United States Court of Appeals for the Federal Circuit

04-1344

ALZA CORPORATION
and JANSSEN PHARMACEUTICA, INC.,

Plaintiffs-Appellees,

v.

MYLAN LABORATORIES INC.,
MYLAN TECHNOLOGIES INC., and MYLAN PHARMACEUTICALS INC.,

Defendants-Appellants.

Gregory L. Diskant, Patterson, Belknap, Webb & Tyler LLP, of New York, New York, argued for plaintiffs-appellees. With him on the brief was Jeffrey I.D. Lewis.

E. Anthony Figg, Rothwell, Figg, Ernst & Manbeck, of Washington, DC, argued for defendants-appellants. With him on the brief were Joseph A. Hynds and Sharon L. Davis.

Appealed from: United States District Court for the District of Vermont

Chief Judge William K. Sessions III

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Defendants-Appellants.

DECIDED: December 10, 2004

Before NEWMAN, Circuit Judge, ARCHER, Senior Circuit Judge, and DYK, Circuit Judge.

Opinion for the court filed by Senior Circuit Judge ARCHER. Opinion concurring-in-part and dissenting-in-part filed by Circuit Judge DYK.

ARCHER, Senior Circuit Judge.

Mylan Laboratories Inc., Mylan Technologies Inc. and Mylan Pharmaceuticals Inc. (collectively "Mylan") appeal the judgment of the United States District Court for the District of Vermont holding that U.S. Patent No. 4,588,580 ("the '580 patent") is not anticipated or obvious in view of U.S. Patent No. 4,470,962 ("the Keith patent") and that the '580 patent is not unenforceable as having been procured by inequitable conduct. Alza Corp. v. Mylan Labs. Inc., 310 F. Supp. 2d 610 (D. Vt. 2004). Because the district court correctly construed the claim term "skin permeable form" to exclude fentanyl citrate, we affirm its validity determinations. Further, because we discern no error in the

district court's finding of a lack of intent to deceive, we affirm the district court's holding that the '580 patent is not unenforceable due to inequitable conduct.

I

Alza Corp. and Janssen Pharmaceutica, Inc. (collectively "Alza") brought an infringement suit against Mylan for infringing the '580 patent. The '580 patent is drawn to a system for the transdermal administration of fentanyl, a powerful narcotic, for an extended period of time at analgetically effective rates.[1] Prior to the '580 patent, transdermal system designs in the form of a patch were based upon two principles: 1) a drug with high solubility should be used, since more drug in solution meant a greater ability to push drug through the skin; and 2) huge drug excesses should be used to super-saturate the system so delivery could be continued for a prolonged period of time.[2] This design, however, was inappropriate for a narcotic, due to the large excesses of a controlled substance that remained in discarded patches which could then be abused. Thus, the inventors of the '580 patent set out to develop a fentanyl patch that minimized the amount of narcotic drug that would be used in the system.

The inventors discovered that the skin permeability of fentanyl – the balance of flux and concentration necessary for adequate delivery to humans – was highly dependent on the chemical form of the drug:

> We have discovered that fentanyl citrate, the form in which fentanyl is presently administered, has such a low skin permeability that it is not at all

[1] At the time the inventors were developing a transdermal system for administering fentanyl, fentanyl was "normally administered as the citrate, either as a bolus injection or infusion or a continuous infusion for the purpose of producing anesthesia or analgesia." '580 patent, col. 1, ll. 22-25.

[2] This is because as drug left solution to go into the skin, excess drug in the patch (above the system's saturation level) would dissolve, replacing the drug that was leaving.

> suitable for transdermal delivery, even with the use of permeation enhancers. Instead, we have found that, in order to obtain the delivery rates noted above, the drug should be incorporated in the transdermal therapeutic system in the form of the base.

'580 patent, col. 3, ll. 10-14. The '580 patent directed to the transdermal administration of fentanyl in the base form issued on May 13, 1986.

Two reexamination proceedings followed. The subject of the first proceeding was an article written by an Alza scientist, Michaels. Michaels taught that high solubility in water is a desirable feature for a transdermally delivered drug. The applicants submitted a declaration explaining that Michaels therefore suggested that fentanyl would not be a suitable transdermal candidate because of its low water solubility. The examiner allowed the claims, reasoning that Michaels did not suggest the use of fentanyl base because of Michaels's desire for high solubility. The subject of the second reexamination proceeding was the Keith patent. The Keith patent is directed principally to a nitroglycerin transdermal patch, but it also includes fentanyl in a list of potential transdermal candidates. Keith teaches using a ten-fold excess of drug to force drug through the skin and keeping the drug in a neutral-to-slightly-acidic solution (pH 6.5 to 7.0) for stability. Gale, one of the '580 patent's inventors, submitted a declaration that due to the pH requirements for stability, the Keith patent taught the use of fentanyl citrate, a form of fentanyl expressly rejected in the '580 patent. Gale concluded that any system disclosed by the Keith patent "would be unsuitable for administering fentanyl at analgetically effective rates." Based on the differences between Keith and the '580 patent, the examiner reaffirmed the '580 patent:

> the form of fentanyl produced under the procedures of the [Keith] patent would be in the citrate salt form. . . . As such, the Keith et al reference fails to teach one having an ordinary skill in the art to make and use a

> device which would transdermally administer a skin-permeable form of fentanyl (or its derivatives) to a human subject at an analgetically effective rate and for a sufficient period of time to induce and maintain analgesia as taught by the patent in Re-examination.

One embodiment of the '580 patent is sold by Janssen as the Duragesic® patch. Mylan developed a generic transdermal fentanyl patch that is a bioequivalent to Duragesic®. Mylan filed an Abbreviated New Drug Application ("ANDA") seeking approval to market its patch before the '580 patent expires. The '580 patent issued on May 13, 1986. It was due to expire in July of 2004; however, following the Food and Drug Administration's approval of the pediatric use of Duragesic®, the patent will now expire on January 23, 2005.[3]

The asserted claims are claim 59 as it depends from claim 11, claim 59 as it depends from claim 15, claim 61 as it depends from claim 31, and claim 27 as it depends from claim 25. Claim 59 as it depends from claim 11 recites

> A process for inducing and maintaining analgesia in a human being by the transdermal administration of [fentanyl base] which comprises:
> transdermally administering to said human being through an area of intact skin,
> a skin permeable form of said [fentanyl base] at an analgetically effective rate and continuing the administration of said [fentanyl base] to said human being at said rate for an extended period of time at least sufficient to induce analgesia;
> wherein said extended period of time is in the range of [at least about 3 days] to seven days.

(emphasis added). Claim 59 as it depends from claim 15 is identical to the above claim, but adds the further limitation "wherein the steady state administration rate of said [fentanyl base] is maintained within the range of about 25 to 150 µg/hr for a substantial portion of said [at least about 3 days]." Claim 61 as it depends from claim 31 recites

[3] At oral argument, both parties conceded that this case will be moot after this date.

> A medical device for inducing and maintaining analgesia in a human being by the continuous transdermal administration to a human being of [fentanyl base] at an analgetically effective administration rate and [for at least about 3 days] comprising, in combination:
> (a) a reservoir for said [fentanyl base] having a skin proximal, material releasing surface area in the range of about 5-100 cm^2, said reservoir containing between 0.1 and 50% by weight of a skin permeable form of said [fentanyl base] in amounts and at a concentration adequate to permit delivery of said [fentanyl base] through the intact [skin] of said human being at a flux within the range of from 0.5 to 10 $\mu g/cm^2/hr$ for at least about 24 hours; and
> (b) means for maintaining said reservoir in material transmitting relationship to said skin.

(emphasis added). Claim 27 as it depends from claim 25 recites

> A medical device for the transdermal administration to a human being of [fentanyl base] at an analgetically effective rate for an extended period of time of at least about 24 hours and sufficient to induce and maintain analgesia which comprises:
> (a) reservoir means containing a skin permeable form of [fentanyl base] in an amount sufficient to deliver said [fentanyl base] at said analgetically effective rate for said extended period of time; and
> (b) means for maintaining said reservoir means in material transmitting relationship to an area of intact skin on said human being,
> wherein said area is in the range of about 5-100 cm^2 and the device delivers said [fentanyl base] through the skin of said human being at a flux within the range of about 0.5 to 10 $\mu g/cm^2/hr$.

(emphasis added).

The claim term at issue here is "skin permeable form." The parties initially agreed on the definition of "skin permeable form": "fentanyl that is in a form that can pass through the skin." However, at trial the district court determined that this definition was not sufficiently precise to answer the questions relevant to the litigation. Accordingly, the court modified the parties' definition of the claim limitation and construed it to mean "fentanyl that is in a form that can pass through the skin, excluding solutions of fentanyl citrate." In view of this construction, the court found that Mylan's

ANDA for a transdermal fentanyl patch was an act of infringement.[4] The court next determined that the Keith reference did not anticipate the '580 patent, because the form of fentanyl that was taught in that reference (fentanyl citrate) was expressly disclaimed by the inventors of the '580 patent in the specification and during the patent's prosecution. Further, the court concluded that the '580 patent would not have been obvious because Mylan had not shown a reason, suggestion, or motivation to combine the teachings of Keith with any reference that teaches one to use the base form of the drug in solution. Finally, in addressing Mylan's contentions of inequitable conduct, the district court found that there was one statement in the declaration submitted by Gale during the second reexamination proceeding that, "although literally true, had the potential to mislead the patent examiner." Id. at 59. However, the court held that it "[could] not find that Gale acted with the requisite deceitful intent." Id. at 60.

Mylan appeals these findings, and we have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

II

Claim construction is an issue of law that we review de novo. Liquid Dynamics Corp. v. Vaughan Co., 355 F.3d 1361, 1367 (Fed. Cir. 2004). Anticipation, on the other hand, is a question of fact and after a bench trial is reviewed under the clearly erroneous standard. Merck & Co. v. Teva Pharms. USA, Inc., 347 F.3d 1367, 1369 (Fed. Cir. 2003). Additionally, a district court's finding of obviousness is reviewed de novo, with any underlying factual findings reviewed for clear error. Winner Int'l Royalty Corp. v. Wang, 202 F.3d 1340, 1348 (Fed. Cir. 2000). Finally, we review a district

[4] Mylan did not appeal this finding of infringement.

court's conclusions on inequitable conduct for an abuse of discretion and its threshold findings on materiality and intent for clear error. Brasseler U.S.A. v. Stryker Sales Corp., 267 F.3d 1370, 1379 (Fed. Cir. 2001).

III

A

In determining the meaning of disputed claim language, a court looks first to the intrinsic evidence of record, examining, in order, the claim language itself, the specification, and the prosecution history. Interactive Gift Express, Inc. v. Compuserve, Inc., 256 F.3d 1323, 1331 (Fed. Cir. 2001) (citing Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996)).

The parties had agreed upon the construction of the term "skin permeable form": "fentanyl that is in a form that can pass through the skin." However, in its claim construction following trial, the district court modified this construction by adding the phrase "excluding solutions of fentanyl citrate."

Here, the term "skin permeable form" when referring to fentanyl base is not plain on its face to one of ordinary skill in the art. As the district court explained, "the base form of fentanyl has been generally described as the skin permeable form of the drug." As such, if "skin permeable form of fentanyl" simply means "the base form of fentanyl," the inclusion of the word "base" in the claims would be redundant. Additionally, "skin permeable" is sometimes used by scientists to refer to flux, the rate at which a drug passes through the skin, and sometimes used to refer to the permeability coefficient, the relationship between flux and the concentration of the drug. Accordingly, the claim term "skin permeable form" is not plain on its face. We, therefore, must look to the

specification and prosecution history to see if they shed any light on what is meant by the term "skin permeable form" in the '580 patent.

The specification states

> We have discovered that fentanyl citrate, the form in which fentanyl is presently administered, has such a low skin permeability that it is not at all suitable for transdermal delivery even with the use of permeation enhancers. Instead we have found that, in order to obtain the delivery rates noted above, the drug should be incorporated in the transdermal therapeutic system in the form of the base.

'580 patent, col. 33, ll. 10-17. This clearly demonstrates to one of ordinary skill in the art that fentanyl citrate (the acidic form of the drug) is not a skin permeable form of fentanyl in the context of the invention of the '580 patent.

The prosecution history confirms that fentanyl citrate is not a skin permeable form of fentanyl as used in the claims. When the Keith reference was before the examiner during the second reexamination proceeding, Gale submitted a declaration detailing the differences between the reference and the claimed invention. Gale explained that Keith taught the production of a diffusion matrix containing fentanyl citrate, which the inventors of the '580 patent had expressly disclaimed:

> [In describing possible diffusion matrices, the Keith patent] teaches that an "appropriate" amount of fentanyl, which is a basic substance, could be either (1) an amount of fentanyl that would not cause the pH of the matrix to increase above 7 or (2) any amount of fentanyl as long as the pH of the matrix is adjusted to 6.5 to 7 with citric acid. Thus, without trying to ascertain a specific quantity of fentanyl that would constitute an "appropriate" amount, I believe it is clear that the disclosure of the Keith patent requires that the fentanyl be present in the matrix at a pH no greater than 7. . . . Because fentanyl has a pK of 8.3, the fentanyl present in the Keith et al. matrix would exist virtually completely in the form of fentanyl citrate. As a result, to the extent that the Keith patent could be considered to disclose making a transdermal fentanyl delivery system by including fentanyl in the diffusion matrices of the Keith patent, such a system would be unsuitable for administering fentanyl at analgetically effective rates. . . . The '580 patent at col. 3, lines 6-14 and col. 1, lines

> 22-25 discloses that the only form of fentanyl that was then being used for medical purposes, fentanyl citrate, is unsuitable for transdermal administration because of its low transdermal flux. . . . Thus, in contrast to our disclosure and claims in the '580 patent, the Keith patent suggests the production of a diffusion matrix containing fentanyl citrate, which we specifically stated in the '580 patent was unsuitable for transdermal delivery, even with permeation enhancers.

Gale Declaration, ¶¶ 8-11 (emphasis added).

Both the prosecution history and the specification disclaimed fentanyl citrate because it was unsuitable for transdermal administration and therefore not a "skin permeable form" of fentanyl. For this reason, we agree with the district court's claim construction of "skin permeable form" as "fentanyl that is in a form that can pass through the skin, excluding solutions of fentanyl citrate."

Mylan and Alza argue this case as if the district court had construed the term "skin permeable form" to mean a fentanyl solution with a pH higher than 7.5. However, it did not. The court simply stated that the skin permeable form excluded fentanyl citrate without restricting that term to any particular range of pH values.

All of Mylan's arguments on claim construction are directed to a purported pH level determined by the district court. However, as we just explained, the district court placed no pH limitation on its construction of "skin permeable form." Mylan contends that the district court's claim construction is contrary to the plain meaning of the term "skin permeable form" and asserts that the proper construction of the term is "fentanyl that is in a form that can pass through the skin," which could include fentanyl citrate

solutions.[5] However, as demonstrated above, such a construction is contrary to the '580 patent's specification and prosecution history's clear disavowal of fentanyl citrate.

Finally, we are not persuaded by Mylan's argument that the district court's construction is inconsistent with the specification. Mylan asserts that because Alza's own data shows adequate flux is obtainable from fentanyl citrate solutions, this somehow disproves the discussion in the specification about the low skin permeability of fentanyl citrate. Alza points out, however, that this argument assumes that "skin permeability" in the specification refers to the flux, which is the rate at which a product flows through the skin, and not to the relationship between that flux and concentration (the "permeability coefficient").[6] The record supports Alza's contention that the discussion of skin permeability in the specification is not about the flux at which the product flows through the skin, but rather the permeability coefficient. Mylan also asserts that this claim construction excludes preferred embodiments disclosed in the patent. Mylan cites no evidence to support its assertion and only speculates based on the Keith matrix which was buffered.[7] Thus, we are unpersuaded by this argument.

B

[5] This is based on the premise that regardless of whether a fentanyl solution contains primarily fentanyl in the base form or primarily fentanyl in the acidic form, it is the base form of the drug that will actually permeate the skin.

[6] Flux describes the rate at which a drug will pass the skin, whereas permeability coefficient describes that rate in proportion to concentration. ("[F]lux, which is the amount that would go through the skin, . . . equals the permeability coefficient times the concentration." Trial Transcript, August 29, 2003, at 85.)

[7] A buffered solution is one that resists a change in pH upon addition of a small amount of acid or base. As such, when adding small amounts of fentanyl base to a solution buffered to remain around pH 7.0, as in the Keith patent, the pH would not be expected to change much, if at all. Such an addition would, however, likely have an effect on an unbuffered solution, such as that taught in the '580 patent.

The district court found that the Keith patent did not teach the claim limitation "skin permeable form," and therefore could not anticipate the claims of the '580 patent. We agree.

As we have stated above, the term "skin permeable form" in the context of the '580 patent is fentanyl that is in a form that can pass through the skin, excluding solutions of fentanyl citrate.

However, the specification of the '580 patent illustrates various solutions considered to be fentanyl citrate. Specifically, in the specification the patentees characterize the form in which fentanyl is "presently administered" as fentanyl citrate. The specific solution referred to is Sublimaze®, a fentanyl citrate solution with a pH of 4 to 7.5. '580 patent, col. 1, ll. 19-23 (citing Physician's Desk Reference 1027-29 (1984)). As such, the specification identifies at least one pH range to explain fentanyl solutions considered to be fentanyl citrate and therefore excluded from the invention. Additionally, in the Gale declaration, the inventors expressly disclaimed the solutions taught by the Keith reference, explaining that the fentanyl present in the Keith matrix would exist virtually completely in the form of fentanyl citrate, because it would have a pH of approximately 7, which was expressly stated as unsuitable for transdermal delivery of fentanyl.

Because the Keith reference teaches adjusting solutions to a pH of 6.5-7.0, it clearly teaches a fentanyl citrate solution that was expressly disclaimed by the '580 patent's inventors. Accordingly, because the Keith reference did not disclose a "skin permeable form" of fentanyl within the meaning of the '580 patent and that limitation

was in each of the asserted claims, the Keith reference does not anticipate the '580 patent.[8]

C

The district court found that "Mylan had not shown a reason, suggestion or motivation to combine the teachings of Keith, to use solutions of fentanyl citrate . . . with any reference that teaches one to use the base form of the drug in solution." Alza, slip op. at 48. We agree. The Keith reference specifically teaches a solution that is approximately 95% fentanyl citrate and only 5% fentanyl base. Indeed, the reference teaches adjusting the solution's pH value to levels that necessarily achieve such a solution. Michaels taught that high solubility in water and oil is a desirable feature for a transdermally delivered drug, therefore suggesting that fentanyl would not be a good transdermal candidate due to its low solubility. As such, Michaels even teaches away from using fentanyl transdermally. We agree with the district court's analysis of the prior art references of record and find that Mylan did not produce evidence of the combinability of those references with the Keith patent to result in the claimed invention of the '580 patent. Mylan's arguments on appeal again rest on the premise that the district court's claim construction is incorrect. Those arguments are moot in view of our affirmance of the district court's claim construction.[9]

[8] Whether other claim limitations are anticipated by the Keith patent was also in dispute in this case. However, because we find that the skin permeable form limitation was not met, we need not consider the other limitations. Additionally, Mylan's enablement arguments are moot in view of our determination that the Keith patent is not an anticipatory reference.

[9] Because Mylan has not made a prima facie case of obviousness, we need not address the parties' assertions regarding the district court's discussion of secondary considerations.

D

Mylan's final challenge on appeal is to the district court's finding of no inequitable conduct. In order to prove inequitable conduct, Mylan must provide clear and convincing evidence of "affirmative misrepresentations of a material fact, failure to disclose material information, or submission of false material information, coupled with an intent to deceive." Purdue Pharma L.P. v. Boehringer Ingelheim GmbH, 237 F.3d 1359, 1366 (Fed. Cir. 2001) (quoting Baxter Int'l, Inc. v. McGaw, Inc., 149 F.3d 1321, 1327 (Fed. Cir. 1998)).

Mylan asserted that Gale engaged in inequitable conduct before the United States Patent and Trademark Office. Specifically, Mylan pointed to seven statements in Gale's declaration during the second reexamination proceeding which it asserted were false and misleading. The district court found that only one of these statements had the potential to be misleading but then examined the totality of the circumstances and found that Gale lacked the requisite intent to deceive in order to find inequitable conduct. Mylan appeals only as to this statement which recites:

> Skin permeability studies conducted by Alza researchers provided the basis for the comments in the '580 patent (col. 3, lines 10-14) regarding the low skin permeability of fentanyl citrate and its unsuitability for transdermal administration. Data generated in these studies supported the conclusion that the skin permeability of fentanyl citrate was too low to permit analgetically effective transdermal fentanyl administration rates to be obtained from reasonably sized transdermal systems.

Dale Decl. at ¶ 12 (emphasis added).

The district court found that the statement was literally true, because the studies did support the researcher's conclusions that they should proceed with a base form of fentanyl because a citrate form would not meet their goals of maximum flux with minimal

total drug. The court went on to say, however, that it had the potential to mislead the examiner, because it was technically possible to use the Keith patent to create a fentanyl transdermal system (albeit one that "might not have been pretty," Alza, slip op. at 58). On the question of intent, the court held "in light of all the circumstances, the Court cannot find that Gale acted with the requisite deceitful intent when he failed to point out that the data he submitted to the patent examiner included values that would suggest that one could also achieve an adequate flux in a transdermal system that used a sufficiently large amount of fentanyl citrate." Id. at 60. We discern no clear error or abuse of discretion in the district court's findings and conclusions. Nothing Mylan argues persuades us otherwise. Indeed, as the court stated, "[i]n context, the statements in Gale's declaration were true. No information was omitted. No information was affirmatively misstated." Id. Gale's declaration simply focused on the key distinctions between his patent and the Keith patent -- that Keith taught the use of a neutral or slightly acidic solution of fentanyl, which made it an unsuitable system for the administration of fentanyl in Gale's opinion, as stated in the '580 patent. Additionally, the district court had the benefit of observing Gale's testimony on direct, as well as cross-examination, and was able to question Gale himself prior to making a determination as to Gale's credibility. On the record before us we will not overturn the trial court's decision.

IV

We affirm the district court's construction of the claim limitation "skin permeable form" and its determinations that the '580 patent was neither anticipated nor obvious by

the Keith patent. Additionally, we affirm the district court's holding that the '580 patent was not unenforceable due to inequitable conduct.

AFFIRMED

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Defendants-Appellants.

DYK, Circuit Judge, concurring-in-part and dissenting-in-part.

I agree with the majority that the patentee effectively disclaimed coverage of the Keith patent in the specification of the '580 patent, and that the Keith patent does not anticipate. However, I write separately because I cannot agree with the majority's affirmance of the district court's finding of no inequitable conduct.

I

Claim 59 as it depends from claim 11 includes the claim language at issue and states:

> A process for inducing and maintaining analgesia in a human being by the transdermal administration of [fentanyl base] which comprises
> transdermally administering to said human being through an area of intact skin,
> a skin permeable form of said [fentanyl base] at an analgetically effective rate and continuing the administration of said [fentanyl base] to said human being at said rate for an extended period of time at least sufficient to induce analgesia

> wherein said extended period of time is in the range of [at least about 3 days] to seven days.

'580 patent (emphasis added). At issue is whether the prior art Keith patent discloses the "skin permeable form" limitation. The Keith patent discloses a transdermal patch using a solution of fentanyl citrate. While the fentanyl citrate itself is not skin permeable, such a fentanyl citrate solution also includes some amount of fentanyl base, which is skin permeable. The patentee's contention is that the pH of the Keith solution, which is directly related to the proportion of base and citrate in the solution, is not covered by the patent.

Conspicuously absent from the claims of the patent is any sort of pH limitation. The majority nonetheless finds that there is such a limitation in the patent. First, the majority, like the district court, construes the disputed limitation "skin permeable form" as meaning "fentanyl that is in a form that can pass through the skin, excluding solutions of fentanyl citrate." Ante at 9. The claim language itself does not exclude "solutions of fentanyl citrate." The majority gets to the exclusion of "solutions of fentanyl citrate" by finding a disclaimer in the specification, which states:

> We have discovered that fentanyl citrate, the form in which fentanyl is presently administered, has such a low skin permeability that it is not at all suitable for transdermal delivery even with the use of permeation enhancers. Instead we have found that, in order to obtain the delivery rates noted above, the drug should be incorporated in the transdermal therapeutic system in the form of the base.

'580 patent, col. 3, ll. 10-17 (emphasis added). The majority concludes that fentanyl citrate was at the time administered by intravenous solution or infusion solution. The question then becomes: what at the time was considered to be a solution of "fentanyl citrate?" The majority determines that such solutions are appropriately defined by their

pH. The patent contains a reference to Sublimaze®, the FDA-approved form of fentanyl citrate, stating that fentanyl's "use as approved by the FDA in the United States is described in the 1984 Physician's Desk Reference, pages 1027 through 1029 with reference to the drug SUBLIMAZE® manufactured by McNeil Lab for Janssen Pharmaceutica, Inc." Id. at col. 1, ll. 18-22. The referenced Physician's Desk Reference described Sublimaze® as "(fentanyl) as the citrate" and described the use of "[s]odium hydroxide for adjustment of pH to 4.0-7.5." (J.A. at 7381.) The majority concludes that the then-presently-administered form of fentanyl citrate thus had a pH of 4.0 to 7.5. A pH within or below that range is thus disclaimed. Since the solution disclosed in Keith had a pH of 6.5 to 7.0, Keith does not anticipate.

This analysis seems to me to be correct and to lead to a finding of no anticipation. I am troubled, however, by the majority's reliance on the admittedly misleading Gale declaration to support this result. Indeed, I think that the Gale declaration raises substantial questions of inequitable conduct.

II

The declaration of Gale, one of the inventors, was submitted by the patentee during reexamination to support patentability over the newly disclosed Keith reference. It stated, in pertinent part:

> 9. Because fentanyl has a pK of 8.3 [sic], the fentanyl present in the Keith et al. matrix would exist virtually completely in the form of fentanyl citrate. As a result, to the extent that the Keith patent could be considered to disclose making a transdermal fentanyl delivery system by including fentanyl in the diffusion matrices of the Keith patent, such a system would be unsuitable for administering fentanyl at analgetically effective rates.
>
> 10. . . . The '580 patent at col. 3, lines 6-14 and col. 1, lines 22-25, discloses that the only form of fentanyl that was then being used for

> medical purposes, fentanyl citrate, is unsuitable for transdermal administration because of its low transdermal flux. . . .
>
> 11. Thus, in contrast to our disclosure and claims in the '580 patent, the Keith patent suggests the production of a diffusion matrix containing fentanyl citrate, which we specifically stated in the '580 patent was unsuitable for transdermal delivery, even with permeation enhancers.

Gale Declaration ¶¶ 9-11 (emphases added). The declaration went on to explain the basis for Gale's belief that a fentanyl citrate system is unsuitable:

> 12. Skin permeability studies conducted by ALZA researchers provided the basis for comments in the '580 patent (col. 3, lines 10-14) regarding the low skin permeability of fentanyl citrate and its unsuitability for transdermal administration. Data generated in these studies supported the conclusion that the skin permeability of fentanyl citrate was too low to permit analgetically effective transdermal fentanyl administration rates to be obtained from reasonably sized transdermal systems. Copies of laboratory notebook entries documenting these studies are attached as Exhibit 2.

Gale Declaration ¶ 12 (emphasis added). Focusing on the underscored portion of paragraph 12, the district court found that "[t]he statement, although literally true, had the potential to mislead the patent examiner." Alza Corp. v. Mylan Labs., No. 2:02-cv-20, 2:02-cv-213, slip op. at 59 (D. Vt. Mar. 25, 2004) There would seem to be no basis for finding the statement "literally true." The data in the studies showed that solutions with a pH of 6.5 to 7.0 would work. The district court specifically credited Gale's trial testimony that the skin permeability of fentanyl at the pHs taught by Keith would in fact "'permit analgetically effective transdermal fentanyl administration to be obtained from reasonably-sized transdermal systems.'" Id. at 58. The district court concluded that "[a] Keith fentanyl transdermal system might not have been pretty, it might not have been marketable, it might have contained massive amounts of residual drug, but it could have gotten an analgesic dose of fentanyl across an area of skin." Id. at 58-59.

The majority, agreeing with the district court, suggests that the district court found the statement to be "literally true, because the studies did support the researcher's conclusions that they should proceed with a base form of fentanyl because a citrate form would not meet their goals of maximum flux with minimal total drug." Ante at 13-14. But the statement in the Gale declaration has nothing to do with the patentee's concerns with the amount of drug ("minimal total drug") being used. It relates only to the unworkability of the Keith disclosure.

III

The district court also found that Gale's misleading statement "was material; the patent examiner based his decision to issue the reexamination certificate on the fact that 'the citrate form of fentanyl has a very low level of transdermal permeability.'" Alza, slip op. at 59. However, the district court, having found that the patentee made a materially misleading statement during reexamination, concluded that there had been no showing of intent, a finding which the majority sustains. That conclusion in my view rests on an entirely erroneous factual predicate—that the patentee's statement was "true." Id. Indeed, the district court explicitly found "that as of 1998 when his declaration was submitted, [Gale] knew that the data also showed that fentanyl, at the pHs taught by the Keith patent, would in fact have high enough skin permeability" to make an analgetically effective, reasonably-sized transdermal system. Id. at 58. I conclude that a remand is necessary to reconsider the issue of intent, particularly since the district court appears to have found that Gale himself knew that the statement was false, and some of the district court's other grounds for finding a lack of intent are problematic at best.

The district court found lack of intent because the patentee requested reexamination based on the Keith patent; the question is not whether the patentee has bad intent before the reexamination, but whether it had bad intent during the reexamination—in concealing the true nature of the Keith disclosure. The district court's reliance on the disclosure of the data underlying the Gale declaration (the Lee data) is also questionable. We have held that a patentee knowing of a misrepresentation made during prosecution cannot cure that misrepresentation by merely supplying "the examiner with accurate facts without calling his attention to the untrue or misleading assertions sought to be overcome." Rohm & Haas Co. v. Crystal Chem. Co., 722 F.2d 1556, 1572 (Fed. Cir. 1983). Here, the patentee made an untrue assertion and simultaneously submitted accurate facts not in accord with that assertion. Such a submission of accurate facts does not cure a false statement.

Therefore, contrary to the majority, I would set aside the district court's decision and remand for further factual findings on the intent component of inequitable conduct.