United States Court of Appeals for the Federal Circuit

APOTEX INC., a Canadian Corporation, AND APOTEX CORP., a Delaware Corporation,
Plaintiffs-Appellants,

v.

UCB, INC., a Delaware Corporation, AND KREMERS URBAN PHARMACEUTICALS, INC., a Delaware Corporation,
Defendants-Appellees,

AND

SCHWARZ PHARMA, INC., a Delaware Corporation, PADDOCK LABORATORIES, LLC, AND PERRIGO COMPANY,
Defendants.

2013-1674

Appeal from the United States District Court for the Southern District of Florida in Nos. 0:12-cv-60706-DMM and 0:12-cv-60707-DMM, Judge Donald M. Middlebrooks.

Decided: August 15, 2014

ROBERT B. BREISBLATT, Katten Muchin Rosenman LLP, of Chicago, Illinois, argued for plaintiffs-appellants.

With him on the brief were ERIC C. COHEN, CRAIG M. KUCHII, and MARTIN S. MASAR III; and HOWARD R. RUBIN and CHRISTOPHER D. JACKSON, of Washington, DC.

ADAM GAHTAN, White & Case LLP, of New York, New York, argued for defendants-appellees. With him on the brief were DIMITRIOS T. DRIVAS, CHRISTOPHER J. GLANCY, AMIT H. THAKORE, and LAURA T. MORAN.

Before REYNA, WALLACH, and HUGHES, *Circuit Judges.*

REYNA, *Circuit Judge.*

Apotex Inc. and Apotex Corp. (collectively, "Apotex") appeal the decision of the United States District Court for the Southern District of Florida finding that: (1) Apotex's U.S. Patent No. 6,767,556 ("the '556 patent") is unenforceable due to inequitable conduct; (2) Apotex is judicially estopped from alleging infringement of the '556 patent by the accused products; (3) the asserted claims are indefinite; (4) Apotex disclaimed coverage of the accused products from the scope of the '556 patent's claims; and (5) Apotex is barred by laches from recovering pre-suit damages. *Apotex, Inc. v. UCB, Inc.*, 970 F. Supp. 2d 1297 (S.D. Fla. 2013). Because the district court did not abuse its discretion in finding inequitable conduct, we *affirm* the district court's judgment on that basis.

BACKGROUND

A. The '556 Patent

The '556 patent, titled "Pharmaceutical Compositions Comprising Moexipril Magnesium," is about ten years old. The patent issued on July 27, 2004, from an application that claims priority to a Canadian application filed on April 5, 2000. Dr. Bernard Charles Sherman, founder and chairman of Apotex, wrote the '556 patent application and is its sole inventor. Dr. Sherman leads the develop-

ment of Apotex's drug formulations and manufacturing processes, and has himself written approximately one hundred patent applications for Apotex. He also directs all litigation for Apotex.

The '556 patent is generally directed to a process for manufacturing moexipril tablets. Moexipril is an angiotensin-converting enzyme ("ACE") inhibitor used to treat hypertension. Like other ACE inhibitors, Moexipril and its acid addition salts (e.g., moexipril hydrochloride) are susceptible to degradation and instability. To improve stability, the '556 patent discloses a process of making moexipril tablets consisting mostly of moexipril magnesium obtained by reacting moexipril or its acid addition salts with an alkaline magnesium compound. '556 patent col. 2 ll. 53–56. This process is captured in claim 1, the only independent claim of the '556 patent:

> 1. A process of making a solid pharmaceutical composition comprising moexipril magnesium, said process comprising the step of reacting moexipril or an acid addition salt thereof with an alkaline magnesium compound in a controlled manner in the presence of a sufficient amount of solvent for a predetermined amount of time so as to convert greater than 80% of the moexipril or moexipril acid addition salt to moexipril magnesium.

In the preferred embodiment, moexipril hydrochloride is reacted with magnesium hydroxide or the magnesium salt of a weak acid (e.g., magnesium carbonate) to obtain moexipril magnesium. *See id.* col. 2 l. 66–col. 3 l. 5. The '556 patent explains that the reaction cannot be accomplished in dry form and must be carried out in the presence of a solvent. *Id.* col. 2 ll. 38–45. After the reaction has occurred and the solvent has evaporated, the dried material can be compressed into tablets. This process is called "wet granulation" and has been known in the pharmaceutical industry since at least the 1980s.

B. The Prior Art

Several methods for stabilizing ACE inhibitors in general, and moexipril in particular, were known in the prior art before Dr. Sherman filed the '556 patent application. U.S. Patent No. 4,743,450 ("the '450 patent"), which issued in 1998 to Warner-Lambert, discloses a method for stabilizing an ACE inhibitor using alkaline magnesium compounds. '450 patent col. 3 ll. 25–35. The examples in the '450 patent use quinapril as the ACE inhibitor and magnesium carbonate as the alkaline stabilizer. *Id.* col. 4 l. 58–col. 5 l. 39. As in the '556 patent, wet granulation is the preferred technique for processing tablets according to the '450 patent. *Id.* col. 4 ll. 26–28.

The two accused products in this case, Univasc and Uniretic, are also prior art to the '556 patent. Both products are moexipril tablets that have been sold in the United States since 1995 and 1997, respectively. Univasc and Uniretic are made in accordance with the process described in the '450 patent, which Defendant UCB, Inc. licenses from Warner-Lambert and has listed in the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book") for both products. The manufacture of Univasc and Uniretic involves the wet granulation of moexipril hydrochloride and magnesium oxide.

The '556 patent discusses the '450 patent and the Univasc product. Specifically, the Background section states that Univasc tablets contain moexipril hydrochloride and magnesium oxide, and are made in accordance with the teachings of the '450 patent. '556 patent col. 2 ll. 16–22. This section also states that the moexipril hydrochloride and alkaline magnesium compound are capable of an acid-base reaction that is difficult to control and results in uncertainty regarding the final composition of the product. *Id.* col. 2 ll. 31–39.

The '556 patent also discusses a 1990 article by Gu et al.[1] ("the Gu article"), which describes the chemistry involved in stabilizing moexipril. Gu examined the degradation of moexipril after mixing it with alkaline stabilizers in both wet granulation and dry powder mixing (dry granulation), concluding that only wet granulation stabilizes moexipril. The Gu article theorizes that such stabilization results from "neutralization" by the outer surface of the granulated material and also possibly because "a portion of the moexipril hydrochloride was converted to the cation salts via granulation" (i.e., moexipril magnesium was obtained). According to the Background section of the '556 patent, the Gu article teaches that only a portion (if any) of the drug may be converted to moexipril magnesium and that stabilization therefore occurs not because of conversion, but because of the presence of the alkaline stabilizing compound in the final product. '556 patent col. 2 ll. 4–11.

C. The Prosecution History

During prosecution before the U.S. Patent and Trademark Office ("PTO"), the '556 patent received three obviousness rejections. First, the Examiner rejected the claims based on the combination of the '450 patent and U.S. Patent No. 4,344,949, which discloses using moexipril tablets to treat hypertension. In response, Dr. Sherman's counsel argued that the cited prior art did not disclose a reaction, but disclosed only combining moexipril hydrochloride and an alkaline magnesium compound. In support, counsel submitted the Product Monograph for Univasc and the portion of the Orange Book that lists Univasc as being covered by the '450 patent, stating:

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[1] Leo Gu et al., *Drug-Excipient Incompatibility Studies of the Dipeptide Angiotensin-Converting Enzyme Inhibitor, Moexipril Hydrochloride: Dry Powder vs. Wet Granulation*, 7 Pharm. Res. 379 (1990).

> Applicant herewith submits the Product Monograph for Univasc® (Moexipril Hydrochloride Tablets) wherein the tablets marketed by Schwarz Pharma (as listed in the FDA Orange Book as per the teachings of United States Patent No. 4,743,450) include magnesium oxide; *unreacted but combined* and functioning as a stabilizer (see first page). The Examiner is referred to those pages. Full reconsideration is respectfully requested.

Joint Appendix ("J.A.") at 12172 (emphasis added).

The Examiner rejected the claims a second time, but this time based on the combination of the '450 patent and the Gu article. The Examiner observed that it would have been obvious to combine the '450 patent's teaching that ACE inhibitor drugs can be stabilized with an alkaline magnesium compound, with Gu's teaching regarding stabilization of moexipril hydrochloride via wet granulation. In response, counsel again distinguished the prior art on the basis that no reaction was taught:

> The Examiner alleges that Gu et al. renders obvious the process of making moexipril magnesium and that Gu discloses a process of making a moexipril alkaline salt by allegedly *reacting* moexipril hydrochloride with an alkaline stabilizing agent. Respectfully no such reaction is taught. The components are merely combined and any reaction is insignificant to the desired end result.

Id. at 12223 (emphasis in original). Dr. Sherman's counsel once more referred the Examiner to the Product Monograph for Univasc and the Orange Book and argued that Univasc includes magnesium oxide "unreacted but combined." *Id.* at 12224.

Unconvinced, the Examiner issued a third and final rejection on obviousness grounds based on Gu and the

'450 patent, finding that the neutralization taught by the cited references constituted a reaction. Dr. Sherman's counsel appealed the final rejection to the PTO's Board of Appeals, arguing that the cited references merely taught combining moexipril hydrochloride with an alkaline stabilizing agent. *Id.* at 12249. Counsel again referred the Board to the Product Monograph for Univasc and the Orange Book and represented that Univasc, made according to the '450 patent, contained "unreacted but combined" moexipril hydrochloride and magnesium oxide. *Id.* at 12251.

At the direction of Dr. Sherman, counsel also submitted the expert declaration of Dr. Michael Lipp, who reinforced the representations regarding the prior art. Specifically, Dr. Lipp explained that the function of a stabilizer is to inhibit or prevent reactions that would degrade the active ingredient, and that a stabilizer needs to be unreacted to perform this function. *See id.* at 12288. According to Dr. Lipp, a person of skill in the art would therefore not expect a reaction to occur between the ACE inhibitor and the alkaline stabilizer disclosed in the '450 patent. *Id.* at 12289. Dr. Lipp relied on Univasc to support his conclusion:

> An additional example particularly relevant to the matter at hand is the UNVASC® [sic] moexipril hydrochloride formulation . . . . The product monograph for the UNVASC [sic] moexipril hydrochloride formulation lists moexipril hydrochloride as being present in the final formulation in addition to magnesium oxide as an alkaline stabilizer, as per the teachings of the '450 patent which is listed on the FDA Orange Book for this formulation. As a result, in my opinion, a skilled formulator reading Harris et al. would not expect a reaction to occur between an alkaline or saccharide stabilizer and an ACE inhibitor drug in the formulations disclosed therein.

Id. at 12288–89.

In a subsequent telephonic interview, the Examiner and Dr. Sherman's counsel agreed to incorporate into claim 1 a limitation requiring "greater than 80%" conversion of the moexipril or moexipril acid addition salt to moexipril magnesium. As a result, the Examiner allowed the '556 patent claims on April 20, 2004. As reasons for allowance, the Examiner stated:

> The primary reason for allowance is that the prior art does not disclose nor fairly suggest a process of making a pharmaceutical composition comprising moexipril magnesium, comprising the step of reacting moexipril or an acid addition salt thereof with an alkaline magnesium compound so as to convert greater than 80% of the moexipril or moexipril acid addition salt to moexipril magnesium. *Rather, the prior art teaches that only a portion of drug (if any) may be converted to the alkaline salt and that the stable product results entirely or primarily not from conversion to alkaline salts, but from stabilization of the moexipril hydrochloride by the presence of the alkaline stabilizing compound in the final product.*

Id. at 12399 (emphasis added).

D. District Court Proceedings

Apotex filed suit on April 20, 2012, accusing UCB of infringing claims 8–12 of the '556 patent by manufacturing and selling Univasc and Uniretic, as well as generic versions thereof. Prior to conducting a jury trial on infringement and invalidity, the district court held a three-day bench trial on claim construction and UCB's equitable defenses.

The district court ruled that the '556 patent is unenforceable due to Dr. Sherman's inequitable conduct before the PTO. Specifically, the district court found that Dr.

Sherman was aware that Univasc was made according to his claimed process, concealed this knowledge from the PTO, and misrepresented the nature of Univasc and the prior art through his counsel's arguments and Dr. Lipp's declaration. The district court also found that Dr. Sherman withheld relevant prior art and submitted results of experiments that he never conducted.

The district court relied on several pieces of evidence in finding that Dr. Sherman was aware that Univasc involved a reaction. For instance, Dr. Sherman conceded during trial that, before filing the '556 patent application, he had a "strong suspicion" and a "belief" that Univasc was made according to his claimed process. Also, on the same day the application was filed, Dr. Sherman conducted tests comparing Univasc to an Apotex moexipril product with no alkaline stabilizer. In his handwritten notes, Dr. Sherman concluded that the Apotex product was "much less stable than the magnesium salt," implying at least a suspicion that Univasc consisted of moexipril magnesium. About a month later, Dr. Sherman's suspicion was confirmed by two Apotex scientists who produced a detailed mass spectrometry report on Univasc and concluded that moexipril in Univasc is "mainly present" as moexipril magnesium.

The court also found that Dr. Sherman was aware of, and involved in, all decisions regarding prosecution of the '556 patent application. The court noted that Dr. Sherman is highly familiar with patent prosecution and patent enforcement litigation. Although Dr. Sherman attempted to disclaim knowledge of the components of Univasc, the prior art, and the statements made to the PTO by his counsel, the district court did not find his testimony to be credible. The district court observed that Dr. Sherman selectively displayed at trial a lack of memory and responsibility that led the court to conclude he was not a credible witness.

The district court also found that Dr. Sherman made several misrepresentations to the PTO regarding the prior art. In particular, Dr. Sherman misrepresented the nature of Univasc and the '450 patent by asserting that the moexipril hydrochloride in Univasc was not reacted but merely combined with an alkaline magnesium compound. The district court also found that Dr. Sherman, in the specification and through Dr. Lipp's declaration, mischaracterized the Gu article by asserting that only a minor portion of the drug, if any, is converted to moexipril magnesium. Lastly, the district court found that Dr. Sherman lied in the '556 patent application by including certain examples of experiments that were never conducted. The court noted that each example is written in the past tense as if it had occurred, but Dr. Sherman admitted at trial that the experiments were made up in his head.

The district court further concluded that Dr. Lipp was only hired to add legitimacy to Dr. Sherman's misrepresentations. The court found that Dr. Sherman failed to inform Dr. Lipp of the true facts about Univasc and shielded him from the truth, which resulted in a declaration that Dr. Sherman knowingly submitted to the PTO to perpetuate his mischaracterizations of the prior art. Dr. Lipp testified that he was specifically asked to limit his discussions to only the documents provided by Apotex, which did not include any information regarding the tests conducted on Univasc or Dr. Sherman's knowledge of the product.

In addition to the misrepresentations, the district court found that Dr. Sherman withheld relevant prior art from the PTO. Specifically, PCT Application No. WO 99/62560, titled "Stabilization of Quinapril Using Magnesium Oxide" ("the '560 PCT"), was cited by the PTO in a 2003 office action for U.S. Application No. 10/060,191 ("the '191 application"), of which Dr. Sherman is also an inventor. The '560 PCT relates to a method for stabilizing

an ACE inhibitor drug, like quinapril, using magnesium oxide, and the Examiner interpreted this reference as disclosing a reaction between a hydrochloride salt and an alkaline base. Given the similarities between the '191 application and the '556 patent and Dr. Sherman's experience, the district court found that Dr. Sherman would have known about the '560 PCT and understood its relevance to the prosecution of the '556 patent. The '560 PCT, however, was never disclosed to the Examiner handling the prosecution of the '556 patent.

The district court found that the foregoing combined misrepresentations and withholding of prior art were material to the prosecution of the '556 patent application. Based on the Examiner's reasons for allowance, the district court concluded that the Examiner adopted Dr. Sherman's repeated misrepresentations verbatim and would not have allowed the claims had he been aware that Univasc contained moexipril magnesium. The district court also found the '560 PCT's disclosure of a reaction between a hydrochloride salt and an alkaline base to be material because of the similarities between the '191 application and the '556 patent, and the fact that the '560 PCT discloses the four basic steps of wet granulation recited in claim 8 of the '556 patent. Although the district court found that the falsification of examples in the '556 patent was alone not sufficiently material, it nonetheless added to the materiality determination when viewed in conjunction with other misrepresentations and omissions.

In the alternative, the district court found that a finding of but-for materiality was not necessary because Dr. Sherman engaged in egregious misconduct during prosecution of the '556 patent application. In addition to the various misrepresentations made by Dr. Sherman, the district court observed that Dr. Sherman abused the patent system by targeting a competitor's existing and widely available product and seeking to obtain a patent

on it through lies and deception for the purpose of suing that competitor.

Regarding intent, the district court found that the single most reasonable inference that could be drawn from the evidence was that Dr. Sherman intended to deceive the PTO. The court based its determination on Dr. Sherman's overall pattern of misconduct and his poor credibility at trial. The district court concluded that Dr. Sherman intentionally violated his duty of candor not only by making repeated misrepresentations to the PTO during prosecution of the '556 patent, but also by including experiment results in the specification as if the experiments had actually been conducted, and by purposely shielding an expert from relevant information to obtain a declaration that misinformed and led the Examiner to finally allow the claims. The court also found that Dr. Sherman's demeanor and evasive testimony at trial were evidence of his intent to deceive the PTO.

The district court therefore held the '556 patent unenforceable due to inequitable conduct. Additionally, the court ruled in favor of UCB on its judicial estoppel and laches equitable defenses, indefiniteness and claim construction. The court entered final judgment against Apotex on September 19, 2013. The jury trial on infringement and invalidity was never held.

Apotex filed a timely appeal. We have jurisdiction pursuant to 28 U.S.C. §1295(a)(1).

DISCUSSION

We affirm the district court's holding that the '556 patent is unenforceable due to Dr. Sherman's inequitable conduct. The district court's findings regarding materiality and intent are not clearly erroneous, and its ultimate determination that Dr. Sherman breached his duty of

candor, good faith, and honesty before the PTO was not an abuse of discretion.[2]

A. Materiality

Clear and convincing evidence demonstrates that Dr. Sherman engaged in material misconduct. First, Dr. Sherman was actively involved in the prosecution of the '556 patent and instigated the representations made on his behalf by his counsel and Dr. Lipp. The '556 patent's specification, written by Dr. Sherman, omits important details regarding the prior art that were determined to have been known to him. Record evidence shows that Dr. Sherman's counsel was in constant communication with him during prosecution and kept him appraised of actions taken by the PTO and arguments made in response, including the representation that the prior art did not involve a reaction. Indeed, Dr. Sherman directly instructed his counsel to continue pressing those arguments and to bolster them through an expert declaration. We see no reason to disturb the district court's finding that Dr. Sherman's attempt to disclaim knowledge and responsibility at trial was not credible.[3] The district court's finding that Dr. Sherman is responsible for the alleged misconduct is not clearly erroneous.

Second, Dr. Sherman made affirmative misrepresentations of material facts. Apotex's internal tests showed that moexipril in Univasc is "mainly present" as moexipril

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[2] *Aventis Pharma S.A. v. Hospira, Inc.*, 675 F.3d 1324, 1334 (Fed. Cir. 2012); *Symantec Corp. v. Computer Assocs. Int'l, Inc.*, 522 F.3d 1279, 1296 (Fed. Cir. 2008).

[3] *See Apotex*, 970 F. Supp. 2d at 1310 n.23; *see also LNP Eng'g Plastics, Inc. v. Miller Waste Mills, Inc.*, 275 F.3d 1347, 1361 (Fed. Cir. 2001) ("This court may not reassess, and indeed is incapable of reassessing, witness credibility and motive issues on review.")

magnesium. Although the tests were conducted in 2001, before the PTO issued its first rejection of the '556 patent claims, Dr. Sherman repeatedly asserted before the PTO that the process of the '450 patent used to manufacture Univasc did not involve a reaction that would produce moexipril magnesium. Years after issuance of the patent, as part of its infringement case, Apotex confirmed through Nuclear Magnetic Resonance (NMR) testing that Univasc indeed contains more than 80% moexipril magnesium. Dr. Sherman's assertions during prosecution regarding the absence of moexipril magnesium in Univasc were false.

Third, Dr. Sherman's misconduct was "but-for material" to the issuance of the '556 patent. The Examiner's rejections were based on the very same prior art that is the subject of Dr. Sherman's misrepresentations. The Examiner allowed the claims only after being convinced that the prior art moexipril tablets were stable not from conversion to moexipril magnesium (i.e., a reaction), but because the alkaline stabilizer was combined and remained present in the final product without reacting with the moexipril. *See* J.A. at 12399. Dr. Lipp's declaration was instrumental in this regard. The Examiner's erroneous belief regarding the prior art corresponds precisely with Dr. Sherman's repeated misrepresentations made through his counsel and the hired expert. We conclude that the PTO would not have allowed the '556 patent but for Dr. Sherman's misconduct.

To be clear, we agree with Apotex that Dr. Sherman had no duty to disclose his own suspicions or beliefs regarding the prior art.[4] There is nothing wrong with advocating, in good faith, a reasonable interpretation of

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[4] *See Mentor H/S, Inc. v. Med. Device Alliance, Inc.*, 244 F.3d 1365, 1378 (Fed. Cir. 2001).

the teachings of the prior art.[5] The misconduct at issue, however, goes beyond failing to disclose a personal belief or alternative interpretations of the prior art; here, Dr. Sherman affirmatively and knowingly misrepresented material facts regarding the prior art.

Because we affirm the district court's finding that the misrepresentations regarding the prior art were but-for material, we need not decide whether Dr. Sherman's conduct rises to the level of egregious misconduct such that materiality could have been presumed.[6] We also need not address the materiality of Dr. Sherman's failure to disclose the '560 PCT or his falsification of examples in the '556 patent. We note, however, that Dr. Sherman's actions, at a minimum, come close to the type of affirmative misconduct that in *Therasense* we held could justify finding inequitable conduct without showing but-for materiality. We find particularly significant and inexcusable the fact that Dr. Sherman arranged for the preparation and submission of an expert declaration containing false statements instrumental to issuance of the patent.

B. Intent

We affirm the district court's finding that clear and convincing evidence establishes Dr. Sherman's intent to deceive the PTO. The district court did not clearly err in finding that Dr. Sherman knew, or at least had a strong suspicion, that he was seeking to patent the very same process used to obtain an already existing and widely available drug. As of the filing of the '556 patent application, Dr. Sherman was aware that some of the assertions he made in the specification regarding the prior art were

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[5] *See Rothman v. Target Corp.*, 556 F.3d 1310, 1328–29 (Fed. Cir. 2009).

[6] *See Therasense, Inc. v. Becton, Dickinson and Co.*, 649 F.3d 1276, 1292–93 (Fed. Cir. 2011) (en banc).

at least misleadingly incomplete, if not plainly inaccurate. Additionally, Dr. Sherman admitted that he never performed the experiments described in the '556 patent, and yet he drafted the examples in the specification entirely in past-tense language. *See* '556 patent col. 5 l. 1–col. 6 l. 16. Dr. Sherman was also aware that additional misrepresentations were made on his behalf to the PTO, and directed his counsel to bolster those misrepresentations by procuring and submitting the declaration of an expert who was deliberately shielded from the truth.

Apotex argues that merely advocating a particular interpretation of the prior art cannot support an inference of deceptive intent. But Dr. Sherman's statements were not mere advocacy for a preferred interpretation; his statements were factual in nature and contrary to the true information he had in his possession. It is immaterial that, at that time, Dr. Sherman had no direct knowledge of UCB's actual manufacturing process or had determined the exact amount of moexipril magnesium present in Univasc. He knew enough to recognize that he was crossing the line from legitimate advocacy to genuine misrepresentation of material facts. In the aggregate, Dr. Sherman's conduct evidences a pattern of lack of candor. We agree with the district court that deceptive intent is the single most reasonable inference that can be drawn from the evidence.[7]

CONCLUSION

The district court did not abuse its discretion in holding the '556 patent unenforceable due to inequitable conduct. In view of this, we need not reach the district court's rulings on claim construction, indefiniteness,

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[7] *See Therasense*, 649 F.3d at 1290 (quoting *Star Scientific Inc. v. R.J. Reynolds Tobacco Co.*, 537 F.3d 1357, 1366 (Fed. Cir. 2008)).

laches and judicial estoppel. The judgment in favor of UCB is hereby

AFFIRMED