No. 08-937

MAR 27 2009

IN THE

Supreme Court of the United States

AVENTIS PHARMA S.A.
and AVENTIS PHARMACEUTICALS, INC.,

Petitioners,

v.

AMPHASTAR PHARMACEUTICALS, INC.
and TEVA PHARMACEUTICALS USA, INC.,

Respondents.

ON PETITION FOR A WRIT OF CERTIORARI TO THE
UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

BRIEF IN OPPOSITION FOR RESPONDENT AMPHASTAR PHARMACEUTICALS, INC.

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QUESTION PRESENTED

The question the petition purports to present was not timely raised below and is not presented by the facts in this case. The district court heard the evidence, made credibility determinations, and specifically found that (a) Aventis intended to deceive the Patent and Trademark Office ("PTO") and (b) "negligence played no role" in the deception. Based on those findings and an earlier determination (not challenged here) that the information that Aventis misrepresented and concealed from the PTO was highly material to patentability, the district court held that Aventis' patent was unenforceable due to inequitable conduct. The Federal Circuit affirmed, finding no clear error in the district court's fact findings and credibility determinations and no abuse of discretion in the ultimate determination of inequitable conduct. The questions actually presented are:

(1) Did the district court commit clear error in finding that Aventis intended to deceive the PTO?

(2) Did the district court abuse its discretion in holding Aventis' patent unenforceable due to inequitable conduct, given Aventis' intent to deceive and the high materiality of the deception?

STATEMENT PURSUANT TO RULE 29.6

Respondent, Amphastar Pharmaceuticals, Inc., has no parent corporation and no publicly held company owns 10% or more of its stock.

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STATEMENT OF THE CASE

This case involved Aventis' intentional, affirmative misrepresentation that the low molecular weight heparin ("LMWH") compounds disclosed in its '618 patent have a "significantly" greater half-life than the LMWHs claimed in prior art European Patent No. 40,144 ("EP 40,144").[1] App. 8a, 10a, 43a-45a, 57a, 59a. The undisputed evidence at trial established that there was no difference in half-life when the compositions were compared at the same dose. App. 45a, 73a.[2] This was readily apparent to Aventis and Dr. Uzan. App. 74a; *see* Appendix to the Federal Circuit Court of Appeals

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[1] Aventis states at p. 2:28-3:1 of its petition, that it invented novel compositions of low molecular weight heparins ("enoxaparin") which were the subject of the '618 patent. The full enoxaparin story did not begin with the '618 patent. Rather, an Aventis scientist by the name of Jean Mardiguian first developed enoxaparin in the early 1980s. Aventis applied for a patent based upon Mardiguian's work in France in 1980. App. 41a-42a, 111a-112a. Aventis filed related applications in Europe and the United States. The European patent application issued as E.P. 40,144 and the related United States application was abandoned. App. 5:7-9; C.A. App. 4064-65.

[2] The contention that the '618 patent disclosed different compositions from E.P. 40,144 was dubious from the outset. The '618 patent used the same three step manufacturing process disclosed in the E.P. 40,144 patent (i.e. salification, esterification, and depolymerization of porcine heparin. (*Compare* C.A. App. 253, Col. 5:4-53 ('618 disclosure) *with* C.A App. 4052, 4054-55 (E.P. 40,144 disclosure). The resulting low molecular weight heparins had the same chemical structure (C.A. App. 10474:12-21) and, as admitted, exhibited no significant difference in half-life when compared at the same dose (App. 73a-74a). *See also infra* note 3.

("C.A. App.") 10084, 10136. Nevertheless, Aventis and Dr. Uzan repeatedly and affirmatively misrepresented that their experimental data showed that the claimed compositions had "significantly" higher half-life. App. 8a, 10a, 43a-45a, 57a, 59a. Not only did Aventis and Dr. Uzan affirmatively misrepresent there was a difference in half-life; they intentionally omitted the dosage information in data given to the PTO that would have revealed the true fact that they were comparing the compositions at different doses and that a same-dose comparison showed no difference in half-life. App. 84a. Thus, this is a case at the extreme end of violating the duty of candor owed by applicants to the PTO. This case involves a party deceiving the PTO into issuing a patent through the knowing falsification of experimental data and through affirmative, highly material misrepresentations regarding that data coupled with the intentional concealment of the known true facts. App. 89a-90a.[3]

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[3] As mentioned in note 1, *supra*, Aventis abandoned its related U.S. application to the E.P. 40,144 patent. Thus, when it came time to market enoxaparin in the United States, Aventis realized that it did not have "market protection." App. 112a; C.A. App. 1895, 4064-65, 10021:9-10022:1. Aventis therefore filed a new patent application (which ultimately issued as the '618 patent), naming Roger Debrie as the inventor, covering the same drug covered by the earlier E.P. 40,144 patent. At the same time that Aventis was contending that the '618 patent covered a new drug during the prosecution of the '618 patent in the United States, Aventis was representing to the French Patent Office that the French precursor to E.P. 40,144 covered enoxaparin in order to obtain a patent term extension in France. C.A. App. 4005. Thus, at the same time Aventis was representing to different government entities that two different patents filed nearly ten years apart covered the same drug.

1. The Proceedings Below Specifically Focused on an Intent to Deceive

Aventis' suggestion that the district court and Federal Circuit wrongly applied a negligence standard in finding inequitable conduct in this case is meritless in light of the proceedings below.

Inequitable conduct was first found on summary judgment by District Judge Timlin. App. 46a, 128a-142a. In so holding, Judge Timlin expressly found an intent to deceive. App. 137a-141a. Aventis appealed, contending that summary judgment was not appropriate on the issue of intent to deceive. App. 46a-47a. Rather, Aventis argued that it was necessary to view Dr. Uzan's live testimony in order to evaluate his credibility and the reasonableness of his explanation. App. 47a, 106a. The Federal Circuit panel affirmed Judge Timlin's ruling that the information at issue was highly material to patentability and agreed that an intent to deceive could reasonably be inferred from the evidence, but held that a trial was needed to determine if Dr. Uzan's innocent explanations for his conduct were credible. App. 46a, 109a.[4]

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[4] Notably, Judge Rader, who dissented in the second appeal, joined the opinion in the first appeal. At page 5:16-22 of the petition, Aventis misstates the holding of the Federal Circuit on the first appeal by contending that as "the party charged with inequitable conduct—[Aventis] was required to demonstrate its innocence in order to prevent a finding of deceptive intent. . . ." The Federal Circuit made no such holding. Rather, the Federal Circuit merely found that Aventis, as the non-movant on a motion for summary judgment, had to raise a genuine issue of material fact. App. 106a; *accord Anderson v. Liberty Lobby Inc.*, 477 U.S. 242, 248 (1986).

On remand, a different district judge (Judge Pfaelzer) followed the Federal Circuit's mandate, held trial on the specific issue of intent to deceive, and found that Aventis did indeed intend to deceive the PTO. App. 40a, 48a.

The entire purpose of the trial on remand was to address the issue of intent to deceive by viewing Dr. Uzan's live testimony. App. 40a, 78a-79a, 86a. After seeing and hearing Dr. Uzan's live testimony, the district court found:

> [B]ased on the totality of the facts and circumstances surrounding Dr. Uzan's repeated omissions, the Court hereby finds the Defendants have shown by clear and convincing evidence that Dr. Uzan intended to deceive the PTO.

App. 90a. Importantly, the district court did not simply leap to a conclusion of intent to deceive. The district court made detailed findings of fact and credibility determinations before specifically finding an intent to deceive. It found:

- The keystone of Aventis' strategy for overcoming the PE's rejections was to distinguish the '618 compositions from the E.P. 40,144 composition based upon their superior half-life. App. 43a; *see* App. 56a-63a; App. 58a ("Aventis attacked sameness based on a difference in properties.").
- Aventis directed the PE to the half-life study of Example 6 of the '618 patent to support Aventis' claims of superior half-life. *Id.*; *see* App. 57a

(quoting Aventis to the PTO) ("[I]t *necessarily follows* that the formulations of the invention could not possibly be the same as those of the European patent. As is notoriously well established, *compounds and their properties are inseparable* and thus, when two compounds exhibit different properties it follows that they *must necessarily be of different structure.*") (emphasis added).[5]

- Throughout the patent prosecution, Aventis and Dr. Uzan affirmatively represented that Example 6 "clearly demonstrate[d]" that the '618 compositions had a significantly longer half-life than the E.P. 40,144 compositions. App. 45a, 59a (quoting Dr. Uzan) ("[Example 6] represents an increase in 250% in half-life and is very significant . . . .").

- Dr. Uzan had compared a 60 mg dose study of the E.P. 40,144 compositions to a 40 mg dose study of the '618 compositions and at no time did Aventis or Dr. Uzan disclose at what dosage the half-life study in subparagraph (3) of Example 6 had been made. *Id.*

- There was no statistically significant difference in half-life when the E.P. 40,144 compositions when compared to the '618 compositions at the

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[5] At pages 3:35-4:2 and 8:9-16 of its petition, Aventis misleadingly contends that Example 6 was intended only to illustrate the "increase in stability" of the '618 compositions over the E.P. 40,144 compositions and not compositional difference. As the district court correctly found, however, it was Aventis who specifically used Example 6 to establish compositional difference during the prosecution of the '618 patent.

same dose, and Aventis and Dr. Uzan "cherry picked" the data selecting the one dose permitting a favorable comparison to E.P. 40,144. *Id.*; App. 74a; *see* App. 73a ("Only the 40 mg dose showed a statistically significant difference over E.P.'144.").[6]

- The different dose comparison was "incapable of proving anything at all about the relative half-lives of the '618 and E.P. '144 LMWHs . . . ." App. 83a; *see* App. 86a ("[The different dose comparison] "could not prove anything the PE wanted to know.").

- Dr. Uzan's prosecution history declarations showed that Dr. Uzan knew the materiality of the misrepresentations he was making to the Examiner. It was "Dr. Uzan's goal" to prove a difference in properties to overcome the examiner's objections, and it was "inconceivable that this fact was unclear to Dr. Uzan." App. 81a ("The language of his First Declaration . . . declares his familiarity with the Second Office Action . . . . The Second Declaration . . . also demonstrates that Dr. Uzan knew the problem of insufficient proof of statistical significance was among [the Examiner's] objections.").

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[6] The Duchier study, from which Dr. Uzan obtained the half-life data relating to the '618 compositions, measured half-life as 20 mg, 40 mg, 60 mg, and 80 mg doses. App. 69a. It was undisputed that there was no statistical difference in half-life between the E.P. 40, 144 compositions when they are compared to the 20 mg, 60 mg, and 80 mg dose studies for the '618 patent. App. 73a-74a. Thus, Aventis and Dr. Uzan cherry-picked the only dose comparison – a different dose comparison of 40 mg to 60 mg – that showed any difference at all. App. 74a.

- "Put simply, Dr. Uzan knowingly gave the PE a narrow answer to her broad question, and then represented that in so doing he had answered her question broadly." App. 83a.[7]

At pages 7-8 of its Petition, Aventis misleading suggests that the district court did not make any finding that Dr. Uzan knew about the materiality of his misrepresentations and omissions. Aventis' Petition for Certiorari ("Pet.") at 7-8. "Regarding knowledge," Aventis refers only to the district court's finding that "Dr. Uzan admitted to knowing that he was comparing the half-lives . . . at different doses." *Id.* at 7. Aventis argues that this fact is of "limited significance." Aventis then argues at page 8 that the district court was "effectively eliminating the requirement that the patent applicant have actual knowledge that the omitted information is material . . . ." *Id.* at 8.

Aventis misleadingly ignores the district court's express finding that Dr. Uzan also knew of the materiality of his misrepresentations and omissions as evidenced by Dr. Uzan's prosecution history declarations. App. 81a. Further, Aventis does not cite this Court to any evidence or testimony from Dr. Uzan that Dr. Uzan did not know the materiality of his misrepresentations and omissions. Thus, there is simply no evidentiary support for any argument from Aventis that the district court's findings of knowledge of materiality were clearly erroneous.

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[7] At page 3:18-22 of its petition, Aventis states that Respondents premised their case on a simple omission made by Dr. Uzan. As can be seen from the district court's decision, Respondents presented a great deal more evidence of intent to deceive than Aventis claims.

The district court also expressly found that "[n]egligence played no role in Aventis and Dr. Uzan's failure to disclose the E.P. '144 dose information." App. 89a. Again, the district court painstakingly made specific findings of fact regarding the absence of negligence. The district court found:

- Aventis and Dr. Uzan concealed "any fact to the PTO even reflecting that a 60 mg dose of the Mardiguian E.P. '144 LMWH was compared" and any fact that would have ignited the examiner's suspicion that the half-life comparison was flawed. App. 84a.

- Aventis and Dr. Uzan also failed to disclose that a dose-ranging analysis was used, and that Dr. Uzan's was allegedly focused only on the prevention of deep vein thrombosis in high-risk patients undergoing orthopedic surgery. Dr. Uzan selected the "clinically relevant dose," and he believed that half-lives of the compositions were dose independent. Example 6 was not "a well-controlled prospective trial, but a meta-analysis comparing data from three different studies performed for three different purposes at three different times."[8]

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[8] Example 6 was misleadingly written as reporting a single well-controlled study. Example 6 began by reporting the results of a "first pharmacokinetic study." Subparagraph (2) stated that the comparison is made "under identical dosage conditions." App. 43a-44a n.3. Subparagraph (3) used half-life data at 4.5 hours, the same time used for the 40 mg dose studies of the '618 compositions whereas the 60 mg study for the claimed composition used 3.7 hours clearly leading to the conclusion that the subparagraph (3) study was done at 40 mg. *Id.*

The district court rejected Dr. Uzan's "clinically relevant dose excuse," holding that it suffered from "a total absence of indicia of credibility." App. 88a-89a.[9] The district court summed up its analysis by finding that "[c]onsistently omitting so many references involves the application of diligence, not the commission of negligence." App. 85a.

Aventis then appealed. The Federal Circuit applied the proper standard of review and found no clear error in the district court's findings of fact and credibility determinations. The Federal Circuit found that the evidence supported a finding of an intent to deceive:

> Here, however, in contrast to any inadvertent omissions made during prosecution, there is sufficient evidence of concealment to warrant a determination that the dose information was intentionally withheld.

App. 30a.

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[9] At page 3:30-35 of its petition, Aventis attempts to downplay Dr. Uzan's involvement in the preparation and prosecution of the '618 patent. This is another late shift in position. Aventis relied heavily on Dr. Uzan in both the preparation and prosecution of the '618 patent and the proceedings below. Dr. Uzan's Example 6 and his declarations were the only source of data used to overcome the examiner's rejections. App. 44a-45a. Indeed, the named inventor, who Aventis did not use as a prosecution expert, did not agree with Dr. Uzan's different dose comparison, testifying that it was "meaningless." App. 67a n.12. Every other person at Aventis involved in the prosecution of the '618 patent claimed not to remember anything about the preparation of the patent application or its prosecution. App. 78a n.17.

In view of the procedural history of this case, and the express findings and rulings of the district court and Federal Circuit, there can be no doubt that the district court and Federal Circuit specifically found an intent to deceive.

2. Aventis Acknowledged Below That the District Court Specifically Found an Intent to Deceive

Though Aventis bases its petition on the contention that the district court applied a negligence standard in finding inequitable conduct in this case, Aventis did not make that argument on appeal to the Federal Circuit. Rather, Aventis repeatedly recognized that the district court had in fact found an intent to deceive. *See* Brief of Plaintiff-Appellants Aventis Pharma S.A. and Aventis Pharmaceuticals at 45, *Aventis Pharma S.A. v. Amphastar Pharmaceuticals, Inc.*, No. 07-1280 (Fed. Cir. May 14, 2008) ("The District Court Clearly Erred In Holding that Dr. Uzan Intended to Deceive the PTO"); *see also id.* at 58 (asserting that "the district court's ultimate holding of inequitable conduct . . . fatally hinges on the clearly erroneous finding that Dr. Uzan intended to deceive the PTO.") Instead, Aventis based its appeal on the contention that the district court committed clear error in finding an intent to deceive based upon the district court's supposed misunderstanding of the prosecution history. *Id.*; App. 18a-20a. The Federal Circuit rejected Aventis' argument, holding that the district court had not committed clear error regarding the prosecution of the '618 patent. App. 21a.

Aventis did not appeal on the ground that the district court's decision was based on negligence. Rather,

Aventis first raised this issue in its petition for rehearing, apparently following Judge Rader's dissent. Even then, Aventis did not make the arguments it makes here. In particular, Aventis did not argue that by finding that Dr. Uzan "knew or should have known" of the materiality of his misrepresentations and omissions the district court eliminated the requirement for an intent to deceive.[10]

Because the question Aventis presents was not timely raised it is not a proper basis for a petition for writ of certiorari. *See United States v. United Foods, Inc.*, 533 U.S. 405, 417 (2001) (refusing to consider arguments not pressed by petitioner below); *Adams v. Robertson*, 520 U.S. 83, 89 n.3 (1997) ("[W]e have

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[10] At page 9:23-30 of its petition, Aventis (again citing Judge Rader's dissent) also improperly suggests that the '618 patent is otherwise valid as evidenced by the PTO's decision to reissue it. As the Federal Circuit majority correctly pointed out, Judge Rader was mistaken regarding the timing of the reissue. App. 12a n.6. Further, the relevance of the reissue was extensively briefed by the parties before the district court. *See* C.A. App. 179-182 (Dkt. Nos. 666, 680, 687, 691, 695). Ironically, Aventis itself contended the reissue was irrelevant to inequitable conduct in order to preclude Amphastar from presenting additional evidence of inequitable conduct during the reissue proceedings. C.A. App. 131-135; *id.* at 4022:20-27 ("[W]hether Aventis committed inequitable conduct in obtaining the '618 patent will be the only issue on appeal. Amphastar's additional allegations of unenforceability based on the prosecution of the reissue patent are irrelevant to the appeal . . . ."). Thus, it is entirely improper for Aventis to even suggest at this late stage that the reissue somehow cured its inequitable conduct or otherwise evidences the validity of the '618 patent. *See Falls City Industries, Inc. v. Vanco Beverage, Inc.*, 460 U.S. 428, 436 n.7 (1983) (holding that issues waived below were not before the Court).

generally refused to consider issues raised clearly for the first time in a petition for rehearing when the state court is silent on the question."). We note that Aventis bears the burden of establishing that the issue raised in its petition was timely raised below. *Adams*, 520 U.S. at 86, 89 n.3.[11]

REASONS FOR DENYING THE PETITION

This case involved knowing affirmative misrepresentations of experimental data and fell at the extreme end of fraud that the courts have long found sufficient to compel patent unenforceability. Aventis and Dr. Uzan, deliberately cherry-picked experimental data to create the appearance of a material difference between a claimed composition and the prior art where none existed. Aventis and Dr. Uzan misleadingly presented data in the patent application itself to suggest that compositions were being compared at "identical dosages" when in fact they were not. These misleading data were then repeatedly and specifically used to overcome the Examiner's rejections.

Never once did Aventis or Dr. Uzan reveal the true dose information for the prior art half-life study or that a different dose comparison was being made. Rather, Aventis and Dr. Uzan affirmatively misrepresented that the false difference in half-life "necessarily" showed that the compositions were different, and that the difference was "statistically significant." App. 5a-11a, 42a-45a, 113a-115a; *see id.* at 100a-101a ("Given the centrality of the

[11] Having acknowledged that the district court found an intent to deceive on appeal and having not timely raised its current issues, the statement in the Petition that the Federal Circuit declined "the invitation to clean its own house" is particularly misplaced.

differences in half-lives to patentability, by failing to disclose that the difference in half-lives at the same dosage was actually lower, Aventis failed to disclose material information to the PTO."). Aventis and Dr. Uzan then offered an after-the-fact excuse that the district court found suffered "from a total absence of indicia of credibility." App. 78a, 88a.

The affirmative misrepresentations and omissions of fact in this case were knowingly false and intended to deceive the Patent Office into issuing a patent. As such, they were well within the type of wrongful conduct this Court has found sufficient to hold patents unenforceable due to inequitable conduct. *See Precision Instrument Mfg. Co. v. Auto. Maint. Mach. Co.*, 324 U.S. 806, 818-19 (1945); *Hazel-Atlas Glass Co. v. Hartford-Empire Co.*, 322 U.S. 238, 251 (1944); *Keystone Driller Co. v. Gen. Excavator Co.*, 290 U.S. 240, 245-47 (1933).

I. THE COURTS BELOW EXPRESSLY FOUND AN INTENT TO DECEIVE SEPARATE FROM MATERIALITY AND EXPRESSLY FOUND THAT AVENTIS AND DR. UZAN WERE NOT MERELY NEGLIGENT

Despite the district court's express credibility determinations and findings of fact, Aventis predicates its petition for certiorari on the contention that the district court failed to find an intent to deceive, but rather found inequitable conduct based upon high materiality applying either a strict liability or negligence standard. The argument is astonishing in view of the great pains that the district court took to make it clear that it was specifically finding an intent to deceive and that it was specifically not basing its decision on negligence.

The district court expressly held that "'[m]ateriality does not,' however, 'presume intent, which is a separate and essential component of inequitable conduct'" App. 49a (quoting *GFI, Inc. v. Franklin, Corp.*, 265 F.3d 1268, 1274 (Fed. Cir. 2001); *Manville Sales Corp. v. Paramount Sys., Inc.*, 917 F.2d 544, 552 (Fed. Cir. 1990)). The district court further recognized that "gross negligence is not, in and of itself, sufficient to satisfy the intent element of inequitable conduct." App. 79a (quoting *Ulead Sys., Inc. v. Lex Computer & Mgmt. Corp.*, 351 F.3d 1139, 1148 (Fed. Cir. 2003)). The district court could not have been more clear that Amphastar and Teva had carried their burden of proving actual intent to deceive by clear and convincing evidence, and that it was not relying on negligence:

> Nevertheless, because affirmatively proving intent is a burden that must lie with Amphastar and Teva at all times, the Court now separately finds that clear and convincing evidence adduced at trial independently reestablishes—and substantially strengthens —those earlier inference of intent . . . .

App. 87a. It is equally clear from the above quote that not only did the district court expressly find an intent to deceive, the district court did not shift the burden to Aventis. *See* App. 87a ("Nevertheless, because affirmatively proving intent is a burden that must lie with Amphastar and Teva at all times . . . ."). Indeed, the district court made a specific finding of intent to deceive (App. 90a) and a specific finding that "negligence played no role" in Aventis' and Dr. Uzan's

misrepresentations and omissions (App. 89a). The Federal Circuit affirmed that the evidence supported those findings. App. 30a.

The express holdings of the district court and Federal Circuit show that neither applied a "sliding scale" that allowed an inference of intent to deceive solely from materiality as Aventis contends. Instead, both courts recognized that intent to deceive must be found separate from materiality. *See* App. 49a (citing *GFI*, 265 F.3d at 1274; *Manville*, 917 F.2d at 552).

That is not to say, however, that a high level of materiality is irrelevant to a party's intent to deceive. Parties rarely confess an intent to deceive. Thus, intent ordinarily must be proven by circumstantial evidence. The degree of materiality naturally affects whether it is appropriate to draw an inference of an intent to deceive: it is easy to forget about relatively inconsequential facts, but much less likely that a person will have innocently overlooked highly consequential facts. Rather than applying a "sliding scale" that eliminates the need to prove intent to deceive, the district court correctly observed "[t]he quantum of proof required to show intent is tied to materiality . . . ." App. 49a. The district court carefully noted at the same time that "[a]lthough 'a lesser quantum of proof is needed to establish the requisite intent' . . . Amphastar and Teva must still prove the predicate facts by clear and convincing evidence."[12]

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[12] At page 8:22-31 of its petition, Aventis mischaracterizes the Federal Circuit's decision by contending that the Federal

(Cont'd)

Thus, the district court was addressing the amount of evidence necessary for Amphastar and Teva to meet their burden, and expressly not dispensing with the need to prove an intent to deceive. *Id.*

Indeed, this court has recognized in other contexts that the reason or motive for a deception (and thus its materiality) cannot be divorced from the intent to deceive. *See, e.g., Claflin v. Commonwealth Ins. Co.*, 110 U.S. 81, 95 (1884):

> [I]f [statements upon a material matter] are knowingly false and willfully made, the fact that they are material is proof of an attempted fraud, because their materiality, in the eye of the law, consists in their tendency to influence the conduct of the party who has an interest in them, and to whom they are addressed.

The Court has also recognized that "intent may be shown by any evidence that has a tendency to persuade the mind of its existence. Hence, in actions for fraud, large latitude is always given to the admission of evidence." *Butler v. Watkins*, 80 U.S. 456, 464 (1872).

(Cont'd)

Circuit placed the burden on Aventis to prove by clear and convincing evidence that Example 6 was not meant to address compositional difference. Contrary to Aventis' argument the Federal Circuit was merely finding that there was no clear error in the district court's finding. App. 23a ("We cannot agree that the district court clearly erred in its determination that the half-life comparisons were, at least in part, intended to show compositional differences.").

II. THE DISTRICT COURT DID NOT CLEARLY ERR IN FINDING AN ABSENCE OF NEGLIGENCE

The district court also took great pains to make it clear that the misleading use of a different dose half-life study in Example 6, coupled with the affirmative misrepresentations during the prosecution that there was a significant difference in half-life, and the omission of the fact that a different dose comparison was being made and the actual dose used for the E.P. 40,144 study, was intentional and not due to negligence. App. 87a-89a. The district court found Aventis' and Dr. Uzan's explanation unsupported and contradicted by other contemporaneous evidence, in addition to being uncorroborated and an apparent after-the-fact fabrication. App. 73a-78a, 88a-89a. The district court specifically found that the explanation suffered from a total absence of credibility. *Id.* In reaching its decision the district court considered the totality of the evidence and rejected Aventis' evidence of alleged good faith as not credible. *Id.*

In spite of the district court's express findings of fact and credibility determinations, Aventis seeks review of the district court's decision contending that the district court found exactly what it expressly ruled out. Aventis' argument necessarily requires that this Court improperly accept Dr. Uzan's discredited "clinically relevant dose" testimony as an established fact. The district court's credibility determination was detailed and fully supported by the evidence. This Court has recognized that the credibility determinations of the trier of fact "can virtually never be clear error." *Anderson v. Bessemer City*, 470 U.S. 564, 575 (1985). In any event, "[a] petition for a writ of certiorari is rarely

granted when the asserted error consists of erroneous factual findings or the misapplication of a properly stated rule of law." S. Ct. R. 10.

III. THERE IS NO CONFLICT AMONG THE LOWER COURTS

Beyond the absence of a factual predicate for Aventis' petition, Aventis' characterization of the law is also incorrect. Aventis contends that there is a conflict among the lower courts regarding whether gross negligence is sufficient to establish inequitable conduct. Aventis cites "five regional circuits" that purportedly rejected the gross negligence standard and three other circuits that purportedly premised inequitable conduct on gross negligence. Pet. at 20. None of these cases are relevant in view of the Federal Circuit's exclusive jurisdiction over patent cases under 28 U.S.C. § 1295(a)(1). No circuit other than the Federal Circuit has addressed the inequitable conduct issue for over 25 years.

Aventis' further contends that there is a conflict within the Federal Circuit with some panels applying a gross negligence standard and others not. This Court has held that such internal circuit conflicts do not support the granting of a petition for certiorari. *Wisniewski v. United States*, 353 U.S. 901, 902 (1957) (refusing to grant certiorari on a question certified by a court of appeals to resolve an intra-circuit conflict):

> Whatever procedure a Court of Appeals follows to resolve these problems-and desirable judicial administration commends consistency at least in the more or less

> contemporaneous decisions of different panels of a Court of Appeals-doubt about the respect to be accorded to a previous decision of a different panel should not be the occasion for invoking so exceptional a jurisdiction of this Court as that on certification. It is primarily the task of a Court of Appeals to reconcile its internal difficulties.

See also Davis v. United States, 417 U.S. 333, 340 (1974). Notably, although Aventis petitioned for the Federal Circuit to revisit this case en banc, the Federal Circuit unanimously agreed that this case was not an appropriate vehicle. Notably, even dissenting Judge Rader did not vote for rehearing, apparently recognizing that his disagreement with the majority turned primarily on his reading of the factual record.

In any event, Aventis' argument is based upon a misreading of Federal Circuit law. The law in the Federal Circuit has been settled since *Kingsdown Medical Consultants, Ltd. v. Hollister, Inc.*, 863 F.2d 867, 876 (Fed. Cir. 1988) (en banc). But *Kingsdown* did not hold that gross negligence was irrelevant to an intent to deceive in all cases, as Aventis apparently contends. Rather, the Federal Circuit held that gross negligence *alone* is insufficient for a finding of inequitable conduct and that the totality of the circumstances must be considered:

> We adopt the view that a finding that particular conduct amounts to "gross negligence" does **not of itself justify** an inference of intent to deceive; the involved

> conduct, viewed in light of all the evidence, including evidence indicative of good faith, must indicate sufficient culpability to require a finding of intent to deceive.

Id. at 876 (emphasis added). Thus, the Federal Circuit merely held that gross negligence **alone** was not sufficient for a finding of inequitable conduct but rather that the totality of the circumstances must be considered.

Aventis' argument stems from the Federal Circuit's rule that intent to deceive can be inferred where the patentee "knew or should have known of the materiality" of the misrepresentation or omission. Aventis contends that this does away with the requirement to prove deceptive intent. Aventis is wrong.[13] "Should have known" comes into play only with respect to knowledge of the materiality of the known misrepresentation, and is entirely appropriate circumstantial evidence of an intent to deceive. In any event, the district court in this case specifically found that Dr. Uzan knew (and not merely should have known) of the materiality of his

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[13] The Federal Circuit has also held that *after* a trial court finds the two requisite thresholds of an intent to deceive and materiality of the misrepresentation, the trial court may balance the degree of materiality with intent in deciding whether the proper remedy is to declare the patent unenforceable. App. 90a. Thus the Federal Circuit gives patentees an extra chance to avoid unenforceability. If anything, this doctrine confirms that Aventis is flat wrong in suggesting that the Federal Circuit applies a rigid rule of "automatic unenforceability."

misrepresentations and omissions, rendering this case a poor vehicle to address the issue. App. 81a.[14]

Aventis focuses only on one aspect of the intent inquiry and therefore misses the larger picture entirely. The Federal Circuit has not ruled out the consideration of evidence that the patentee should have known of the materiality or even gross negligence. Rather, that the patentee should have known of materiality or was grossly negligent in avoiding any knowledge of materiality can be considered in the context of other circumstantial evidence from which an intent to deceive can be inferred. As explained in *Hewlett-Packard Co. v. Bausch & Lomb, Inc.*:

> Although the proof of gross negligence may be circumstantial evidence which gives rise to an inference of intent to mislead in some instances, the label "gross negligence" covers too wide a range of culpable conduct to create such an inference in all cases. Thus, grossly negligent conduct may or may not compel an inference of an intent to mislead. Such an inference depends

[14] The district court also found in the alternative that Dr. Uzan "must (and should) have known what experimental question he was answering . . . ." App. 82a. This was not a determination of negligence, but rather an application of circumstantial evidence to find intent. The district court found under the circumstances that any claim by Aventis and Dr. Uzan that he did not know the materiality of the representations he made to the Patent Office in his prosecution declarations was not credible. App. 82a ("After all, Aventis can scarcely disagree that Dr. Uzan ought to have been aware of the nature of the questions he was called on to answer before the PTO."). Based upon the totality of the circumstances a finding of intent to deceive was appropriate regardless of whether Aventis admitted Dr. Uzan knew the materiality of his misrepresentations or contended that he did not.

> upon the totality of the circumstances, including the nature and level of culpability of the conduct and the absence or presence of affirmative evidence of good faith.

882 F.2d 1556, 1562 (Fed. Cir. 1989) (citing *Kingsdown*, 863 F.2d at 876); *see Manville*, 917 F.2d at 552 (affirming a finding of no inequitable conduct explaining: "As we noted in *Hewlett-Packard* . . . 'grossly negligent conduct may or may not compel an inference of an intent to mislead.' Here it did not.") (citation omitted).

In short, there is no conflict in the Federal Circuit, or between the circuits. Rather, the outcome of each case, including those cited by Aventis, depended on the particular circumstantial evidence present in each respective case and whether an inference of an intent to deceive was proper in view of the totality of the evidence.[15]

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[15] For example, Aventis cites the dissenting opinions from two post-*Kingsdown* decisions in *Ferring B.V. v. Barr Labs., Inc.*, 437 F.3d 1181, 1191, 1196 (2006) (Newman, J., dissenting); *Praxair, Inc. v. ATMI, Inc.*, 543 F.3d 1306, 1329 (Fed. Cir. 2008) (Lourie, J., dissenting). The majority in *Ferring* did not rely solely on what the patent prosecutor "should have known." Rather, the majority affirmed the district court's finding of inequitable conduct based upon the patentee's knowledge of the past relationships of the two declarants, the undisputed fact that the patentee knew the materiality of the information (i.e. the examiners concern about the identity of the affiants), the fact that the examiner had specifically requested "non-inventor" affidavits, and the absence of any evidence of good faith. *Ferring*, 437 F.3d at 1191-92. In *Praxair*, the majority found that the patentee knew about the prior art reference in addition to having known or should have known of its materiality along with high materiality. 543 F.3d at 1318. The dissents merely disagree as to whether the facts supported an inference of intent to deceive.

The same is true in this case. Judge Rader disagreed with the majority and the district court, however, he did not consider the totality of the circumstances and improperly substituted his view of the evidence for that of the district court.[16] That is not, however, the role of the appellate court. *See Anderson v. Bessemer City*, 470 U.S. 564, 574 (1985) ("[I]f the district court's account of the evidence is plausible in light of the record viewed in its entirety the court of appeals may not reverse it even though convinced that had it been sitting as the trier of fact, it would have weighed the evidence differently."); *Kingsdown*, 863 F.2d at 872 ("This standard plainly does not entitle a reviewing court to reverse the finding of the trier of fact simply because it is convinced that it would have decided the case differently.").

The "should have known" rule addresses attempts to avoid a finding of deceptive intent through "studied

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[16] Judge Rader made several factual mistakes in his dissent including the timing of the reissue (*compare* App. 38a *with* App. 12a n.6), his assumption that Dr. Uzan allegedly revealed the error in the different dose study (*Compare* App. 37a *with* App. 84a, 100a-105a (Rader joining in majority)), and his assertion that Example 6 makes the different dose comparison apparent (*id.*). Judge Rader also failed to take into account the use of "4.5 hours" for both the subparagraph (1) and (3) studies and the statement in Example 6 that the study was "under identical dosage conditions." App. 43a-44a n.3. Judge Rader further found that a different dose comparison was scientifically reasonable without any support whatsoever. App. 36a. Judge Rader also improperly weighed Dr. Uzan's credibility, finding that Dr. Uzan was free of deceptive intent because of his caliber and reputation as a scientist. App. 36a. Judge Rader effectively substituted his judgment on facts he deemed important and his credibility determinations of a witness he did not observe testify for the district court's. *Anderson*, 470 U.S. 574.

ignorance." *Hewlett-Packard*, 882 F.2d at 1562. Thus, cases such as *Bressler, U.S.A.I., L.P. v. Styker Sales Corp.*, 267 F.3d 1370, 1384 (Fed. Cir. 2001) and *FMC Corp. v. Hennessy Industries, Inc.*, 836 F.2d 521, 526 n.6 (Fed. Cir. 1987) criticized by Aventis involved "studied ignorance" as part of the circumstantial evidence supporting an inference of an intent to deceive.

IV. THERE IS NO CONFLICT BETWEEN THE FEDERAL CIRCUIT'S APPROACH AND THIS COURTS PRECEDENTS

As noted above, this Court has held that "large latitude is always given to the admission of evidence" to establish an intent to deceive. *Butler v. Watkins*, 80 U.S. 456, 464 (1872). In particular, this Court has held that evidence of gross negligence can be taken into account when finding an intent to deceive. For example, as early as 1895, this Court recognized that a person could be held criminally liable for an evil intent where "his negligence in failing to inform himself [was] so gross as to characterize his conduct as fraudulent." *Cochran v. United States*, 157 U.S. 286, 294 (1895); *see also United States v. Yermian*, 468 U.S. 63, 75 n.14 (1984) (holding that the defendant's knowledge that the statement was false coupled with the fact that the defendant should have known the statement was being made to the government was sufficient to preclude "the possibility that criminal penalties were imposed on the basis of innocent conduct."). Further, as Justice Souter recognized "deliberate indifference is thus treated, as it is elsewhere in the law, as tantamount to intent." *Board of County Comm'rs v. Brown*, 520 U.S. 397, 419 n.1 (1997) (dissent) ("To consciously ignore or to deliberately close one's eyes to a manifest danger is recklessness, a mental

state that the law commonly substitutes for intent or actual knowledge.")

In the same manner, a patentee's false representation to the Patent Office, actual knowledge of that falsity, coupled with a finding that under the circumstances the patentee knew or should have known (i.e. studied ignorance) of the materiality of the false representation and a finding that the patentee's innocent explanations for its misconduct are incredible, are sufficient circumstantial evidence to support a finding of intent to deceive. Thus, the Federal Circuit's decisions are completely consistent with the past rulings of this Court and basic principles of fraud.

Since the district court found that Dr. Uzan knew the materiality of his misrepresentations and omissions as evidenced by his prosecution declarations, the district court's inference of intent to deceive were fully supported by what Dr. Uzan knew, not just what he should have known. Thus, the above debate will have no impact on the ultimate merits or outcome in this case.

V. THERE IS NO SOUND REASON TO OVERTURN THIS COURT'S LONG STANDING EQUITABLE RULE REGARDING PATENTS OBTAINED BY INEQUITABLE CONDUCT

Ultimately, Aventis seeks to confine the type of circumstantial evidence that a court can consider in determining an intent to deceive. Yet this Court has long recognized that a person accused of fraud or deception is not likely to admit having an intent to deceive. Thus, as this Court has held, "[c]ircumstantial evidence is not only sufficient, but may also be more certain, satisfying

and persuasive than direct evidence." *Michalic v. Cleveland Tankers, Inc.*, 364 U.S. 325, 330 (1960). If a person accused of fraud is not likely to admit having a deceptive intent, it is just as probable that such a person will not admit to knowing that the other person was actually deceived (i.e. knowing of the materiality of the misrepresentation.) If circumstantial evidence is necessary, and indeed "more certain, satisfying and persuasive" to prove the former, it is just as probative of the latter.

Lost in Aventis' arguments is the purpose behind the inequitable conduct doctrine.[17] The inequitable

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[17] Aventis warns of the coming "plague" of inequitable conduct cases as if use of the word alone could compel a result in its favor. The "plague" that the Federal Circuit addressed in *Burlington Indus. Inc. v. Dayco Corp.* was over the practice of alleging inequitable conduct simply as a matter of course. 849 F.2d 1418, 1422 (Fed. Cir. 1988). There is no evidence of that practice recurring. Further, the data from the University of Houston Law Center do not support Aventis' argument. Since 2000, patentees have defeated inequitable conduct allegations over 75% of the time, and only 20 patents per year have been found unenforceable. Even the latter number is inflated by one unusual 2007 case in which 15 patents were held unenforceable due to a pattern of similar misconduct.

This case is certainly no evidence of a returning "plague." Neither Amphastar nor Teva alleged inequitable conduct until discovery produced clear evidence of Aventis' knowing misrepresentations to the PTO regarding the half-life data. And every judge to review the facts (including Judge Rader in the first appeal) has concluded that an intent to deceive could properly be inferred. App. 108a. That may not always be the case, but the harm to the public caused by a few ill-advised allegations of inequitable conduct is insignificant in comparison to the harm that would be caused by allowing patentees to knowingly submit false data to the Patent Office.

conduct doctrine stems from this Court's judgment that the doctrine is essential to the duty of candor patent applicants owe the Patent Office. *Precision Instrument*, 324 U.S. at 816. That duty arises from the constitutional mandate that patents be granted only to true inventions and only for a limited period of time. *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 6 (1966). When a patent is wrongfully issued through inequitable conduct the "injury to the public through a weakening of the Patent System is manifest." *Norton v. Curtiss*, 433 F.2d 779, 796 (C.C.P.A. 1970). An improperly issued patent not only injures the Patent System but potentially costs the public millions of dollars (if not billions as in this case) in increased pricing resulting from an improperly patent-backed monopoly.[18] The PTO cannot possibly know every material fact regarding patentability (i.e. offers for sale, public uses, prior art publications, etc.) and thus, must necessarily rely on the good faith and candor of patent applications.

The misrepresentations in this case struck at the point where the PTO is most susceptible to fraud. The misrepresentation present here related to experimental data used to distinguish the prior art in order to

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[18] Aventis goes outside the record pointing out that the patent in this case related to a drug in which Aventis has had sales in the "billions" of dollars over the life of the '618 patent. If Aventis is permitted to go outside the record, Aventis should also be required to acknowledge that (according to publicly available information) Aventis charges **five times** the amount for the drug at issue in the United States as Aventis charges in Europe. There could not be a more dramatic real world illustration of how a fraudulent obtained patent harms the public.

overcome the Examiner's rejections. The experimental data purported to establish superior properties and thus a novel composition. The Examiner twice advised Aventis that the PTO does not have the facilities or capabilities to conduct testing on its own. App. 7a n.2, 21a. As such the PTO must rely on an applicant's representations regarding experimental results. To carve out an exception to the inequitable conduct doctrine based upon the claim that the patentee (while knowing the falsity of the representations) did not know that the experimental data would have been relied upon by the Examiner (i.e. did not know it was material) would sanction "studied ignorance," and cripple the PTO where it is most vulnerable.

CONCLUSION

This is not a case of simple or even gross negligence. Rather, the overwhelming evidence established that Aventis and Dr. Uzan knowingly "cherry-picked" data to falsely create the appearance of a half-life difference between the LMWH from the '618 patent and the E.P. '144 patent. Aventis and Dr. Uzan then misrepresented the data while omitting key facts that would have shown the misrepresentations to be false.

At trial, Aventis offered an incredible, uncorroborated, after-the-fact fabricated story that was disproved on every level, which, according to the district court, "suffered from a total absence of credibility." App. 78a, 88a. Aventis would have this Court accept rejected testimony as established fact, ignore the express holdings of the lower courts, and adopt arguments raised for the first time in a petition for certiorari. This Court should decline the invitation and deny the petition.

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Respectfully submitted,

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