United States District Court,
E.D. Virginia, Norfolk Division.

AVENTIS PHARMA DEUTSCHLAND GMBH and King Pharmaceuticals, Inc,
Plaintiffs.
v.
LUPIN LTD. and Lupin Pharmaceuticals, Inc,
Defendants.

Civil Action No. 2:05cv421

May 11, 2006.

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MEMORANDUM OPINION AND ORDER

ROBERT G. DOUMAR**, District Judge.**

This case involves an action for patent infringement and inducement of infringement of an invention of pharmaceutical compound protected by U.S. Patent No. 5,061,722 (the '722 patent), which was issued on October 29, 1991. The '722 patent covers ramipril, a pharmaceutical compound. Aventis Pharma Deutschland GMBH ("Aventis") and King Pharmaceuticals, Inc. ("King") are the plaintiffs in this case (collectively referred to as "Aventis"). Lupin Ltd., a generic drug company, and Lupin Pharmaceuticals, Inc. are the defendants (collectively referred to as "Lupin").

Presently before the Court is the claim construction of the terms "a compound" and "said compound or salt being substantially free of other isomers" found in claim 1 of the '722 patent. As explained in detail herein, the Court **FINDS** that "a compound" is a fairly broad term meaning "a chemically distinct substance formed by union of two or more ingredients (as elements) in definite proportion by weight and definite structural arrangement." Ortho-McNeil Pharmaceuticals Inc. v. Mylan Labs., Inc., 348 F.Supp.2d 713, 728 (N.D.W.Va.2004). The Court also **FINDS** that "said compound or salt being substantially free of other isomers" means that ramipril, the "said compound," is largely but not necessarily free of other isomers. In other words, "substantially free of other isomers" qualifies the compound by indicating that it may not be

100% pure or 100% free of other isomers. Finally, the Court **FINDS** that the phrase "substantially free of other isomers" is not indefinite.

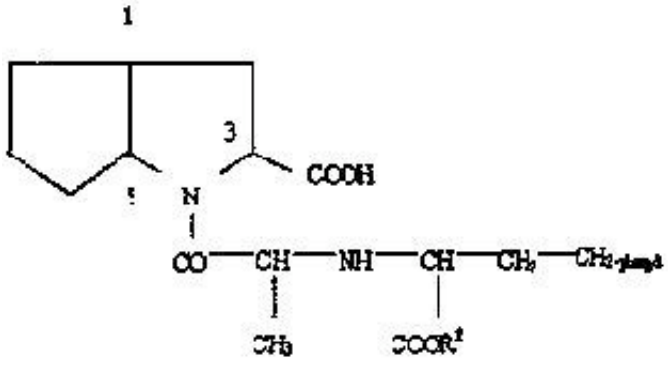
I. Background

A. Overview

On March 18, 2005, Lupin submitted an "Abbreviated New Drug Application" ("ANDA") to the Food and Drug Administration ("FDA") seeking approval to market generic versions of the ramipril capsules developed by Aventis. Pursuant to the ANDA content requirements relating to the status of the '722 patent, Lupin certified that Aventis' patent "is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted" under paragraph IV of the provision, which is commonly known as "paragraph IV certification." *See* s. 355(b)(2)(A)(iv); Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1352 (Fed.Cir.2003). As required by s. 355(j)(2)(B), Lupin then sent a notification letter to Aventis about its ANDA application on June 8, 2005. The present action arose when, after receiving the notification letter from Lupin, Aventis subsequently filed suit in this Court on July 19, 2005 alleging infringement and inducement of infringement.

On May 5, 2006, this Court held a Markman hearing. The '722 patent has five claims. In a joint statement to the Court, the parties agreed that one claim, claim 1, requires construction. Claim 1 reads in its entirety as follows, with the portions of the claim requiring construction bolded:

A compound of the formula



or a physiologically acceptable salt thereof, wherein R ^{2} 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.**
'722 patent.

B. The Invention

At the outset, the Court compliments counsel on both sides for the illustrations that were provided at the Markman hearing and the briefs submitted explaining the chemistry involved with the invention in this case.

Ramipril is an "enzyme inhibitor" used to treat high blood pressure. The ramipril molecule has five carbon atoms known as "chiral carbons." A chiral carbon is a carbon atom having four different groups chemically bonded to it. It can exist in two possible three dimensional configurations, known as the "R-configuration" and the "S-configuration." The terms "S" and "R" are ways in which chemists describe a right-hand or left-hand version of a compound. (Markman Hearing Trans. 13: 8-12.) Such molecules are "stereoisomers" or isomers, which means they have the same constituent atoms but are arranged in a unique pattern. The same molecules in a configuration may be arranged differently in three-dimensional space.

When a molecule, such as ramipril, has five chiral carbons, there are thirty-two possible configurations of the chiral carbons. These chiral carbons may be thought of as having five positions. The number one position could be in S, with the rest of the positions in R. Another possibility is that positions one and two could be in S, with positions three, four, and five in R. Id. at 17-18. In this way, thirty-two combinations are possible ($2^5 = 32$). Id. at 18: 17-18.

Ramipril has one specific chiral combination, the "S-configuration." The parties refer to this as the 5-S configuration. The thirty-one other configurations are known as ramipril's isomers. Accordingly, in this case, ramipril is a compound having the chemical composition described above with its five chiral carbons in the "S-configuration." Id. at 19: 1-4, 9.

II. Claim Construction

A. Standard of Review

Patents consist of "claims," and claim construction is a matter of law to be determined by the Court. Markman v. Westview Instruments, Inc., 517 U.S. 370, 388 (1996). By interpreting the words used in a claim, courts explain the scope of the claim, which ultimately defines the scope of the patented invention. *See* Gart v. Logitech, Inc., 254 F.3d 1334, 1339-40 (Fed.Cir.2001); HERBERT F. SCHWARTZ, PATENT LAW AND PRACTICE s. 5.I (4th ed.2003). "It is a 'bedrock' principle of patent law that 'the claims of a patent define the invention to which the patentee is entitled to exclude.' " Phillips v. AWH Corp., 415 F.3d 1303, 1312 (Fed.Cir.2005).

"When construing patent claims, the Court must look first to the intrinsic evidence in the record: 'The claims, the specification, and the prosecution history.' " Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed.Cir.1995), *aff'd.,* 517 U.S. 370 (1996). These sources are not considered equal; rather, they are a "hierarchy of analytical tools." Digital Biometrics, Inc. v. Identix, Inc., 149 F.3d 1335, 1344 (Fed.Cir.1998). "The actual words of the claim are the controlling focus." *Id.; see also* Ortho-McNeil Pharmaceuticals Inc., 348 F.Supp.2d at 721-22 ("With these varying sources of information, the Court must be careful to always focus on interpreting the claim language as written."). While the specification and the prosecution history are the best tools for "plac[ing] the claim language in its proper technological and temporal context," the claim language as used by "skilled artisans at the time of the invention" controls unless the intrinsic evidence found in the specification and prosecution history "*compels* a contrary conclusion." SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1338-39 (Fed.Cir.2005) (emphasis added).

The language used in the claim is the first and most important step of the court's analysis. Ortho-McNeil Pharmaceuticals Inc., 348 F.Supp.2d at 722. The United States Court of Appeals for the Federal Circuit has often stated that the words of a claim "are generally given their ordinary and customary meaning." Phillips,

415 F.3d at 1312 (quoting *Vitronics Corp. v. Conceptronic, Inc.,* 90 F.2d 1576, 1582 (Fed.Cir.1996)). When interpreting technical terms in a patent document, however, a court should give it the "meaning that it would be given by persons experienced in the field of the invention" at the time the patent application was filed. Hoechst Celanese Corp. v. BP Chems. Ltd., 78 F.3d 1575, 1578 (Fed.Cir.1996); Phillips, 415 F.3d at 1313. *See also* Honeywell Intern., Inc. v. Int'l Trade Comm'n, 341 F.3d 1332, 1338 (Fed.Cir.2003) (a court must "give a claim term the full range of its ordinary meaning as understood by persons skilled in the relevant art"). Inventors, not surprisingly, "are typically persons skilled in the field of the invention." Phillips, 415 F .3d at 1313. For this reason, "the inventor's words that are used to describe the invention-the inventor's lexicography-must be understood and interpreted by the court as they would be understood and interpreted by a person in that field of technology." *Id.* FN1

FN1. As discussed *infra,* the written description-the "specification"-and the prosecution thus become important when understanding the context in which the claim terms were written. Phillips, 415 F.3d at 1313.

Second in the "hierarchy of tools" is the specification, a written description describing the invention. Phillips, 415 F.3d at 1315. The specification has been described as "a concordance for the claims," which is "based on the statutory requirement that the specification 'describe the manner and process of making and using' the patented invention." *Id.* (internal citation omitted). The United States Court of Appeals for the Federal Circuit has instructed that the best way to "understand[ ] a technical term is the specification from which it arose, informed, as needed, by the prosecution history." *Id.*

The prosecution history is the third most important tool used to construe a claim. *Id.* The prosecution history of a patent contains:

... all express representations made by or on behalf of the applicant to the examiner to induce a patent grant .... Such representations include amendments to the claims and arguments made to convince the examiner that the claimed invention meets the statutory requirements of novelty, utility, and nonobviousness. Thus, the prosecution history (or file wrapper) limits the interpretation of claims so as to exclude any interpretation that may have been disclaimed or disavowed during prosecution in order to obtain claim allowance.

Jonsson v. Stanley Works, 903 F.2d 812, 818 (Fed.Cir.1990). "The Court should consult the prosecution history to determine whether the patent applicant 'consistently and clearly use[s] a term in a manner either more or less expansive than its general usage in the relevant community." OrthoMcNeil, 348 F.Supp.2d at 723. Furthermore, the "prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." Phillips, 415 F.3d at 1317. The statements in the prosecution history, however, must be "clear and unmistakable" in order to limit the scope of a claim. Resqnet.com, Inc. v. Lansa, Inc., 346 F.3d 1374, 1378 (Fed.Cir.2003).

B. "A Compound"

Here, Aventis, the owner of the '722 patent, maintains that "a compound" in claim 1 refers to one of the three types of claims in the pharmaceutical field: compound claims, formulation claims, and methods-of-use claims. Pl.'s Pre-Trial Claim Construction Brief at 5. Moreover, it also maintains that "[c]ompound claims are the broadest [and] they cover the drug compound itself." Id. FN2 Lupin, on the other hand, construes "a

compound" in claim 1 to mean "a singular molecular entity with the chemical formula set for in claim 1, that further has the so-called (S, S, S, S, S) configuration." Def.'s Pre-Trial Claim Construction Brief at 1. In Lupin's view, claim 1 is "directed to a single isomer of a compound that corresponds to the listed structure." The distinction between the parties' constructions appears to be this: Aventis maintains that the term "a compound" is being used in a broad and more general sense, while Lupin urges that, in the context of claim 1, "a compound" refers only to ramipril itself and that this version of ramipril includes only a single isomer of the compound. However "a compound" is read, the parties seem to agree that the term is used to refer to ramipril in the context of claim 1.

FN2. At the hearing, Aventis described claim 1 as a "genus" claim, stating that the compound described in claim 1 is a specific entity that "covers more than one compound." (Markman Hearing Trans. 20: 14). Indeed, looking at the '722 patent in its entirety, it appears that this is the case as subsequent claims 2 and 3 seem to provide for alternative versions of claim one. Aventis described these claims as "species claims," which relate to a "particular molecule." Id. 20: 19. As MOY'S WALKER ON PATENTS explains:
Two patent claims can be dominant and subservient to each other by being drawn respectively to a genus and an included specie. This relationship broadly resembles the taxonomic organization employed in fields such as zoology. A generic claim uses terms that define the invention to include a class of individual embodiments, each of which shares one or more characteristics in common. A specific claim defines its invention as one of the embodiments in the class.

1 MOY'S WALKER ON PATENTS s. 4:27 (4th ed.). The fact that claim 1 is a "genus claim," however, does not change this Court's view that claim 1 uses the term "a compound" broadly and that claim 1 goes on to define the term in the context of the claim as the chemical compound that is ramipril. To be sure, Aventis does not appear to make a contrary argument, as it has said that compound claims "cover the drug compound itself." Pl.'s Pre-Trial Claim Construction Brief at 5 (Doc. 85).
As the parties do not spend a lot of time on this point, the Court will try not to belabor this issue either. In this Court's view, the plain language of claim 1 uses the term "a compound" like it uses the word "formula"- as a fairly broad term. The substance recited in the claim has to be called something, and what it is called is "a compound." In *Schering Corp. v. Geneva Pharmaceuticals,* the United States Court of Appeals for the Federal Circuit described compound claims as "encompass[ing] compounds defined by structure only." 339 F.3d 1373, 1375 (Fed.Cir.2003) (also describing claims listing "a compound" followed by the formula of the compound as "compounds" and going on to read compound claims broadly). In this Court's view, this indicates that the term "a compound" refers to a "structure" made up of specific chemical constituents. In Ortho-McNeil Pharmaceuticals, 348 F.Supp.2d at 728, the district court provided a definition that conforms with this understanding, defining "compound" as that which is "a chemically distinct substance formed by union of two or more ingredients (as elements) in definite proportion by weight and definite structural arrangement ." FN3 (quoting WEBSTER'S THIRD NEW INT'L DICTIONARY 466 (2002)). The Court adopts this definition for the purposes of this case.

FN3. The district court went on to say that molecules may also be compounds, as a "molecule is a unit of matter that is the smallest particle of an element or chemical combination of atoms (as a compound) capable of retaining chemical identity with the substance in mass." Ortho-McNeil Pharmaceuticals, 348 F.Supp.2d at 728 (internal quotations omitted). In this case, neither party appears to argue that "a compound" in this case refers only to a portion or particular molecule of the ramipril drug; consequently, this Court will not do so either.

The Court observes that, contrary to what Lupin seems to argue, the fact that claim 1 goes on to give content to what compound is involved in the claim does not narrow the plain meaning of the word "compound" or the term "a compound." Rather, the term is used to indicate a "chemically distinct substance"-what that substance consists of must be explained in the formula provided and in the rest of the claim. The Court therefore **FINDS** that the term "a compound" is a fairly broad term meaning "a chemically distinct substance formed by union of two or more ingredients (as elements) in definite proportion by weight and definite structural arrangement ." *Id*.

C. "Said Compound or Salt Being Substantially Free of Other Isomers"

1. The Parties' Arguments

While the term "a compound" does not appear to be particularly contested by the parties, the phrase "said compound or salt being substantially free of other isomers" is hotly contested. Aventis maintains that the phrase means "that other isomers may be present so long as the presence of other isomers does not materially affect the basic properties of the recited compound." Pl.'s Pre-Trial Claim Construction Brief at 1. Aventis argues that, given the qualifier "substantially," "[a] person of ordinary skill in the pharmaceutical arts would *not* construe the condition-'free of'-to mean a purity of 100.00%." *Id*. at 6-7. In addition, in Aventis' view, the prosecution history "establishes that 'substantially free of other isomers' carries the same meaning as the phrase "consisting essentially of," a term of art in patent law that allows for the presence of other components beyond the claimed compound as long as they do not materially affect the basic characteristics of the claim compound." *Id*. at 8.

Lupin, in contrast, maintains that, properly construed, claim 1 "does not have any detectable isomers." Def.'s Pre-Trial Claim Construction Brief at 9.

In other words, a compound is the pure 5(S)-isomer or "being substantially free of other isomers" if one cannot "see" it, i.e., it contains no detectable amount of other isomers by NMR or TLC testing. Conversely, a compound with the 5(S)-isomer that contains detectable amounts of other isomers that a test method can "see," is not pure or "substantially free of" other isomers. This is the only construction that is consistent with the intrinsic evidence and the inventors' own understanding and use of these phrases before the PTO.

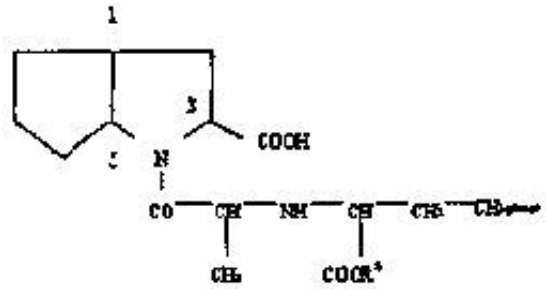
Id. Lupin relies heavily on the prosecution history of the patent to make this argument, and its arguments are discussed more fully in the analysis below.

2. Claim Construction of "Said Compound or Salt Being Substantially Free of Other Isomers"

I. The Language of Claim 1

The Court shall begin with the language of claim 1. Again, in its entirety, the claim reads as follows:

A compound of the formula



or a physiologically acceptable salt thereof, wherein R ^{2} 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.**
'722 patent.
Beginning with "substantially free," the words particularly contested by the parties, the Court observes at the outset that the United States Court of Appeals for the Federal Circuit has defined the "term 'substantial' [as] a meaningful modifier implying 'approximate,' rather than 'perfect.' " Playtex Prod., Inc. v. Procter & Gamble Co., 400 F.3d 901, 907 (Fed.Cir.2005) (quoting Liquid Dynamics Corp. v. Vaughan Co., Inc., 355 F.3d 1361 (Fed.Cir.2004)). The Federal Circuit has also stated that, "ordinarily ... 'substantially' means ... 'largely but not wholly that which is specified.' " Ecolab, Inc. v. Envirochem, Inc., 264 F.3d 1358 (Fed.Cir.2001) (quoting WEBSTER'S NINTH NEW COLLEGIATE DICTIONARY 1176 (9th ed.1983)). In *Ecolab,* the appellate court went on to note that,"like the term 'about,' the term 'substantially' is a descriptive term commonly used in patent claims to 'avoid a strict numerical boundary to the specified parameter.' " *Id.* (quoting Pall Corp. v. Micron Separations, Inc., 66 F.3d 1211, 1217 (Fed.Cir.1995)). "Substantially," unless contradicted or defined differently by the intrinsic evidence, "avoids the strict 100% nonuniformity boundary." *Id.* The *Playtex* court similarly emphasized that it has "refused to impose a precise numeric constraint" on phrases such as "substantially uniform thickness" unless "something in the prosecution history imposed the 'clear and unmistakable disclaimer' needed for narrowing beyond this plain-language interpretation." Playtex, Inc., 400 F.3d at 907. *See also* Glaxo Group Ltd. v. Ranbaxy Pharmaceuticals, Inc., 262 F.3d 1333, 1337-38 (Fed.Cir.2001) (construing "essentially free" and concluding that the prosecution history defined "essentially free from crystalline material" as a maximum crystalline cefuroxime axetil content of less than 10%).

In this case, "substantially" modifies "free," a term that the parties agree means "pure" in this context. Given the definitions above, the fact that "substantially" modifies "free" indicates that "free" is something "approximate, rather than perfect." *Id.* "Substantially free" therefore means something less than "100% free" or "100% pure." *See* Ecolab, Inc., 264 F.3d at 1358. To conclude otherwise, the Court would be reading "substantially" out of the claim. Reading express limitations out of claims is impermissible. Maxwell v. J. Baker, Inc., 86 F.3d 1098, 1105 (Fed.Cir.1996) (holding that a court cannot construe claims to read an express limitation out of the claim). "Courts can neither broaden nor narrow claims to give the patentee something different than what he has set forth." Texas Instruments Inc. v. U.S. Int'l Trade Comm'n, 988 F.2d 1165, 1171 (Fed.Cir.1993) (internal citation omitted).

Of course, given the technical nature of claim 1, "substantially free" must be understood as one of ordinary skill in the art at the time of the invention would use the phrase. Apotex, 403 F.3d at 1338-39. The inventor's words used to describe the invention in the prosecution history are good indications of how

persons skilled in the field of invention would use the term. Phillips, 415 F.3d at 1313. Accordingly, a review of the of the '722 patent prosecution history and a consideration of how persons of ordinary skill in the art would use the phrase are merited.FN4

FN4. The parties agree that the specification does not inform the terms "substantially free" in claim 1.

ii. The Prosecution History

"[T]he prosecution history provides evidence of how the [Patent and Trade Office ("PTO")] and the inventor understood the patent." Phillips, 415 F.3d at 1317. This is so because "it was created by the patentee in attempting to explain and obtain the patent," and it is possible that the "inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id*. As the *Phillips* court explained, however, reviewing the prosecution history is not an easy task.

[B]ecause the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of the negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes.

Id. Statements made in the prosecution history therefore must be "clear and unmistakable" in order to limit the scope of a claim beyond its plain-language interpretation. Playtex, Inc., 400 F.3d at 907; Resqnet.com, Inc., 346 F.3d at 1378.

a) Aventis' Construction

Aventis contends that "substantially free of other isomers" has the same meaning as "consisting essentially of," a term of art in patent law that allows for the presence of other components beyond the claimed compound as long as they do not materially affect the basic characteristics of the claim compound." Pl.'s Pre-Trial Claim Construction Brief at 8. To make this argument, Aventis asks the Court to take several steps in logic that are not supported by the prosecution history or the caselaw.

Aventis first points out that claim 24, which was subsequently cancelled, was added during the prosecution of the patent to clarify that the claimed compounds were "substantially free of other isomers." *Id*. Claim 24 differed from claim 19 only in that it used the language "consisting essentially of" instead of "substantially free of other isomers." *Id*. The Examiner ultimately asked Aventis to cancel claim 24 because "[it] appear[ed] to be claiming the same compounds free of other isomers as claim 19." *Id*. at Ex. I (Examiner Record dated April 19, 1991). Aventis did so. Based on this cancellation, Aventis now asserts that the applicants essentially defined the phrase "substantially free of other isomers" to mean the same thing as "consisting essentially of." The cancellation of claim 24, in other words, is dispositive on the meaning of "substantially free of other isomers." Notably, Aventis provides no legal support for its last assertion that the cancellation of one claim is dispositive as to the meaning of another.

Assuming, then, that "substantially free" means the same thing as "consisting essentially of," Aventis notes that "consisting essentially of" is a term of art in patent law that has a clearly defined meaning, namely, that "[a] patent claim using this phrase allows for the presence of ingredients that do not materially affect the basic properties of the invention." *Id*. at 9 (citing PPG Indus. v. Guardian Indus. Corp., 156 F.3d 1351, 1354 (Fed.Cir.1998)). Aventis further supports its argument by pointing out that the United States Court of Appeals for the Federal Circuit has held that " 'consisting essentially of' as used in the pharmaceutical arts

does not exclude the presence of impurities." *Id*. (citing Abbott Lab. v. Baxter Pharmaceuticals Prod., Inc., 334 F.3d 1274, 1331 n. 2 (Fed.Cir.2003); Talbert Fuel Sys. Patents Co. v. Unocal Corp., 275 F.3d 1371, 1375 (Fed.Cir.2002)). Aventis thus urges this Court to graft the meaning of "consisting essentially of" as a term of art onto the phrase "substantially free."

The Court has several problems with Aventis' construction and concludes that it impermissibly broadens the scope of the claim by reading "free of other isomers" as "free of impurities" generally.FN5 *See* Texas Instruments Inc., 988 F.2d at 1171 ("[c]ourts can neither broaden nor narrow claims to give the patentee something different than what he has set forth."). While Aventis argues that the cancellation suggests that "substantially free of other isomers" and "consisting essentially of" were redundant phrases, the Court perceives a difference between the two. "Substantially free of" focuses on what *is not* included in a substance or compound. "Consisting essentially of" focuses on what *is* included in a compound. The Court observes that, while claim 24 was indeed cancelled, the Examiner represents it was done so because it "appear[ed] to be claiming the same compounds free of other *isomers* as claim 19." Pl.'s Pre-Trial Claim Construction Brief at Ex. I (Examiner Record dated April 19, 1991) (emphasis added). In this way, the Examiner focused on what the same compounds were *free of* and specifically pointed out "other isomers." The phrase "consisting essentially of ramipril" simply does not indicate what should not be there-either isomers or elephants could be lurking around as possible unwanted materials. "Substantially free of other isomers," on the other hand, indicates that *other isomers* should not be in the compound in significant quantities. The phrase is much narrower.

FN5. The Court is not deciding that isomers are not impurities in the context of ramipril; rather, the Court is deciding that the claim is limited to being free of "other isomers," regardless of whether they are impurities or not.

The Court also rejects Aventis' effort, after equating the two phrases, to read into "substantially free of" the meanings associated with the term of art "consisting essentially of." A term of art is "a word or phrase having a specific, precise meaning in a given specialty, apart from its general meaning in ordinary contexts." BLACK'S LAW DICTIONARY 1483 (7th ed.1999). Even assuming "consisting essentially of" is a term of art, the Court can only wonder why it wasn't used, given it has a "specific, precise meaning." The fact that a term of art was not used suggests an intent not to use it. Moreover, *PPG Industries* defines "consisting essentially of" as "a transition phrase commonly used to signal a partial open claim in a patent." PPG Indus., 156 F.3d at 1354. That Aventis would even suggest that claim 1 is a partially open claim is quite surprising, as it would indicate that ramipril is a compound "open to unlisted ingredients." *Id*. To be sure, Aventis urges that these unlisted ingredients would be those "that do not materially affect the basic and novel properties of the invention." *Id*. Such ingredients, Aventis argues, would be nothing more than "impurities ." Yet even this construction is broader than what is provided for in claim 1 by the phrase "substantially free of other isomers." As far as the Court reads claim 1, ramipril is a well-defined chemical compound that is not open to "unlisted ingredients" or various "impurities" but may possibly contain "other *isomers*." There is nothing in the prosecution history to suggest otherwise.

b) Lupin's Construction

While Aventis provides a construction that is impermissibly broad, Lupin provides one that is impermissibly narrow. Lupin gives great weight to the fact that the phrase at issue was included after Aventis lost an interference proceeding with a company called Schering over who was the first person to invent ramipril.

That proceeding involved U.S. Patent No. 4,587,258 (the '258 patent) and the parent '284 application. According to Lupin, Aventis represented to the PTO that its invention in the '722 patent was distinct from the '258 patent because its claims were narrower based on the fact that its invention was "substantially free of other isomers." Id. at 12. Moreover, Aventis, in Lupin's view, analogized this term as "substantially *pure* isomers." Id. (emphasis added). The Examiner apparently rejected this effort "under 35 U.S .C. s. 112 for lack of support." Id. at 14. Lupin urges this rejection was addressed by a declaration of one of the inventors, Dr. Hansjorg Urbach, who "noted that the synthetic procedures employed in Example 1 would eventually lead only to the 5(S) isomer, not the other undesired isomers." Id. According to Lupin, Dr. Urbach referenced thin layer chromatography ("TLC") and "column chromatography" to show that "[i]n each of the both separated products no other isomer could be detected." Id. at 15. By explaining that the product was one where "no other isomer could be detected," Lupin argues that Aventis essentially limited the term "being substantially free of other isomers" to a "pure" compound being "free from other detectable isomers." Id.

Aventis, for its part, maintains that Lupin misreads the prosecution history. Aventis emphasizes that the PTO rejection occurred not because the claim was "indefinite" under 35 U.S.C. s. 112, paragraph 2, but because, under 35 U.S.C. s. 112, paragraph 1, there was "no embodiment in the specification that falls within the scope of those claims." FN6 Pl.'s Pre-Trial Claim Construction Brief at 14. The distinction, according to Aventis, is significant because it suggests the Examiner understood the meaning of the claims, but objected because no embodiment was disclosed. Id.

FN6. Under 37 C.F.R. s. 1.71(b), the specification "must set forth the precise invention for which a patent is solicited, in such manner as to distinguish it from other inventions and from what is old. It must describe completely a specific embodiment of the process, machine, manufacture, composition of matter or improvement invented, and must explain the mode of operation or principle whenever applicable. The best mode contemplated by the inventor of carrying out his invention must be set forth."

Given these arguments, the Court begins by observing that the fact that Aventis represented to the Examiner that it added claim 19 (which subsequently became claim 1 in the '722 patent) "to make it clear that these isomeric compounds and salts are substantially free of other isomers, i.e. are substantially pure isomers" does not alter this Court's view that the term "substantially" is being utilized as qualifier-the fact that it appears, in this sentence, to be qualifying both the compound and the isomers themselves does not necessitate the conclusion, as Lupin argues, that somehow the isomers themselves have been defined as 100% pure. *See* Def.'s Pre-Trial Claim Construction Brief at 12 (citing the Preliminary Amendment dated April 7, 1989 at 9). Nor is this Court's view changed by the fact that Aventis also represented that "it is evident from the form of the claims submitted *abinitio* in this application ... that substantially pure isometric compounds having five chiral centers, all in the S-configuration, were defined or intended to be defined by Applicants." Id. (citing the Preliminary Amendment dated April 7, 1989 at 19). Once again, "substantially" is modifying the purity of "isometric compounds." Undoubtedly, all of the five chiral centers are supposed to be in the S-configuration, as the language of claim 1 itself represents. Yet this emphasis on the configuration of isomers does not expressly change the phrase "substantially free of other isomers" or "substantially pure isomers" to mean 100% pure isomers, as Lupin contends. Id. If anything, it indicates to the Court that the chiral centers in the S-configuration should be "substantially pure isomers" in addition to the fact that the compound itself should be "substantially free of other isomers." The problem for Lupin is that the term "substantially" qualifies both possibilities, indicating that 100.00% pure isomers of any kind are not described.

Lupin goes on, however, to urge that Aventis narrowed the scope of "substantially free of other isomers" to mean a "pure" compound when Reinhard Becker, one of the inventors of the '722 patent, allegedly argued that the term was analogous to pure isomers when he compared

the ACE-inhibiting effect of two pure isomers (i.e., isomers have all five chiral centers in the S-configuration) according to original claim 19 and new claim 19 ... with a *mixture* of isomers of the same formula having five chiral centers, but in which not all of these centers were in the S-configuration as they are in the compounds and salts claimed in both claim 19 of the parent application and now-more explicitly-in new claim 19 of the present application.

Id. (citing the Preliminary Amendment dated April 7, 1989 at 20)(emphasis in original). Lupin then makes much of the statement by the Examiner that, "[h]ence, new claim 19 in the present application makes explicit the isometric purity of the compounds recited therein." Id. (citing the Preliminary Amendment dated April 7, 1989 at 21). Lupin, however, does not quote the rest of the paragraph following this statement, which reads:

Namely, claims 19-23 as presented herein explicitly define compounds and salts thereof having five chiral centers, all of which are in the S-configuration and which are *substantially free of other isomers*. While it is urged the original claims 19-23 of the parent application read on or are intended to read on such *substantially pure isomers,* and were so understood to read by both Applicants and the Patent Office, new claim 19 of the present application makes this limitation explicit.

Id. As this Court reads the prosecution history, what the application makes explicit is that the isometric purity of the invention is "substantially free of other isomers" and contains "substantially pure isomers." It does not make explicit Lupin's contention that there are "no other detectable isomers."

Lupin also argues that the Examiner's rejection of the application and Aventis' response to this rejection reveals that the term "substantially free of other isomers" means "pure isomers." The Examiner rejected the application for two reasons. Claim 22, not at issue here, was rejected under 35 U.S.C. s. 112, paragraph 2, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Id. (Examiner's Action dated Oct. 4, 1989 at 2). Claims 19-23, which subsequently became claims 1-5 of the '722 patent, were rejected as being unpatentable in Interference proceeding 101,833, under 35 U.S.C. 102(g).FN7 The Examiner concluded that the judgment rendered in the interference proceeding applied, stating: "[t]he term 'being substantially free of other isomers' is not considered to be a limitation which distinguishes the instant claims from the claims involved in the interference." Id.

FN7. 35 U.S.C. s. 102(g) provides:
during the course of an interference conducted under section 135 or section 291, another inventor involved therein establishes, to the extent permitted in section 104, that before such person's invention thereof the invention was made by such other inventor and not abandoned, suppressed, or concealed, or (2) before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

In response to this rejection, Aventis filed another amendment. Id. (Amendment dated April 4, 1990). Aventis contended that "claims 19-23 to the specific isomer, *substantially free of other isomers,* represent a separate patentable invention over the broad count of the interference is not inconsistent with the judgment rendered in the interference because the judgment was not referring to these specific claims." Id. (Amendment dated April 4, 1990 at 8) (emphasis added). In the Amendment, Aventis went on to note that the "specific '5S' isomer is claimed as being *substantially free of other isomers*" and that the "Examiner will search in vain for similar disclosure of these specific 5 S compounds *substantially free of other isomers* in any of the prior, predecessor applications...." Id. (Amendment dated April 4, 1990 at 9-10)(emphasis added). Aventis then pointed to several examples in the parent application that do not indicate the 5-S configuration. "Accordingly," Aventis urged, "there is no teaching of any isomers in which all chiral centers are in the S-position and which are *substantially free of other isomers* as is the case of the compounds in claims 19-23." Id. (Amendment dated April 4, 1990 at 12) (emphasis added). After reviewing this portion of the prosecution history, nowhere does the Court find that the phrase "substantially free of other isomers" clearly and unmistakably means "100% pure" or "no other detectable isomers."

Even so, Lupin attempts to support its arguments by pointing to the methods Aventis used to show when a product is substantially free of other isomers. On June 21, 1990, the Examiner once again rejected claims 19-23. Id. (Office Action dated June 21, 1990). This time she rejected the claims under 35 U.S.C. s. 112, paragraph 1, which states:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The Examiner rejected the claims under this provision because

the specification, as originally filed, does not provide support for the invention as now claimed. There is no express support in the specification for the limitation "being substantially free of other isomers." Additionally, the working examples do not indicate the exact purity obtained.

Id. (Office Action dated June 21, 1990 at 2). In response to this rejection, Aventis submitted the declaration of Dr. Hansjorg Urbach, one of the inventors, who, at the outset, stated that Example 1 of the specification was the only example involving the "5-S" compound. Id. (Urbach Decl. at 2). FN8 He then provided a series of drawings explaining the "reaction scheme described in Example 1." Id. At the conclusion of these schematic depictions, which were explained subsequently in the declaration, he stated:

FN8. Example 2 is described as a "mixture of cis, endo "SSS" and "RRR" Intermediate compounds. Id.

Thus, the methods of Example I(1)-I(5) lead only to a single compound in which each of the five chirality centers in the compound has the S-configuration, *being substantially free of other isomers* .
The methods of Example I(1)-I(5), establishing that the necessary and only reasonable construction to be given the disclosure of Application Serial No. 07/296,513 is that the methods provide only the "5S"

compound being *substantially free of other isomers,* are now examined in greater detail.

Id. (Urbach Decl. at 8-9) (emphasis added).
In spite of Dr. Urbach's use of the phrase "substantially free of other isomers," Lupin emphasizes that the two methods Dr. Urbach utilized to distinguish and/or separate isomeric mixtures-TLC and column chromatography-led him to conclude that "no other diastereomer could be detected"-in other words, no other isomers could be "seen." Id. (Urbach Decl. at 16). Unfortunately for Lupin, although the tests did not detect any other isomers, the Court is unconvinced that this fact clearly and unmistakably changes the meaning of the phrase "substantially free of other isomers." If no isomers were detected, the tests simply revealed that Example 1 produces a version of ramipril "substantially free of other isomers," just as the application stated. The tests do not compel the conclusion that no isomers may ever be detected or that 100% purity is guaranteed.

Moreover, the Urbach Examples were provided in response to the Examiner's paragraph 1 rejection, which relates to the support (or lack thereof) provided in the specification. It was not a rejection under s. 112, paragraph 2 for indefiniteness. Thus neither the Examiner's question nor Dr. Urbach's response was related to the meaning of "substantially free of other isomers." Indeed, if the phrase had not been understandable to the Examiner, she would have rejected claim 19 (later claim 1 of the '722 patent) under paragraph 2. In any event, in order to accept Lupin's argument that Dr. Urbach's declaration reveals that he chose to be his own "lexicographer" and change the ordinary meaning of "substantially free," the Court would have to find the plain and ordinary meaning of this phrase " *clearly disclaimed* " during the prosecution of the patent. E-Pass Tech. Inc. v. 3Com Corp., 343 F.3d 1364, 1370 (Fed.Cir.2003) (emphasis added); Playtex, Inc., 400 F.3d at 907. It has not been. Contrary to Lupin's assertions, the Court sees nothing that would clearly and unmistakably indicate that Aventis (or Dr. Urbach) intended to limit the phrase "substantially free of other isomers" to "no detectable isomers."

iii. Persons of Ordinary Skill in the Art

Aventis maintains that a person of ordinary skill in the art would understand the phrase "substantially free of" "to mean something less than 100.00% purity." FN9 Pl.'s Pre-Trial Claim Construction Brief at 5. Aventis asserts that persons of ordinary skill in the art understand "there is no such thing as a 100.00% pure compound." *Id*. at 6. In Ortho-McNeil Pharmaceuticals, Inc., 348 F.Supp.2d at 729, an expert testified "there is always that molecule hiding somewhere in the corner. There is no such thing as an absolutely 100 percent .0000 pure substance." *Id*. The district court in that case agreed that the "realities of science would [lead] a skilled artisan to conclude that the purity was not 100 percent." *Id*. at 730.

FN9. The Court addresses how a person of ordinary skill in the art would understand "substantially free of other isomers" after the prosecution history because the discussion includes, in part, evidence not found in the prosecution history, *i.e.,* extrinsic evidence.

Indeed, Lupin's own chemist seems to agree. On April 18, 2006, in a deposition related to this matter, Girij Pal Singh responded in the following way when asked about when he prepared a "pure sample of Isomer-1."

Q. I think you used the word pure to describe it a minute ago, didn't you?

A. Purity.

Q. You said-I just want to make sure, you said pure Isomer-1?

A. Pure Isomer-1. Pure means, you know, the quality may be more than 95 percent, 98 percent.

Q. So it wasn't 100 percent of Isomer-1?

A. No, it was not 100 percent. I recall, perhaps, you know, I need to see the document, it was 95 or 98 percent purity.

Q. And you considered that pure?

A. That's pure, more than 95%.

Id. at Ex. F, Singh Tr. at 59: 20, 24; 60: 2-12. Given this testimony, like the district court in *OrthoMcNeil Pharmaceuticals,* this Court concludes that the "realities of science would [lead] a skilled artisan to conclude that the purity was not 100 percent." 348 F.Supp.2d at 730. In other words, a person having ordinary skill in the art would conclude that "substantially free" means "largely free" but something less than 100% free. A person of ordinary skill in the art would not read the phrase as meaning "no detectable isomers."

For all of the above reasons, based on the plain language of the claim, the prosecution history, and how a person having ordinary skill in the art would understand the claim, the Court **FINDS** that "said compound or salt being substantially free of other isomers" means that ramipril, the "said compound," is largely but not necessarily free of other isomers. In other words, "substantially free of other isomers" qualifies the compound by indicating that it may not be 100% pure or 100% free of other isomers.

III. Indefiniteness

A. Standard of Review

Under the Patent Act, s. 112, paragraph 2 requires that a patent specification conclude with one or more claims "particularly pointing out and distinctly claiming subject matter which the applicant regards as his invention." 35 U.S.C. s. 112, para. 2. "[T]he standard for assessing whether a patent claim is sufficiently definite to satisfy the statutory requirement [is] as follows: If one skilled in the art would understand the bounds of the claim when read in light of the specification, then the claim satisfies section 112 paragraph 2." Exxon Research & Eng'g Co. v. United States, 265 F.3d 1371, 1375 (Fed.Cir.2001). The claims at issue must be "sufficiently precise to permit a potential competitor to determine whether or not he was infringing." *Id*. "The standard of indefiniteness is somewhat high; a claim is not indefinite merely because its scope is not ascertainable from the face of its claims." Amgen, Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1342 (Fed.Cir.2003). Instead, indefiniteness requires a claim to be "insolubly ambiguous, and no narrowing construction can properly be adopted." *Id*. (quoting Exxon Research & Eng'g Co., 265 F.3d at 1375).

Issued patents are also entitled to a statutory presumption of validity. *Id*. (citing 35 U.S.C. s. 282 (2000)). When indefiniteness is alleged, however, general principles of claim construction apply. *Id*. Thus, the court should focus on the intrinsic evidence found in the patent specification and prosecution history. *Id*. Extrinsic evidence such as expert testimony may be used if necessary. "What matters is for the court to attach the

appropriate weight to be assigned to those sources in light of the statutes and policies that inform patent law." *Id.* at 1324 (quoting Phillips, 415 F.3d at 1314). "Furthermore, a difficult issue of claim construction does not ipso facto result in a holding of indefiniteness." Datamize, LLC v. Plumtree Software, Inc., 417 F.3d 1342, 1347 (Fed.Cir.2005).

B. Analysis

Lupin argues that "the limitation 'substantially free of other isomers' is a relative or subjective term of degree that, standing alone, provides no objective standard for measuring or determining infringement." Def.'s Pre-trial Claim Construction Brief at 21. Aventis, of course, argues otherwise. The parties do not spend a lot of time on this issue; rather, their claim construction arguments largely support their positions.

The Court **FINDS** that the limitation "substantially free of other isomers" is not fatally indefinite. Given the analysis *supra* and in the context of this case, the Court has no trouble finding that "substantially free of other isomers" is not indefinite given its plain-meaning and the fact that it would indicate to a person of ordinary skill in the art that the compound was largely free of other isomers but not 100% pure. As the United States Court of Appeals for the Federal Circuit observed:

Expressions such as "substantially" are used in patent documents when warranted by the nature of the invention, in order to accommodate the minor variations that may be appropriate to secure the invention. Such usage may well satisfy the charge to "particularly point out and distinctly claim" the invention, and indeed may be necessary in order to provide the inventor with the benefit of his invention. In *Andrew Corp. v. Gabriel Elecs. Inc.,* the court explained that usages such as "substantially equal" and "closely approximate" may serve to describe the invention with precision appropriate to the technology and without intruding on the prior art. The court again explained in *Ecolab Inc. v. Envirochem, Inc.* that "like the term 'about,' the term 'substantially' is a descriptive term commonly used in patent claims to 'avoid a strict numerical boundary to the specified parameter."

Verve, LLC v. Crane Cams, Inc., 311 F.3d 1116, 1120 (Fed.Cir.2002) (internal citations omitted). Indeed, the *Verve* court went on to say that "[i]t is well established that when the term 'substantially' serves reasonably to describe the subject matter so that its scope would be understood by persons in the field of the invention, and to distinguish the claimed subject matter from the prior art, it is not indefinite." *See also* Andrew Corp. v. Gabriel Elecs. Inc., 847 F.2d 819, 821-22 (Fed.Cir.1988) (noting that terms such as "substantially equal" and "closely approximate" are "ubiquitous in patent claims" and that such usages, when serving reasonably to describe the claimed subject matter to those of skill in the field of the invention, have been accepted in patent examination and upheld by the courts). In this case, the prosecution history reveals Aventis included the phrase "substantially free of other isomers" in order to distinguish their claims from the prior art. In such a situation, using the term "substantially" is not indefinite.

Moreover, the ability of one skilled in the art to identify a claimed compound by testing indicates that the claim is not invalid for indefiniteness. Morton Int' l, Inc. v. Cardinal Chem. Co., 5 F.3d 1464, 1470 (Fed.Cir.1993). There is no indication in the prosecution history (or anywhere else) that a chemist would not be able to identify the compound ramipril as defined in claim 1. SmithKline Beecham Corp., 403 F.3d at 1340 (stating, when the claim recites in clear terms a discernible chemical structure, "it would be difficult to imagine a more clear and definite claim."). Lupin makes much of that fact that the claim does not indicate just how many "other isomers" are permitted for it to determine whether infringement has occurred. "The test for indefiniteness," however, "does not depend on a potential infringer's ability to ascertain the nature of

its own accused product to determine infringement, but instead on whether the claim delineates to a skilled artisan the bounds of the invention." Id. at 1340-41. Accordingly, the Court is satisfied that claim 1 is not indefinite, as one skilled in the art would be able to identify the claimed compound in claim 1. Indeed, Lupin itself has been able to identify the compound described in claim 1 to such an extent that it has filed an application for a generic version of ramipril with the FDA.

IV. Conclusion

While the parties' arguments concerning "substantial" have been substantial, and while the Court's resulting analysis is not a pithy one, the Court has little difficulty concluding that "substantially free of other isomers" means what it says, namely, that the compound modified-ramipril-is largely free of other isomers and is not guaranteed to be 100% pure. For the reasons the Court has explained, the Court **FINDS** the following:

-> "A compound" is a fairly broad term meaning a chemically distinct substance formed by union of two or more ingredients (as elements) in definite proportion by weight and definite structural arrangement.

-> "Said compound or salt being substantially free of other isomers" means that ramipril, the "said compound," is largely but not necessarily free of other isomers. In other words, "substantially free of other isomers" qualifies the compound by indicating that it may not be 100% pure or 100% free of other isomers.

-> The phrase "substantially free of other isomers" is not indefinite.

The Clerk is **DIRECTED** to send a copy of this Order to all counsel of record by facsimile and U.S. Mail.

IT IS SO ORDERED.

E.D.Va.,2006.
Aventis Pharma Deutschland GmbH v. Lupin Ltd.

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