United States Court of Appeals for the Federal Circuit

AVENTIS PHARMA S.A. AND SANOFI-AVENTIS U.S., LLC,
Plaintiffs-Appellants,

v.

HOSPIRA, INC.,
Defendant-Appellee,

and

APOTEX INC. AND APOTEX CORP.,
Defendants-Appellees.

2011-1018

Appeal from the United States District Court for the District of Delaware in consolidated case nos. 07-CV-0721 and 08-CV-0496, Chief Judge Gregory M. Sleet.

Decided: April 9, 2012

GEORGE F. PAPPAS, Covington & Burling, LLP, of Washington, DC, argued for plaintiffs-appellants Aventis Pharma S.A., et al.. With him on the brief were CHRISTOPHER N. SIPES, KEVIN B. COLLINS, MICHAEL N. KENNEDY, and ROGER A. FORD.

JAMES F. HURST, Winston & Strawn, LLP, of Chicago, Illinois, argued for defendant-appellee, Hospira, Inc. With him on the brief was IMRON T. ALY. Of counsel on the brief were STEFFEN N. JOHNSON, GEOFFREY P. EATON, and JACOB R. LOSHIN, of Washington, DC. Of counsel was ANDREW NICHOLS.

RICHARD T. RUZICH, Duane Morris LLP, of Washington, DC, argued for defendants-appellees, Apotex Inc., et al. With him on the brief were ARTHUR M. DRESNER, KERRY B. MCTIGUE, KRISTINA CAGGIANO and MATTHEW C. MOUSLEY. Of counsel on the brief was SHASHANK UPADHYE, Apotex, Inc., of Toronto, Ontario, Canada.

Before LINN, DYK, and PROST, *Circuit Judges*.

PROST, *Circuit Judge*.

Aventis Pharma S.A. and Sanofi-Aventis U.S., L.LC. (collectively "Sanofi") filed suit against Hospira, Inc. ("Hospira") and Apotex Inc. and Apotex Corp. (collectively "Apotex") under 35 U.S.C. § 271(e) for infringement of U.S. Patent Nos. 5,750,561 ("'561 patent") and 5,714,512 ("'512 patent"). After a bench trial, the district court found, inter alia, that claim 5 of the '561 patent and claim 7 of the '512 patent were invalid for obviousness under 35 U.S.C. § 103, that claim 7 of the '512 patent was not infringed, and that both the '561 and '512 patents were unenforceable for inequitable conduct. Sanofi has appealed. For the reasons set forth below, we affirm.

I. BACKGROUND

The '561 and '512 patents are pharmaceutical patents related to the administration of the chemotherapy cancer drug docetaxel, which is marketed under the brand-name Taxotere. The patents are assigned to Aventis Pharma S.A., and Sanofi-Aventis U.S., L.L.C. is the holder of the New Drug Application for Taxotere. Docetaxel is a successor to the cancer drug paclitaxel, marketed as Taxol, and the composition for docetaxel was covered by now-expired U.S. Patent No. 4,814,470 ("'470 patent"). Both docetaxel and paclitaxel belong to the class of compounds known as taxanes.

Taxanes are administered through an intravenous infusion, accomplished by slowly delivering the drug in a diluted aqueous solution called a "perfusion." Taxanes, however, have low solubility in water and tend to precipitate, i.e., form solid clumps, and come out of solution. To delay precipitation, taxanes are mixed with additives like surfactants and ethanol; these additives stabilize the perfusion and delay the amount of time before precipitation occurs. The taxane is combined with the additives to form a "stock solution" which is then mixed into an injectable aqueous solution, such as saline, to form a perfusion.

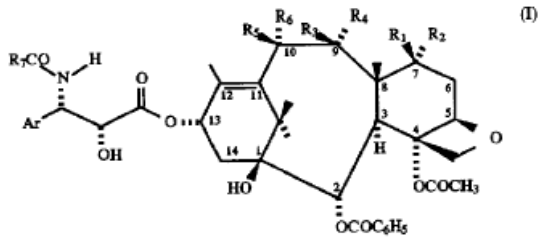
In the prior art, the surfactant Cremophor was used with taxanes to form the stock solution, but it was known to trigger serious allergic reactions, including anaphylactic shock. '561 patent col.1 ll.59-63; '512 patent col.2 ll.31-35. The '561 and '512 patents relate to using surfactants other than Cremophor with docetaxel and decreasing the amount of ethanol to reduce alcohol intoxication and anaphylactic effects in patients. After Hospira and Apotex applied for Federal Drug Administration ("FDA")

approval to market generic versions of Taxotere, Sanofi filed suit against them for infringement of the '561 and '512 patents. Only claim 5 of the '561 patent and claim 7 of the '512 patent are at issue on appeal.

The '561 patent is titled "Compositions containing taxane derivatives" and describes taxane compositions, including a perfusion that avoids anaphylactic and alcohol intoxication manifestations. Claim 5 of the '561 patent recites:

> 5. A perfusion, which contains approximately 1 mg/ml or less of compound of formula as defined in claim 1, and which contains less than 35 ml/l of ethanol and less than 35 ml/l of polysorbate, wherein said perfusion is capable of being injected without anaphylactic or alcohol intoxication manifestations being associated therewith.

The '512 patent is titled "New compositions containing taxane derivatives," and discloses taxane compositions with reduced ethanol. Claim 7 depends from claims 1 and 6. As corrected by a Certificate of Correction, those claims recite:

> 1. A composition comprising a compound of the formula
>
> (I)
>
> 
>

> in which Ar is unsubstituted phenyl, R_7 is phenyl or tert butoxy, R_6 is hydrogen, R_5 is acetyloxy or hydroxy, R_3 and R_4 taken together form an oxo radical, R_1 is hydroxy and R_2 is hydrogen, said composition being dissolved in a surfactant selected from polysorbate, polyoxyethylated vegetable oil, and polyethoxylated castor oil, said composition being essentially free or free of ethanol.
>
> 6. The composition of claim 1, wherein R_5 is hydroxy and R_7 is tert butoxy.
>
> 7. The composition of claim 6, wherein said surfactant is polysorbate.

After a bench trial, the court found that claim 7 of the '512 patent was invalid as obvious and not infringed by Hospira or Apotex. With respect to claim 5 of the '561 patent, the court found that Hospira and Apotex did infringe but concluded that the claim was obvious. The court also determined that the '512 and '561 patents were unenforceable for inequitable conduct.

II. DISCUSSION

On appeal, Sanofi challenges the district court's construction of two claim terms: "perfusion" in claim 5 of the '561 patent and "essentially free or free of ethanol" in claim 7 of the '512 patent. Based on the district court's constructions, Sanofi argues that the court erred in finding that both claims were invalid for obviousness under 35 U.S.C. § 103 and that Apotex's and Hospira's accused products did not infringe claim 7 of the '512 patent. Additionally, Sanofi contends that the court erred in finding that the '561 and '512 patents were unenforceable

for inequitable conduct. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

A. Claim 5 of the '561 Patent

Claim construction is a question of law reviewed de novo. *Cybor Corp. v. FAS Techs.*, 138 F.3d 1448, 1454-55 (Fed. Cir. 1998) (en banc). Claim terms generally are construed in accordance with the ordinary and customary meaning they would have to one of ordinary skill in the art in light of the specification and the prosecution history. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc).

Before the district court, the parties initially agreed to construe "perfusion" in claim 5 of the '561 patent as "a solution suitable for infusion into patients including at least active pharmaceutical ingredient and an aqueous infusion fluid such as physiological saline or glucose." *Aventis Pharma S.A. v. Hospira, Inc.*, 743 F. Supp. 2d 305, 332 (D. Del. 2010). The parties, however, later realized that they did not agree on the meaning of the phrase "suitable for infusion into patients" in their proposed construction, leading Sanofi to ask the district court to require that the claimed "perfusion" also be effective for treatment, safe, and stable (i.e., not precipitate) for at least eight hours. The court declined to impose these additional limitations and instead construed "perfusion" to mean "an injectable solution containing the active pharmaceutical ingredient and an aqueous infusion fluid." *Id.* at 333. On appeal, Sanofi argues that the district court erred in not construing "perfusion" to include these additional efficacy, safety, and stability limitations.

We can easily dispose of Sanofi's first two limitations. Neither the claims, the specification, nor the prosecution

history suggest that the claimed perfusion must satisfy certain safety or efficacy standards. We previously have refused to impose such limitations when not required by the language of the claims or the specification, *see Mitsubishi Chem. Corp. v. Barr Labs., Inc.*, 435 F. App'x 927, 934-35 (Fed. Cir. 2011); *Iovate Health Scis., Inc. v. Bio-Engineered Supplements & Nutrition, Inc.*, 586 F.3d 1376, 1382 (Fed. Cir. 2009), and decline to do so here.

Regarding Sanofi's eight-hour stability limitation, Sanofi does not contend that "perfusion," as that term is normally understood in the art, includes such a limitation. Instead, Sanofi argues that based on how the term is used in the context of the '561 patent, the claimed "perfusion" must demonstrate at least eight hours of stability. *See* Oral Argument 3:05-3:10, *available at* http://www.cafc.uscourts.gov/oral-argument-recordings/2011-1018/all. This court recently reiterated the stringent standard for narrowing a claim term beyond its plain and ordinary meaning in *Thorner v. Sony Computer Entertainment America L.L.C.*, 669 F.3d 1362 (Fed. Cir. 2012). There, we explained that we will only interpret a claim term more narrowly than its ordinary meaning under two circumstances: "1) when a patentee sets out a definition and acts as [its] own lexicographer, or 2) when the patentee disavows the full scope of a claim term either in the specification or during prosecution." *Id.* at 1365.

"To act as its own lexicographer, a patentee must 'clearly set forth a definition of the disputed claim term' other than its plain and ordinary meaning." *Id.* (quoting *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002)). In other words, "the patentee must 'clearly express an intent' to redefine the term." *Id.* This clear expression need not be in *haec verba* but may be inferred from clear limiting descriptions of the invention

in the specification or prosecution history. Similarly, to disavow claim scope, "[t]he patentee may demonstrate intent to deviate from the ordinary and accustomed meaning of a claim term by including in the specification expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope." *Id.* at 1366 (quoting *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1325 (Fed. Cir. 2002)). Moreover, "[i]t is . . . not enough that the only embodiments, or all of the embodiments, contain a particular limitation" to limit a claim term beyond its ordinary meaning. *Id.* Here, because neither exception applies, the district court correctly did not include an eight-hour stability limitation in its construction of "perfusion."

We begin our analysis with the language of the claims. *Phillips*, 415 F.3d at 1312. Claim 5 requires that the "perfusion" be "capable of being injected without anaphylactic or alcohol intoxication manifestations," but contains no limitations with respect to the claimed perfusion's stability. Had the patentee similarly intended to require that the "perfusion" display a certain duration of stability, it could have included such a limitation in the claim but notably did not. By expressly identifying the specific characteristics of the "perfusion," i.e., that it is not associated with "anaphylactic or alcohol intoxication manifestations," the plain language of claim 5 indicates that the term has its ordinary meaning subject only to those specifically enumerated limitations.

This interpretation of "perfusion" also is consistent with the teachings of the specification. Although the specification does refer to perfusions with a stability of at least eight hours, *see* '561 patent col.2 ll.43-45 ("The new perfusions [referring to examples in the specification] are stable from a physical standpoint, that is to say no pre-

cipitation phenomenon is seen to appear within approximately 8 hours."), and the disclosed examples of perfusions have stabilities exceeding eight hours, *see id.* at col.2 l.59-col.3 l.26, these general descriptions of the characteristics of embodiments do not suffice to limit the claims. *See Thorner*, 669 F.3d at 1366 ("It is likewise not enough that the only embodiments, or all of the embodiments, contain a particular limitation."). Indeed, the specification expressly instructs that the disclosed examples "are not to be considered as limiting the invention." '561 patent col.2 ll.53-54. Moreover, in contrast to the specification's discussion of anaphylactic and alcohol intoxication manifestations, nothing in the specification indicates that a minimum stability of eight hours is an essential feature of the claimed perfusion or an advantage of the perfusion over the prior art. *See Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906-09 (Fed. Cir. 2004) (distinguishing cases where the court narrowly construed an otherwise broad claim term).

Nor does the prosecution history evidence a clear and unmistakable disavowal of claim scope. The prosecution history can offer insight into the meaning of a particular claim term, but the "[c]laim language and the specification generally carry greater weight." *HTC Corp. v. IPCom GmbH & Co.*, 667 F.3d 1270, 1276 (Fed. Cir. 2012). Here, the patentee's observation during prosecution that the perfusions in the Tarr reference demonstrated signs of precipitation after four hours and thirty minutes neither indicates that the claimed perfusion has a special definition nor clearly and unmistakably manifests the patentee's intention to limit claim 5 to perfusions that are stable for at least eight hours. The Tarr reference was not directed to the two-solvent solution of claim 5 but to a prior art three-solvent solution; the argument was that

the presence of the third solvent materially affected the characteristics of the claimed composition.

Lastly, we reject Sanofi's argument that the district court improperly relied on extrinsic evidence in the form of expert testimony in construing this claim term. According to Sanofi, because the intrinsic evidence alone dictates the proper construction of perfusion, any extrinsic evidence is irrelevant. A district court, however, has the discretion to take expert testimony into account in determining the ordinary meaning of a claim term to one skilled in the art. *Phillips*, 415 F.3d at 1319 ("[B]ecause extrinsic evidence can help educate the court regarding the field of the invention and can help the court determine what a person of ordinary skill in the art would understand claim terms to mean, it is permissible for the district court in its sound discretion to admit and use such evidence."). Here, the district court heard testimony from both sides' experts, including testimony from Sanofi's expert, Dr. Howard Burris, which was consistent with the intrinsic evidence and supports the conclusion that the ordinary meaning of a perfusion does not include the stability limitation proposed by Sanofi. Consequently, the district court did not err in relying on extrinsic evidence in construing this claim term.

In sum, we conclude that the patentee did not narrow the ordinary meaning of "perfusion" in claim 5 of the '561 patent by either acting as its own lexicographer or disclaiming claim scope and therefore agree with the district court that a "perfusion" is simply "an injectable solution containing the active pharmaceutical ingredient and an aqueous infusion fluid."

Having affirmed the court's claim construction, we next address the district court's conclusion that claim 5

was invalid as obvious under 35 U.S.C. § 103. A patent is invalid for obviousness "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(a). "Obviousness is a question of law based on underlying findings of fact." *In re Kubin*, 561 F.3d 1351, 1355 (Fed. Cir. 2009). These underlying factual inquiries are (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; and (4) any relevant secondary considerations, such as commercial success, long felt but unsolved needs, and the failure of others. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007) (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 legal determination that an invention is obvious de novo and the court's underlying factual determinations for clear error. *Eli Lilly & Co. v. Teva Pharms. USA, Inc.*, 619 F.3d 1329, 1336 (Fed. Cir. 2010).

The district court found that claim 5 was obvious in light of the prior art, including the Guéritte-Voegelein reference ("GV reference") and the *Dictionnaire Vidal* ("*Vidal* reference"). During oral argument, Sanofi's counsel confirmed that under the district court's construction of "perfusion," Sanofi did not dispute that claim 5 was obvious based on the prior art. Oral Argument 22:23-22:45. Because we have affirmed the district court's construction of "perfusion," we also affirm the district court's judgment that claim 5 of the '561 patent is invalid under 35 U.S.C. § 103.

B. Claim 7 of the '512 patent

Sanofi argues that the district court erred in construing the claim term "essentially free or free of ethanol" in claim 7 of the '512 patent as meaning that the claimed perfusion contains "the same amount of ethanol as a stock solution with no more than 5% ethanol by volume." *Aventis*, 743 F. Supp. 2d at 359. We need not resolve this issue, however, because its resolution does not require reversal of the district court's obviousness determination.

Claim 7 of the '512 patent claims a "composition," which the parties agree can be either a stock solution or a perfusion. With respect to stock solutions, the parties also agree that the phrase "essentially free or free of ethanol" in claim 7 means "no more than 5% ethanol by volume." *Id.* Relying on this construction, the district court found that claim 7 was obvious, noting that the "the specification and claims of the prior art '470 Patent[,] . . . disclose and contemplate both ethanol-containing and essentially ethanol-free *stock solutions* . . . ." *Id.* at 337 n.15 (emphasis added). Sanofi has not addressed the district court's obviousness finding with respect to stock solutions in its opening brief. To the extent that Sanofi's conclusory statement in its reply that there is not "art in the record of polysorbate stock solutions containing less than 5% ethanol," amounts to a challenge to the invalidity finding, that argument is waived. *Advanced Magnetic Closures, Inc. v. Rome Fastener Corp.*, 607 F.3d 817, 833 (Fed. Cir. 2010) ("This court has consistently held that a party waives an argument not raised in its opening brief."). Thus, regardless of whether the court correctly construed "essentially free or free of ethanol" as it relates to perfusions, the district court's unchallenged finding that the claimed stock solutions were obvious in light of the prior art also renders the "composition" in claim 7

obvious. *See Titanium Metals Corp. v. Banner*, 778 F.2d 775, 782 (Fed. Cir. 1985) ("It is . . . an elementary principle of patent law that when, as by a recitation of ranges or otherwise, a claim covers several compositions, the claim is 'anticipated' if *one* of them is in the prior art."). We accordingly affirm the district court's judgment that claim 7 of the '512 patent is invalid under 35 U.S.C. § 103.

C. Inequitable Conduct

Sanofi also appeals the district court's determination that both the '512 and '561 patents are unenforceable for inequitable conduct. As an initial matter, Sanofi contends that the district court abused its discretion in allowing Hospira and Apotex to amend their pleadings after the scheduling order deadline to add allegations related to inequitable conduct without first finding that Hospira and Apotex had established "good cause" as required by Federal Rule of Civil Procedure 16(b)(4). We review a district court's granting of a motion to amend pleadings under the law of the regional circuit. *Creative Compounds, L.L.C. v. Starmark Labs.*, 651 F.3d 1303, 1309 (Fed. Cir. 2011). In the Third Circuit, such decisions are reviewed for an abuse of discretion. *Race Tires Am., Inc. v. Hoosier Racing Tire Corp.*, 614 F.3d 57, 73 (3d Cir. 2010). Under Rule 16(b)(4), a scheduling order "may be modified only for good cause and with the judge's consent." Fed. R. Civ. P. 16(b)(4).

Here, the parties do not dispute that the scheduling order—and consequently Rule 16(b)(4)'s "good cause" requirement—apply to Hospira's amendment. With respect to Apotex's amendment, however, both Apotex and Hospira argue that Apotex was never subject to the scheduling order and therefore did not need to demonstrate good cause to amend its pleadings. Assuming

without deciding that the deadlines in the scheduling order covered both Apotex and Hospira, we cannot say that the district court abused its discretion in allowing the amendments. Hospira timely asserted a claim for inequitable conduct in its original counterclaims but, shortly after deposing named-inventor Jean-Louis Fabre, moved to amend its allegations after the scheduling order deadline to specifically identify the withheld *Vidal* and GV references. The district court granted the motion, finding that "the timing of Hospira's motion [did] not appear to have been the product of bad faith" and that Sanofi would not be unduly prejudiced by the amendment. Apotex then filed a motion to amend its counterclaims to add a claim of inequitable conduct, which the district court also granted. Given the circumstances of this case, including the temporal proximity of the amendments to inventor Fabre's deposition, there was good cause for the amendments, and the district court did not abuse its discretion in allowing them. Consequently, we turn to the merits.

The district court found that the *Vidal* and GV references were material to patentability and that inventor Fabre intentionally withheld them with the intent to deceive the U.S. Patent and Trademark Office ("PTO"). Based on these findings, the court concluded that the '512 and '561 patents were unenforceable for inequitable conduct. Sanofi argues that we should reverse the court's inequitable conduct judgment because Fabre explained why he did not disclose these references to the PTO and, thus, the court's finding that he acted with the intent to deceive was not the single most reasonable inference that could be drawn from the evidence. Additionally, Sanofi contends that these references were not material to patentability because they were duplicative of references that were before the PTO. In response, Apotex and

Hospira argue that the district court's intent findings are supported by both the evidence and the court's credibility determinations. Regarding materiality, they maintain that the district court properly applied the but-for materiality analysis in concluding that the references were material to patentability. We agree with Apotex and Hospira.

In reviewing the district court's inequitable conduct determination, we review the court's underlying factual findings for clear error and its ultimate decision as to inequitable conduct for an abuse of discretion. *Star Scientific, Inc. v. R.J. Reynolds Tobacco Co.*, 537 F.3d 1357, 1365 (Fed. Cir. 2008). To prevail on an inequitable conduct defense, a defendant must establish both the materiality of the withheld reference and the applicant's intent to deceive the PTO. *Therasense, Inc. v. Becton, Dickinson & Co.*, 649 F.3d 1276, 1290 (Fed. Cir. 2011) (en banc). In *Therasense*, this court rejected the "sliding scale" approach to proving inequitable conduct "where a weak showing of intent may be found sufficient based on a strong showing of materiality, and vice versa." *Id.* Instead, we instructed that "[i]ntent and materiality are separate requirements." *Id.* Additionally, we held that but-for materiality is the standard for evaluating the materiality prong of the analysis unless there is affirmative egregious misconduct. *Id.* at 1292. In this case, although the district court did not have the benefit of our *Therasense* opinion when it rendered its inequitable conduct decision, the court nevertheless found that the withheld references were but-for material to patentability and made distinct intent and materiality findings rather than employing the now-abrogated sliding scale approach. Consequently, as set forth below, we conclude that the court's inequitable conduct determination withstands even the more rigorous standard adopted in *Therasense*.

1. Materiality

A prior art reference "is but-for material if the PTO would not have allowed a claim had it been aware of the undisclosed prior art." *Therasense*, 649 F.3d at 1291. Unlike the clear and convincing evidence standard for invalidating a patent in the district court under 35 U.S.C. §§ 102 and 103, the standard for establishing but-for materiality in the inequitable conduct context only requires a preponderance of the evidence, "giv[ing] claims their broadest reasonable construction." *Id.* at 1291-92. As a result, when a "claim is properly invalidated in district court based on the deliberately withheld reference, then that reference is necessarily material" for purposes of the inequitable conduct inquiry. *Id.* at 1292. On the other hand, even if the withheld reference is not sufficient to invalidate the claim in district court, "the reference may be material if it would have blocked patent issuance under the PTO's different evidentiary standards." *Id.*

Here, we have affirmed the district court's finding that the '561 and '512 patents were invalid based on, inter alia, the withheld GV and *Vidal* references. Because such references are necessarily material to patentability, the district court did not err in finding that the materiality requirement was established.

2. Intent

To satisfy the intent requirement, "the accused infringer must prove by clear and convincing evidence that the applicant knew of the reference, knew that it was material, and made a deliberate decision to withhold it." *Id.* In *Therasense*, we confirmed that inequitable conduct requires clear and convincing evidence of a specific intent

to deceive the PTO and that "the specific intent to deceive must be 'the single most reasonable inference able to be drawn from the evidence.'" *Id.* (quoting *Star Scientific*, 537 F.3d at 1366). "This court reviews the district court's factual findings regarding what reasonable inferences may be drawn from the evidence for clear error." *Id.* at 1291. In this case, the district court heard extensive testimony from inventor Fabre regarding both the *Vidal* and GV references, and the court's finding that Fabre acted with a specific intent to deceive the PTO in withholding those references is not clearly erroneous.

The *Vidal* reference discloses Sandoz's experience using polysorbate 80 as a surfactant with the cancer drug etoposide. During the trial, Fabre testified that he did not cite the *Vidal* reference to the PTO because the etoposide-type experiments he and his co-inventors performed with doxcetaxel resulted in perfusions that did not demonstrate eight hours of stability. According to Fabre, he believed that these experiments were failures and that he therefore did not need to disclose the *Vidal* reference to the PTO. Sanofi argues that based on this testimony the district court erred in finding that Fabre had the specific intent to deceive the PTO because that finding was not the single most reasonable inference that could be drawn. We disagree.

The district court considered Fabre's explanation for withholding the *Vidal* reference and expressly rejected it based on both the evidence presented and the finding that Fabre lacked credibility. Specifically, the district court relied on Fabre's testimony that he learned of replacing Cremophor with polysorbate 80 from the *Vidal* reference and that the Sandoz experience disclosed in the reference was one of the "main factors that shaped [his] thinking" in choosing polysorbate 80 and led him to believe that

replacing Cremophor with polysorbate 80 would avoid anaphylactic manifestations. *Aventis*, 743 F. Supp. 2d at 351-53. This testimony also was consistent with a Sanofi internal memorandum acknowledging the side effects associated with Cremophor and noting that Sandoz had used polysorbate 80 (i.e., "TWEEN") instead of Cremophor in its etoposide product. *Id.* at 351; J.A. 5666.

In making its intent finding, the district court also emphasized that in Fabre and his co-inventors' submissions to the PTO, they cited the Rowinsky reference, which identified the "problem" the inventors were trying to solve—i.e., the anaphylactic reactions associated with Cremophor—but did not cite the *Vidal* reference, which revealed the "solution"—i.e., the switch from Cremophor to polysorbate 80. *Aventis*, 743 F. Supp. 2d at 352. The court found that "[t]here simply is no justification for telling the [PTO] about the prior art disclosing the problem [Fabre] examined while concealing key prior art disclosing the solution he chose." *Id.* at 353.

Finally, in addressing Fabre's excuse that he withheld the *Vidal* reference because the etoposide-type experiments he and his co-inventors performed were failures, the court found that Fabre's testimony was not credible. The court determined that during Fabre's direct examination he did not address all of the etoposide-type experiments that he and his colleagues had undertaken but rather only reviewed those experiments that demonstrated low stability and thus supported Fabre's excuse for not disclosing the reference. The remaining experiments discussed during Fabre's cross-examination, however, displayed stabilities ranging from five hours and forty minutes to over thirty hours. *Id.* at 352-53; J.A. 5566-69. Fabre attempted to downplay the significance of these experiments by stating that they were not "eto-

poside-type formulations." But the district court found that Fabre's testimony was contrary to the titles of the Sanofi documents detailing those experiments and lacked credibility: "The court does not find credible Fabre's witness-stand assertion, twenty years after the documents were prepared, that the contemporaneous description of these formulations as 'etoposide-type' did not reflect how Sanofi's researchers actually viewed the formulations." *Aventis*, 743 F. Supp. 2d at 353. Based on the evidence and his assessment of Fabre's testimony, the court found that Fabre "knew that the *Vidal* reference and the other etoposide prior art were relevant to the patentability of his alleged invention, but nonetheless chose not to disclose it to the patent office." *Id.* From this finding, the court concluded that Fabre acted with the intent to deceive the PTO when he withheld the *Vidal* reference. *Id.*

In light of the evidence before the district court supporting the finding of a specific intent to deceive, coupled with the deference we must afford to the district court's credibility determinations, we cannot conclude that the court's finding that Fabre withheld the *Vidal* reference with the specific intent to deceive the PTO was clearly erroneous.

We reach the same conclusion with respect to the GV reference. The GV reference describes the relationship between the structure and activity of various analogues of paclitaxel including docetaxel and names one of Fabre's colleagues as an author. Specifically relevant to the patentability of the patents at issue, the reference states: "Moreover Taxotere (13a) showed a better solubility in excipient system (polysorbate 80/ethanol, 1:1) . . . ." J.A. 5631. Fabre testified that he did not cite the GV reference to the PTO because he only read a March 1990 draft

of the reference which did not include this sentence disclosing the polysorbate 80/docetaxel formulation.

Again, the district court found that this testimony was not credible and relied on the other evidence presented during the trial in finding that Fabre withheld the reference with the specific intent to deceive the PTO. The court explained that Fabre was the project leader of Sanofi's Taxotere development, had to approve the GV reference for publication, and had testified that he reviewed the article "with some care to make sure that it was a proper article for the company to be publishing." *Id.* at 353-54. The court further highlighted Fabre's testimony that in March 1992, he was dissatisfied with the clinical brochure for Taxotere because it did not list the GV reference and affirmatively took steps to ensure that the reference was identified. Six months later, however, when Fabre signed his patent declaration, he failed to disclose the reference to the PTO. *Id.* at 353. Relying on this evidence, the district court found that Fabre "'reviewed . . . with some care' the final version of the GV reference prior to signing the patent declaration, was aware of the reference's materiality to the prosecution of his patents, and purposefully decided not to disclose it despite this knowledge." *Id.* at 354. Thus, contrary to Sanofi's contention, in concluding that Fabre acted with a specific intent to deceive the PTO, the district court did not rely solely on its finding that Fabre was not credible but instead viewed Fabre's testimony in light of the other evidence to reach its intent conclusion. Based on the evidence presented, this finding was not clearly erroneous.

Relying on these materiality and intent findings, the district court found the patents were unenforceable due to inequitable conduct. *Id.* at 354. Based on the district

court's thorough discussion of its factual findings and its well-reasoned analysis that is consistent with *Therasense*, this determination was not an abuse of discretion. We accordingly affirm.

III. CONCLUSION

We have considered Sanofi's additional arguments for reversing the district court's decision and conclude that they similarly lack merit. Consequently, for the reasons set forth above, the district court's judgment that claim 5 of the '561 patent and claim 7 of the '512 patent are invalid for obviousness and that the '561 and '512 patents are unenforceable for inequitable conduct is affirmed.

AFFIRMED