

FILED
U.S. COURT OF APPEALS FOR
THE FEDERAL CIRCUIT

Appeal No. 2006-1530, -1555

SEP 25 2007

United States Court of Appeals
for the
Federal Circuit

JAN HORBALY
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AVENTIS PHARMA DEUTSCHLAND GMBH,

Plaintiff-Cross Appellant.

- and -

KING PHARMACEUTICALS, INC.,

Plaintiff-Cross Appellant.

- v. -

LUPIN LTD. and LUPIN PHARMACEUTICALS, INC.,

Defendants-Appellants.

APPEAL FROM THE UNITED STATES DISTRICT COURT FOR
THE EASTERN DISTRICT OF VIRGINIA IN CASE NO. 2:05-CV-421,
JUDGE ROBERT G. DOUMAR

PETITION FOR REHEARING AND REHEARING EN BANC

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Dated: September 25, 2007

**CERTIFICATE OF INTEREST OF AVENTIS PHARMA DEUTSCHLAND
GMBH**

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I. The full name of every party or amicus represented by me is:

Aventis Pharma Deutschland GmbH

II. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

sanofi-aventis Deutschland GmbH

III. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

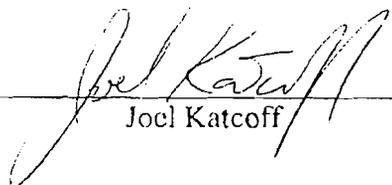
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IV. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:

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1. The full name of every party represented by me is:

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2. The name of the real party in interest represented by me is:

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3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

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Dated: September 24, 2007



Eric Stops

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I. STATEMENT OF COUNSEL:

Based on our professional judgment, we believe the panel decision is contrary to the following decisions of the Supreme Court of the United States or the precedents of this Court: *Graham v. John Deere Co.*, 383 U.S. 1 (1966); *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct 1727 (2007); *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339 (Fed. Cir. 2003); *Estee Lauder Inc. v. L'Oreal, S.A.*, 129 F.3d 588 (Fed. Cir. 1997); *Forest Labs., Inc. v. Ivax Pharms. Inc.*, 2007 WL 2482122 (Fed. Cir. Sept. 5, 2007); *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 252 F.3d 1306 (Fed. Cir. 2001); *Rosco, Inc. v. Mirror Lite Co.*, 304 F.3d 1373 (Fed. Cir. 2002); *Takeda Chem. Indus. Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007); *Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339 (Fed. Cir. 2000); 35 U.S.C. § 103(a); Fed. R. Civ. P. 52.

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

1. May this Court, in the face of established precedent to the contrary, find a chemical compound obvious in the absence of any finding by *any* court (including this Court) of a reasonable expectation of success?
2. May this Court substitute the “capability of a skilled artisan” standard of enablement in place of the very different “reasonable expectation of success”

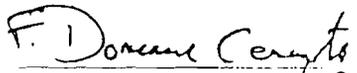
standard required for a finding of obviousness?

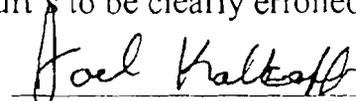
3. Does the Supreme Court's *KSR* decision so radically alter this Court's jurisprudence on the obviousness of chemical compounds that this Court may disregard a district court finding of a lack of any motivation to make the claimed compound, and substitute its own findings of fact for those of the district court?

4. May this Court find that the *composition* of third party's laboratory sample is prior art under § 102(g), even though (1) the district court never found that there was a *contemporaneous* appreciation of the sample's composition, and (2) there is *no* documentation or corroborated evidence of such an appreciation?

5. May this Court reverse on a ground that was not raised by appellants, thus depriving appellees a fair and full opportunity to address the issue?

6. May this Court substitute its own findings of fact for those of the district court, without finding the district court's to be clearly erroneous?


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II. POINTS OF LAW AND FACT OVERLOOKED OR MISAPPREHENDED BY THE PANEL:

1. The Panel disregarded established precedent that obviousness requires a reasonable expectation of success in achieving the patented invention.

2. The Panel disregarded the district court's well-supported findings establishing that there was no reasonable expectation that separating a mixture to obtain ramipril substantially free of other isomers would be successful.

3. The Panel misapplied *KSR* in refusing to give deference to the district court's factual finding that "a person of ordinary skill in the art would not by clear and convincing evidence have necessarily been motivated to isolate Ramipril in the 5(S) configuration substantially free of other isomers." (A76).

4. In view of the fact that there was no district court finding, no documentation, and no corroborated evidence of a contemporaneous appreciation of what isomers were in lab sample SCH 31925, the Panel erred in concluding that the composition of that sample was prior art under 35 U.S.C. § 102(g).

5. By basing its reversal on a finding that the patented invention would have been obvious over SCH 31925 in combination with other references -- an argument that appellants did not raise on appeal -- the Panel deprived appellees of a full and fair opportunity to be heard on the issue.

6. The Panel employed hindsight in finding no unexpected results while disregarding the district court's finding that the superiority of ramipril substantially free of other isomers as compared to a mixture would *not* have been expected.

III. PRELIMINARY STATEMENT:

After a nine day bench trial during which extensive evidence was presented,

the district court, having considered all the evidence before it, found that the appellant did not establish a *prima facie* case of obviousness of any claim of U.S. Patent No. 5,061,722 (“722 patent”) on any of the grounds presented. (A73). Among other things, the district court found: (1) “a person of ordinary skill in the art would not by clear and convincing evidence have necessarily been motivated to isolate Ramipril in the 5(S) configuration substantially free of other isomers” (A76); (2) “having other isomers in the mixture did not seem to be of great concern to the Schering scientists” (A78); “nor was this separation [of ramipril from its isomers] particularly easy to do” (A78); and at the time of the invention, “there was no expectation that Ramipril substantially free of other isomers would be more or less potent than a mixture” (A77-78).

The Panel did not find any of these findings to be clearly erroneous. Nor did the Panel find that the district court had misapplied this Court’s precedents. Instead, the Panel invoked *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007), and then proceeded to make its own findings of fact that contradicted those of the district court. But as other panels of this Court have recognized, *KSR* does not overturn this Court’s jurisprudence regarding the *prima facie* obviousness of chemical compounds, and certainly does not permit this Court to transgress its proper role under Fed. R. Civ. P. 52 as a court of review, not a finder of fact.

Moreover, the Panel failed to apply this Court’s precedents holding that

obviousness requires clear and convincing evidence of a reasonable expectation of success. Indeed, the Panel ignored that requirement altogether: the “reasonable expectation of success” requirement is not even mentioned in its opinion. The Panel’s failure to address the issue is critical, because the district court’s findings, supported by the evidence, show that no such expectation existed.

The Panel also departed from the governing law and facts with regard to the content of the prior art. The Panel’s decision was based on the premise that the isomeric *composition* of a certain laboratory sample -- SCH 31925 -- made by Schering scientists is prior art under 35 U.S.C. § 102(g). But the composition of that sample could be prior art under § 102(g) only if there was clear and convincing and corroborating evidence that the Schering scientists had a contemporaneous appreciation of what isomers were in that sample. Contrary to the Panel’s statement, the district court never made such a finding; and, indeed, it could not have made such a finding because all of the evidence is to the contrary.

The Panel’s reliance on SCH 31925 to find obviousness suffers from another infirmity: the appellants, Lupin Ltd. and Lupin Pharmaceuticals, Inc. (“Lupin”), never argued that ground on appeal. Because appellees never had an opportunity to address the issue, fairness requires a rehearing.

Finally, the Panel impermissibly employed hindsight and substituted its own factfinding for that of the district court in concluding that the appellees had failed

to establish unexpected results. Given the district court's finding that "there was no expectation that Ramipril substantially free of other isomers would be more or less potent than a mixture" (A77-78) -- which has not been found clearly erroneous -- it was improper for the Panel to make a contrary finding on appeal.

IV. ARGUMENT:

A. The Panel Opinion Ignores Well Established Precedent Which Requires a Showing of Reasonable Expectation of Success

It has long been the law that a finding of obviousness requires a showing that there was a reasonable expectation of success in achieving the patented invention at the time the invention was made. *Takeda Chem. Indus. Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1360-62 (Fed. Cir. 2007); *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1354 (Fed. Cir. 2003); *Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000). This principle was endorsed by the Supreme Court in *KSR*, 127 S. Ct. at 1742 (obviousness established where there "are a finite number of identified, predictable solutions" which led to "anticipated success").

The Panel, however, did not even mention the "reasonable expectation of success" requirement, much less apply it. That alone is grounds for rehearing.

The district court explicitly found that "separation [of the 5(S) ramipril isomer from a mixture of isomers was not] particularly easy to do." (A77-78). Hence, the district court found that there was *no* reasonable expectation that

separating a mixture of isomers to obtain ramipril substantially free of other isomers would be successful. (A73, A77-78).

The district court's finding was not, and has not been found to be, clearly erroneous. Indeed, the evidence of record supports it. The Schering scientists who made SCH 31925 expressly testified that they had *no* reasonable expectation that separating SCH 31925 into individual isomers would be successful. Dr. Neustadt testified that whether the 31925 mixture could be separated was "[n]ot easy to predict" and that "there might or might not be an efficient separation achievable," even when applying the same technique that had successfully separated isomers of a 6,5 bicyclic compound. (A3143, A3145). Similarly, Dr. Smith testified that the same technique that separated isomers in a 6,5 bicyclic compound (reverse phase liquid chromatography) did *not* succeed in separating the isomers when applied to Sample 31925, which is a 5,5 bicyclic compound. (A2816-17, A2819).

The Panel disregarded the district court's findings and the supporting record, and instead declared that "there is no evidence that separating 5(S) and SSSSR ramipril was outside the capability of an ordinary skilled artisan." (Op. at 16). This, however, is the test for enablement, not obviousness. That a person of ordinary skill in the art may ultimately achieve separation without undue experimentation does not mean that she reasonably expected that such a separation would be successful. While "there is no 'prediction'" involved in determining

enablement, *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999), obviousness is all about predictability. The two standards are different.

The Panel stated that “the ‘944 patent specifically taught that stereoisomers of ramipril ‘can be separated by conventional chromatographic or fractional crystallization methods.’” (Op. at 16). The Panel’s statement, however, is contrary to the district court’s explicit finding that “this portion of the [‘944] patent is referring to a 6,5 compound having a ‘cis, syn’ configuration and *not* a 5,5 compound, which is Ramipril.” (A77) (emphasis added). This finding was not found clearly erroneous; and the Panel inappropriately acted as a fact finder in reaching a contrary conclusion.

B. The Panel Misapplied *KSR* in Failing to Defer to the District Court’s Finding that a Person of Ordinary Skill Would Not Have Had a Reason or Motivation to Separate Ramipril From Its Isomers

In finding that Lupin had failed to prove *prima facie* obviousness, the district court applied this Court’s decision in *Yamanouchi*. The Panel reversed, concluding that *KSR* changed the law of obviousness as applied to claims to chemical compounds. Yet a different panel of this Court, in *Takeda* 492 F.3d at 1356, characterized *KSR* as “consistent with” prior Federal Circuit law concerning the obviousness of claims to chemical compounds. And, in *Forest Labs., Inc. v. Ivax Pharms, Ltd*, 2007 WL 2482122 (Fed. Cir. 2007), another panel did not even cite *KSR* in affirming the patentability of a single isomer over its racemic mixture in

the prior art. Appellees respectfully submit that the Panel's reading of *KSR* to change this Court's well-developed, long-standing law of obviousness regarding chemical compounds is inconsistent with the Court's prior decisions in *Takeda* and *Forest Labs*, both of which indicate that *KSR* has a far more limited bearing, if any, on the law of obviousness in pharmaceutical and chemical cases than the Panel has attributed to it here.

While *KSR* does hold that there is no "rigid" requirement that the motivation to make the patented invention be *explicit* in the prior art, the district court did not rely on the absence of such an explicit disclosure. To the contrary, the court looked to the real-world evidence that "having other isomers in the mixture did not seem to be of great concern to the Schering scientists." (A78). Indeed, as discussed below, those scientists did not even contemporaneously appreciate or care what isomers were in the mixture. The district court's finding regarding lack of motivation to separate was amply supported. (A2913, A3146).

KSR does not authorize the disregard of factual findings of the district court that are not clearly erroneous. Here, the district court applied the very standard for *prima facie* obviousness that the *Takeda* panel said is "consistent with the legal principles enunciated in *KSR*," 492 F.3d at 1356, and found: "the Court **FINDS** that a person of ordinary skill in the art would not by clear and convincing evidence have necessarily been motivated to isolate Ramipril in the 5(S)

configuration substantially free of other isomers.” (A76). Under long-standing Federal Circuit precedent, this finding is a pure question of fact, which must be upheld on appeal unless clearly erroneous. *See, e.g., In re Gartside*, 203 F.3d 1305, 1315-16 (Fed. Cir. 2000); *In re Berg*, 320 F.3d 1310, 1312 (Fed. Cir. 2003).

But the Panel did *not* find the district court’s finding to be clearly erroneous; instead, it invoked *KSR* and then proceeded to make its own findings of fact which contradicted those of the district court. Appellees submit that the Panel thus departed from the proper role of an appellate court under Fed. R. Civ. P. 52.

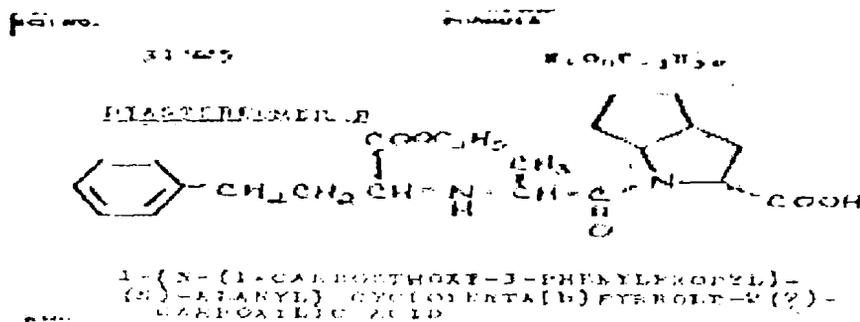
C. The Panel Opinion Contradicts the Consistent Precedent of This Court on What Constitutes Prior Art Under 35 U.S.C. § 102(g) And Is Improperly Premised on Appellate Fact Finding

It is established law that to show that an invention is prior art under 35 U.S.C. § 102(g), there must be clear and convincing proof of “contemporaneous recognition and appreciation of the limitations of the claimed invention, not merely fortuitous inherency.” *Mycogen Plant Sc., Inc. v. Monsanto Co.*, 252 F.3d 1306, 1314 (Fed. Cir. 2001); *accord* *Estee Lauder Inc. v. L’Oreal, S.A.*, 129 F.3d 588, 593 (Fed. Cir. 1997) (“It is well-settled that conception and reduction to practice cannot be established *nunc pro tunc*. There must be contemporaneous recognition and appreciation of the invention.”) (citation omitted).

The Panel found SCH 31925 made by Dr. Smith qualified as prior art under 35 U.S.C. § 102(g). The Panel asserted that the district court found that Dr. Smith

“appreciated” in 1981 that SCH 31925 contained ramipril having the 5(S) configuration and the SSSSR isomer. (Op. at 7). The Panel further stated, “testing by the end of March 1981 confirmed the mixture’s . . . stereochemistry.” *Id.*

The Panel’s statements are neither supported by the district court’s findings, nor by the evidence. The district court did not find that Dr. Smith knew, in 1981, what isomers were present in SCH 31925.¹ Indeed, Dr. Smith’s 1981 lab notebook, reproduced below, demonstrates that she did not appreciate what isomers were contained in SCH 31925. The notebook identifies the configuration of only *one* of the five chiral centers in SCH 31925 -- the rest are unidentified, indicated only by a squiggly line or a question mark, or nothing at all. (A7133-34):



Even Lupin’s expert witness interpreted this notebook entry as showing that

¹ The district court said only that Dr. Smith “envisioned the 5(S) isomer, just as she contemplated all possible isomers.” (A70). However, this statement has nothing to do with the composition of SCH 31925; it refers to a Dr. Smith’s “invention disclosure” (A16554-59) which contains generic formulas covering millions of possible compounds and includes a statement that the disclosure “contemplates all possible stereoisomers.” (See A19-20; A3274-75, A3359-60, A16555, A16559).

Dr. Smith did *not* know the stereochemistry of SCH 31925. (A2443-45). Further, contrary to the Panel's inappropriate appellate fact finding, it is undisputed that SCH 31925 was *never* tested for its stereochemistry. (A2849-50, A2965-66).

Dr. Smith admitted in her testimony that there were no contemporaneous documents showing the 5(S) structure of ramipril. (A2969). The only evidence in the record about the identity of the isomers supposedly contained in SCH 31925 comes from Dr. Smith's testimony in 2006, a quarter century after SCH 31925 was prepared. At her deposition, she was questioned about her understanding of the components of SCH 31925 *as of 2006*: "*Do you have an understanding as to what the stereoconfiguration of the SCH 31925 compound is?*" (A2821) (emphasis added). Dr. Smith responded by providing a hindsight reconstruction of which isomers were supposedly contained in the sample from the perspective of 2006 -- not 1981. She even dated her lab notebook page to indicate that her testimony reflected her thinking in 2006. (A16745). Thus, while the district court states that Dr. Smith "made" a mixture containing the all (S) and SSSSR stereoisomers (A23), it was able to deduce this only in hindsight. There was no evidence of contemporaneous appreciation.

Moreover, to show an alleged prior invention is prior art under 35 U.S.C. § 102(g), there must be corroboration. *Rosco, Inc. v. Mirror Lite Co.*, 304 F.3d 1373, 1382 (Fed. Cir. 2002) (alleged prior inventor's uncorroborated testimony "is

insufficient to constitute clear and convincing evidence” of prior invention); *TypeRight Keyboard Corp. v. Microsoft Corp.*, 374 F.3d 1151, 1159 (Fed. Cir. 2004) (“Corroboration is required of any witness whose testimony is asserted to invalidate a patent.”). Dr. Smith’s testimony, even if construed as reflecting her knowledge of the components of SCH 31925 in 1981, was uncorroborated and is therefore insufficient as clear and convincing proof of prior art under 35 U.S.C. § 102(g). The Panel overlooked this corroboration requirement.

D. The Panel’s Ground for Reversal Was Not Raised By Lupin On Appeal, and Thus Deprived Appellees The Right To Be Heard on The Issue

The Panel reversed based on its conclusion that the ‘722 patent would have been obvious over SCH 31925 in combination with other references. Lupin, however, never argued this ground on appeal. Lupin relied on SCH 31925 only for arguing anticipation; it did not rely on SCH 31925 for obviousness. (Lupin’s obviousness argument was based on the “Schering References” and enalapril. SCH 31925 is not included within the definition of “Schering References”). Hence, the issue of whether SCH 31925 in combination with other references would have rendered the ‘722 patent obvious was not placed before the Panel by Lupin, and was not addressed by appellees in their brief.

Whether the ‘722 patent would have been obvious over a combination of SCH 31925 with other references is not a pure legal issue; it should not have been

raised by the Panel for the first time in its decision. Because the Panel deprived appellees of a full and fair opportunity to be heard on the issue, fundamental fairness requires that a rehearing be granted.

E. The Panel Opinion Impermissibly Employed Hindsight and Substituted Its Own Factfinding for That of the District Court In Concluding that Appellees Failed to Establish Unexpected Results

The Panel ruled that appellees failed to establish that ramipril substantially free of other isomers exhibited unexpected results, stating that “[t]he potency of pure 5(S) ramipril is precisely what one would expect, as compared to a mixture containing other, inert or near-inert stereoisomers.” (Op. at 17). The Panel’s finding is based on pure hindsight. At the time of the invention of the ‘722 patent, the potency of the other isomers of ramipril was unknown. The fact that other isomers are “inert or near inert” was part of the invention, not something known to persons skilled in the art. (A3393-94, A3400-01).

Moreover, the Panel disregarded a finding of fact by the district court that is diametrically opposed to what the Panel determined on appeal. The district court explicitly stated: “the evidence shows that, as of 1981, there was no expectation that Ramipril substantially free of other isomers would be more or less potent than a mixture.” (A77-78). This finding is not, and has not been found to be, clearly erroneous, and is in fact supported by ample evidence. (A3391-94, A3400-01,

A9399-404). It is inappropriate for the Panel to act as its own factfinder and ignore the trial court's findings of fact.

The Panel Opinion acknowledged that the district court found that that "5(S) ramipril is 18 times as potent as the next most potent isomer, the RRSSS form," and that this result was unexpected. (Op. at 16). The Panel, however, stated that this was the "wrong comparison," and that it was necessary to show instead that 5(S) ramipril had unexpected results over the SCH 31925 mixture. In fact, unrebutted evidence shows that that 5(S) ramipril did have unexpected superiority over *any* mixture of its stereoisomers, including SCH 31925. (A3400-01).

CONCLUSION

For the foregoing reasons, appellees Aventis and King's petition for rehearing and rehearing *en banc* should be granted and the district court affirmed.

Dated: September 25, 2007
Respectfully submitted,

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ADDENDUM

United States Court of Appeals for the Federal Circuit

2006-1530, -1555

AVENTIS PHARMA DEUTSCHLAND GMBH,

Plaintiff-Cross Appellant,

and

KING PHARMACEUTICALS, INC.,

Plaintiff-Cross Appellant,

v.

LUPIN, LTD.

and LUPIN PHARMACEUTICALS, INC.,

Defendants-Appellants.

Joel Katcoff, Kaye Scholer LLP, of New York, New York, argued for plaintiff-cross appellant Aventis Pharma Deutschland GmbH. With him on the brief were Benjamin C. Hsing, Sapna Walter Palla, and Tatiana N. Alyonycheva.

F. Dominic Cerrito, Jones Day, of New York, New York, argued for plaintiff-cross appellant King Pharmaceuticals, Inc. With him on the brief were Daniel L. Malone, Eric Stops, and Jonathan A. Muenkel.

Deanne M. Mazzochi, Rakoczy Molino Mazzochi Siwik LLP, of Chicago, Illinois, argued for defendants-appellants. With her on the brief were William A. Rakoczy, Paul J. Molino, and Alice L. Riechers.

Appealed from: United States District Court for the Eastern District of Virginia

Judge Robert G. Doumar

United States Court of Appeals for the Federal Circuit

2006-1530, -1555

AVENTIS PHARMA DEUTSCHLAND GMBH,

Plaintiff-Cross Appellant,

and

KING PHARMACEUTICALS, INC.,

Plaintiff-Cross Appellant,

v.

LUPIN, LTD. and LUPIN PHARMACEUTICALS, INC.,

Defendants-Appellants.

DECIDED: September 11, 2007

Before MAYER and LINN, Circuit Judges, and ROBERTSON, District Judge.

LINN, Circuit Judge.

This is a patent infringement action concerning the pharmaceutical compound ramipril, which is marketed by King Pharmaceuticals, Inc. ("King") as a blood pressure medication under the name Altace®. Lupin Ltd. and Lupin Pharmaceuticals, Inc. (collectively, "Lupin") appeal from a final judgment of infringement entered by the United States District Court for the Eastern District of Virginia in favor of King and Aventis Pharma Deutschland GmbH ("Aventis"). Aventis Pharma Deutschland GmbH v. Lupin Ltd., No. 2:05-CV-421 (E.D. Va. July 18, 2006). The district court concluded at

Hon. James Robertson, District Judge, United States District Court for the District of Columbia, sitting by designation.

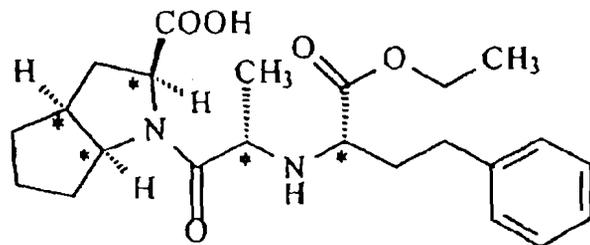
summary judgment that Lupin's filing of an Abbreviated New Drug Application (ANDA) for a generic version of ramipril infringed Aventis's U.S. Patent. No. 5,061,722 ("the '722 patent") under the doctrine of equivalents, and concluded after a bench trial that the asserted claims of the '722 patent were not invalid.¹ Lupin appeals from these decisions. Aventis cross-appeals from the district court's decision to dismiss its claim of willful infringement. For the reasons that follow, we conclude that the subject matter of the asserted claims of the '722 patent would have been obvious. Accordingly, we reverse. The cross-appeal and the remaining issues raised by the parties are deemed moot and are not addressed.

I. BACKGROUND

A. The Claimed Technology

The patent at issue in this appeal is directed to the pharmaceutical compound ramipril in a formulation "substantially free of other isomers." Ramipril, like many complex organic molecules, is one of a family of stereoisomers. As the district court explained in greater detail in its opinion regarding validity, Aventis Pharma Deutschland GmbH v. King Pharms., Inc., No. 2:05-CV-421 (E.D. Va. July 17, 2006) ("Invalidity Opinion"), an isomer of a compound is a separate compound in which each molecule contains the same constituent atoms as the first compound, but with those atoms arranged differently. A stereoisomer is an isomer in which the same atoms are bonded to the same other atoms, but where the configuration of those atoms in three dimensions differs. The following structural formula represents ramipril:

¹ Aventis is the owner of the '722 patent, and King is its exclusive licensee. Both parties are plaintiff-cross appellants. For convenience, and because Aventis and King have adopted each other's arguments on appeal pursuant to Fed. R. App. P. 28(i), we refer to them collectively as "Aventis."



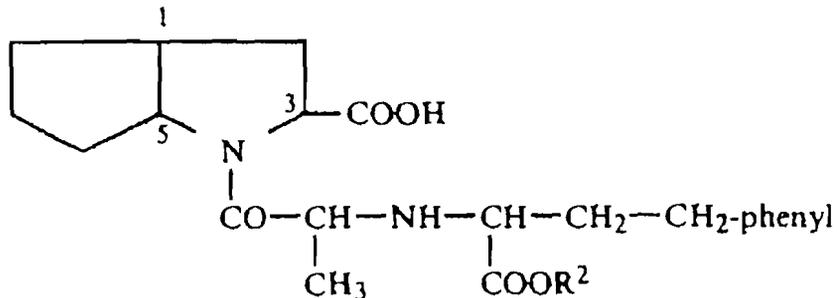
Each of the five carbon atoms marked with an asterisk can be spatially oriented in two different ways.² For example, the dashed triangle leading from the leftmost marked carbon to a hydrogen ("H") atom indicates that the hydrogen atom lies below the planes of the two five-sided rings of which the carbon atom is a part. The hydrogen atom may also lie above the planes of the rings, resulting in a structure that is a stereoisomer of ramipril. Because there are five carbon atoms that may take either of two orientations—or five "stereocenters," as such atoms are known—ramipril is one of 2^5 , or 32, stereoisomers. There are a number of different ways of naming these stereoisomers; one comparatively simple system, used by both parties and by the district court, involves labeling each stereocenter with an "R" or an "S" depending on its configuration. Using this system, all five stereocenters in ramipril are in the "S" configuration, so it is known as an "SSSSS" or "5(S)" stereoisomer. Other stereoisomers would include RRRRR, SSSSR, RRSSS, etc.

Some of the prior art references also use the terms "enantiomer" and "diastereomer." Enantiomers are stereoisomers that are mirror images of each other, like left and right hands. Diastereomers are stereoisomers that are not enantiomers.

² As is customary in chemical diagrams, carbon atoms may be indicated by an intersection of two line segments; in such cases, hydrogen atoms that are bonded to the carbons may be omitted from the diagram for simplicity and should be inferred.

The asserted claims of the '722 patent read as follows:

1. A compound of the formula



or a physiologically acceptable salt thereof, wherein R² is hydrogen, methyl, ethyl, or benzyl, and wherein hydrogen atoms on the ring carbon atoms in the 1- and 5-positions are in the cis-configuration relative to one another, the carboxyl group on the ring carbon atom in the 3-position is in the endo position relative to the bicyclic ring system, and the chirality centers in the chain and on the ring carbon atom in the 3-position all have the S-configuration, said compound or salt being substantially free of other isomers.

2. A compound or salt as in claim 1 which is N-(1-S-carboethoxy-3-phenyl-propyl)-S-alanyl-cis,endo-2-azabicyclo-[3.3.0]-octane-3-S-carboxylic acid or a salt thereof.

4. A hypotensive composition for reducing blood pressure comprising a hypotensively effective amount of a compound or salt as in claim 1 and a pharmaceutically acceptable excipient therefor.

5. A method for reducing blood pressure in a patient which comprises administering to said patient a hypotensively effective amount of a compound or salt as in claim 1.

Claim 1, the only independent claim, covers a small genus of compounds, each of which has a different functional group at location R². The language of the claim, "wherein hydrogen atoms on the ring carbon atoms in the 1- and 5-positions are in the cis-configuration relative to one another, the carboxyl group on the ring carbon atom in the 3-position is in the endo position relative to the bicyclic ring system, and the chirality centers in the chain and on the ring carbon atom in the 3-position all have the S-configuration," limits claim 1 (and thus all the other claims) to the 5(S) stereoisomer.

When the R² functional group is ethyl, the compound of claim 1 is ramipril. This is the compound claimed specifically by claim 2.

B. The Development of Ramipril

Ramipril is one of a family of drugs known as "Angiotensin-Converting Enzyme inhibitors," or "ACE inhibitors." ACE inhibitors inhibit a biochemical pathway that constricts blood vessels and therefore are useful for treating high blood pressure. The earliest ACE inhibitors, dating back to the late 1960s, were based on the venom of the Brazilian Viper, which was known to reduce blood pressure. The active compound isolated from viper venom, known as BPP_{5a}, has six stereocenters, all of which are in the S configuration. Synthetic ACE inhibitors have been developed by making structural modifications to this venom and to successive generations of ACE inhibitors. For example, captopril, the first synthetic ACE inhibitor, consists of part of the BPP_{5a} molecule with a sulfur atom at the end. Captopril retains two stereocenters from BPP_{5a}, both of which remain in the S configuration.

Ramipril's immediate predecessor is an ACE inhibitor known as enalapril that was introduced by Merck in 1980. Enalapril has three stereocenters. In a published article, Merck scientists explained that the all-S (SSS) stereoisomer of enalapril was found to have 700 times the potency of the SSR stereoisomer. A.A. Patchett et al., A New Class of Angiotensin-Converting Enzyme Inhibitors, 288 Nature 280 (Nov. 20, 1980), available at J.A. 15475. The Merck article taught how to separate the all-S isomer using standard chromatography techniques.

Both Aventis and its competitor Schering sought to create new ACE inhibitors based on enalapril. Soon after enalapril's introduction, Dr. Elizabeth Smith, a chemist at

Schering, conceived of the structure of ramipril and recorded it in her laboratory notebooks. Ramipril has the same overall structure as enalapril, with one distinction: where ramipril has two linked five-sided carbon rings (a "5,5 fused ring system"), depicted, in the chemical diagrams above, on the left side of the molecule, enalapril has only a single ring. The addition of the second ring gives rise to two more stereocenters than are present in enalapril; thus, ramipril has the same three stereocenters as enalapril, plus two new ones that span the fused ring system and are therefore known as "bridgehead" carbons, for a total of five as discussed above.

Based on the work of Dr. Smith, Schering filed U.S. Patent Application No. 06/199,886 ("the '886 application") on October 23, 1980. Thereafter, the U.S. Patent and Trademark Office ("PTO") granted Schering Patent No. 4,587,258 ("the '258 patent," issued May 6, 1986) and No. 5,348,944 ("the '944 patent," issued Sept. 20, 1994), both claiming priority from the '886 application via a series of continuations and continuations-in-part. The '886 application, the '258 patent, and the '944 patent disclose the structure of ramipril but do not describe how its stereocenters should be configured.

Example 20 of the '886 application discloses a method for making ramipril and is contained in the published specification of the '944 patent. '944 patent, col. 15, ll. 1-15. The title of Example 20 encompasses only eight of the 32 stereoisomers of ramipril, but there is some suggestion in the record that, in fact, Example 20 would have produced only four stereoisomers in practice. Invalidity Opinion at 22-23. The district court described one of the experts testifying on the topic as "somewhat credible" and did not make any explicit findings as to which stereoisomers Example 20 would create. Id. at

23. For purposes of this appeal, it is sufficient to observe that it is uncontested that Example 20 yields a mixture of several, but not all, stereoisomers of ramipril, one of which is the 5(S) form. It appears likely that in some of these stereoisomers, the "bridgehead" carbons are in the R configuration.

In February 1981, Dr. Smith synthesized a mixture of 5(S)-configuration ramipril and its SSSSR stereoisomer, which mixture came to be known as SCH 31925. To make SCH 31925, Smith followed the process disclosed in Example 20, with one "tweak": she used a catalytic hydrogenation step instead of the mercuric acetate oxidation step taught by Example 20. The record is unclear as to why Smith used that step, but there has been no showing that Smith was attempting to select particular stereoisomers. However, the district court found, and Aventis does not dispute on appeal, that SCH 31925—the product of the process as modified by Smith—contains exactly two isomers, the 5(S) and SSSSR forms, and was successfully produced by Dr. Smith. In both the 5(S) and SSSSR forms, the two "bridgehead" carbons are in the S configuration. In light of the teachings of Example 20, Dr. Smith's written laboratory notebooks, and the test results that Dr. Smith obtained within weeks of SCH 31925's synthesis, we see no clear error in the district court's findings that Dr. Smith had conceived of the various stereoisomers and appreciated which of them SCH 31925 contained. See id. at 22–23, 68–69. Moreover, in vivo testing completed by the end of March 1981 confirmed the mixture's therapeutic activity as well as its stereochemistry. We agree with the district court that Dr. Smith did not separate the 5(S) and SSSSR isomers, and there is no evidence that she conceived of a purified formulation containing only 5(S) ramipril. Id. at 69.

In October 1981, Dr. Volker Teetz, an Aventis chemist, also synthesized ramipril. Id. at 23. On November 5, 1981, Aventis filed a German precursor to the application that would become the '722 patent-in-suit. On November 3, 1982, Aventis filed the first in a chain of U.S. patent applications that led to the '722 patent. In all these applications, Aventis claimed the benefit of the German application. There is no dispute that Aventis is entitled to the November 5, 1981 priority date.

On May 6, 1986, Schering's '258 patent issued. Shortly thereafter, Schering granted Aventis a royalty-bearing license under the '258 patent. Around the same time, the PTO declared Interference No. 101,833 between the '258 patent and a pending continuation application belonging to Aventis. The interference settled. Schering agreed to reduce Aventis's royalty payment and to disclaim some of its patent claims. In exchange, Aventis conceded priority as to the primary subject matter of the '258 patent—the structure, production, and therapeutic use of ramipril, without specification of particular stereoisomers. Aventis retained the right to prosecute its application as to the 5(S) stereoisomer of ramipril in formulations "substantially free of other isomers," which it contended (and still contends) represents a separately patentable invention.

The dispute about patent rights having been resolved between Schering and Aventis, Aventis proceeded to seek FDA approval of ramipril (apparently in a substantially pure 5(S) form). On January 28, 1991, the FDA granted approval, and Aventis began to sell ramipril under the name Altace®. Acting as Schering's agent, Aventis sought and obtained an extension of the '258 patent's term on the basis of the period of regulatory review by the FDA.

On October 29, 1991, the '722 patent issued.

C. Procedural History

The '258 patent expired on January 27, 2005. On March 18, 2005, Lupin filed an ANDA seeking approval for a generic version of ramipril. In response, pursuant to 35 U.S.C. § 271(e)(2)(A), Aventis sued Lupin for infringement, including willful infringement, of the '722 patent in the United States District Court for the Eastern District of Virginia.

The district court granted Lupin's Rule 12(c) motion for judgment on the pleadings as to Aventis's claim for willful infringement and dismissed that claim, leaving only counts alleging non-willful infringement. Aventis Pharma Deutschland GmbH v. King Pharms., Inc., No. 2:05-CV-421 (E.D. Va. Jan. 18, 2006). After construing the claims, see Aventis Pharma Deutschland GmbH v. King Pharms., Inc., No. 2:05-CV-421 (E.D. Va. May 11, 2006), the district court considered the issue of infringement pursuant to motions filed by both sides for summary judgment. The district court declined to grant summary judgment to either party as to literal infringement, finding disputed issues of material fact as to whether Lupin's formulation of ramipril was "substantially free of other isomers." Aventis Pharma Deutschland GmbH v. King Pharms., Inc., No. 2:05-CV-421, slip op. at 11-16 (E.D. Va. June 5, 2006). However, the district court granted summary judgment of infringement under the doctrine of equivalents, subject to a subsequent ruling as to the '722 patent's validity. Id.

The district court then held a bench trial on validity. During the trial, the district court orally granted Aventis's motion for judgment as a matter of law that the '722 patent was not unenforceable for inequitable conduct. On July 17, 2006, the district court issued its opinion on validity, concluding that the '722 patent was neither anticipated nor

obvious. Invalidity Opinion at 87. Although the district court "reache[d] this decision reluctantly" and observed that "[i]f the standard . . . had been by a preponderance of the evidence rather than by clear and convincing evidence, the Court might have determined this case in Lupin's favor," id. at 1–2, the court concluded that the prior art did not teach ramipril "substantially free of other isomers," nor would a person of ordinary skill in the art "have necessarily been motivated to isolate Ramipril in the 5(S) configuration substantially free of other isomers," id. at 75.

Lupin appeals. Aventis cross-appeals, asserting error in the district court's finding that the filing of an ANDA cannot give rise to willful infringement. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

II. DISCUSSION

A. The Relevant Prior Art

The record contains a litany of potential prior art references, only some of which are summarized in Part I.B above, and the prosecution histories of both the '722 patent and Schering's ramipril patents are complex. Accordingly, and because Aventis challenges the prior art status of a number of the references that Lupin cites, we begin by identifying and describing the references on which our decision depends and explaining why we consider them to be prior art.

Least controversial are the various references regarding BPP_{5a}, captopril, and enalapril. It is uncontested that these references were publicly disclosed or published well before the development of ramipril and that both Schering's and Aventis's efforts towards developing ramipril were based on this body of earlier knowledge. Notably, all of the stereocenters in the most therapeutically active stereoisomers of these prior art

compounds are in the S configuration, and this fact was taught by, among other references, Merck's enalapril article in Nature.

Unlike these earlier references, however, Aventis challenges the prior art status of the '944 patent.³ The '944 patent, it observes, is a continuation-in-part of Schering's U.S. Patent Application No. 06/258,484 ("the '484 application"), itself a continuation-in-part of the '886 application. Because Schering had abandoned the '484 application before the '944 patent's filing date, Aventis argues, 35 U.S.C. § 120 bars the '944 patent from benefiting from the earlier '886 filing date. Lupin responds that the PTO cured this defect by reviving the '484 application nunc pro tunc. We need not and do not decide Aventis's challenge on this ground, however, because Aventis presents it for the first time on appeal. In the district court, the '944 patent was relied upon as prior art and its status went unchallenged. Accordingly, the issue is waived. See Sage Prods., Inc. v. Devon Indus., Inc., 126 F.3d 1420, 1426 (Fed. Cir. 1997). We thus consider the '944 patent entitled to the '886 filing date and treat it as prior art to the '722 patent. The '944 patent discloses Example 20 and also contains the following teaching: "When diastereomeric products result from the synthetic procedures, the diastereomeric products can be separated by conventional chromatographic or fractional crystallization methods." '944 patent, col. 10, ll. 28-31.

Finally, we rely, as did the district court, on Dr. Smith's synthesis of SCH 31925, which qualifies as prior art under 35 U.S.C. § 102(g) as of a date no later than the end of March 1981, several months before Aventis's own synthesis of ramipril. See E.I. du

³ Aventis also challenges the prior art status of the '258 patent on the ground that it is a continuation-in-part containing previously undisclosed new matter. We need not resolve this issue because we do not rely on the '258 patent.

Pont de Nemours & Co. v. Phillips Petroleum Co., 849 F.2d 1430, 1436–37 (Fed. Cir. 1988) (discussing use of § 102(g) prior art in § 103 obviousness determinations). Section 102(g) affords prior art status to an “invention [that] was made in this country by another inventor who had not abandoned, suppressed, or concealed it.” 35 U.S.C. § 102(g). Aventis argues that Dr. Smith “abandoned, suppressed, or concealed” SCH 31925, but we see no error in the district court’s implicit rejection of this argument. A very similar method to the one Dr. Smith used had already been disclosed in the ’886 patent application, the exact method was subsequently disclosed in the ’258 patent, and the composition was developed in the course of extensive ongoing research and development and concurrent ongoing patent prosecution. There has been no showing either that Smith “intentionally suppress[ed] or conceal[ed] h[er] invention” or that an “inference of suppression or concealment can be drawn based on an unreasonable delay in making the invention publicly known.” Flex-Rest, LLC v. Steelcase, Inc., 455 F.3d 1351, 1358 (Fed. Cir. 2006). Accordingly, SCH 31925—a mixture of 5(S) ramipril with its SSSSR stereoisomer—is part of the prior art.

B. Obviousness of Claims 1 and 2

We turn to the question of obviousness. “Obviousness is a question of law, reviewed de novo, based upon underlying factual questions which are reviewed for clear error following a bench trial.” Alza Corp. v. Mylan Labs., Inc., 464 F.3d 1286, 1289 (Fed. Cir. 2006). The key question is whether the 5(S) stereoisomer of ramipril, in a form substantially free of other isomers,⁴ would have been obvious over the prior art

⁴ We note that the parties dispute the claim construction of “substantially free of other isomers.” We need not address this question directly, however, because their dispute centers on how much of another isomer a composition might contain while

listed above to one of ordinary skill in the art at the time of the '722 patent's priority date. See 35 U.S.C. § 103(a). Such a composition is precisely the subject matter of claim 2 of the '722 patent, but the question is dispositive of the obviousness of claim 1 as well, because claim 1 is to a broader genus containing the same subject matter. See, e.g., Eli Lilly & Co. v. Barr Labs., Inc., 251 F.3d 955, 971 (Fed. Cir. 2001) (noting that a "genus claim limitation is anticipated by, and therefore not patentably distinct from, [a] species claim").

The district court held that Lupin failed to meet its burden of proof by clear and convincing evidence that a person of ordinary skill in the art would have been motivated to purify 5(S) ramipril into a composition substantially free of other isomers. Invalidity Opinion at 74–75. The district court saw this as a close case based principally on the absence of a clear and convincing showing of motivation. Since the date of that decision, however, the Supreme Court decided KSR International Co. v. Teleflex Inc., 127 S. Ct. 1727 (2007), which counsels against applying the "teaching, suggestion, or motivation" ("TSM") test as a "rigid and mandatory formula[]." See KSR, 127 S. Ct. at 1741. It remains necessary to show "some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness," but such reasoning "need not seek out precise teachings directed to the specific subject matter of the challenged claim." See id. (quoting In re Kahn, 441 F.3d 977, 988 (Fed. Cir. 2006)). Requiring an explicit teaching to purify the 5(S) stereoisomer from a mixture in which it is the active

still remaining "substantially free of other isomers." Whatever the answer to this question might be, it is undisputed that SCH 31925 and the other mixtures of ramipril isomers in the prior art are mixtures that are not substantially free of isomers other than the 5(S) form, whereas the claimed composition of 5(S) ramipril is ipso facto "substantially free" enough.

ingredient is precisely the sort of rigid application of the TSM test that was criticized in KSR.

In the chemical arts, we have long held that "structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed compositions, creates a prima facie case of obviousness." Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd., No. 06-1329, slip op. at 9 (Fed. Cir. June 28, 2007) (quoting In re Dillon, 919 F.2d 688, 692 (Fed. Cir. 1990) (en banc)); see also In re Papesch, 315 F.2d 381 (C.C.P.A. 1963). The "reason or motivation" need not be an explicit teaching that the claimed compound will have a particular utility; it is sufficient to show that the claimed and prior art compounds possess a "sufficiently close relationship . . . to create an expectation," in light of the totality of the prior art, that the new compound will have "similar properties" to the old. Dillon, 919 F.2d at 692; see also In re Wilder, 563 F.2d 457, 460 (C.C.P.A. 1977) ("[O]ne who claims a compound, per se, which is structurally similar to a prior art compound must rebut the presumed expectation that the structurally similar compounds have similar properties."). Once such a prima facie case is established, it falls to the applicant or patentee to rebut it, for example with a showing that the claimed compound has unexpected properties. Dillon, 919 F.2d at 692.

The analysis is similar where, as here, a claimed composition is a purified form of a mixture that existed in the prior art. Such a purified compound is not always prima facie obvious over the mixture; for example, it may not be known that the purified compound is present in or an active ingredient of the mixture, or the state of the art may be such that discovering how to perform the purification is an invention of patentable

weight in itself. However, if it is known that some desirable property of a mixture derives in whole or in part from a particular one of its components, or if the prior art would provide a person of ordinary skill in the art with reason to believe that this is so, the purified compound is prima facie obvious over the mixture even without an explicit teaching that the ingredient should be concentrated or purified. See In re May, 574 F.2d 1082, 1090–94 (C.C.P.A. 1978) (holding isolated stereoisomer nonobvious over racemic mixture of stereoisomers, after conceded prima facie showing of obviousness, because isolated stereoisomer was unexpectedly nonaddictive); In re Adamson, 275 F.2d 952, 954–55 (C.C.P.A. 1960) (holding isolated stereoisomer obvious over racemic mixture of stereoisomers, given insufficient showing of any unexpected result); see also In re Merz, 97 F.2d 599, 601 (C.C.P.A. 1938) (holding, prior to the enactment of § 103, that an applicant “is not entitled to a patent on [an] article which after being produced has a greater degree of purity than the product produced by former methods” unless the purification results in “properties and characteristics which were different in kind from those of the known product rather than in degree”). Ordinarily, one expects a concentrated or purified ingredient to retain the same properties it exhibited in a mixture, and for those properties to be amplified when the ingredient is concentrated or purified: isolation of interesting compounds is a mainstay of the chemist's art. If it is known how to perform such an isolation, doing so “is likely the product not of innovation but of ordinary skill and common sense.” KSR, 127 S. Ct. at 1742.

The record suggests that when Dr. Smith synthesized SCH 31925, she understood that the 5(S) form of ramipril was the mixture's therapeutically active ingredient. Even if she did not, however, the prior art provides a sufficient reason to

look to the 5(S) configuration. The SCH 31925 composition contained only the 5(S) and SSSSR stereoisomers of ramipril. Importantly, these forms differ by the configuration of only one carbon atom, and that atom is not one of the "bridgehead" carbons. Rather, that carbon atom is in the part of the ramipril molecule that is common to the enalapril molecule. In enalapril, as in captopril and BPP_{5a} before it, all of the stereocenters are in the S configuration; the Merck article taught that the SSS configuration of enalapril is 700 times as potent as the SSR form. The close structural analogy between 5(S) and SSSSR ramipril and SSS and SSR enalapril would have led a person of ordinary skill to expect 5(S) and SSSSR ramipril to differ similarly in potency. Moreover, the '944 patent specifically taught that stereoisomers of ramipril "can be separated by conventional chromatographic or fractional crystallization methods." '944 patent, col. 10, ll. 28–31. Aventis's protestations notwithstanding, there is no evidence that separating 5(S) and SSSSR ramipril was outside the capability of an ordinarily skilled artisan.

Aventis attempts to rebut this prima facie case of obviousness by arguing that purified 5(S) ramipril exhibited unexpected results in the form of increased potency. In support, Aventis points to the district court's finding that 5(S) ramipril is 18 times as potent as the next most potent isomer, the RRSSS form. Invalidity Opinion at 44. Aventis is correct that, on the basis of the record, the RRSSS and 5(S) forms might have been expected to have comparable potencies; both of them have only S-configured stereocenters in the part of the ramipril molecule that is common to enalapril, as the R stereocenters in the RRSSS form are the "bridgehead" carbons. This, however, is the wrong comparison. The prior art supporting prima facie obviousness included the SCH 31925 mixture, and so Aventis must show that 5(S) ramipril had

unexpected results not over all of its stereoisomers, but over that mixture, which did not contain the RRSSS form. And the potency of pure 5(S) ramipril is precisely what one would expect, as compared to a mixture containing other, inert or near-inert stereoisomers. All evidence suggests, and the district court found, that potency varies with the absolute amount of the 5(S) isomer in a mixture. Invalidity Opinion at 37. That is, a 30 milligram dose of a mixture that is 1/3 5(S) ramipril has the same effectiveness as a 10 milligram dose of pure 5(S) ramipril. Id. Aventis has thus failed to show unexpected results that would tend to rebut a prima facie case of obviousness. See Pfizer v. Apotex, 480 F.3d 1348, 1368–69 (Fed. Cir. 2007) (holding obvious a patent claim to amlodipine besylate over prior art disclosing the small genus of pharmaceutically acceptable amlodipine salts, where there was an insufficient showing that the properties of amlodipine besylate, purportedly superior for the purpose of mass-manufacturing tablets, were unexpectedly superior to other obvious-to-try salts); cf. Forest Labs., Inc. v. Ivax Pharms., Inc., No. 07-1059, slip op. at 10–11 (Fed. Cir. Sept. 5, 2007) (holding that prima facie obviousness of a claim to a particular stereoisomer over a racemic mixture was rebutted where the particular stereoisomer showed unexpected benefits and evidence indicated that the isomers would have been difficult for a person of ordinary skill in the art to separate).

In sum, we hold that claims 1 and 2 of the '722 patent, which cover the 5(S) stereoisomer of ramipril in a composition substantially free of other isomers, are invalid under 35 U.S.C. § 103 over the SCH 31925 mixture, the '944 patent, and the enalapril references in the prior art.

C. Obviousness of Claims 4 and 5

Two asserted claims of the '722 patent remain for discussion. Claim 4 addresses a "hypotensive composition" of the compound in claim 1 "comprising a hypotensively effective amount" of the compound "and a pharmaceutically acceptable excipient therefor." Claim 5 addresses a "method for reducing blood pressure" by administering the compound of claim 1. The parties argue this case by discussing the invalidity of the '722 patent as a whole, but "we must evaluate obviousness on a claim-by-claim basis." DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co., 464 F.3d 1356, 1372 (2006). However, the parties do not challenge the district court's observation that "all the claims rise or fall with the validity of claim 1," Invalidity Opinion at 17, and with good reason. The added limitations of claims 4 and 5 appear almost verbatim in virtually all the prior art patents, including the '944 patent and its parent '886 application. E.g., '944 patent, claims 3–4, col. 36, ll. 43–52. The prior art thus reveals that it was well understood by ordinarily skilled artisans that ACE inhibitors were to be used in the manner these claims describe. Accordingly, we hold that claims 4 and 5 of the '722 patent are also invalid as obvious.

III. CONCLUSION

Having concluded that all asserted claims of the '722 patent are invalid as obvious, we need not reach Lupin's remaining arguments in favor of reversal. Likewise, Aventis's cross-appeal is moot. Because Lupin is entitled to entry of judgment in its favor, the judgment of the district court is

REVERSED.

CERTIFICATE OF SERVICE

**United States Court of Appeals
for the Federal Circuit**

Appeal Nos. 2007-1530, -1555

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AVENTIS PHARMA DEUTSCHLAND GMBH,
Plaintiff-Cross Appellant,

and
KING PHARMACEUTICALS, INC.,
Plaintiff-Cross Appellant,

v.
LUPIN LTD. and LUPIN PHARMACEUTICALS, INC.,
Defendants-Appellants.

-----)
I, John C. Kruesi, Jr., being duly sworn according to law and being over the age of 18, upon my oath depose and say that:

I am retained by KAYE SCHOLER LLP, Attorneys for Plaintiff-Cross Appellant.

On the **25th Day of September 2007**, I served the within **Petition for Rehearing and Rehearing En Banc** upon:

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King Pharmaceuticals, Inc.*

via Federal Express, by depositing 2 true copies of each, enclosed in a properly addressed wrapper, in an official depository of the Federal Express.

Unless otherwise noted, the original and 18 copies have been hand-delivered to the Court on the same date as above.

September 25, 2007

