IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

In re: Rosuvastatin Calcium Patent Litigation	:	
	:	MDL No. 08-1949
		PUBLIC VERSION
AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals Inc., and Shionogi Seiyaku Kabushiki Kaisha,	:	
Plaintiffs,	:	
v.	:	Civ. No. 07-805-JJF-LPS
Mylan Pharmaceuticals Inc.,	:	
Defendant.	:	
AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals Inc., and Shionogi Seiyaku Kabushiki Kaisha,	:	
Plaintiffs,	:	
v.	:	Civ. No. 07-806-JJF-LPS
Sun Pharmaceutical Industries Ltd.,	:	
Defendant.	:	

AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals Inc., and Shionogi Seiyaku Kabushiki Kaisha, Plaintiffs, v. Sandoz Inc., Defendant.	:	Civ. No. 07-807-JJF-LPS
AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals Inc., and Shionogi Seiyaku Kabushiki Kaisha, Plaintiffs, v. Par Pharmaceutical Inc., Defendant.	:	Civ. No. 07-808-JJF-LPS
AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals Inc., and Shionogi Seiyaku Kabushiki Kaisha, Plaintiffs, v. Apotex Inc. and Apotex Corp., Defendants.	:	Civ. No. 07-809-JJF-LPS

AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals Inc., and Shionogi Seiyaku Kabushiki Kaisha, Plaintiffs, v. Aurobindo Pharma Ltd. and Aurobindo Pharma USA Inc., Defendants.	:	Civ. No. 07-810-JJF-LPS
AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals Inc., and Shionogi Seiyaku Kabushiki Kaisha, Plaintiffs, v. Cobalt Pharmaceuticals Inc. and Cobalt Laboratories Inc., Defendants.	:	Civ. No. 07-811-JJF-LPS
AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals Inc., and Shionogi Seiyaku Kabushiki Kaisha, Plaintiffs, v. Aurobindo Pharma Ltd. and Aurobindo Pharma USA Inc., Defendants.	:	Civ. No. 07-359-JJF-LPS

AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals Inc., and Shionogi Seiyaku Kabushiki Kaisha,	:	
Plaintiffs,	:	
v.	:	Civ. No. 08-426-JJF-LPS
Teva Pharmaceuticals USA, Inc.,	:	
Defendant.	:	

REPORT AND RECOMMENDATION REGARDING CLAIM CONSTRUCTION

This multidistrict litigation consolidates nine separate actions for patent infringement filed by Plaintiffs AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals, Inc., and Shionogi Seiyaku Kabushiki Kaisha (collectively "AstraZeneca" or "Plaintiffs") against Defendants Mylan Pharmaceuticals, Inc. ("Mylan"), Sun Pharmaceutical Industries, Ltd. ("Sun"), Sandoz, Inc. ("Sandoz"), Par Pharmaceutical, Inc. ("Par), Apotex Inc. and Apotex Corp. ("Apotex"), Aurobindo Pharma Ltd. and Aurobindo Pharma, USA Inc. ("Aurobindo"), Cobalt Pharmaceuticals Inc. and Cobalt Laboratories Inc. ("Cobalt"), and Teva Pharmaceuticals USA, Inc. ("Teva") (collectively "Defendants"). AstraZeneca holds all substantial rights in U.S. Reissue Patent RE37,314 (the "'314 patent"), which covers a rosuvastatin calcium drug AstraZeneca manufactures and sells under the brand name "Crestor®." Each of the Defendants is involved in some way with the filing of an Abbreviated New Drug Application ("ANDA") with the U.S. Food and Drug Administration ("FDA"). The matter has

been referred to me for all purposes through and including the pretrial conference. *See* Civ. No. 805 (D.I. 9). This Report and Recommendation provides my recommended construction of the disputed claim terms.

BACKGROUND

A. Procedure

Pursuant to the Scheduling Order (Civ. No. 805 D.I. 25), on January 27, 2009 AstraZeneca, Mylan, Cobalt, Par, and Apotex filed a Joint Claim Chart identifying the claim terms needing construction (D.I. 52).[1] The parties briefed their positions on claim construction and, on March 10, 2009, I conducted a Markman hearing. *See* March 10, 2009 Hearing Transcript (D.I. 116) ("Tr."). The terms in dispute and requiring construction relate to Claim 6 and Claim 8 of the '314 patent.

B. The '314 Patent

The '314 Patent, entitled "Pyrimidine Derivatives," claims priority to Japanese patent application No. 3-188015, which was filed on July 1, 1991. The U.S. application was filed on June 12, 1992 and issued as U.S. Patent No. 5,260,440 (the "'440 patent") on November 9, 1993. The '440 patent's owner, Shionogi Seiyaku Kabushiki Kaisha ("Shionogi"), requested reissue, and, as a result, the '314 patent was issued on August 7, 2001.

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[1]Defendants Aurobindo, Sandoz, Sun, and Teva did not propose claim constructions or participate in the Joint Claim Construction Chart submission. Unless otherwise indicated, all Docket Index ("D.I.") references hereinafter are to MDL No. 08-1949.

Claim 6, the first of the two claims in dispute, reads:

> *6. The compound 7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-methylsulfonylamino)pyrimidin-5-yl)-(3R, 5S)-dihydroxy-(E)-6-heptenoic acid in the form of a non-toxic pharmaceutically acceptable salt thereof.*

(D.I. 52, Ex. 1, '314 patent at Col. 16, lines 30-33)

Claim 8, which is also in dispute, reads:

> *8. The compound of claim 6 in the form of a calcium salt.*

(*Id.* at Col. 16, line 35)

There are two issues to be decided. First, is the language set out in Claim 6 (and on which Claim 8 depends) to be read as a "unitary" term, as AstraZeneca contends, or, instead, must certain terms that are part of the claim language be individually construed, as the Defendants contend? Second, regardless of the answer to the first question, must the claims be construed to exclude the monocalcium bis form of any compounds alleged to fall within the scope of Claims 6 and 8?

LEGAL STANDARDS

"It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (internal quotation marks omitted). Construing the claims of a patent is a question of law. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 977-78 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370, 388-90 (1996). "[T]here is no magic formula or catechism for conducting claim construction." *Phillips*, 415 F.3d at 1324. Instead, the court is free to attach the appropriate weight to appropriate sources "in light of the statutes and policies that inform

patent law." *Id.*

"[T]he words of a claim are generally given their ordinary and customary meaning . . . [which is] the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Id.* at 1312-13 (internal citations and quotation marks omitted). "[T]he ordinary meaning of a claim term is its meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321 (internal quotation marks omitted). The patent specification "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

While "the claims themselves provide substantial guidance as to the meaning of particular claim terms," the context of the surrounding words of the claim also must be considered. *Phillips*, 415 F.3d at 1314. Furthermore, "[o]ther claims of the patent in question, both asserted and unasserted, can also be valuable sources of enlightenment . . . [b]ecause claim terms are normally used consistently throughout the patent . . . ." *Id.* (internal citation omitted).

It is likewise true that "[d]ifferences among claims can also be a useful guide . . . . For example, the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1314-15 (internal citation omitted). This "presumption is especially strong when the limitation in dispute is the only meaningful difference between an independent and dependent claim, and one party is urging that the limitation in the dependent claim should be read into the independent claim." *SunRace Roots Enter. Co., Ltd. v. SRAM Corp.*, 336 F.3d 1298, 1303 (Fed. Cir. 2003).

Occasionally, "the specification may reveal a special definition given to a claim term by

the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips*, 415 F.3d at 1316. It also bears emphasis that "[e]ven when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004) (internal quotation marks omitted), *aff'd*, 481 F.3d 1371 (Fed. Cir. 2007).

In addition to the specification, a court "should also consider the patent's prosecution history, if it is in evidence." *Markman*, 52 F.3d at 980. The prosecution history, which is "intrinsic evidence," "consists of the complete record of the proceedings before the PTO [Patent and Trademark Office] and includes the prior art cited during the examination of the patent." *Phillips*, 415 F.3d at 1317. "[T]he 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." *Id.*

A court also may rely on "extrinsic evidence," which "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Markman*, 52 F.3d at 980. For instance, technical dictionaries can assist the court in determining the meaning of a term to those of skill in the relevant art because such dictionaries "endeavor to collect the accepted meanings of terms used in various fields of science and technology." *Phillips*, 415 F.3d at 1318. In addition, expert testimony can be useful "to ensure that the court's understanding of the technical aspects of the patent is consistent with that

of a person of ordinary skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Id.* Nonetheless, courts must not lose sight of the fact that "expert reports and testimony [are] generated at the time of and for the purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence." *Id.* Overall, while extrinsic evidence "may be useful" to the court, it is "less reliable" than intrinsic evidence, and its consideration "is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." *Id.* at 1318-19.

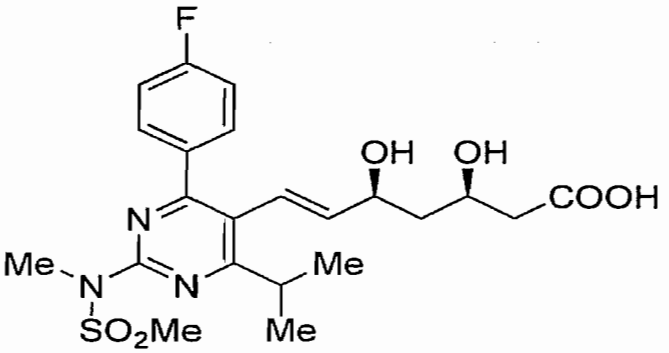
Finally, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998). Thus, if possible, claims should be construed to uphold validity. *See In re Yamamoto*, 740 F.2d 1569, 1571 (Fed. Cir. 1984).

CONSTRUCTION OF THE DISPUTED TERMS

A. Claim 6

Claim 6 recites "[t]he compound 7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)pyrimidin-5-yl)-(3R, 5S)-dihydroxy-(E)-6-heptenoic acid in the form of a non-toxic pharmaceutically acceptable salt thereof." Plaintiffs construe Claim 6 as "a unitary term meaning a non-toxic pharmaceutically acceptable salt form of the named compound, 7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)pyrimidin-5-yl)-(3R, 5S)-dihydroxy-(E)-6-heptenoic acid." (D.I. 52 at 4) Defendants respond that Claim 6 "cannot be properly construed in its entirety as a unitary term" and, instead, identify three elements of the

claim – "acid," "a non-toxic pharmaceutically acceptable salt," and "in the form of"– as terms requiring construction. *Id.*[2] Defendants construe "acid" as a compound with the following structure:



Defendants construe "a non-toxic pharmaceutically acceptable salt" to mean "a compound wherein the hydrogen depicted in the above structural drawing at the 'R4' position, as defined in the '314 patent's formula (I) at Ex.1, col. 1, lines 40-57, is removed and replaced with 'a cation capable of forming a non-toxic pharmaceutically acceptable salt.'" (D.I. 68 at 28; *see also* D.I. 52 at 6) Finally, Defendants maintain that the phrase "in the form of" is indefinite, and, therefore, is not amenable to construction. (D.I. 68 at 28; *see also* D.I. 52 at 5)

Proper construction of a claim and its terms requires a Court to determine how one of ordinary skill in the field of the invention "would understand the claim in the context of . . . the

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[2]The parties' dispute as to whether Claim 6 can be construed as a unitary term or whether it contains various terms requiring individual construction applies equally to Claim 8. Plaintiffs construe Claim 8, which recites "[t]he compound of Claim 6 in the form of a calcium salt," as covering "the calcium salt of the compound of Claim 6, and . . . not exclud[ing] the monocalcium bis form of the compound of Claim 6." (D.I. 52 at 6) Defendants' objection to the Claim 6 term "in the form of" due to that term's "indefiniteness . . . is equally applicable to Claim 8." *Id.* at 5. Defendants suggest in their briefs that the Claim 8 elements "compound of Claim 6" and "a calcium salt" also require individual construction (D.I. 68 at 3), but do not propose constructions for those terms in their briefs or in the parties' Joint Claim Construction Chart.

description in the specification, with due deference to the prosecution history." *On Demand Machine Corp. v. Ingram Industries, Inc.*, 442 F.3d 1331, 1337 (Fed. Cir. 2006). The prosecution history is significant because "it reveals the course of dealing with the [PTO], which may show a particular meaning attached to the terms, or a position taken by the applicant to ensure the patent would issue." *Markman*, 52 F.3d at 991. Here, while the Defendants characterize the Plaintiffs' proposed unitary construction as "essentially redrafting the claims," Tr. at 88, a careful review of the back-and-forth between Shionogi and the PTO reveals precisely how the claim language came about. This prosecution history also supports the Plaintiffs' position as to what one of ordinary skill in the art would understand Claim 6 to cover.

1. *Origins of "in the form of" language in the prosecution history*

Of the three elements of Claim 6 that they argue require construction, the Defendants' principal dispute is with the "in the form of" language, which, as Defendants observe, is "plainly important to the claim (since the PTO was unwilling to issue a claim that lacked this language)." (D.I. 69, Ganem Decl. ¶ 38) Defendants insist that "in the form of" is "ambiguous to the person of ordinary skill." *Id.* However, as Defendants concede, there is no mystery as to where this language came from; it was suggested to Shionogi during the prosecution history by the PTO.

When Shionogi initially requested reissue of the '440 patent in August 1998, Shionogi included new claims (including Claim 6 and Claim 8) which it argued would narrow the scope of the invention disclosed in the original '440 patent. As initially proposed in connection with the reissue application, Claim 6 read:

> The compound **(+)-** 7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)pyrimidin-5-yl)-(3R, 5S)-dihydroxy-(E)-6-heptenoic acid **or** a non-toxic pharmaceutically acceptable salt thereof.

(D.I. 52 Ex.4 at AZ 411220, AZ 411248 (emphasis added)) PTO Examiner Ford repeatedly rejected the claim in this form on the grounds that it was "outside the reissue statute," *id.* at AZ 411328, because it included stereochemistry that Ford believed could not be predicted from the original patent. Shionogi sought an interview with Examiner Ford, after which Shionogi removed the "(+)" notation from Claim 6 for redundancy but kept the conjunction "or," signaling its continuing intention (at that point) to claim both the acid and salt forms of the compound recited in Claim 6.

Thereafter, two new PTO representatives – C. Tsang, SPRE, and R. Schwartz, TCPS – held a telephone interview with counsel for Shionogi. The interview summary indicates that it was agreed that Shionogi's "generic claim to pharmaceutically acceptable **salt of the acid** recited in Claim 6 would not broaden the original claims because the claim to the salt is subsumed within original Claim 1 and is supported by specific examples of the sodium and calcium salts." (D.I. 52 Ex. 4 at AZ 411430) (emphasis added) Shionogi subsequently amended Claim 6 to remove the acid from coverage and only "recite that the claimed compound is in the form of a non-toxic pharmaceutically acceptable salt." *Id.* at AZ 411433. This change was accomplished with a minimum of alterations to the proposed claim language, as the new Claim 6 simply substituted "in the form of" for "or," to read:

> The compound 7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)pyrimidin-5-yl)-(3R, 5S)-dihydroxy-(E)-6-heptenoic acid **in the form of** a non-toxic pharmaceutically acceptable salt thereof.

Id. (emphasis added).

Examiner Ford, who had not participated in the most recent interview, rejected this revised claim, finding that "[n]o material change is made by this proposed amendment." *Id.* at AZ 411440. Shionogi appealed, noting that its most recent amendment "to Claim 6, amending 'or' to read 'in the form of' with respect to the non-toxic pharmaceutically acceptable salt," was presented to the PTO "following suggestions made during a . . . telephone interview" with Schwartz and Tsang. *Id.* at AZ 411447. Following another telephone interview with Schwartz as well as PTO Examiner R. Raymond, Shionogi again submitted its amended claims, again replacing "or" with "in the form of." Shionogi noted that the "in the form of" amendment came at the behest of the PTO: "In accordance with the suggestion of Examiner Raymond, Claim 6 is amended above to recite that the claim compound is in the form of a non-toxic pharmaceutically acceptable salt." *Id.* at AZ 411492. While Shionogi continued to "believe that [its] previous claims were in appropriate form and allowable," it submitted the "in the form of" amendment "to expedite prosecution." *Id.* at AZ 411493. The amended claims were allowed and reissue patent '314 was issued. *Id.* at AZ 411500-01.

Thus, the prosecution history reveals that in adopting "in the form of," Shionogi acted on the PTO's suggestion that it would be advisable to claim the "pharmaceutically acceptable salt of the acid recited in Claim 6," *id.* at AZ 411430, and to jettison Shionogi's claim to the acid itself. Shionogi used the PTO's own suggested language to accomplish this end. The PTO then allowed the amended claim.

2. *Defendants' proposed constructions*

The Defendants maintain that "it is not entirely clear what the phrase 'in the form of' was

meant to include versus exclude." (D.I. 69, Ganem Decl. ¶ 38) Their expert posits three possibilities for "what it means for an 'acid' to be 'in the form of a 'salt'": (1) it refers to an impossibility, "since an acid is not the same thing as a salt," possessing different properties and a different chemical structure; (2) "the language informs how the salt has been derived from the acid," though the use of "thereof" at the end of the claim "already conveys the information that the salt is to originate from the acid, and such a reading would render the 'in the form of' language redundant;" or (3) the language "involves a specification definition," though, according to Defendants, this cannot be true either, because the specification uses "in the form of" in a different context and, further, "names salt species by placing the salt term before the chemical compound name, and changing the end of the name from 'ic' to '[o]ate,'" a familiar method for using chemical nomenclature to name compounds. *Id.* ¶¶ 36, 34. None of Defendants' proposed constructions is persuasive, particularly in light of the prosecution history.

a. *"Acid" does not require individual construction*

Defendants' proposal that "acid . . . in the form of a salt thereof" might mean that the claimed invention must simultaneously be an acid and a salt – which is an impossibility – is contradicted by the prosecution history. From the outset, Shionogi and the PTO viewed the acid of the claimed compound as something different from the claimed compound "in the form of a . . . salt thereof." Shionogi initially wanted its claim to cover the acid and the salt, the PTO twice proposed that the claim cover just the salt and not the acid, and – after Shionogi agreed to draft the acid out of the claim – the PTO allowed the claim to just the salt. Knowing this, one of ordinary skill in the art would not read Claim 6 as covering just an acid that is simultaneously a salt. Furthermore, because the claim does not call for an acid but rather an acid in the form of a

salt, there is no need to construe "acid."

b. *Defendants' proposed process limitation*

In support of their second position, that "in the form of" might "inform[] how the salt has been derived from the acid," the Defendants offer the following construction of the claim language "a non-toxic pharmaceutically acceptable salt":

> a compound wherein the hydrogen depicted in the [ ] structural drawing [of the specification] at the "R4" position, as defined in the '314 patent's formula (I) at Ex.1 , col. 1, lines 40-57, is removed and replaced with "a cation capable of forming a non-toxic pharmaceutically acceptable salt."

(D.I. 68 at 28; *see also* D.I. 52 at 6) In other words, Defendants construe the claim as limiting the "salts" of Claim 6 to compounds that start out as the heptenoic acid and are then formed by a prescribed method (i.e., substituting "a cation capable of forming a non-toxic pharmaceutically acceptable salt" for hydrogen at the R4 position). *See* D.I. 68 at 27-28.

I reject Defendants' position because it impermissibly reads into the claim a process limitation that was not recited by the patentee. "An invention claimed in purely structural terms generally resists functional limitation." *Toro Co. v. White Consol, Industries, Inc.*, 266 F.3d 1367 (Fed. Cir. 2001); *see also Vanguard Prods. Corp. v. Parker Hannifin Corp.*, 234 F.3d 1370, 1372 (Fed. Cir. 2000) ("A novel product that meets the criteria of patentability is not limited to the process by which it was made.").

One of the preferred embodiments of the '314 patent is not formed by the process Defendants would read into the claim. Example 7 describes how the calcium salt of rosuvastatin is formed from a mixture including the sodium salt of rosuvastatin, *not* by removing hydrogen from the heptenoic acid compound and replacing it with a cation. *See* D.I. 52, Ex. 1, '314 patent

at Column 13, line 59 - Column 14, line 8; *see also* D.I. 75 Bartlett Decl. ¶ 30 (noting that "[a] person of ordinary skill in the art would understand that the procedure of Example 7 describes the conversion of the sodium salt of rosuvastatin directly into the calcium salt."). As the Federal Circuit has repeatedly held, "it is unlikely that an inventor would define [her] invention in a way that excluded the preferred embodiment, or that persons of a skill in [her] field would read the specification in such a way." *Hoechst Celanese Corp. v. BP Chemicals Ltd.*, 78 F.3d 1575, 1581 (Fed. Cir. 1996); *see also Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996) ("Such an interpretation is rarely, if ever, correct and would require highly persuasive evidentiary support."). There is nothing in the record here to recommend such a conclusion.[3]

Therefore, and because I do not see a process limitation in Claim 6, I recommend against adopting Defendants' individual construction of the claim element "a non-toxic pharmaceutically acceptable salt."

c. *Claim 6 is not ambiguous*

Defendants' third proposal with respect to "in the form of" relies on purported inconsistencies between the way Shionogi argues it uses this phrase in Claim 6 and how it employed the same phrase in the patent specification. According to Defendants, these

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[3]Defendants have particularly sought to rely on *In re Gabapentin*, 503 F.3d 1254, 1263 (Fed. Cir. 2007), in which the Federal Circuit upheld a district court's construction of "anion of a mineral acid" as "anion derived from a mineral acid." The Federal Circuit noted that, in that case, such construction gave "full meaning to every word of the entire claim," because if "the patentees intended the anion to refer to any anion, regardless of its source, the patentees could have simply claimed 'anions' and omitted the phrase 'of a mineral acid.'" *Id.* The Court also noted, however, that "claims must be read in view of the specification, of which they are a part," and in *Gabapentin*, the specification taught a multi-step process that supported the Court's construction. *Id.* Here, by contrast, the specification does not support such a process limitation. Indeed, the preferred embodiment of Example 7 is strong evidence against reading a process limitation into Claim 6.

inconsistencies demonstrate that "in the form of" is not explicitly defined in the specification and, consequently, as used in Claim 6 the phrase is "insolubly ambiguous." (D.I. 68 at 32)

I agree that Shionogi did not act as its own lexicographer and provide a definition of "in the form of" in the specification. But there is nothing about how "in the form of" is used in the specification – for example, to refer to "compound[s]" that "may be orally administered in the form of tablets, powders, capsules and granules," (D.I. 52 Ex. 1, '314 patent at Column 4, lines 17-21) – that renders the use of this same phrase in Claim 6 ambiguous. To the contrary, in the context of Claim 6, and particularly in light of the prosecution history, "in the form of" has a discernible meaning which is consistent with a unitary interpretation of the entirety of Claim 6.[4] I am thus persuaded that "one of ordinary skill in the art of organic chemistry would understand [the claim] to cover the non-toxic pharmaceutically acceptable salts of a single carboxylic acid." (D.I. 75, Bartlett Decl ¶ 40) Therefore, "the claim [is] sufficiently clear to avoid invalidity on indefiniteness grounds." *Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001).

Defendants' expert, Dr. Ganem, suggests that Claim 6 is ambiguous because the specification (but not the claim) uses chemical nomenclature to describe the salt form of a compound, "placing the salt term before the chemical compound name, and changing the end of the name from 'ic' to '[o]ate.'" (D.I. 69, Ganem Decl. ¶ 37) Dr. Ganem also contends that

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[4]Plaintiffs cite several prior-art examples of the use of "an . . . acid in the form of a salt." *See* D.I. 67 at 13-17 (citing, e.g., U.S. Pat. No. 4,900,668, column 6, lines 25-28: "The process of claim 1, wherein said lactic acid is in the form of a salt selected from the group consisting of the sodium, potassium, ammonium and calcium salts of D-(-)-lactic acid"). While I do not give great weight to these other materials, they generally support Plaintiffs' contention that "acid in the form of a salt" is not insolubly ambiguous.

Plaintiffs' construction of "in the form of" renders the last word of the claim, "thereof," redundant. *Id.* I do not agree with Dr. Ganem's conclusions. For reasons already noted, how some terms are used in the specification does not necessarily alter the meaning of those disputed terms in the context of Claim 6, especially given the prosecution history. Moreover, while "thereof" could have been removed when Shionogi amended Claim 6 to replace "or" with "in the form of" and the claim would have remained intelligible, retaining "thereof" only serves to emphasize that the claim refers just to a salt of the claimed compound.

3. *Recommended construction of Claim 6*

I agree with the Plaintiffs that Defendants' proposed construction of certain elements within Claim 6 amounts to a "word-by-word definition, removed from the context of the invention, [that] leads to an overall result that departs significantly from the patented invention." *On Demand*, 442 F.3d at 1344. Instead, one of ordinary skill in the art would read and understand the entirety of Claim 6 as a whole. The prosecution history shows how Shionogi's originally-proposed claim to an acid as well as a salt was amended to claim only a salt, in a manner that nonetheless retained much of the originally-proposed language.

Thus, I recommend construing Claim 6 as:

> A non-toxic pharmaceutically acceptable salt of the compound 7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)pyrimidin-5-yl)-(3R, 5S)-dihydroxy-(E)-6-heptenoic acid.[5]

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[5]This is essentially the construction Plaintiffs propose, though the wording of their proposed construction has varied slightly. *See* Joint Claim Construction Chart, D.I. 52 at 4 ("a unitary term meaning a non-toxic pharmaceutically acceptable salt form of the named compound, 7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)pyrimidin-5-yl)-(3R, 5S)-dihydroxy-(E)-6-heptenoic acid."); Plaintiff's Opening Brief, D.I. 67 at 10 ("Claim 6 should be construed as a unitary term, 'The compound [ ] in the form of a non-toxic pharmaceutically acceptable salt thereof,' which means a non-toxic pharmaceutically acceptable salt form of the

This construction is entirely consistent with the PTO's suggestion to Shionogi that a "generic claim to pharmaceutically acceptable salt of the acid recited in Claim 6 would not broaden the original claims. . . ."[6] (D.I. 52, Ex. 4 at AZ 411430)

B. The "Monocalcium Bis" Form Of The Claimed Compound Is Not Excluded

Defendants construe Claims 6 and 8 as excluding "what was described during prosecution as the monocalcium bis form of any compounds alleged to fall within the claim scope." (D.I. 52 at 4, 6) (emphasis added) "Monocalcium bis" refers to the ratio of heptenoate ions to the calcium ions in a salt: "When one mandates a 'bis' structure, there must be two anion structures attached to the [single calcium] cation." (D.I. 69 Ganem Decl. ¶ 44) Defendants argue, based on the prosecution history, that Shionogi initially tried to claim a "monocalcium bis" compound in Claim 8 but, after a series of rejections by the PTO, "affirmatively withdrew and rewrote" Claim 8 to cover a "calcium salt" that does not include the "monocalcium bis" form of the compound.

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specified heptenoic acid compound."); Plaintiffs' Reply Brief, D.I. 73 at 6 (describing "the simple and straightforward construction proposed by AstraZeneca: 'a pharmaceutically acceptable salt of [the named] acid'").

[6]Defendants contend that this construction may broaden the scope of the claim "based on the facial meaning of the phrase, pharmaceutically acceptable salt[]." *See* D.I. 116, Tr. at 72. However, it is clear from the specification that a "cation capable of forming a non-toxic pharmaceutically acceptable salt" refers to an "alkali metal ion, alkaline earth metal ion, [or an] ammonium ion." D.I. 52, Ex. 1, Column 2, lines 16-18. The specification gives several examples of alkali metal and alkaline earth metal, including calcium. *Id.*, lines 18-21. "Especially, sodium and calcium are preferred." *Id.*, line 21. In this way, the specification imposes a limitation on the universe of claimed salts, as Plaintiffs themselves acknowledge. *See* D.I. 116, Tr. at 7 ("It is the [P]laintiff's position that Claim 8 covers one specific salt, that being the calcium salt of the acid which is named in Claim 6. And that Claim 6 covers a relatively small group of salts, including that calcium salt, and, as defined in the specification of the patent.").

(D.I. 68 at 37) Plaintiffs disagree, insisting that the "monocalcium bis" interpretation of the claims was never disclaimed. I agree with Plaintiffs, as I do not find a disclaimer of "monocalcium bis" anywhere in the prosecution history.

A patent application's "prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution." *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576 (Fed. Cir. 1995); *see also Standard Oil Co. v. Am. Cynamid Co.*, 774 F.2d 448, 452 (Fed. Cir. 1985) (claim interpretations "disclaimed or disavowed during prosecution in order to obtain claim allowance" must be excluded). "[S]ubject to any clear and unmistakable disavowal of claim scope, the [claim] term . . . takes the full breadth of its ordinary meaning." *Innova/Pure Water, Inc. v. Safari Water Filtration Systems, Inc.*, 381 F.3d 1111, 1120 (Fed. Cir. 1998). The prosecution history here reveals that while Shionogi removed the words "monocalcium bis" from Claim 8, it never disavowed its position that the "non-toxic pharmaceutically acceptable salt" of Claim 6 and "calcium salt" of Claim 8 could be a "monocalcium bis."

As originally submitted by Shionogi, proposed Claim 8 claimed:

> 8. The compound **monocalcium bis** ((+)-7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)pyrimidin-5-yl)-(3R, 5S)-dihydroxy-(E)-6-heptenoate).

(D.I. 52 Ex. 4 at AZ 411334) (emphasis added) Shionogi declared that "[t]he sole claims now pending in this application are directed to a single compound . . . particularly its . . . calcium salt (Claim 8) form[]," further noting that "the calcium salt is exemplified in Example 7 . . . as the calcium salt of the compound." *Id.* at AZ 411340. After PTO Examiner Ford twice rejected the proposed Claim 8 as "not reasonable to expect from Claim 1" of the '440 patent, *id.* at AZ

411361, Shionogi and Ford met for an interview, at which the parties agreed, among other things, that Shionogi's "[b]is Claim 8 [would be] rewritten as calcium salt." *Id.* at AZ 4100375. The interview summary provides no explanation of the purpose of the agreed-upon rewrite.

Shionogi then submitted an amended Claim 8 – "The compound of claim 6 in the form of a calcium salt." – which Shionogi explicitly described to the PTO as "**identical in scope**" to the previously proposed Claim 8, only "now dependent on Claim 6 to clarify [its] relationship to the Claim 6 compound." *Id.* at AZ 411378, AZ 411380 (emphasis added). Shionogi further explained that while the previous "monocalcium bis" designation had "come[] from the disclosure of calcium as a suitable cation capable of forming a non-toxic pharmaceutically acceptable salt . . . , and the fact that calcium is divalent[,] the need for the bis-designation has been obviated by placing Claim 8 in dependent form, limiting the compound of Claim 6 to the calcium salt thereof." *Id.* at AZ 411389-90. Shionogi emphasized to the PTO that while the previous "monocalcium bis" designation was "supported by the specification disclosure, the present claims have been clarified by the deletion of these terms [i.e., "bis"] **without altering the scope of these claims**." *Id.* at AZ 411389 (emphasis added).

Thus, the prosecution history shows that while the words "monocalcium bis" were removed from the text of Claim 8, Shionogi never disclaimed any right to a "monocalcium bis" compound. By rewriting Claim 8 to cover "the compound of Claim 6 in the form of a calcium salt," Shionogi continued to make it plain to the PTO – as it would be clear as well to a person of ordinary skill in the art – that the claimed salt was a "monocalcium bis," with the relative number of calcium cations and rosuvastatin anions in the claimed salt made evident by the scientific fact that calcium has a +2 charge and each molecule of the rosuvastatin (the compound of Claim 6) to

which it bonds has a -1 charge.[7] Thus, "[t]he calcium salt of rosuvastatin would necessarily contain two molecules of the rosuvastatin anion for every calcium cation." (D.I. 75 Bartlett Decl. ¶ 31)

It is worth noting that if Shionogi relinquished coverage of a "monocalcium bis" salt from Claim 6 and Claim 8, it would have taken the unusual step of excluding a preferred embodiment of the '314 patent. Example 7 of the patent refers to the "Calcium salt of the compound (Ia-1),"[8] and describes a procedure that "a person of ordinary skill in the art would understand [involves] the conversion of the sodium salt of rosuvastatin directly into the calcium salt." (D.I. 75 Bartlett Decl. ¶ 30) The elemental analysis of the compound as reported in Example 7 "contains half of a calcium cation . . . for each rosuvastatin anion," thereby disclosing a "monocalcium bis" salt (i.e., a one-to-two ratio of calcium-to-rosuvastatin). (D.I. 75 Bartlett Decl. ¶¶ 31-32) As noted above, it is highly unlikely that an inventor would define her invention in a way that excluded the preferred embodiment, or that a person of ordinary skill in the art would read the claim that way.

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[7]Among those of ordinary skill in the art there are multiple ways of referring to the salt formed by two rosuvastatin anions and one calcium cation, **[REDACTED]**

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

Defendants' objection to Plaintiffs' introduction of Exhibits AA, BB, and CC (Tr. at 5) is hereby overruled. While these documents are extrinsic evidence, they are relevant here to confirm that to one of ordinary skill in the art there are multiple ways of referring to the same chemical compound, some of which use the word "bis" and some of which do not.

[8]Shionogi's appellate brief to the PTO declares that "[t]he calcium salt of reissue Claim 8 is described in Example 7 . . . and would have a structure equivalent to Figure (Ia-1) except taking into account that calcium is divalent," (D.I. 52 Ex. 4 at AZ 411449) (emphasis added), reinforcing that Shionogi was not – and had not – disclaimed a "bis" salt.

Hoechst, 78 F.3d at 1581. To find such an exclusion "would require highly persuasive evidentiary support," *Vitronics Corp.*, 90 F.3d at 1583, which is absent here.

Defendants try, but fail, to identify an explicit disavowal of "monocalcium bis" by Shionogi in the prosecution history.[9] Defendants' reliance on *Rheox, Inc. v. Entact, Inc.*, 276 F.3d 1319 (Fed. Cir. 2002), is misplaced. In *Rheox*, the Federal Circuit found that a patentee's deletion of references to two varieties of calcium orthophosphate from its proposed claims constituted a disclaimer of those varieties from the term "calcium orthophosphate," even though this meant reading out a preferred embodiment of the patent. *Rheox* involved a patent directed to a method of treating lead-contaminated soil by application of a calcium orthophosphate-based composition. The prosecution history showed that in initially rejecting the patentee's proposed claims, the PTO examiner emphasized that prior art taught the use of water-soluble phosphates – "such as monocalcium orthophosphate and [triple superphosphate]" – as treatment agents. *Id.* at 1322. Because these monocalcium and tricalcium orthophosphates in the prior art were also within the scope of the patentee's initially proposed claims, the claims were rejected. Thereafter,

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[9]Defendants argued at the hearing that Shionogi disclaimed the "bis" by telling the PTO that, by placing the revised Claim 8 in a dependent form in Claim 6, Shionogi had "obviated" the need for designating the claimed salt "monocalcium bis." According to Defendants, Shionogi's statement was tantamount to an admission that the amendment obviated the need to consider, or "discuss," whether Shionogi was claiming the "monocalcium bis" because Shionogi was no longer claiming it. *See, e.g.,* D.I. 116, Tr. at 109-110, 120 (arguing that Shionogi "told the PTO that any need for further discussion on this is obviated by our amendment. . . . [T]o obviate the need for further discussion is to say, I concede. I waive. I'm done"), 123, 136, 138-139. Defendants are incorrect. Shionogi simply represented to the PTO that it had selected another way to describe the claimed salt that obviated the need to use the words "monocalcium bis." Shionogi never represented that the amendment obviated the need to consider the interpretation that the claimed salt was a "bis" salt, *i.e.,* a salt containing two anions of rosuvastatin for every one calcium cation. In fact, Shionogi stressed to the PTO that rewriting Claim 8 did not narrow the scope of the claim which, prior to the rewrite, had explicitly claimed the "monocalcium bis." (D.I. 52, Ex.4 at AZ 411389-90)

the patentee met with the examiner to argue "a difference based on [the patentee's] use of slightly soluble phosphates versus the soluble phosphates of [the prior art]," and filed an amendment deleting all references in the claims to monocalcium orthophosphate and tricalcium superphosphate. *Id.* The patentee further "indicated that it made these cancellations . . . to distinguish the invention from the water-soluble compounds" of the prior art. *Id.* at 1322-23. Considering "the totality of the prosecution history," the Federal Circuit concluded that the patentee had relinquished coverage to monocalcium orthophosphate and tricalcium superphosphate. *Id.* at 1326. Thus, *Rheox* was the "rare[]" case in which "the prosecution history requires a claim construction that excludes some but not all of the preferred embodiments." *Id.* at 1327.

This is not such a case. There is no indication in the record that the deletion of the "monocalcium bis" designation by Shionogi was motivated by a need to overcome a prior art problem. More importantly, assessing the totality of the prosecution history reveals that Shionogi's avowed reason for rewriting Claim 8 was to make it "dependent on Claim 6 [in order] to clarify [its] relationship to the Claim 6 compound." (D.I. 52, Ex. 4 at AZ 411380) Shionogi removed the words "monocalcium bis" from Claim 8, but intended the alteration to be only a linguistic one, as it repeatedly insisted that the revised amendments were "identical in scope" to the previously proposed claims, which had explicitly claimed the "bis" salt. *Id.* at AZ 411380, AZ 411989-90. PTO Examiner Ford appears to have recognized there was no substantive change, as he continued to reject Shionogi's proposed claim amendments, even after they were shorn of the "bis"-designation. *See id.* at AZ 411427-28, AZ 411438-42. Shionogi then appealed, and, after a further amendment to Claim 6 that did not affect the "bis" salt of Claim 8,

a different PTO examiner accepted the proposed amendments. *Id.* at AZ 411493, AZ 411499-411501. Thus, there is no evidence that the PTO relied on any disclaimer of "monocalcium bis" in issuing the '314 patent, nor is there any evidence of such a disclaimer by Shionogi.

RECOMMENDED DISPOSITION

For the foregoing reasons, I recommend:

1. Claim 6 be construed as:

> "A non-toxic pharmaceutically acceptable salt of the compound 7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)pyrimidin-5-yl)-(3R, 5S)-dihydroxy-(E)-6-heptenoic acid."

2, Claim 8 be construed as:

> "The compound of Claim 6 in the form of a calcium salt."

This Report and Recommendation is filed pursuant to 28 U.S.C. § 636(b)(1)(B), Fed. R. Civ. P. 72 (b)(1), and D. Del. LR 72.1. The parties may serve and file specific written objections within ten (10) days after being served with a copy of this Report and Recommendation. Fed. R. Civ. P. 72(b). The failure of a party to object to legal conclusions may result in the loss of the right to de novo review in the district court. *See Henderson v. Carlson*, 812 F.2d 874, 878-79 (3rd Cir. 1987); *Sincavage v. Barnhart*, 171 Fed. Appx. 924, 925 n.1 (3d Cir. 2006).

The parties are directed to the Court's Standing Order In Non-Pro Se Matters For Objections Filed Under Fed. R. Civ. P. 72, dated April 7, 2008, a copy of which is available on the Court's website, www.ded.uscourts.gov/StandingOrdersMain.htm.

Dated: May 4, 2009

Honorable Leonard P. Stark
UNITED STATES MAGISTRATE JUDGE