is contradicted by the references cited by Dr. Jacobs that the court failed to consider. J.A. 9; *see also id.* ("[T]here was no reason for the [person of ordinary skill in the art] to focus on an ODT vardenafil because of the rarity of ODT formulations."). All six of the prior art references disregarded by the district court identify ED drugs as ODT formulations. Chang identifies ED drugs as one of five drug classes considered candidates for fast-dissolving tablets. J.A. 19024. Boolell states ED drugs such as sildenafil and vardenafil can be "administered orally, buccally or sublingually in the form of tablets" and "may also be administered as fast-dispersing or fast-dissolving dosage forms." J.A. 19689–90 ¶¶ 49–54, 63. Fryburg provides the same disclosure, limited to vardenafil. J.A. 19677 at 6:31–39. Bell-Huff, Furitsu, and Chen show that between 1999 and 2001, more than one company sought patent protection on ODT formulations of ED drugs. Bell-Huff is directed to "rapidly disintegrating oral dosage forms which contain sildenafil." J.A. 19683 ¶ 2. Furitsu is titled "Tablets Immediately Disintegrating in the Oral Cavity" and is directed to phosphodiesterase inhibitors, the class in which vardenafil, sildenafil, and tadalafil belong. J.A. 19077. And Chen is directed to sildenafil formulations, one example of which includes a "fast dissolving tablet." J.A. 19797. All of these references indicate a person of ordinary skill in the art would have considered ODT formulations applicable to ED

drugs. And several of these references indicate a person of ordinary skill in the art would have considered ODT formulations to be applicable to vardenafil in particular.

Bayer argues that Watson's arguments concerning many of its references, such as Chang, Boolell, and Fryburg, were insignificant and the district court did not clearly err by failing to address them. It argues that while Watson asserts on appeal that the district court ignored its key prior art, Watson flooded the district court with references without adequately addressing them. We do not agree.

Watson produced a significant number of references to support its argument that a person of ordinary skill in the art would have been motivated to formulate an ODT formulation of vardenafil. While it may at times be unwise for a party to rely on numerous prior art references when challenging a patent on obviousness grounds, Watson's approach was not untenable here. Watson produced these nine references to support a narrow point: they each "disclosed formulating vardenafil and other approved ED drugs into ODTs." J.A. 935. Its expert, Dr. Jacobs, addressed each of these nine references after he was asked, "were there any references that discussed formulating erectile dysfunction drugs in particular into ODTs?" J.A. 448–50 at 310:20–319:1. Chang, Boolell, and Fryburg were the first three references he discussed. J.A. 448–49 at 310:20–313:13. Watson addressed the same nine references in its post-trial briefing under the heading, "The Prior Art Suggested Formulating Vardenafil and Other Approved ED Drugs as ODTs." J.A. 935. While Watson's discussion of the various references was at times succinct, Dr. Jacobs' testimony and Watson's arguments were tailored to the simple point that ODT formulations of ED drugs were known. It is unnecessary, for example, to delve deeply into the meaning of a patent application directed to an "intraoral quickly disintegrating tablet containing a phosphodiesterase inhibitor" to

explain that application discloses an ODT formulation of an ED drug. J.A. 19077 (Furitsu); *see* J.A. 450 at 316:23–318:10 (Dr. Jacobs' testimony); J.A. 936–37 (Watson's post-trial briefing). Chang's listing of "drugs for [ED]" among five types of drugs that can be considered for ODTs speaks for itself. J.A. 19024; *see* J.A. 448 at 310:24–311:16 (Dr. Jacobs' testimony); J.A. 937 (Watson's post-trial briefing). Watson clearly presented and preserved its arguments relating to the prior art for the vardenafil ODT limitation. In light of these references, the district court clearly erred in determining that one of skill would not have been motivated to make ODT formulations of ED drugs.

Dr. Wicks' testimony does not cast doubt on the weight of Watson's evidence regarding the vardenafil ODT limitation. Many of the references Watson relies on for this limitation were unchallenged by Dr. Wicks. For example, Dr. Wicks did not present testimony on Chang's disclosure that ED drugs can be considered candidates for ODTs. He did not question or critique any of the three patent applications directed to ODT formulations of ED drugs—Bell-Huff, Furitsu, and Chen. His only discussion of Bell-Huff concerned the immediate-release limitation, and he did not mention Furitsu or Chen at all. Rather, Dr. Wicks' testimony that a person of ordinary skill in the art would not have considered ODTs applicable to ED drugs, on which the district court relied, was expressly limited to the Habib and Fu references. *See* J.A. 9; J.A. 676 at 853:25–854:4 (Q: "Okay. So in light of the information that we saw in Habib and Fu, if the person of ordinary skill were to think about alternate formulations of vardenafil, would they focus on ODTs?" A: "No. There's no indication that they're applicable."). In fact, Dr. Wicks expressly conceded that the prior art described ED drugs as candidates for ODT formulations. J.A. 690 at 911:23–912:2. This case does not present a situation in which the district court's credibility determination can be

understood to discount the prior art references it failed to address based on one expert's characterization of the prior art. *See, e.g.*, *Senju Pharm. Co. v. Lupin Ltd*, 780 F.3d 1337, 1351 (Fed. Cir. 2015) (deferring to district court's credibility determination to credit competing testimony regarding the prior art's teaching).

It is well within the district court's discretion to credit one expert's competing testimony over another. We "must give due regard to the trial court's opportunity to judge the witnesses' credibility." Fed. R. Civ. P. 52(a)(6); s*ee FilmTec Corp. v. Hydranautics*, 982 F.2d 1546, 1553 (Fed. Cir. 1992) ("We will not invade the province of the district court to judge matters of credibility."). But a district court cannot, through a credibility determination, ignore the wealth of evidence, especially as in this case where the expert did not even address it. The district court's finding that ODTs were not considered applicable to ED drugs is clearly erroneous in light of Watson's evidence. *See* J.A. 9.

The remainder of the district court's findings underlying the motivation to formulate vardenafil ODT focused too heavily on the commercial availability of ODT formulations of ED drugs as of the '950 patent's priority date. *See, e.g.*, J.A. 9 (finding "it important that prior art references from 2004 listing ODTs on the market and likely to come to market in the next few years did not list any drugs for the treatment of erectile dysfunction"); J.A. 10 ("[N]o ODT of an erectile dysfunction drug was on the market by March 2005."). It is unclear why the district court found it important that no ODT ED drug had gained FDA approval as of '950 patent's priority date. The motivation to combine inquiry is not limited to what products are forthcoming or currently available on the market. Particularly given the lengthy FDA approval process, the pharmaceutical industry is no exception. Any motivation, "whether articulated in the references themselves or supported by evidence of the knowledge of a

skilled artisan, is sufficient." *Outdry Techs. Corp. v. Geox S.p.A.*, 859 F.3d 1364, 1370–71 (Fed Cir. 2017). Here, the motivation to formulate an ODT version of vardenafil is plainly evident from the face of multiple prior art references disclosing ODT formulations of ED drugs. No further rationale for developing vardenafil ODT was necessary. On review of the entire record evidence before the district court, we are left with the definite and firm conviction that the district court clearly erred when it found there would not have been a motivation to formulate vardenafil ODT.

B. Sorbitol and Mannitol Limitation

Claim 9 requires the vardenafil ODT formulation contain a mixture of sorbitol and mannitol, and claim 11 more generally requires that the ODT formulation contain at least two sugar alcohols, one of which must be sorbitol. Neither party disputes that it was known—if not necessary—to include a sugar alcohol in ODT formulations. The parties' dispute rests on whether a person of ordinary skill in the art would have been motivated to select the claimed combination of sugar alcohols, sorbitol and mannitol.

The district court found a person of ordinary skill in the art would not have been motivated to use mannitol and sorbitol in an ODT formulation, finding Dr. Wicks' testimony on this limitation more credible than Dr. Jacobs'. It found Dr. Jacobs' reliance on the Bauer reference unpersuasive because Bauer's disclosure that the combination of mannitol and sorbitol could optimize tableting properties was based on a 1978 article. J.A. 12 (citing J.A. 467 at 385:19–386:12; J.A. 18593–94 (Bauer)). It noted Dr. Jacobs relied on the Pharmaburst reference, which advertised an off-the-shelf excipient containing a combination of mannitol and sorbitol, but found it contained no working examples or experimental data. J.A. 12–13 (citing J.A. 454–55 at 335:23–336:1). It found

Dr. Jacobs' testimony that a skilled artisan would have been motivated to use a mixture of sorbitol and mannitol to avoid the need for specialized packaging unpersuasive in light of his contrary testimony that "there is no need for specialized packaging" when a particular manufacturing process is employed. J.A. 13 (citing J.A. 453 at 328:3–15 (discussing the Joshi reference); J.A. 446 at 301:16–302:1). It found persuasive Dr. Wicks' testimony that "every ODT on the market in the relevant prior art time frame contained only a single sugar alcohol: mannitol," and that "there were no known problems with the use of mannitol in the existing ODTs." J.A. 12 (citing J.A. 683 at 884:1–19; J.A. 685 at 891:11–17). It found "there was nothing in the prior art that would have given the [person of ordinary skill in the art] a reason to use sorbitol in addition to mannitol in an ODT." J.A. 12 (citing J.A. 686 at 894:12–15).

We do not question the district court's credibility determinations. However, the district court's analysis for the sorbitol and mannitol limitation again focused on the commercial availability of products while failing to address relevant prior art. Upon consideration of the entire record and under a proper analysis, we conclude that the district court clearly erred in finding a person of ordinary skill in the art would not have been motivated to formulate an ODT with sorbitol and mannitol.

The parties do not dispute that as of the '950 patent's priority date, a company named SPI Pharma marketed an off-the-shelf ODT excipient product called Pharmaburst. The parties agree Pharmaburst existed in three different forms: two using only mannitol and a third, Pharmaburst B2, containing mannitol and sorbitol. The '950 patent specification uses Pharmaburst B2 in an example. *See* '950 patent at 6:31–34. Thus there can be no question that it was known as of the '950 patent's priority date to use sorbitol and mannitol in ODT formulations.

Dr. Jacobs testified that the Norman reference, not addressed by the district court, discloses examples of ODT formulations using sorbitol and mannitol created by SPI Pharma. *See* J.A. 19727–28 at Exs. 1, 3, and 4; J.A. 453–54 at 331:21–332:23 (Dr. Jacobs' testimony). The district court mentioned Dr. Jacobs relied on the Sparks reference, J.A. 12, but did not explain why Sparks' examples using sorbitol and mannitol in ODT formulations were not relevant to whether a skilled artisan would have used sorbitol and mannitol in vardenafil ODT, or give any reason why that reference would not inform the obviousness analysis. *See* J.A. 19671 at Exs. 1, 2 (explaining tablet disintegration times of 3 and 7 seconds); J.A. 453 at 330:18–331:23 (Dr. Jacobs' testimony). Dr. Wicks likewise provided no rebuttal testimony regarding these references. Other than critiquing its lack of examples or experimental data, J.A. 12–13, the district court's decision does not otherwise mention the Pharmaburst advertisement, or its disclosure that it is "an 'off the shelf' excipient which allows you to develop your own quick dissolve formulations in-house quickly and much more cost effectively." J.A. 18554; *see also* J.A. 454–55 at 335:18–337:9 (Dr. Jacobs' testimony). Its decision does not mention Ghosh's similar disclosure that Pharmaburst "is a highly flexible, rapidly disintegrating excipient that imparts a smooth creamy mouth feel, and is manufactured under cGMPs." J.A. 19173; J.A. 455 at 337:13–23 (Dr. Jacobs' testimony).

The district court clearly erred when it found "there was nothing in the prior art that would have given the [person of ordinary skill in the art] a reason to use sorbitol in addition to mannitol in an ODT." J.A. 12. The Joshi reference states using sorbitol with mannitol in ODTs is advantageous because it "enable[s] strong binding and result[s] in a more robust tablet at low compression forces." J.A. 19820–21; J.A. 938 (Watson's post-trial briefing). It explains that, "[i]n addition to contributing to

the robustness of tablets, the sorbitol also imparts a sweet taste and a unique texture to the mannitol, thereby improving the ODT formulation's mouthfeel" without affecting pharmacopeial conformity standards.[4] J.A. 19821. Particularly in light of the district court's finding that a person of ordinary skill in the art "would have expected a vardenafil ODT to have a bitter taste," J.A. 10, these disclosures are relevant to whether a skilled artisan would have been motivated to use sorbitol and mannitol in vardenafil ODT. The district court's finding that nothing in the prior art provided a reason to use sorbitol in addition to mannitol in an ODT is clearly erroneous in light of Watson's evidence. *See* J.A. 12.

The district court's remaining findings on the motivation to use sorbitol and mannitol in an ODT formulation[5] focused solely on the ODT market as of the '950 patent's priority date. *See* J.A. 12 ("[E]very ODT on the market in the relevant prior art time framed contained only a single sugar alcohol: mannitol."); *id.* ("[T]here were no known problems with the use of mannitol in the existing ODTs."). Dr. Wicks likewise critiqued Pharmaburst because it was not "in any approved product in the United States as of March 2005." J.A. 683 at 884:20–23; *see also* J.A. 684 at 885:2–15 (testifying that a person of ordinary skill in

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[4] While the district court found part of Dr. Jacobs' testimony regarding Joshi—that it would have been desirable to add sorbitol to mannitol to avoid the need for specialized packaging—unpersuasive, it never addressed Joshi's express disclosures regarding the benefits of using sorbitol with mannitol. *See* J.A. 13 (citing J.A. 453 at 328:3–15).

[5] Because it is not necessary to our analysis, we do not address the district court's finding that the Bauer reference was not relevant because it was based on a 1978 article. *See* J.A. 12.

the art would look to currently-available ODT products to know whether the FDA considered the excipients safe and effective). Accepting fully Dr. Wicks' testimony on this point, the motivation to combine inquiry for drug formulations is not limited to what already has or could gain FDA approval. We have previously explained:

> There is no requirement in patent law that the person of ordinary skill be motivated to develop the claimed invention based on a rationale that forms the basis for FDA approval. Motivation to combine may be found in many different places and forms; it cannot be limited to those reasons the FDA sees fit to consider in approving drug applications.

Allergan, Inc. v. Sandoz Inc., 726 F.3d 1286, 1292 (Fed. Cir. 2013). While FDA approval may be relevant to the obviousness inquiry, *see id.* at 1291–92, a lack of FDA approval cannot negate an otherwise apparent motivation to formulate a product. The district court clearly erred in finding no motivation to use sorbitol and mannitol in ODTs; Watson's evidence expressly demonstrated that sorbitol and mannitol in ODTs was known in the art and that there were advantageous reasons to use them.

C. Immediate-Release Limitation

The district court found that even if a skilled artisan would have been motivated to make an ODT formulation of vardenafil, the prior art taught away from formulating vardenafil ODT as immediate release. J.A. 10–11. The parties agree that only two types of ODT formulations were known in the art: immediate-release ODTs, which are released in the mouth, and delayed-release ODTs, which are released in the stomach. The district court found, based again on expert testimony, that a person of ordinary skill in the art would have expected vardenafil ODT to have a bitter taste, which would have discouraged him from creating a formulation that releases vardenafil

in the mouth. J.A. 10. It also found a person of ordinary skill in the art would have been concerned with using an immediate-release formulation because it would be expected to increase bioavailability, and Levitra's label suggested an increase in vardenafil blood levels would be a problem for older men. J.A. 11. The district court found these two concerns would have taught away from an immediate-release formulation. *Id.*

We do not disturb the district court's findings relating to vardenafil's expected bitter taste and increased bioavailability, but the district court erred when it elevated those findings to teaching away. "A reference teaches away when it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1354 (Fed. Cir. 2012) (quoting *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006) (alterations omitted)). The district court did not find that a person of ordinary skill in the art would have believed vardenafil's expected bitter taste and increased bioavailability would have likely rendered an immediate-release formulation unproductive. Instead, the district court's analysis focused on whether a person of ordinary skill in the art would "necessarily have made an immediate-release ODT rather than a delayed-release ODT." J.A. 10; *see* J.A. 11 (finding teaching away based on these "two fundamental concerns when considering an immediate-release formulation over a delayed release ODT formulation"). But the teaching away inquiry does not focus on whether a person of ordinary skill in the art would have merely *favored* one disclosed option over another disclosed option. In assessing whether prior art teaches away, that "better alternatives exist in the prior art does not mean that an inferior combination is inapt for obviousness purposes." *In re Mouttet*, 686 F.3d 1322, 1334 (Fed. Cir. 2012). When there are only two possible formulations and both are

known in the art at the time, the fact that there may be reasons a skilled artisan would prefer one over the other does not amount to a teaching away from the lesser preferred but still workable option. The district court's finding that a person of ordinary skill in the art would have first pursued a delayed-release formulation over an immediate-release formulation is insufficient to support a finding of teaching away.

The evidence before the district court supports its finding that a person of ordinary skill in the art may have preferred a delayed-release formulation over immediate release—not that an immediate-release formulation was unlikely to be productive in vardenafil ODT. Rather than testify that a skilled artisan would have believed the taste of vardenafil is too bitter to formulate as an immediate-release ODT, Dr. Wicks merely testified that "the consideration would lead them to a delayed-release ODT." J.A. 678 at 863:22–864:7 (answering "would the person of ordinary skill have a reason to make a formulation of vardenafil, an ODT formulation, that releases the drug in the mouth, the immediate-release type?"). Nor did Dr. Wicks point to prior art suggesting vardenafil would have tasted too bitter. Dr. Wicks conceded "[t]he taste of vardenafil was not reported in the literature" and disclaimed that a person of ordinary skill in the art "would have assumed that vardenafil was as bitter as sildenafil." J.A. 694 at 925:16–926:4. When asked about bioavailability concerns due to Levitra's label, Dr. Wicks again focused on why those concerns would have caused a skilled artisan to prefer a delayed-release formulation. *See* J.A. 681 at 874:17–23 (testifying "the making of a delayed-release ODT would be far simpler"). Dr. Wicks opined that the bioavailability concerns "would clearly teach away from making an immediate-release formulation," but when asked why, he answered "[b]ecause you would get much greater control with a delayed-release formulation." J.A. 681 at 873:8–25. This testimony

supports the district court's finding that the taste and bioavailability of vardenafil raised concerns, and that a skilled artisan may have *preferred* a delayed-release formulation, but it does not support a finding of teaching away. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 425–26 (2007) (holding expert's declaration did not support finding teaching away because it did not indicate the prior art system "was somehow so flawed that there was no reason to upgrade it").

While the district court did not clearly err in its fact finding that a skilled artisan would have had concerns over an immediate-release formulation due to vardenafil's expected bitter taste and bioavailability, obviousness "does not require that the motivation be the *best* option, only that it be a *suitable* option from which the prior art did not teach away."[6] *Par Pharm., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1197–98 (Fed. Cir. 2014). We determine whether a skilled artisan would have found the claimed combination obvious weighing the four *Graham* factors, which includes the district court's fact findings regarding the bitter taste and bioavailability of immediate release formulations. *See Apple Inc. v. Samsung Elecs. Co.*, 839 F.3d 1034, 1048 (Fed. Cir. 2016) (en banc).

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[6] We also note the district court did not address record evidence that may have alleviated concerns with an immediate-release formulation, including that Pharmaburst "is a highly flexible, rapidly disintegrating excipient that imparts a smooth creamy mouth feel, and is manufactured under cGMPs." J.A. 19173. It did not address evidence that using sorbitol with mannitol in ODTs benefited tableting properties, taste, and mouth-feel. J.A. 19820–21 (adding sorbitol to ODTs "imparts a sweet taste and a unique texture to the mannitol, thereby improving the ODT formulation's mouthfeel").

D. Objective Evidence

The district court found Watson's copying of the claimed invention and Staxyn's unexpected increased duration of action compared to Levitra supported its conclusion of nonobviousness. J.A. 16–19. We do not disturb these findings. Copying is one of the objective indicia we have held is probative of nonobviousness. *Apple*, 839 F.3d at 1052. Both Bayer's evidence of copying and unexpected results weigh in favor of the nonobviousness of the claimed combination.

E. Legal Conclusion of Obviousness

We consider whether the claimed invention would have been obvious de novo based on underlying findings of fact. *Pfizer*, 480 F.3d at 1359. Watson demonstrated by clear and convincing evidence that there would have been a motivation to formulate an ODT version of vardenafil. In fact, the prior art was explicit in the suggestion to make such a combination and the district court clearly erred in its fact finding to the contrary. The prior art of record expresses a clear motivation to formulate ODT versions of ED drugs and that multiple companies were formulating ODT versions of ED drugs. *See* J.A. 19024, 19077, 19683 ¶ 2, 19797. Watson also demonstrated by clear and convincing evidence that there was an express motivation in the prior art to use sorbitol and mannitol as the excipients in the ODT formulation of the ED drug and the district court clearly erred in its fact finding to the contrary. Pharmaburst B2 was a known, off-the-shelf ODT excipient product that permitted formulation of ODT products "in-house quickly and much more cost effectively." J.A. 18554. The district court did not clearly err in its fact finding that a person of ordinary skill in the art would have had concerns using an immediate-release formulation due to vardenafil's expected bitter taste and bioavailability; however, it clearly erred when it concluded that those findings taught away from the immediate

release. Bayer presented evidence of copying and unexpected results that weigh in favor of a conclusion of non-obviousness.

Weighing all four *Graham* factors, we conclude claims 9 and 11 of the '950 patent would have been obvious. The repeated suggestion in the prior art to make an ODT formulation of an ED drug and the suggestion to use the combination of sorbitol and mannitol as excipients are strong evidence of a motivation to make the claimed combination. The parties agree that ODTs were known to exist as either immediate-release or delayed-release formulations. A skilled artisan motivated to formulate vardenafil ODT would have been faced with a design need for its release profile, and an immediate-release formulation would have been one of two options. *See KSR*, 550 U.S. at 402 ("When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp."). While a skilled artisan may have preferred a delayed-release formulation over the claimed immediate-release formulation, "that the prior art as a whole suggests the desirability of a particular combination need not be supported by a finding that the prior art suggests that the combination claimed . . . is the preferred, or most desirable, combination." *In re Fulton,* 391 F.3d 1195, 1200 (Fed. Cir. 2004). Weighing this evidence together with the objective evidence of unexpected results and copying, we conclude that a skilled artisan would have found the claimed combination obvious. The district court's final judgment is reversed.

CONCLUSION

For the reasons discussed above, we reverse the district court's holding that Watson failed to prove by clear and convincing evidence that claims 9 and 11 of the

'950 patent would have been obvious.

REVERSED

COSTS

Costs to Watson.