IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BRISTOL-MYERS SQUIBB COMPANY and PFIZER INC.,	)	
Plaintiffs and Counterclaim-Defendants	)	
v.	)	C.A. No. 17-374-LPS (CONSOLIDATED)
AUROBINDO PHARMA USA INC. and AUROBINDO PHARMA LTD.,	)	
Defendants and Counterclaim-Plaintiffs.	)	

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MEMORANDUM OPINION

October 18, 2018
Wilmington, Delaware

STARK, U.S. District Judge:

This is a patent infringement case arising under the Hatch Waxman Act. Plaintiffs Bristol-Myers Squibb Co. and Pfizer Inc. (collectively, "Plaintiffs") sued multiple Defendants who seek to market a generic form of Plaintiffs' Eliquis (apixaban) drug product before the expiration of U.S. Patent Nos. 9,326,945 ("'945 patent") and 6,967,208 ("'208 patent").[1] (*See generally* D.I. 124)

Presently before the Court are the parties' disputes over the meaning of certain terms in the asserted claims. Some defendants[2] have also filed a motion to strike an article relied upon by Plaintiffs. (*See* D.I. 258, 259, 271) The parties submitted technology tutorials (D.I. 202, 203), comments to the opposing side's technology tutorial (D.I. 235, 236), claim construction briefs (D.I. 204, 206, 243, 245), and supporting declarations (D.I. 205, 207, 208, 209, 244, 246, 247). The Court held a claim construction hearing on September 6, 2018. (*See* D.I. 296) ("Tr.")

I. LEGAL STANDARDS

The ultimate question of the proper construction of a patent is a question of law. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 837 (2015) (citing *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 388-91 (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 quotation marks omitted).

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[1]Out of the 25 defendants Plaintiffs initially sued, 14 have settled. (*See* D.I. 206 at 1) The '945 patent is asserted against all 11 remaining Defendants (D.I. 204 at 2 n.4) while the '208 patent is asserted against just six of them (*see* D.I. 206 at 1 n.1; D.I. 204 at 1 n.2).

[2]These defendants are Unichem Laboratories Ltd., Sunshine Lake Pharma Co., Ltd., and HEC Pharm USA Inc. ("Moving Defendants"). (D.I. 258)

"[T]here is no magic formula or catechism for conducting claim construction." *Id.* 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).

It is also possible that "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 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." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)) (internal quotation marks omitted).

In addition to the specification, a court "should also consider the patent's prosecution history, if it is in evidence." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370 (1996). 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.*

In some cases, "the district court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Teva*, 135 S. Ct. at 841. Extrinsic evidence "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 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. Where the intrinsic record unambiguously describes the scope of the patented invention, reliance on any extrinsic evidence is improper. *See Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999) (citing *Vitronics*, 90 F.3d at 1583).

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). It follows that "a claim interpretation that would exclude the inventor's device is rarely the correct interpretation." *Osram GmbH v. Int'l Trade Comm'n*, 505 F.3d 1351, 1358 (Fed. Cir. 2007) (quoting *Modine Mfg. Co. v. U.S. Int'l Trade Comm'n*, 75 F.3d 1545, 1550 (Fed. Cir. 1996)).

II. CONSTRUCTION OF DISPUTED TERMS

A. '208 Patent

The '208 patent is entitled "Lactam-containing Compounds and Derivatives Thereof as Factor Xa Inhibitors." The "invention relates generally to lactam-containing compounds and derivatives thereof which are inhibitors of trypsin-like serine protease enzymes, especially factor Xa, pharmaceutical compositions containing the same, and methods of using the same as anticoagulant agents for treatment of thromboembolic disorders." ('208 patent, 1:19-25)

1. "pharmaceutically acceptable salts"[3]

Plaintiff Original: "derivative wherein the compound is modified by making an acid or base salt" Revised: "derivative wherein the compound is modified by making an acid or base salt acceptable for use in the pharmaceutical arts, such as the salts disclosed at U.S. Patent No. 6,967,208, column 116, lines 51-67, and in Remington's Pharmaceutical Sciences, 17th ed., Mack Publishing Company, Easton, Pa., 1985, p. 1418"[4]
Defendants "derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof, which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio"
Court "derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof, which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio"

[3]This term appears in asserted claims 1, 8, 13, 26, 27, 52, and 55 of the '208 patent.

[4]In their responsive brief, Plaintiffs proposed a revised construction, which they argue is "coextensive with their original proposed construction." (D.I. 243 at 4)

The parties agree that the patent defines "pharmaceutically acceptable," but they dispute whether that definition applies to the term "pharmaceutically acceptable salts." Defendants say yes while Plaintiffs say no.

Plaintiffs argue that in the context of the patent, a person of ordinary skill in the art ("POSA") would understand that "the definition of 'pharmaceutically acceptable' is limited to 'compounds, materials, compositions, and/or dosage forms' and envisions 'contact with the tissues of human beings and animals'" and "appears only in the context of 'pharmaceutically acceptable carriers.'" (D.I. 206 at 14, 17) Defendants counter that the term is a "term of art in the pharmaceutical sciences" and well understood by a POSA to mean "salts that are pharmaceutically acceptable," which requires "the salt form be safe for human administration." (D.I. 204 at 5, 6)

Both sides focus on the patent specification, which provides, in the part most pertinent to this dispute:

> The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.
>
> As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, [the following list of examples].

('208 Patent, 116:40-67)

Defendants' construction essentially reads the patent's express definition of

"pharmaceutically acceptable" into the patent's express definition of "pharmaceutically acceptable salts." This is a logical approach. Its correctness is supported by the fact that nothing in the patent suggests that "pharmaceutically acceptable" takes on a different meaning when read in conjunction with the word "salts."

Plaintiffs agree that the claimed salts must be "acceptable for use in the pharmaceutical arts," as reflected in Plaintiffs' revised construction. (D.I. 243 at 3) But Plaintiffs' revised construction provides no guidance as to the meaning of "acceptable for use in the pharmaceutical arts." Defendants' construction incorporates the meaning of "pharmaceutically acceptable" as defined in the patent, which is how a POSA would understand the term is being used to modify salts in the context of the patent.

Plaintiffs contend that the "specification does not define the word 'salts' alone." (D.I. 243 at 6) But in defining "pharmaceutically acceptable salts" the patent tells a POSA that the patentee understands a salt to be "derivatives of disclosed compounds wherein the parent compound is modified by making acid or base salts thereof." ('208 Patent, 116:48-51; *see also id.* at 117:1-7 (noting "pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound that contains a basic or acidic moiety by conventional chemical methods . . . [such as] reacting the free acid or base forms of these compounds with . . . appropriate base or acid")

In Plaintiffs' view, a pharmaceutically acceptable salt of the type claimed in the patent "need not come directly into contact with human tissue" (D.I. 206 at 15) and does not have "independent safety limitations like the ones Defendants are seeking to introduce" (D.I. 243 at 8). Plaintiffs also insist that a POSA would understand that "pharmaceutically acceptable salts" in

the patent do not include "dangerous salts, like cyanide, mercury, or arsenic salts." (D.I. 206 at 17) While Plaintiffs may be correct as a matter of common sense, their position is flawed in the context of claim construction. The patent does not support the conclusion that the patentee intended its definition of "pharmaceutically acceptable" to modify "compound" but not to also modify "salts," particularly given it is undisputed that "salts" are also "compounds." Also, Plaintiffs contend that the patentee defined the term "pharmaceutically acceptable," but Plaintiffs then want to exclude from that express definition salt forms that are toxic, even though such salt forms would be within the literal definition expressly provided in the patent. As a matter of claim construction, the Court is not persuaded Plaintiffs are correct. (Nor, it would seem, would the patent provide the public, and potential competitors, adequate notice of the scope of Plaintiffs' claims, if Plaintiffs' construction were adopted.)

The Court's conclusion is based on the intrinsic evidence. Nonetheless, the Court does not believe that the extrinsic evidence submitted by the parties – including Defendants' expert declaration (*see* D.I. 205 at ¶¶ 27-30), Defendants' journal articles (*see* D.I. 204 at 14-16), and the evidence purporting to show "there is no pharmaceutically acceptable salt form of Apixaban" (D.I. 315; *see also* D.I. 324 (Plaintiffs disagreeing)) – changes the outcome.

B. The '945 Patent

The '945 patent, "Apixaban Formulations," "relates to apixaban pharmaceutical formulations comprising crystalline apixaban particles having a maximum size cutoff; and methods of using them, for example, for the treatment and/or prophylaxis of thromboembolic disorders." ('945 patent at 1:10-15)

1. "apaxiban particles have a D_{90}"[5]

Plaintiff and Certain Defendants plain meaning (i.e., no construction necessary)
Unichem and Sunshine Lake ("Unichem") "D_{90} is measured by laser light scattering (such as Malvern light scattering) of bulk apixaban particles"
Court plain and ordinary meaning

The dispute between Plaintiffs and Unichem is whether the undisputed size limitation – that at least 90% of apixaban particles are equal to or below a given size – must be measured solely and exclusively by laser light scattering, such as Malvern light scattering. Plaintiffs contend Unichem is improperly attempting to "rewrite the claims and import new limitations that are not contemplated by the intrinsic record" (D.I. 206 at 18), while Unichem counters that its construction is supported by the intrinsic record, particularly the patent's emphasis on the importance to practicing the invention of meeting the size limitation. (D.I. 204 at 17) The Court agrees with Plaintiffs.[6]

A POSA would understand the meaning of this term in the patent's context based on the commonly understood meanings of "particle" and "D_{90}." The specification refers to particles as

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[5]This term appears in asserted claims 1 and 12 of the '945 patent. Only two defendants, Unichem and Sunshine Lake, seek construction of this term; the remaining nine defendants argue that the term should be given its plain and ordinary meaning, which, in their view, refers to 90% of volume, not 90% of particles. (*See* D.I. 204 at 24)

[6]Unichem filed a motion to strike an article relied upon by Plaintiffs. (*See* D.I. 258, 259, 271, 278) The Court will deny the motion. There is nothing inappropriate about Plaintiff's use of the article as impeachment evidence, to challenge Unichem's expert. As Plaintiffs point out, Unichem could have objected to the article during deposition, or addressed it in re-direct, a supplemental declaration, or in their responsive claim construction brief. (D.I. 271 at 5)

"individual drug substance particles" of a certain size range. ('945 patent at 3:20-22; *see also id.* at 2:13-15 (noting "notation D_x means that X% of the volume of particles have a diameter less than a specified diameter D"); *id.* at 2:15-17 (noting "D_{90} of 89 μm means that 90% of the volume of particles in an apixaban composition have a diameter less than 89 μm"))

Nothing in the patent requires particle size to be measured one and only one way, in particular only by a laser light scattering method using only bulk apaxiban particles, as Unichem contends. (*See* D.I. 204 at 17-23) The claims themselves simply disclose "[a] solid pharmaceutical composition . . . wherein the crystalline apixaban particles ***have*** a D_{90} equal to or less than about 89 μm," irrespective of whether the apixaban particles is bulk apixaban or whether the particle size is measured using laser light scattering technique. ('945 patent at 9:50-54) (Claim 1) (emphasis added) The claims are silent as to a method of measurement.

While the specification explains that "particle sizes stipulated herein and in the claims refer to particle sizes were determined using a laser light scattering technique" (*id.* at 2:21-23), this explanation of how the inventors themselves measured particle size does not – as a matter of claim construction law – exclude the possibility that other methods of measurement might alternatively be used by a POSA. Unichem points to no language of exclusion or disclaimer that could support its proposed construction. Indeed, the patent contains language suggesting that laser light scattering is not the only measurement method a POSA might use. (*See id.* at 3:37-39 ("Particle size distribution ***can*** be measured by laser light scattering technique as known to those skilled in the art and as further disclosed and discussed below. ") (emphasis added); *id.* at 6:15-16 ("As noted, average particle size ***can*** be determined by Malvern light scattering, a laser light scattering technique. ") (emphasis added)) Nor does Unichem point to a clearly-expressed intent

by the patentee to act as its own lexicographer with respect to this term. The focus of the claimed invention is on the surprising and unexpected finding that a certain particle size range of apixaban has better dissolution or absorption rate inside the body, not on the specific technique through which the particle size is measured. (*See id.* at 1:64-2:3 (noting in "Summary of the Invention" section that "[s]urprisingly and unexpectedly . . . apixaban particles having a D_{90} (90% of the volume) less than 89 microns (μm) lead to consistent in-vivo dissolution in humans"); *id.* at 1:56-60 (noting "large particles of apixaban drug substance [above claimed range] resulted in less than optimal exposures") *id.* at 2:52-54 ("It has surprisingly been found . . . that the particle size that impacts apixaban absorption rate is about a D_{90} of 89 μm."); *see also id.* at 9:29-32 ("FIGS. 3 and 4 illustrate the dissolution data that shows that while particle size impacts dissolution, controlling the particle size to less than 89 microns will result in a dissolution rate that will ensure consistent in-vivo exposures. "))[7]

Nothing in the extrinsic evidence leads to a different conclusion.

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[7] The prosecution history also shows the focus of the invention is on a certain particle size range of apixaban and not on any specific method of measuring the particle size. (*See* D.I. 182 Ex. 5 at BMSAPIX0009369 (noting "data in the application demonstrate that the claimed pharmaceutical composition that comprises crystalline apixaban provide in vivo exposures bioequivalent to that from an apixaban solution, provided that the ***apixaban particles have a particle size within claimed range***") (emphasis added); *id.* at BMSAPIX0010470, BMSAPIX0010472; *see also id.* at BMSAPIX0010466-68 (distinguishing prior art based on patent's focus on claimed particle size range, not on any specific method of measuring particle size)

III. CONCLUSION

The Court construes the disputed terms as explained above. An appropriate Order follows.