2018-2361

United States Court of Appeals for the Federal Circuit

PERSION PHARMACEUTICALS LLC,

Plaintiff-Appellant,

– v. –

ALVOGEN MALTA OPERATIONS LTD.,

Defendant-Appellee.

On Appeal from the United States District Court for the District of Delaware in Case No. 1:16-cv-00139-WCB Honorable William C. Bryson, Circuit Judge

COMBINED PETITION FOR REHEARING AND REHEARING *EN BANC*

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JANUARY 27, 2020

CERTIFICATE OF INTEREST

Counsel for Plaintiff-Appellant Persion Pharmaceuticals LLC certifies the following:

1. The full name of every party or amicus represented by me is: **Persion Pharmaceuticals LLC.**

2. The real parties in interest are: **Persion Pharmaceuticals LLC.**

3. All parent corporations and any publicly held companies that own 10% or more of the stock of the parties I represent are: **Currax Holdings USA LLC and Currax Holdings LLC.**

4. The names of all law firms and the partners or associates that appeared for the parties now represented by me in the trial court or are expected to appear in this court (and who have not or will not enter an appearance in this case) are:

Daniel M. Silver, Benjamin A. Smyth, and Michael P. Kelly (McCarter & English, LLP); David G. Varghese and Christopher J. Stankus (formerly Fitzpatrick, Cella, Harper & Scinto).

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal are: **None**.

Dated: January 27, 2020

/s/ Dominick A. Conde
Dominick A Conde

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STATEMENT OF COUNSEL

Based on my professional judgment, I believe the panel decision is contrary to the following decisions of the Supreme Court of the United States and precedents of this Court: *KSR Int'l Co. v. Teleflex Inc*., 550 U.S. 398, 421 (2007); *Anderson v. Bessemer City*, 470 U.S. 564, 575 (1985); *Honeywell Int'l Inc. v. Mexichem Amanco Holding S.A. De C.V.*, 865 F.3d 1348, 1354 (Fed. Cir. 2017); *W.L. Gore & Associates, Inc. v. Garlock, Inc*., 721 F.2d 1540, 1555 (Fed. Cir. 1983); *Jamesbury Corp. v. United States*, 518 F.2d 1384, 1398 (Ct. Cl. 1975).

Based on my professional judgment, I believe this appeal requires an answer to one or more precedent-setting questions of exceptional importance:

1. Whether it is proper to rely on the description of the invention in a patent-in-suit when combining references under 35 U.S.C. § 103?
2. Whether the panel erred by failing to follow Supreme Court and Federal Circuit precedent holding that inconsistent findings constitute clear error?
3. Whether the panel erred by failing to follow this Court's precedential authority holding that inherency cannot render obvious claims that recite unknown and unpredictable properties?

January 27, 2020

/s/ Dominick A. Conde
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I. Introduction

For written description, the District Court found that nothing in the art, except for Example 8 of the patents-in-suit, provided guidance as to which formulations could be used in the claimed method. In contrast, for obviousness, the District Court found that prior art allegedly provided guidance on a formulation that could be used in the claimed method. The panel held that those findings do not contradict each other based solely on an erroneous belief that Example 8 could have provided guidance under § 103.

First, while considering the specification's description of invention under § 112 is hornbook law, that description cannot render its claims obvious, and Example 8 therefore is irrelevant to § 103. Rehearing is necessary because the panel failed to maintain this distinction in its analysis. Second, besides improperly invoking Example 8, the panel did not address the inconsistencies in the District Court's decision. Supreme Court and Federal Circuit precedent precludes affirming decisions predicated on inconsistent findings. Third, the panel failed to consider the District Court's finding that a POSA—without resort to Example 8—had no "way of predicting which formulations would work and which would not[.]" Appx99. That finding forecloses obviousness based on inherency under the proper standard that this Court should reaffirm *en banc* to eliminate the ambiguity from different panels' divergent tests for inherency under § 103.

II. Background

A. The Patents-in-Suit

Because the liver metabolizes most opioids, patients with hepatic impairment generally experience significantly higher blood levels of drug when given the same dose as given to patients without hepatic impairment, which can lead to serious side effects, including sedation, respiratory depression, or death. Appx53, Appx306-309 (11:18-12:6, 12:14-14:9), Appx588-589 (293:19-294:2), Appx2791 (2:41-47), Appx3937, Appx3942, Appx3117. At least five prior art extended-release opioids therefore required ***lowering*** the starting dose for patients with hepatic impairment. Appx2792 (3:10-4:29), Appx1014-1019 (719:6-724:12), *see also* Appx2768, Appx3134, Appx3175, Appx3910.

The patents-in-suit claim a new method of treating pain in patients with mild or moderate hepatic impairment by administering an ***unadjusted*** starting dose of an extended-release opioid formulation containing hydrocodone as the only active ingredient.[1] This simplified the treatment of pain in hepatically impaired patients by eliminating the need to determine the correct starting dose for each individual patient. Appx531-532 (236:11-237:5), Appx539 (244:8-17). It also allowed

[1] Certain claims require particular pharmacokinetic profiles (quantitative measures of hydrocodone blood concentration) in hepatically impaired patients relative to unimpaired patients instead of, or in addition to, an express "no adjustment" limitation.

hepatically impaired patients to receive sufficient medication without risking inadequate pain relief from a lower starting dose. Appx1019-1020 (724:19-725:22).

B. The District Court Decision

The District Court held the asserted claims obvious in view of Devane, Jain, and the Vicodin/Lortab labels. While Devane discloses the formulation that the inventors of the patents-in-suit tested in the hepatic impairment clinical study reported in Example 8 of the patents-in-suit, ***it does not disclose any pharmacokinetic data for hepatically-impaired patents***. Appx37, Appx41-42. That is, Devane gave no guidance as to how the formulation would work in hepatically-impaired patients—it makes no mention of hepatically-impaired patients. Jain states that an extended-release hydrocodone-acetaminophen ***combination*** formulation produced ***qualitatively*** similar pharmacokinetics in patients with moderate, mild, and no hepatic impairment, but does not disclose: (1) a starting dose for hepatically impaired patients; (2) quantitative pharmacokinetic data for hepatically impaired patients; or (3) any ingredients of the formulation except for hydrocodone and acetaminophen. Appx584-586 (289:9-291:8), Appx593-594 (298:17-299:15), Appx598 (303:1-4), Appx599-600 (304:23-305:10), Appx999-1001 (704:21-706:15). The Vicodin/Lortab labels provide no information for extended-release products because they are for

immediate-release hydrocodone-acetaminophen combination products, and thus they fail to disclose a starting dose when administering extended-release products to patients with mild or moderate hepatic impairment, or any pharmacokinetic data for hepatically impaired patients. Appx61, Appx70.

The District Court found that POSAs "frequently expressed the view that dosages of opioids need to be ***adjusted*** for persons suffering from hepatic impairment in order to avoid a dangerous build-up of the opioid in the patient's bloodstream." Appx8.[2] It concluded, however, that a POSA would have been motivated to administer an unadjusted starting dose of Devane's formulation to patients with mild or moderate hepatic impairment. While the District Court recognized that Devane does not disclose anything about hepatic impairment (and therefore does not anticipate the asserted claims (Appx37, Appx41-42)), it found that a POSA would "look to Jain and to the Vicodin and Lortab labels ***for [] guidance*** as to the appropriate dosing levels of Devane's formulation for patients with mild or moderate hepatic impairment." Appx78.

The District Court held the patents invalid under § 112 for the opposite reason: "***nothing in the state of the art as of July 2012 . . . would have provided guidance*** as to which of the broadly claimed formulations would work [in the

[2] Unless indicated otherwise, emphases have been added.

claimed method] and which would not." Appx105. The District Court thus found, in the written description context, that neither Devane, nor Jain, nor the Vicodin/Lortab labels provided guidance as to which if any extended-release hydrocodone-only formulations would produce the claimed pharmacokinetic profile and not require an adjusted starting dose for patients with mild or moderate hepatic impairment.

C. The Panel Affirmance

The panel affirmed in a precedential decision ("Op."), rejecting Persion's argument that the District Court's § 103 and § 112 findings contradicted each other. According to the panel, "Persion's entire argument with respect to [the inconsistency] issue" omitted "critical context," namely, the District Court's finding that Example 8 of the patents-in-suit provides guidance under § 112. Op. 19-20.

In addition, while the panel acknowledged that prior art did not expressly disclose the claimed pharmacokinetic properties, it nevertheless found those properties inherent in the combination of Devane, Jain, and the Vicodin/Lortab labels. Op. 10-13.

III. Argument

A. This case should be reheard to restore the distinction between the state of the art under § 103 and § 112, emphasizing the need to exclude the patent-in-suit's disclosure from obviousness combinations.

The panel or the full Court should rehear this case because the panel created confusion in the law by conflating the state of the art under § 103 and § 112.

1. The panel mischaracterized the patents' description of the invention as prior art.

The panel attempted to reconcile the District Court's § 103 and § 112 findings by emphasizing that, in the written description context, the District Court found "nothing in the state of the art as of July 2012 that would have provided guidance as to which of the broadly claimed formulations would work and which would not, *with the exception of the single embodiment described in Example 8*." Op. 19. (emphasis original) (citation omitted). Based on the emphasized language concerning Example 8, the panel held that "the district court found that the ***prior art*** provided adequate guidance" under both § 103 and § 112. Op. 19-20. But Persion properly omitted the District Court's discussion of Example 8 when contrasting the obviousness and written description findings ***because Example 8 embodies the invention, including the pharmacokinetic data—not prior art—and thus has no bearing on obviousness***.

The panel obscured its reliance on the invention by incorrectly characterizing the "embodiment described in Example 8" as "the Devane

formulation." Op. 19. Example ***6*** discloses the Devane formulations (*e.g.*, ingredients and amounts). *Compare* Appx2800-2801 (20:59-22:29) *with* Appx3624 ([0099]-[0101]). Example 8 does not disclose formulations, but rather describes the inventors' clinical study results—the pharmacokinetic data that was missing in the prior art. As the District Court explained:

> ***Example 8 describes the clinical study*** of the pharmacokinetic effects of Zohydro ER on subjects with hepatic impairment, as compared to normal subjects. ***The example relates the study results***, which showed that the increases in serum concentration of hydrocodone in patients with liver dysfunction, as compared to normal patients, were modest. . . . [and] "would not be considered large enough to require dosage adjustment for patients with hepatic impairment."

Appx97-98 (citations omitted).

2. The panel's decision upsets settled law on the difference between the state of the art under § 112 and § 103.

The District Court properly looked to Example 8 for guidance under § 112 because the written description inquiry requires consideration of the patents-in-suits' disclosure. 35 U.S.C. § 112 ¶ 1 ("The specification shall contain a written description of the invention[.]"). The obviousness inquiry, by contrast, prohibits reliance on the patents-in-suits' disclosure. *Jamesbury Corp. v. United States*, 518 F.2d 1384, 1398 (Ct. Cl. 1975) ("[Obviousness] determinations must be made without resorting to the teaching of the patent at bar[.]"); *Orexo AB v. Actavis Elizabeth LLC*, 903 F.3d 1265, 1271 (Fed. Cir. 2018) ("It is inappropriate to use

the template provided by the inventor, to render the inventor's contribution obvious.").

The panel disrupted this well-settled law, which guards against "the distortion caused by hindsight bias." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007); *Orexo*, 903 F.3d at 1271 (reversing where district court held claims obvious based "upon the hindsight knowledge of the structure and benefits described in" the patent-in-suit); *Jamesbury*, 518 F.2d at 1398 (courts must avoid "the deceptive and oftentimes unwitting use of hindsight" under § 103). By conflating Example 8 with the prior art, the panel blurred the critical difference between the state of the art under § 112 and § 103.

The legal error is significant. Infringers will seize upon the decision to inject the patent-in-suit's disclosure into obviousness combinations. Rehearing is required to restore the longstanding distinction between the state of the art under § 103 and § 112, and thereby ensure that obviousness remains grounded in preexisting knowledge rather than "*ex post* reasoning." *KSR*, 550 U.S. at 421; *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1138 (Fed. Cir. 1985) ("The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time.").

B. This case should be reheard because the panel did not reconcile inconsistent written description and obviousness findings.

The panel or the full Court should rehear this case because the panel failed to address inconsistencies in the District Court's written description and obviousness findings.

1. Inconsistencies have not been addressed.

The panel's efforts to reconcile the District Court's findings under § 112 and § 103 depended entirely on the panel's improper reliance on Example 8 as prior art. Op. 19-20. Inconsistencies therefore remain unresolved under the proper legal framework where a patent's disclosure does not render obvious its claims.

In addition to the above inconsistency regarding the lack of guidance in the art, the panel did not disturb the finding that a POSA would have had "virtually infinite number of potential formulation[]" choices, without any understanding of "what component or combination of components was responsible for the [inventors'] pharmacokinetic results" or "how those pharmacokinetic results could be obtained." Appx93, Appx96-99. That finding also contradicts the obviousness holding. *See In re Cyclobenzaprine Hydrochloride Extended Release Capsule Patent Litig.*, 676 F.3d 1063, 1071, 1073-74 (Fed. Cir. 2012) (reversing obviousness holding where prior art provided no indication "as to which of many possible choices is likely to be successful," and "no evidence [showed] that skilled artisans would have known how to achieve" invention) (citation omitted). The

District Court further found "[i]dentifying the formulation is ***essential to the invention***," and it is "critical that the formulation be described with sufficient specificity," yet "the identity of the hydrocodone formulations that would have a similar effect on subjects with and without hepatic impairment ***was not known***." Appx103-104. The panel did not address this finding, which contradicts the District Court's finding that Jain's formulation with unknown ingredients rendered the invention obvious because it produced "similar" pharmacokinetics in patients with and without hepatic impairment.[3]

Nor did Alvogen resolve the inconsistencies in the District Court's written description and obviousness findings. Instead, Alvogen dismissed them because they originated in "different legal contexts." DE 33 at 30. But factual statements apply without regard to legal context. For example, in *Hybritech Inc. v. Monoclonal Antibodies, Inc*., 802 F.2d 1367, 1384 (Fed. Cir. 1986), the district court held claims obvious in part because "the 'existence of monoclonal antibodies *having the affinity constants claimed in the patent was well known*.'" (emphasis

[3] The panel's conclusion that prior art provided guidance on the "sole formulation" tested by the inventors—but no others—would lack support even if the inconsistencies were disregarded. Op. 19-20. Jain discloses nothing about its extended-release formulation except that it contained certain amounts of hydrocodone and acetaminophen. *See* Section II(B), *supra*. Jain's teachings thus do not relate to the "Devane formulation." Nor do the Vicodin/Lortab labels for ***immediate-release*** combination products provide guidance specific to Devane's formulation. *See id.*

original). "The [district] court then about-faced and held [the patent deficient under §112] because it fails to teach how to make monoclonal antibodies." *Id*. In view of those "internally inconsistent" findings under § 103 and § 112, this Court reversed. *Id.* at 1374-75, 1384; *see also Nalpropion Pharms., Inc. v. Actavis Labs. FL, Inc*., 934 F.3d 1344, 1350 (Fed. Cir. 2019) (expert's testimony on obviousness undermined his credibility in written description context); *Allergan, Inc. v. Sandoz, Inc*., 796 F.3d 1293, 1309 (Fed. Cir. 2015) (finding adequate written description in view of statement regarding obviousness); *Vanmoor v. Wal-Mart Stores, Inc*., 201 F.3d 1363, 1366 (Fed. Cir. 2000) (infringement allegation rendered patent invalid).

In holding the claims invalid for lack of written description, the District Court was required to—and did—analyze "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue." *Ariad Pharm., Inc. v. Eli Lilly & Co*., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (citation omitted); *see Pozen Inc. v. Par Pharm., Inc.*, 696 F.3d 1151, 1167 (Fed. Cir. 2005) (limitation had adequate support in view of knowledge in the art). The written description and obviousness inquiries thus require analysis of the same prior art. If nothing in that art provided guidance for achieving the invention under § 112, as the District Court found, then nothing—neither Devane, nor Jain, nor the Vicodin/Lortab labels—could have provided such guidance under § 103.

2. Inconsistent findings mandate reversal under binding precedent on the standard of review.

The Supreme Court has held that inconsistent findings warrant reversal under the clearly erroneous standard of review that applies here. *Anderson v. Bessemer City*, 470 U.S. 564, 575 (1985) (singling out "internally inconsistent" findings as an example of clear error); *United States v. Singer Mfg. Co*., 374 U.S. 174, 190, 192-194 & n.9 (1963) (reversing and holding "inconsistent" findings clearly erroneous). This Court routinely recognizes that inconsistent findings require reversal even under more deferential standards of review. *IBG LLC v. Trading Techs. Int'l, Inc.*, 757 F. App'x 1004, 1008 (Fed. Cir. 2019) ("We conclude that the Board's reasoning with regard to the '132 and '304 patents is internally inconsistent and therefore arbitrary and capricious."); *Polygroup Ltd. MCO v. Willis Elec. Co*., 780 F. App'x 880, 884 (Fed. Cir. 2019) ("We do not regard . . . internally inconsistent findings as supported by substantial evidence."), citing *Honeywell Int'l Inc. v. Mexichem Amanco Holding S.A. De C.V.*, 865 F.3d 1348, 1354 (Fed. Cir. 2017) (finding the Board's analysis flawed due to internal inconsistencies); *see Tandon Corp. v. United States Int'l Trade Comm'n*, 831 F.2d 1017, 1019 (Fed. Cir. 1987) ("greater weight and finality" given to findings under "substantial evidence" standard compared to "clearly erroneous" standard).

The panel's decision contravenes this precedent. It is the first decision by this Court to affirm despite undisputed inconsistencies between material findings,

and it should be reheard to bring it into accordance with Supreme Court and Federal Circuit precedent.

C. This case should be reheard to resolve a split in the law on inherency in the context of obviousness.

The Court should rehear this case *en banc* to clarify the law on inherency in the context of obviousness.

1. Three different versions of § 103 inherency law exist.

Panels have set forth at least three variants of § 103 inherency law, which the District Court called "tricky," "maddening," and "not very informative" (SAppx1 (350:1-11)), and the full Court has never spoken on it.

First, panels have rejected any use of inherency under § 103. In *In re Spormann*, 363 F.2d 444, 448 (C.C.P.A. 1966), for example, the Court reversed an obviousness rejection that relied on inherency because "the inherency of an advantage and its obviousness are entirely different questions." *Id.* at 448 ("That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown."); *see W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1555 (Fed. Cir. 1983) ("Inherency and obviousness are distinct concepts").

Second, panels have held that inherency may apply under § 103, but only to ***predictable*** properties:

> What is important regarding properties that may be inherent, but unknown, is whether they are unexpected. All properties of a composition are inherent in that composition, but unexpected properties may cause what may appear to be an obvious composition to be nonobvious. . . . Thus, the Board here, ***in dismissing properties of the claimed invention as merely inherent, without further consideration as to unpredictability and unexpectedness, erred as a matter of law***.

Honeywell, 865 F.3d at 1355. For example, in *Application of Shetty*, 566 F.2d 81, 86 (C.C.P.A. 1977), the Board rejected as obvious a claim to a method of using a compound in an amount effective to curb appetite. It found curbing appetite inherent in a combination of prior art that expressly disclosed the claimed compound and dose. *Id.* On appeal, the Court reversed because the Board made no showing as to the "predictability" of the appetite curbing property. *Id.*

Third, panels have recently found properties inherent under § 103 irrespective of predictability. *Hospira, Inc. v. Fresenius Kabi USA, LLC*, Nos. 2019-1329, 2019-1367, 2020 U.S. App. LEXIS 545, at *19 (Fed. Cir. Jan. 9, 2020) (finding analysis of a POSA's expectations "unnecessary": "[i]f a property of a composition is in fact inherent, there is no question of a reasonable expectation of success in achieving it"). The District Court here followed this approach, finding the pharmacokinetic profile inherent without mentioning predictability. Appx69.

2. <u>The full Court should address § 103 inherency in this case</u>.

Accordingly, to the extent inherency applies at all under § 103, diametric standards could govern it depending on the composition of the panel assigned to a

case. The panel in *Honeywell* adhered to a test that hinges on predictability, whereas the panel in *Hospira* held that the district court erred in even considering the predictability of inherent properties. This case presents the ideal opportunity for clarifying the law on inherency under § 103 because the District Court, Alvogen, and Persion agree that prior art did not expressly disclose the claimed pharmacokinetic properties, so Persion would undisputedly prevail under the first approach that rejects inherency under § 103. Appx37, Appx41; *Spormann*, 363 F.2d at 448.

In addition, apart from its improper reliance on Example 8, the panel did not address the District Court's finding that a POSA would have had no way of predicting whether a formulation would achieve the claimed PK profile without testing it in hepatically impaired patients, which no one had done for Devane's formulations prior to the inventions in the patents-in-suit. Op. 19-20; Appx99-100. Thus, the panel did not disturb the District Court's unpredictability finding. Nor could it. Alvogen's expert testimony accorded with the District Court's findings on unpredictability. Appx591 (296:11-25), Appx596 (301:12-20), Appx633-634 (338:25-339:22), Appx880 (585:8-23). So Persion would undisputedly prevail under the second approach that turns on predictability of allegedly inherent properties. *Honeywell*, 865 F.3d at 1354-55.

Moreover, the panel's decision cannot stand because the first two approaches antedate the third approach that the District Court followed and the panel affirmed. *In re Bose Corp*., 580 F.3d 1240, 1245-46 (Fed. Cir. 2009) (recognizing that earlier precedents are binding). The District Court's approach also contradicts the panel's acknowledgement that inherency must be "circumscribed" in the obviousness context. Op. at 12, quoting *Par Pharms., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1195-96 (Fed. Cir. 2014) ("[T]he use of inherency, a doctrine originally rooted in anticipation, ***must be carefully circumscribed in the context of obviousness***. . . . A party must, therefore, meet a ***high standard*** in order to rely on inherency to establish the existence of a claim limitation in the prior art in an obviousness analysis[.]") If predictability does not matter for inherency under § 103, then the inherent obviousness test would not be "circumscribed"; it would be identical to the "necessarily present" inherent anticipation test under § 102. *Compare Schering Corp. v. Geneva Pharms., Inc*., 339 F.3d 1373, 1377 (Fed. Cir. 2003) ("[A] prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is ***necessarily present***, or inherent, in the single anticipating reference."), *with Hospira*, 2020 U.S. App. LEXIS 545, at *21 (affirming inherency finding under § 103 because a "limitation was ***necessarily present*** in the prior art").

IV. Conclusion

The petition for panel rehearing and rehearing *en banc* should be granted.

Dated: January 27, 2020

Respectfully submitted,

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ADDENDUM

United States Court of Appeals for the Federal Circuit

PERSION PHARMACEUTICALS LLC,
Plaintiff-Appellant

v.

ALVOGEN MALTA OPERATIONS LTD.,
Defendant-Appellee

2018-2361

Appeal from the United States District Court for the District of Delaware in No. 1:16-cv-00139-WCB, Circuit Judge William C. Bryson.

Decided: December 27, 2019

DOMINICK A. CONDE, Venable LLP, New York, NY, argued for plaintiff-appellant. Also represented by CHRISTOPHER P. BORELLO, JOSHUA DANIEL CALABRO, ZACHARY GARRETT.

CHAD A. LANDMON, Axinn Veltrop Harkrider, LLP, Hartford, CT, argued for defendant-appellee. Also represented by MATTHEW BECKER, THOMAS K. HEDEMANN, DAVID KEELER LUDWIG, EDWARD M. MATHIAS; CHRISTOPHER MICHAEL GALLO, Washington, DC.

Before O'MALLEY, REYNA, and CHEN, *Circuit Judges*.

REYNA, *Circuit Judge*.

Persion Pharmaceuticals LLC appeals from a decision of the U.S. District Court for the District of Delaware finding the asserted claims of U.S. Patent Nos. 9,265,760 and 9,339,499 invalid as obvious and lacking adequate written description. Because we find no reversible error in the district court's obviousness determination, we affirm on that basis and do not reach the written description issue.

BACKGROUND

I. The Asserted Patents

Persion Pharmaceuticals LLC ("Persion")[1] owns U.S. Patent Nos. 9,265,760 ("the '760 patent") and 9,339,499 ("the '499 patent"), both entitled "Treating Pain in Patients with Hepatic Impairment." Both patents share a common written description[2] and priority date and are directed to methods of treating pain in patients with mild or moderate hepatic impairment using extended-release hydrocodone-only formulations. Hepatic impairment is compromised liver functionality.

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[1] Pernix Ireland Pain DAC and Pernix Therapeutics, LLC (collectively, "Pernix") were the named plaintiffs before the district court and the original appellants in this case. During the pendency of this appeal, Persion acquired the patents at issue from Pernix, and we granted leave for Persion to be substituted as a party. *See* Order, *Persion Pharm. LLC v. Alvogen Malta Operations LTD*, No. 2018-2361 (Fed. Cir. May 23, 2019), ECF No. 63. For convenience, we refer to Persion as the plaintiff and appellant in this opinion.

[2] For convenience, this opinion cites to the written description of the '760 patent.

Hydrocodone is an opioid that is widely used to treat pain and has been FDA approved since 1943. It is marketed in both extended-release and immediate-release formulations and is often combined with other active ingredients. Like many opioids, hydrocodone is primarily metabolized in the human liver. If liver function is impaired, metabolism of opioids is slowed. Thus, the same dose of hydrocodone may pose a higher risk of overdose in a patient with hepatic impairment than in a healthy patient due to potential build-up of the drug in the patient's bloodstream.

The '760 and '499 patents cover the formulation for Zohydro ER, Persion's extended-release hydrocodone-only drug product. When Zohydro ER's prior owner sought approval to market the drug from the U.S. Food and Drug Administration ("FDA"), the FDA required the owner to conduct a clinical study to determine the potential effect of the drug on patients with hepatic impairment. The study showed that use of Zohydro ER did not result in substantially higher concentrations of hydrocodone in the bloodstream of subjects with mild and moderate hepatic impairment than in subjects without hepatic impairment.

Following this study, the researchers filed patent applications directed to their discovery, which later issued as the '760 and '499 patents. Example 8 of the patents describes the Zohydro ER clinical study and its results. *Id.* col. 22 l. 52–col. 23 l. 48. However, the patent claims are not limited to the use of the Zohydro ER formulation but instead cover methods of using any extended-release formulation with "hydrocodone bitartrate as the only active ingredient" to treat pain in patients with mild or moderate

hepatic impairment.[3] '760 patent col. 24 ll. 1–5, col. 25 ll. 13–17, '499 patent col. 24 ll. 1–5, col. 26 ll. 9–13.

The relevant claims of the '760 and '499 patents can generally be grouped into two sets: the "non-adjustment" claims and the "pharmacokinetic" claims. The non-adjustment claims are directed to administering a starting dose of hydrocodone to a patient having mild or moderate hepatic impairment without adjusting the dose relative to a patient with a healthy liver. Independent claim 1 of the '760 patent is representative of the non-adjustment claims, and recites:

> 1. A method of treating pain in a patient having mild or moderate hepatic impairment, the method comprising:
>
> > administering to the patient having mild or moderate hepatic impairment a starting dose of an oral dosage unit having hydrocodone bitartrate as the only active ingredient, wherein the dosage unit comprises an extended release formulation of hydrocodone bitartrate, and wherein the starting dose is not adjusted relative to a patient without hepatic impairment.

'760 patent col. 23 l. 66–col. 24 l. 7.

The pharmacokinetic claims recite pharmacokinetic parameters either as absolute values or in relation to values in a healthy patient. Independent claim 12 of the '760

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[3] Hydrocodone bitartrate is a salt of hydrocodone used to deliver hydrocodone to the human body. *Pernix Ireland Pain DAC v. Alvogen Malta Operations Ltd.*, 323 F.Supp.3d 566, 575 (D. Del. 2018) (citing '760 patent col. 13 ll. 13–15).

patent is representative of the pharmacokinetic claims, and recites:

> 12. A method of treating pain in a patient having mild or moderate hepatic impairment, the method comprising:
>
> administering to the patient having mild or moderate hepatic impairment an oral dosage unit having hydrocodone bitartrate as the only active ingredient, wherein the dosage unit comprises an extended release formulation of hydrocodone bitartrate,
>
> wherein the dosage unit provides a release profile of hydrocodone that:
>
> (1) does not increase average hydrocodone $AUC_{0–inf}$ in subjects suffering from mild hepatic impairment relative to subjects not suffering from renal or hepatic impairment in an amount of more than 14%;
>
> (2) does not increase average hydrocodone $AUC_{0–inf}$ in subjects suffering from moderate hepatic impairment relative to subjects not suffering from renal or hepatic impairment in an amount of more than 30%;
>
> (3) does not increase average hydrocodone C_{max} in subjects suffering from mild hepatic impairment relative to subjects not suffering from renal or hepatic impairment in an amount of more than 9%; and

> (4) does not increase average hydrocodone C_{max} in subjects suffering from moderate hepatic impairment relative to subjects not suffering from renal or hepatic impairment in an amount of more than 14%.

'760 patent col. 25 ll. 11–35.

II. Prior Art

A. Devane

U.S. Patent Publication No. 2006/0240105 ("Devane") is entitled "Multiparticulate Modified Release Composition" and was published on October 26, 2006. Devane is directed to a controlled-release composition that provides both immediate and extended release of one or more active ingredients. J.A. 3616 (Devane, ¶¶ 26–27). Devane teaches that one active ingredient that can be used with these compositions is hydrocodone. J.A. 3615 (Devane, ¶ 17); J.A. 3620 (Devane, ¶ 70). As an example, Devane discloses the Zohydro ER formulation and describes an in vivo study in which the formulation is used to treat pain. J.A. 3625–26 (Devane, ¶¶ 103–06); J.A. 6, 490; Appellee's Br. 4.

B. Jain

U.S. Patent Publication No. 2010/0010030 ("Jain") is entitled "Extended Release Hydrocodone Acetaminophen and Related Methods and Uses Thereof" and was published on January 14, 2010. Jain is directed to methods of treating pain using an extended-release formulation containing about 15 milligrams of hydrocodone and about 500 milligrams of acetaminophen. J.A. 3631 (Jain, Abstract). This formulation is known as Vicodin CR. J.A. 3647 (Jain, ¶ 34). Jain describes several clinical studies involving Vicodin CR, including a study conducted to determine the effects of hepatic insufficiency on the pharmacokinetics of Vicodin

CR. J.A. 3649 (Jain, ¶ 64). The results of the study demonstrated that pharmacokinetic parameters for hydrocodone "were similar in normal subjects and subjects with mild and moderate hepatic impairment." *Id.* The results further demonstrated that the pharmacokinetic parameters for acetaminophen "were similar in normal subjects and subjects with mild hepatic impairment, and 34 to 42% higher in subjects with moderate hepatic impairment." *Id.*

C. Vicodin and Lortab Labels

Vicodin and Lortab are both immediate-release formulations of hydrocodone and acetaminophen that are used to treat pain. J.A. 3121, 3230. The 2011 labels for these products provide safety information and instructions for use. J.A. 3121, 3230–33. Although both labels state that these drugs "should be used with caution in . . . those [patients] with severe impairment of hepatic . . . function," neither label includes any precautions or dosage restrictions for patients with mild or moderate hepatic impairment. J.A. 3121, 3231.

III. District Court Proceedings

On March 4, 2016, Persion sued Alvogen Malta Operations Ltd. ("Alvogen") for infringement of claims 1–4, 11–12, 17, and 19 of the '760 patent. After the '499 patent issued, Persion filed an amended complaint additionally asserting infringement of claim 1 of that patent. Persion alleged that Alvogen infringed these claims by filing an Abbreviated New Drug Application ("ANDA") seeking to market a generic version of Zohydro ER.[4]

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[4] Alvogen filed its ANDA with the FDA prior to the issuance of the '760 and '499 patents. Other patents at issue in this case, however, were listed in FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations"

After a bench trial, the district court concluded that Alvogen would indirectly infringe the asserted claims because its product label would induce doctors and patients to administer Alvogen's product in an infringing manner. *Pernix Ireland Pain DAC v. Alvogen Malta Operations Ltd.*, 323 F. Supp. 3d 566, 579 (D. Del. 2018). The district court also concluded that the asserted claims are not invalid as anticipated by Devane. *Id.* at 594. These rulings are not at issue on appeal.

The district court next determined that the asserted claims are invalid as obvious over Devane in view of Jain, the state of the prior art at the time of invention, and the Vicodin and Lortab labels. *Id.* at 595–96, 610. Specifically, the district court found that in light of the teachings of Jain and the Vicodin and Lortab labels, a person of ordinary skill in the art would have been motivated to administer the extended-release hydrocodone bitartrate formulation disclosed in Devane to patients with mild or moderate hepatic impairment at an unadjusted dose and would have had a reasonable expectation of success in so doing. *Id.* at 609–10, 615. The district court further found that the pharmacokinetic limitations in the pharmacokinetic claims are "inherent in any obviousness combination that contains the Devane formulation" because the recited pharmacokinetic parameters were "necessarily present" in the Zohydro ER formulation described in both Devane and the asserted patents. *Id.* at 607. Finally, the district court found that the objective factors of unexpected results, long-felt but unmet need, and failure of others did not weigh in favor of finding nonobviousness.

In addition, the district court determined that the asserted claims of the '760 and '499 patents are invalid under 35 U.S.C. § 112(a) for lack of adequate written description

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publication, otherwise known as the "Orange Book," for Zohydro ER at the time Alvogen filed its ANDA.

support. *Id.* at 624–25. The district court found that the written description discloses only the formulation described in Example 8, which is the same as both the Zohydro ER and the Devane formulations. *Id.* at 575, 619. The district court explained that, by contrast, the claims of the '760 and '499 patents "are broadly cast in generic form," and "are not limited to that single disclosed formulation." *Id.* at 618–19. The district court concluded that because "[t]he pharmacokinetic data and dissolution profile for the Devane formulation provide no guidance as to whether other formulations would satisfy the functional limitations of the claims," the asserted claims of the '760 and '499 patents were not supported by the written description as required by § 112(a). *Id.* at 623, 625.

Persion timely appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

Obviousness is a question of law with underlying factual findings relating to the scope and content of the prior art; differences between the prior art and the claims at issue; the level of ordinary skill in the pertinent art; the presence or absence of a motivation to combine or modify with a reasonable expectation of success; and any objective indicia of non-obviousness. *Acorda Therapeutics, Inc. v. Roxane Labs., Inc.*, 903 F.3d 1310, 1328 (Fed. Cir. 2018) (citing *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007)); *Ariosa Diagnostics v. Verinata Health, Inc.*, 805 F.3d 1359, 1364 (Fed. Cir. 2015). "The inherent teaching of a prior art reference is a question of fact." *PAR Pharm., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1194 (Fed. Cir. 2014) (quoting *In re Napier*, 55 F.3d 610, 613 (Fed. Cir. 1995)) (internal quotation marks omitted).

In an appeal from a bench trial, we review the district court's factual findings for clear error and the district court's legal conclusion on obviousness de novo. *Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd.*, 719 F.3d 1346,

1354 (Fed. Cir. 2013). Under the clearly erroneous standard of review, we defer to the district court's factual findings unless, considering the totality of the evidence, we are "left with the definite and firm conviction that a mistake has been committed." *Zenith Radio Corp. v. Hazeltine Research, Inc.*, 395 U.S. 100, 123 (1969) (quoting *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 395 (1948)).

Persion raises four primary challenges to the district court's obviousness conclusion. First, Persion contends that the district court improperly relied on inherency to conclude that Devane discloses the pharmacokinetic limitations of the asserted claims. Second, Persion argues that the district court improperly relied on pharmacokinetic profiles from drugs other than extended-release single-active-ingredient hydrocodone formulations and from patients other than those with hepatic impairment in reaching its obviousness conclusion.[5] Third, Persion contends that the district court erred by finding the asserted claims obvious before considering the objective indicia factors. Fourth, Persion argues that the district court's factual findings concerning obviousness are inconsistent with its findings concerning the lack of written description support. We address each argument in turn.

A. Inherency

"[I]nherency may supply a missing claim limitation in an obviousness analysis." *PAR*, 773 F.3d at 1194–95; *see also Endo Pharm. Sols., Inc. v. Custopharm Inc.*, 894 F.3d 1374, 1381 (Fed. Cir. 2018) ("An inherent characteristic of a formulation can be part of the prior art in an obviousness

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[5] Persion characterizes several of its arguments as challenging the district court's legal errors. *See, e.g.*, Appellant's Br. 24, 26, 29. It is clear, however, that Persion's arguments are directed to the district court's factual findings, which we review for clear error.

analysis even if the inherent characteristic was unrecognized or unappreciated by a skilled artisan."). It is long settled that in the context of obviousness, the "mere recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not distinguish a claim drawn to those things from the prior art." *In re Oelrich*, 666 F.2d 578, 581 (C.C.P.A. 1981). The Supreme Court explained long ago that "[i]t is not invention to perceive that the product which others had discovered had qualities they failed to detect." *Gen. Elec. Co. v. Jewel Incandescent Lamp Co.*, 326 U.S. 242, 249 (1945).

We too have previously explained that "an obvious formulation cannot become nonobvious simply by administering it to a patient and claiming the resulting serum concentrations," because "[t]o hold otherwise would allow any formulation—no matter how obvious—to become patentable merely by testing and claiming an inherent property." *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1354 (Fed. Cir. 2012). In *In re Kao*, we found that the claimed controlled-release oxymorphone formulation was obvious because an inherent pharmacokinetic property of oxymorphone that was present in controlled-release oxymorphone "add[ed] nothing of patentable consequence." 639 F.3d 1057, 1070 (Fed. Cir. 2011). In *In re Kubin*, we found an inherent property obvious, explaining that "[e]ven if no prior art of record explicitly discusses the [limitation], the . . . application itself instructs that [the limitation] is not an additional requirement imposed by the claims on the [claimed protein], but rather a property necessarily present in [the claimed protein]." 561 F.3d 1351, 1357 (Fed. Cir. 2009). Our predecessor court similarly concluded that it "is not the law" that "a structure suggested by the prior art, and, hence, potentially in the possession of the public, is patentable . . . because it also possesses an [i]nherent, but hitherto unknown, function which [the patentees] claim to have discovered." *In re Wiseman*, 596 F.2d 1019, 1023 (C.C.P.A. 1979).

Inherency, however, is a "high standard," that is "carefully circumscribed in the context of obviousness." *PAR*, 773 F.3d at 1195. Inherency "may not be established by probabilities or possibilities," and "[t]he mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." *Oelrich*, 666 F.2d at 581 (emphasis added) (quoting *Hansgirg v. Kemmer*, 102 F.2d 212, 214 (C.C.P.A. 1939); *see also In re Rijckaert*, 9 F.3d 1531, 1533–34 (Fed. Cir. 1993). Rather, inherency renders a claimed limitation obvious only if the limitation is "necessarily present," or is "the natural result of the combination of elements explicitly disclosed by the prior art." *PAR*, 773 F.3d at 1195–96; *see also Alcon Research, Ltd. v. Apotex Inc.*, 687 F.3d 1362, 1369 (Fed. Cir. 2012) (relying on inherency where the claims recited "a property that is necessarily present" in the prior art). "If . . . the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient" to render the function inherent. *Oelrich*, 666 F.2d at 581 (quoting *Hansgirg v. Kemmer*, 102 F.2d 212, 214 (C.C.P.A. 1939)).

On appeal, Persion contends that the district court erred in applying the inherency doctrine in its obviousness analysis because Devane does not teach administering its hydrocodone-only formulation to patients with mild or moderate hepatic impairment. Thus, Persion asserts, "'the natural result flowing from the operation as taught' in Devane cannot be the claimed [pharmacokinetic] values for [hepatically impaired] patients." Appellant's Br. 37 (quoting *Oelrich*, 666 F.2d at 581); Reply Br. 19.

To the extent Persion contends that inherency can only satisfy a claim limitation when all other limitations are taught in a single reference, that position is contrary to our prior recognition that "inherency may supply a missing claim limitation in an obviousness analysis" where the limitation at issue is "the natural result of the *combination of*

prior art elements." *PAR*, 773 F.3d at 1194-95 (emphasis added, internal quotations omitted). Here, the district court specifically found that Devane, together with Jain, the state of the prior art at the time of invention, and the Vicodin and Lortab labels, taught the combination of elements that inherently result in the claimed pharmacokinetic parameters. The district court found that a person of ordinary skill in the art would have been motivated, with reasonable expectation of success, to administer an unadjusted dose of the Devane formulation to hepatically impaired patients. There was also no dispute that the Devane formulation, which was identical to the Zohydro ER formulation described in the patents in suit, necessarily exhibited the claimed parameters under these conditions. *Pernix*, 323 F. Supp. 3d at 607, 610. In this context, the district court did not err by finding that the pharmacokinetic limitations of the asserted claims were inherent and added no patentable weight to the pharmacokinetic claims.

B. Evidence of Obviousness

Persion also argues that the district court clearly erred in its obviousness findings by relying on pharmacokinetic data from formulations and patient groups not covered by the asserted claims. Persion asserts that pharmacokinetic data for drug products with more than one active ingredient, for immediate-release hydrocodone products, or for hydrocodone-only products administered to unimpaired patients is irrelevant to the obviousness inquiry in this case because that data would not allow a person of ordinary skill in the art to predict the correct dose of its claimed hydrocodone-only extended-release formulation for hepatically impaired patients. Appellant's Br. 24–28, 30–36. On this basis, Persion argues that Jain would not have provided a person of ordinary skill in the art "with any reasonable expectation that a hydrocodone-only dosage form could be dosed the same way in patients with and without [hepatic impairment]." Appellant's Br. 35; Reply Br. 7–14. Also on this basis, Persion contends that Devane's

pharmacokinetic data is "irrelevant to Jain's formulation" because "none of the data in Devane is for [hepatically impaired] patients." Appellant's Br. 31; Reply Br. 16. We do not find these arguments persuasive because we find no clear error in the district court's analysis.

The district court provided several reasons for its conclusion that a person of ordinary skill in the art would have considered other types of drug products in developing a hydrocodone-only extended-release formulation. *Pernix*, 323 F. Supp. 3d at 608–09. In particular, the district court found that in light of acetaminophen's hepatotoxicity, a person of skill in the art would have expected that an acetaminophen-free hydrocodone formulation, such as the one disclosed in Devane, would have been even safer for patients with hepatic impairment than the combination formulations disclosed in Jain and other references. *Id.* at 608. While Persion asserts that Jain "extols the 'significantly greater benefits' of acetaminophen-containing combination products," and thus undermines the district court's finding of a motivation to remove acetaminophen from Jain's formulation, Appellant's Br. 30, Jain only discusses these benefits in comparison to a *placebo* used in its clinical study, not to hydrocodone alone, J.A. 3652, ¶ 89 (emphasis added). Thus, nothing in the text of Jain leads us to conclude that the district court clearly erred in combining the teachings of Jain with the Devane formulation.

Persion also asserts that the district court improperly relied on the FDA's acceptance of safety data for Vicoprofen, an immediate-release combination hydrocodone and ibuprofen drug, as part of the New Drug Application ("NDA") for Zohydro ER. Appellant's Br. 24–25. The district court found that the FDA's willingness to accept such data supports the view that a combination product containing hydrocodone would have been relevant to a person of ordinary skill evaluating the appropriate administration of the Devane formulation. *Pernix*, 323 F. Supp. 3d at 608–09. Persion argues this finding was clearly erroneous

because the FDA did not find the Vicoprofen data sufficient to establish the proper dosing of Zohydro ER for hepatically impaired patients and had previously refused to rely on such "combination products" data in evaluating another hydrocodone-only product. Appellant's Br. 25. However, as the district court explained, "[t]he standard to find a motivation to combine is far below what is sufficient to prove safety and efficacy to the FDA," and therefore, "[t]he fact that the FDA found the comparison [between Vicoprofen and Zohydro ER] insufficient to satisfy its safety and efficacy standards does not speak to the issue of obviousness." *Pernix*, 323 F. Supp. 3d at 611. We find no clear error in the district court's conclusion that the FDA's approval requirements do not undermine the force of the evidence as to obviousness. *Id.* In light of the record as a whole, we find no clear error in the district court's findings on the relevance of combination product data to a person of ordinary skill considering the administration of a hydrocodone-only product.

Persion also challenges the district court's reliance on Jain's description of the pharmacokinetic parameters of hydrocodone in healthy subjects and in subjects with mild or moderate hepatic impairment as "similar." Persion argues that Jain does not define "similar" and the district court erred by "presuming" that "similar" meant "less than 34 to 42%" because a presumption is not evidence. Appellant's Br. 32–34. Jain, however, expressly distinguishes "similar" pharmacokinetic results from those that are "34 to 42% higher." J.A. 3649; *see also Pernix*, 323 F. Supp. 3d at 613. Thus, the district court did not merely presume to know what Jain meant by "similar," contrary to Persion's argument. We find no clear error in the district court's interpretation of Jain or in its conclusion that because Jain discloses "similar" pharmacokinetic values for both hepatically impaired and unimpaired patients, a person of ordinary skill in the art would understand that no dose

adjustment would be necessary in administering hydrocodone to hepatically impaired patients.

Persion next challenges the district court's reliance on Devane's study of healthy patients in finding that the presence of acetaminophen had no appreciable effect on the pharmacokinetic profile for hydrocodone. *See Pernix*, 323 F. Supp. 3d at 610. The district court credited the testimony of Alvogen's expert that the relevant pharmacokinetic parameter values disclosed in Devane's study for a hydrocodone-only product and a hydrocodone-acetaminophen product are "virtually identical values." *Id.* Relying on Devane's study, the district court found that a person of ordinary skill in the art would have appreciated that hydrocodone and acetaminophen are metabolized differently, and accordingly, would not have been deterred from relying on combination products containing acetaminophen for guidance about the dosing of the Devane formulation. *Id.* Persion asserts that pharmacokinetic data for hepatically unimpaired patients is irrelevant to motivation or expectation of success for administration of a drug to patients with hepatic impairment. Appellant's Br. 31. We disagree. Persion provides no support for its assertion, and we find no clear error in the district court's crediting of expert testimony that relied on the Devane data in discussing how a person of ordinary skill in the art would have understood the effect of acetaminophen on the metabolism of hydrocodone in a combination product. *See Pernix*, 323 F. Supp. 3d at 609 (citing J.A. 552, Trial Tr. 257:1–8); *see also* J.A. 551:21-25.

Persion also contends that the district court erred by taking judicial notice of the FDA's recommendation to "limit the strength of acetaminophen in prescription drug products." Specifically, Persion asserts that Alvogen had expressly dropped an obviousness combination that included the FDA's statement and thus Persion was deprived of an adequate opportunity to respond to the statement during trial. Appellant's Br. 29 (citing *Pernix*, 323 F. Supp.

3d at 609). However, the district court relied on the FDA's statements not as part of a prior art combination, but only in rebutting Pernix's assertion that there was no motivation to combine the teachings of Devane with the hydrocodone-acetaminophen formulations described in Jain and the Vicodin and Lortab labels. In rejecting Persion's argument, the district court relied on three additional bases for finding a motivation to combine that were independently supported by other evidence presented at trial. *Pernix*, 323 F. Supp. 3d at 609–10. Thus, regardless of whether the district court's consideration of the FDA's statement was proper, we find no clear error in the court's finding that there was a motivation to combine in light of the evidence as a whole.

In sum, after reviewing the entire evidentiary record, we are not left with any conviction that the district court has made a mistake. *See Zenith*, 395 U.S. at 123. We therefore reject Persion's challenge to the district court's factual findings, which are not clearly erroneous.

C. Objective Indicia

Persion argues that the district court erred by finding the asserted claims obvious before considering the asserted objective indicia of nonobviousness, which Persion contends clouded the district court's analysis of the objective indicia. Appellant's Br. 38–43. Relying on *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litigation*, Persion argues that the district court's finding of obviousness was premature. 676 F.3d 1063, 1075 (Fed. Cir. 2012). We disagree. Unlike the trial court in *Cyclobenzaprine*, the district court here considered Persion's evidence of objective indicia together with the other evidence presented at trial on the issue of obviousness. *See, e.g.*, *Pernix*, 323 F. Supp. 3d at 615–16 (considering whether Persion's objective indicia arguments were "supported by other evidence adduced at trial"); *id.* at 616–17 (considering the inventors' testimony directed to the unexpected

results factor in the context of "all the evidence at trial"). While the district court's discussion of objective indicia follows its discussion of the asserted prior art, the substance of the court's analysis makes clear that it properly considered the totality of the obviousness evidence in reaching its conclusion and did not treat the objective indicia as a mere "afterthought" relegated to "rebut[ting]" a prima facie case. *Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1357–58 (Fed. Cir. 2013); *Cyclobenzaprine*, 676 F.3d at 1075.

The remainder of Persion's arguments amount to challenges against the district court's weighing of the objective indicia. For example, Persion argues that in addressing the failure of others, the district court did not give any weight to evidence of Cephalon, Inc.'s failure to develop its Vantrela drug in a manner that would not require a dose adjustment for hepatically impaired patients. Appellant's Br. 39–40. The district court, however, expressly considered this evidence and determined that it did not warrant a finding of nonobviousness. The district court found that Cephalon, Inc.'s failure was not persuasive in light of evidence demonstrating that others had succeeded in making a hydrocodone drug that did not require a dose adjustment. *Pernix*, 323 F. Supp. 3d at 617. In addition, the district court heard trial testimony that the FDA would not have required a dose adjustment for administering Vantrela to patients with hepatic impairment. *See* J.A. 596–97 (Trial Tr. 301:21–302:4). Persion additionally argues that the district court improperly dismissed the testimony of the inventors regarding unexpected results. Appellant's Br. 40–42. However, the district court considered this testimony, and we see no clear error in the court's discounting of the evidence in light of the inventors' failure to account for the teachings in Jain. *Pernix*, 323 F. Supp. 3d at 616–17. Overall, we find no clear error with the district court's assessment of the objective indicia evidence.

D. Internal Inconsistency

Lastly, Persion argues that the district court's obviousness decision must be reversed because its obviousness findings are at odds with its findings concerning the written description issue. Persion states that, for example, in finding a lack of written description support for the asserted claims, the district court "found [that] 'nothing in the state of the art as of July 2012 . . . would have provided guidance as to which [ER hydrocodone-only] formulations would [achieve the claimed PK profile] and which would not[.]'" Appellant's Br. 22 (quoting *Pernix*, 323 F. Supp. 3d at 627) (emphasis omitted). Persion asserts this statement contradicts the district court's finding that a person of ordinary skill in the art "would 'look to Jain and to the Vicodin and Lortab labels for [] guidance as to the appropriate dosing levels of Devane's formulation for patients with mild or moderate [hepatic impairment].'" *Id.* (quoting *Pernix*, 323 F. Supp. 3d at 612) (emphasis omitted). We reject this argument as we see no inconsistency in the district court's findings.

Persion's entire argument with respect to this issue is based on incomplete quotations from the district court's opinion. For example, a complete reading of the district court's statement above belies Persion's assertion that the district court's findings are inconsistent. The district court stated that "there was nothing in the state of the art as of July 2012 that would have provided guidance as to which of the broadly claimed formulations would work and which would not, *with the exception of the single embodiment described in Example 8*." *Pernix*, 323 F. Supp. 3d at 627 (emphasis added). The embodiment described in Example 8 of the common written description of the '760 and '499 patents is the Devane formulation, which formed the basis for the district court's obviousness findings. *Id.* at 575, 619. In contrast to the "essentially limitless number of formulation species" covered by the claims of the '760 and '499 patents, the district court found that the prior art provided

adequate guidance with respect to the sole formulation described in Example 8: the Devane formulation. *Id.* at 618–19, 622–23. Thus, there is no inconsistency between the statement Persion quotes and the district court's conclusion that a person of ordinary skill in the art would have been motivated to combine Devane with Jain and the Vicodin and Lortab labels to arrive at the claimed invention.

For the same reason, we reject Persion's argument that the district court's findings with respect to reasonable expectation of success are inconsistent with its findings concerning the lack of written description. Persion asserts that the district court "found that there was no 'way of predicting which formulations would work and which would not[,]' stating that 'testing results would be fundamental to determining which formulations would satisfy the asserted claims[.]'" Appellant's Br. 20 (quoting *Pernix*, 323 F. Supp. 3d at 624, 628). According to Persion, this necessity for experimentation contradicts the district court's finding that a person of ordinary skill would have had a reasonable expectation of success in combining Devane with Jain and the Vicodin and Lortab labels. *Id.* at 20–21. Once again, however, Persion omits critical context from its quote that demonstrates the district court was addressing formulations other than the one described in Example 8. *See Pernix*, 323 F. Supp. 3d at 623 (declining to credit expert testimony that "the specification would provide guidance to a person of skill in the art regarding how to make a formulation that would satisfy the limitations of the asserted claims, *except for the Devane formulation set forth in Example 8 or compositions closely similar to that one*") (emphasis added). In context, there is no inconsistency between the district court's findings underlying its obviousness and lack of written description determinations, and we will not reverse the district court on this basis.

CONCLUSION

We have considered Persion's remaining arguments and find them unpersuasive. We conclude that the district court correctly applied inherency to find that the claimed pharmacokinetic limitations of the asserted claims added no patentable weight over the combination of Devane and other prior art references. We further conclude that the district court's factual findings concerning obviousness are not clearly erroneous. We therefore affirm the district court's decision that the asserted claims of the '760 and '499 patents are invalid as obvious under 35 U.S.C. § 103. We do not reach the district court's decision concerning the lack of written description support.

AFFIRMED

COSTS

Each party will bear its own costs.

CERTIFICATE OF SERVICE

I hereby certify that on January 27, 2020, I electronically filed the foregoing with the Clerk of the Court for the United States Court of Appeals for the Federal Circuit by using the appellate CM/ECF system.

I certify that all participants in the case are registered CM/ECF users and that service will be accomplished by the appellate CM/ECF system.

I further certify that the required paper copies have been sent to the court within the requested time frame

Dated: January 27, 2020

/s/ Dominick A. Conde
Dominick A. Conde

Counsel for Plaintiff-Appellant
Persion Pharmaceuticals LLC

CERTIFICATE OF COMPLIANCE

Undersigned counsel certifies that this petition complies with the type-volume limitation of Fed. R. App. P. 35(b)(2)(A) because it contains 3,728 words, excluding the parts of the petition exempted by Fed. R. App. P. 32(f).

Undersigned counsel further certifies that this petition complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6) because this petition has been prepared in a proportionally spaced 14-point Times New Roman typeface using Microsoft Word 2010.

Dated: January 27, 2020

/s/ Dominick A. Conde
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