UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ASTRAZENECA AB, et al. Plaintiffs, v. HANMI USA, INC., et al. Defendants.	Civil Action No. 11-760 (JAP) **OPINION**

PISANO, District Judge.

Plaintiffs AstraZeneca AB, Aktiebolaget Hässle, AstraZeneca LP, KBI Inc. and KBI-E Inc. (collectively, "AstraZeneca" or "Plaintiffs") bring this patent infringement against defendants Hanmi, Inc., Hanmi Pharmaceutical Co., Ltd., Hanmi Fine Chemical Co., Ltd. and Hanmi Holdings Co., Ltd. (collectively, "Hanmi" or "Defendants") alleging that Hanmi infringed two of AstraZeneca's patents by filing with the U.S. Food and Drug Administration ("FDA") a New Drug Application ("NDA") seeking approval to market their esomeprazole strontium products prior the expiration of certain patents held by AstraZeneca. The patents at issue are U.S Patent No. 5,714,504 (the " '504 patent") and U.S. Patent No. 5,877,192 (the " '192 patent") (together, the "patents-in-suit"), which cover pharmaceutical compositions containing alkaline salts of esomeprazole and methods of the use of such compositions to treat gastric acid related diseases. Presently before the Court is the parties' request for claim construction.

I. BACKGROUND

AstraZeneca manufactures and markets Nexium, a capsule drug product containing an esomeprazole salt as the active ingredient. Hanmi is seeking approval from the United States Food and Drug Administration to manufacture esomeprazole strontium capsules in the United States. As part of its NDA, Hanmi submitted a Paragraph IV certification asserting that the '504 patent and the '192 patent are invalid or will not be infringed by their NDA product. Hanmi provided notice to AstraZeneca of its filing by letter dated December 29, 2010, and this lawsuit followed.

The '504 and '192 patents relate to, inter alia, pharmaceutical compounds containing esomeprazole salt active ingredients and methods to treat gastric acid related diseases by administering them. More specifically, the asserted claims of the '504 patent (claims 1–7 and 10) are directed to "pharmaceutical formulation[s]" containing an "alkaline salt" of esomeprazole and methods of use thereof for "inhibiting gastric acid secretion" and "treatment of gastrointestinal inflammatory disease." The asserted claims of the '192 patent (1–7, 10–19 and 21–23) are directed to methods for the "treatment of gastric acid related diseases" with esomeprazole "or a pharmaceutically acceptable salt thereof" and to methods for the "production of a medicament for treating gastric acid related diseases" containing the same.

The parties have requested that the Court construe certain disputed terms in each of the patents-in-suit.[1] The Court having held a claim construction hearing on the relevant issues, this Opinion addresses the proper construction of the disputed terms.

[1] The parties each submitted opening and responsive Markman briefs and supporting materials. Pursuant to an Ordered entered March 12, 2012, AstraZeneca was permitted to file an additional reply brief.

II. LEGAL STANDARD

In order to prevail in a patent infringement suit, a plaintiff must establish that the patent claim "covers the alleged infringer's product or process." *Markman v. Westview Instrs., Inc.*, 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996). "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 quotations omitted) (citing *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996) ("we look to the words of the claims themselves ... to define the scope of the patented invention"). Consequently, the first step in an infringement analysis involves determining the meaning and the scope of the claims of the patent. *Johnson Worldwide Assocs., Inc. v. Zebco Corp.*, 175 F.3d 985, 988 (Fed. Cir. 1995). Claim construction is a matter of law, *Markman v. Westview Instrs., Inc.*, 52 F.3d 967, 979 (Fed.Cir.1995) *aff'd* 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996), therefore, it is "[t]he duty of the trial judge ... to determine the meaning of the claims at issue," *Exxon Chem. Patents, Inc. v. Lubrizoil Corp.*, 64 F.3d 1553, 1555 (Fed. Cir. 1995).

Generally, the words of a claim are given their "ordinary and customary meaning," which is defined as "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." *Phillips*, 415 F.3d at 1312–13 (citations omitted). In this regard, the Federal Circuit has noted that

> It is the person of ordinary skill in the field of the invention through whose eyes the claims are construed. Such person is deemed to read the words used in the patent documents with an understanding of their meaning in the field, and to have knowledge of any special meaning and usage in the field. 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. Thus the

> court starts the decisionmaking process by reviewing the same resources as would that person, viz., the patent specification and the prosecution history.

Id. (quoting *Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1477 (Fed. Cir. 1998)).

In order to determine the meaning of a claim as understood by a person skilled in the art, a court may look to various sources from which the proper meaning may be discerned. These sources include intrinsic evidence, which consists of "the words of the claims themselves, the remainder of the specification, [and] the prosecution history," *id.* at 1314, and extrinsic evidence "concerning relevant scientific principles, the meaning of technical terms, and the state of the art," *id.*

When considering the intrinsic evidence, the court's focus must begin and remain on the language of the claims, "for it is that language that the patentee chose to 'particularly point[ ] out and distinctly claim[ ] the subject matter which the patentee regards as his invention.' " *Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1331 (Fed.Cir.2001) (quoting 35 U.S.C. § 112, ¶ 2). The specification is often the best guide to the meaning of a disputed term. *Honeywell Int'l v. ITT Indus.*, 452 F.3d 1312, 1318 (Fed.Cir.2006). It is improper, however, to import limitations from the specification into the claims. *Seachange Int'l v. C–COR Inc.*, 413 F.3d 1361, 1377 (Fed. Cir. 2005). The court may also consider as intrinsic evidence a patent's prosecution history, which is evidence of "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.

While a court is permitted to turn to extrinsic evidence, such evidence is generally of less significance and less value in the claim construction process. *Id.* at 1317. Extrinsic evidence is evidence that is outside the patent and prosecution history, and may include expert testimony, dictionaries, and treatises. *Id.* The Federal Circuit has noted that caution must be exercised in the use of extrinsic evidence, as this type of evidence may suffer from inherent flaws affecting its reliability in the claim construction analysis. *Id.* at 1319 ("We have viewed extrinsic evidence in general as less reliable than the patent and its prosecution history in determining how to read claim terms."). While "extrinsic evidence may be useful to the court, ... it is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." Extrinsic evidence may never be used to contradict intrinsic evidence. *Id.* at 1322–23.

III. CONSTRUCTION OF CLAIM TERMS

A. '504 Patent

1. "*alkaline salt*"

The term "alkaline salt" appears in independent claims 1, 6 and 7 and by dependence in claims 2 and 4. Claim 1 is representative: "A pharmaceutical formulation for oral administration comprising a pure solid state alkaline salt of the (-)-enantiomer of 5-methoxy-2[[(4-methoxy-3, 5-dimethyl-2-pyridinyl)methyl]sulfinyl]- 1H-benzimidazole and a pharmaceutically acceptable carrier." '504 patent, claim 1.

Hanmi contends that the term "alkaline salt" as used in the claims should be construed as "Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+} or $N^+(R)_4$ salt." AstraZeneca construes the term as "a basic salt (here, a salt in which (-)-omeprazole is negatively charged) that is suitable for use in a pharmaceutical formulation." Both parties agree that "alkaline salt" is not defined in the

claims. Hanmi asserts, however, that the specification clearly defines the term as encompassing only the Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+} or $N^+(R)_4$ salts and no others. AstraZeneca responds that the specification merely identifies these salts as examples of alkaline salts.

The Court finds AstraZeneca's arguments unavailing and agrees with Hanmi that here the patentee has given a definition to "alkaline salts" which governs construction of this term. The '504 patent is clear and consistently states that the compounds of the invention are the identified five inorganic salts (Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+}) and the one organic genus of salts ($N^+(R)_4$) of an enantiomer of omeprazole. For example, the Abstract of the '504 patent specification describes the subject matter of the patent as follows:

> "The novel optically pure compounds Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+} and $N^+(R)_4$ salts of [the enantiomers of omeprazole] … processes for the preparation thereof and pharmaceutical preparations containing the compounds as active ingredients, as well as the use of the compounds in pharmaceutical preparations and intermediates obtained by preparing the compounds."

'504 patent, Abstract.

The "Detailed Description of the Invention" similarly states that "[t]he present invention refers to the new Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+} or $N^+(R)_4$ salts of the single enantiomers of omeprazole, where R is an alkyl with 1-4 carbon atoms, i.e. Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+} or $N^+(R)_4$ salts of (+)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl] sulfinyl]-1H-benzimidazole and (-)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl] sulfinyl]-1H-benzimidazole, where R is an alkyl with 1-4 carbon atoms." '504 patent, col. 2, lines 42-49 (emphasis added). Thus, the specification unambiguously establishes that the "present invention" is limited to the six named salt species.

AstraZeneca argues that the term "alkaline salts" should be given a broad and ordinary meaning, and contends that the term is not limited to merely the salts identified in the

specification. In particular, it points to the doctrine of claim differentiation, which creates a presumption against constructions that would render a claim meaningless in its entirety by making it identical in scope to another claim. *See Phillips*, 415 F.3d at 1315 (noting that "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"). Here, for example, claim 1 reads "A pharmaceutical formulation for oral administration comprising a pure solid state alkaline salt …" and dependent claim 3 reads: "The pharmaceutical formulation according to claim 1 wherein the alkaline salt is a Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+} or $N^+(R)_4$ salt." Thus, the doctrine creates a presumption that "alkaline salts" in claim 1 is broader than the six salt species identified in claim 3. However, the doctrine of claim differentiation is "not a hard and fast rule and will be overcome by a contrary construction dictated by the written description or prosecution history." *Seachange Int'l, Inc. v. C–COR, Inc.*, 413 F.3d 1361, 1369 (Fed. Cir.2 005). Indeed, "[c]laim differentiation is a guide, not a rigid rule." *Laitram Corp. v. Rexnord, Inc.*, 939 F.2d 1533, 1538 (Fed. Cir. 1991)). In light of the relevant intrinsic evidence, the Court is not persuaded by AstraZeneca's claim differentiation argument.

AstraZeneca also points to the following sentence in the specification, placing great emphasis on the term "exemplified by" in arguing that the salt forms in claims 3 and 10 are merely examples: "Alkaline salts of the single enantiomers of the invention are, as mentioned above, beside the sodium salts (compounds Ia and Ib) and the magnesium salts (compounds IIa and IIb), exemplified by their salts with Li^+, K^+, Ca^{2+} or $N^+(R)_4$, where R is an alkyl with 1-4 C-atoms." '504 patent, col. 5, lines 7-11. However, the Court agrees with Hanmi that when read in context this phrase does not broaden the scope of the subject matter described earlier in the specification, which limits the inventions scope to the six identified salts. The

Court, therefore, adopts Hanmi's proposed construction and construes "alkaline salt" to mean Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+} or $N^+(R)_4$ salt.

2. "*(-)-enantiomer of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole*"

This term stands alone in claims 1, 3-7 and 10, and is modified by the term "optically pure" in claim 2. The Court has previously construed this claim term in a related action, *AstraZeneca v. Dr. Reddy's Laboratories, Ltd.*, 05-5553 (JAP) (the "DRL Action"). In that action, the Court construed the term "(-)-enantiomer of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole" to mean (-)-omeprazole of high optical purity, specifically, in at least 94% enantiomeric excess ("e.e."). Where "(-)-enantiomer of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole" appear in the claims modified by the term "optically pure," the Court construed this to mean (-)-omeprazole that was essentially free of the (+)-enantiomer of omeprazole, specifically, in at least 98% e.e. AstraZeneca urges the Court to adopt those constructions here.

Hanmi, on the other hand, has asked the Court to reconsider its earlier construction of this term. Raising argument similar to those raised in the DRL Action, Hanmi proposes that the Court construe term "(-)-enantiomer of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole" to mean "(-)-omeprazole" or "(-)-enantiomer of omeprazole." Where the term is modified by "optically pure," Hanmi proposes that the Court construe the term to mean "essentially free of (+)-omeprazole alkaline salt, i.e., the single enantiomer."

The Court has carefully considered Hanmi's arguments but remains unpersuaded that its earlier construction should be modified. For the reasons set forth in its Opinion in the DRL Action, the Court shall construe "(-)-enantiomer of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole" to mean "(-)-omeprazole in at least 94% enantiomeric excess," and when the term is modified by "optically pure", "in at least 98% enantiomeric excess."

3. *"administration of…"; "administration to…" and "a mammal including man in need of treatment"*

The term "administration of" appears in claim 6, while "administration to a mammal including man in need of such treatment" appears in claim 7. Claim 6 reads as follows:

> A method of inhibiting gastric acid secretion comprising the oral *administration of* a pharmaceutical formulation comprising a therapeutically effective amount of a pure solid state alkaline salt of the (-)-enantiomer of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole and a pharmaceutically acceptable carrier.

Claim 7 of the '504 patent reads as follows:

> A method for the treatment of gastrointestinal inflammatory disease comprising the oral *administration to a mammal including man in need of such treatment* of a pharmaceutical formulation comprising a therapeutically effective amount of a pure solid state alkaline salt of the (-)-enantiomer of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1Hbenzimidazole and a pharmaceutically acceptable carrier.

AstraZeneca argues that no construction is necessary for these disputed terms as their ordinary and customary meaning would be clear to one skilled in the art. Hanmi, on the other hand, contends that the "administration" terminology in claims 6 and 7 means "the prescription by a physician or other licensed healthcare professional, dispensing and ingestion," and Hanmi further contends that the phrase "a mammal including man in need of

such treatment" means "a mammal including man whom the need for treatment of gastrointestinal inflammatory disease is recognized and/or appreciated by the physician or other licensed healthcare professional."

Turning first to the "administration" terms, the Court finds that Hanmi's proposed definition lacks support and is somewhat at odds with the claim language itself. Hanmi's proposed definition would define "administration" to include "prescription by a physician or other licensed healthcare professional," as well as "dispensing." Hanmi contends that this construction is consistent with the views of a person of ordinary skill in the art in the mid-1990's," since what is claimed is a method of treatment, only a physician is capable of determining the "therapeutically effective amount" and the drug product is only available by prescription. In support of its construction, Hanmi relies in large part upon generalities about the manner in which prescription drugs ultimately reach patients. The Court finds, however, that Hanmi has not shown that such requirements should be read into the terms at issue here. Further, in both claim 6 and 7 the term "administration" is modified by "oral," that is, the claims read: "oral administration". Thus, a person of ordinary skill in the art would understand the term administration to refer to the means of delivering the medication to an individual. *See* Declaration of Dr. David Johnson ¶¶ 28-32. In light of this, Hanmi's proposed construction of the administration terms is inconsistent with the plain language of the claims.

Hanmi similarly has not shown that "a mammal including man in need of such treatment" requires a construction other than its ordinary and customary meaning. Consequently, because the Court finds that the meaning of the claim terms "administration of…"; "administration to…" and "a mammal including man in need of treatment" would be

clear to one skilled in the art, the Court declines to construe them at this time and their ordinary and customary meaning will apply.

A. '192 Patent

1. "*pharmaceutically acceptable salt*"

The '192 patent states that it incorporates by reference the "description of the salt forms of the single enantiomers of omeprazole and the process for making the same" from the application that ultimately issued as the '504 patent. '192 patent, col. 1, lines 10-12. As such, AstraZeneca contends that the term "pharmaceutically acceptable salt" should be given the same meaning as "alkaline salt" in the '504 patent. As noted above, that construction proposed by AstraZeneca was "a basic salt (here, a salt in which (-)-omeprazole is negatively charged) that is suitable for use in a pharmaceutical formulation." The Court rejected AstraZeneca's proposed construction of "alkaline salt" for the '504 patent claims. *See supra*.

Hanmi proposes a number of alternative constructions for "pharmaceutically acceptable salt." First, it proposes -- in what it describes as its "main" construction -- that the term "pharmaceutically acceptable salt" be given the same meaning as "alkaline salt" in the '504 patent. Indeed, in its Non-Infringement and Invalidity Contentions, Hanmi asserted that the '192 patent was "limited to the expressly described salt species in the '504 patent." *See* Non-infringement and Invalidity Contentions, D.I. 87-1 at 37). As noted above, the Court determined that Hanmi's proposed construction -- "Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+} or $N^+(R)_4$ salt" -- is the appropriate construction of "alkaline salt" in the '504 patent.

Second, Hanmi proposes an "alternative" construction as follows: "an acid or alkaline pharmaceutically acceptable nontoxic salt." This construction is derived from the specification of the '192 patent, which states in the relevant part:

> The pharmaceutical compositions of the present invention comprise the (-)-enantiomer of omeprazole as active ingredient, or pharmaceutically acceptable salt thereof, and may also contain a pharmaceutically acceptable carrier and optionally other therapeutic ingredients. *The term "pharmaceutically acceptable salt" refers to both acid and alkaline pharmaceutically acceptable nontoxic salts.* Composition comprising other therapeutic ingredients are especially of interest in the treatment of Helicobacter infections.

'192 patent, col. 4, lines 9-17 (emphasis supplied).

Finally, Hanmi proposes that the Court "meld" these constructions to arrive at "a combined construction where the acid component is broadly defined and the alkaline component is restricted per the '504 patent's definition." Hanmi Opening Br. at 21-22.

One reason Hanmi provides multiple constructions is because Hanmi challenges the validity of the incorporation into the '192 patent of the description of the salt forms of (-)-omeprazole from the parent '512 application. The relevant language reads: "The description of the salt forms of the single enantiomer of omeprazole and the process for making the same is herein incorporated by reference to copending Ser. No. 08/376512." '192 patent, col. 1, lines 10-13. Hanmi contends that if this incorporation is effective, the specification will contain conflicting information bearing on the construction of "pharmaceutically acceptable salt."

As noted by the Federal Circuit, incorporation by reference "provides a method for integrating material from various documents into a host document ... by citing such material in a manner that makes clear that the material is effectively part of the host document as if it were explicitly contained therein." *Zenon Environmental, Inc. v. U.S. Filter Corp.*, 506 F.3d 1370, 1378 (Fed. Cir. 2007); *Cook Biotech Inc. v. Acell, Inc.*, 460 F.3d 1365, 1376 (Fed. Cir. 2006) (quoting *Advanced Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000)). In order to incorporate by reference, "the host document must identify with

detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents." *Id.* The determination of whether material has been properly incorporated by reference into a host document, and the extent to which it has been incorporated, is a question of law. *Id.* In making that determination, "the standard of one reasonably skilled in the art should be used to determine whether the host document describes the material to be incorporated by reference with sufficient particularity." *Id.* at 1378-79 (quoting *Advanced Display*, 212 F.3d at 1282).

The Court finds this incorporation effective for its purposes here, as the plain language of the incorporation statement is clear. As such, it further finds that Hanmi's "main" proposed construction is appropriate. Because of its reference to the "salt forms of the single enantiomers of omeprazole" as described in the '504 patent, the '192 patent would be understood by one skilled in the art to be focused on the alkaline salts of esomeprazole. As discussed above, these are limited in the '504 patent to the six named species. Thus, the Court shall construe "pharmaceutically acceptable salt" in the '192 patent as "Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+} or $N^+(R)_4$ salt."

2. "*consisting essentially of the (-)-enantiomer of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole*"

This term appears in independent claims 1, 2 and 12. The Court previously construed this term in the DRL Action to mean (-)-omeprazole in at least 98% enantiomeric excess. AstraZeneca asks the Court to adopt that construction here. Hanmi contends that the term should be construed to mean " (-)-omeprazole or the (-)-enantiomer of omeprazole that may also contain substances that do not materially affect the claimed novel properties." The Court is again unpersuaded by Hanmi's arguments that a change to the Court's prior

construction is warranted. For the same reasons in the DRL action, the Court shall construe the term "consisting essentially of the (-)-enantiomer of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole" to mean (-)-omeprazole in at least 98% enantiomeric excess.

3. "*administering to a mammal in need of treatment*"

This term appears in independent claims 1 and 2 of the '192 patent. Claim 1 is representative:

> A method for treatment of gastric acid related diseases by inhibition of gastric acid secretion comprising *administering to a mammal in need of treatment* a therapeutically effective amount of a proton pump inhibitor consisting essentially of the (-)-enantiomer of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole or a pharmaceutically acceptable salt thereof, so as to effect decreased interindividual variation in plasma levels (AUC) during treatment of gastric acid related diseases.

AstraZeneca argues that no construction of this term is necessary as its ordinary and customary meaning would be apparent to one skilled in the art. Hanmi proposes the following construction: "the prescription by a physician or other licensed healthcare professional, dispensing and delivery by any suitable means." Hanmi contends that this construction "tracks the views of a person of ordinary skill in the art in the mid-1990's," since what is claimed is a method of treatment, and "only a physician can determine the 'therapeutically effective amount [and] the drug product is only available by prescription." Hanmi Opening Br. at 29. However, for the same reasons as discussed above with similar terms in the '504 patent, the Court rejects Hanmi's proposed construction. As the ordinary and customary meaning would be clear to one skilled in the art, the Court concludes that no construction of this term is necessary.

IV. CONCLUSION

For the reasons set forth above, the disputed claim terms will be construed as indicated. An appropriate Order shall accompany this Opinion.

/s/ Joel A. Pisano
JOEL A. PISANO, U.S.D.J.

December 10, 2012