UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

MERCK SHARP & DOHME CORP., *Plaintiff*, v. ACTAVIS LABORATORIES FL, INC., ANDRX CORPORATION, ACTAVIS PHARMA, INC. AND ACTAVIS, INC., *Defendants.*	)	Civil Action No: 15-cv-6075 (PGS)(DEA) **MEMORANDUM AND ORDER**

SHERIDAN, U.S.D.J.

This matter comes before the Court on a Second Amended Joint Claim Construction and Prehearing Statement (hereinafter "Joint Claim Construction") regarding U.S. Patent No. 5,661,151 ("the '151 patent"), submitted by Merck Sharp & Dohme Corp. ("Merck" or "Plaintiffs") and Actavis Laboratories FL, Inc., Andrx Corporation, Actavis Pharma, Inc. and Actavis, Inc. (collectively, "Actavis") pursuant to L. Pat. R. 4.3. (*See* D.I. 128).

The '151 patent is directed to the synthesis and clinical use of antifungal compound posaconazole, which is used for treating or preventing fungal infections. Noxafil®, a brand name pharmaceutical drug for treating or preventing fungal infections, especially in people with weak immune systems, includes the active ingredient poscanazole.

In order to market and sell Noxafil®, Merck listed the '151 patent in the Food and Drug Association's ("FDA") Approved Drug Products with Therapeutic Equivalence Applications, commonly known as the Orange Book. *See* 21 U.S.C. § 355(B)(1). Thereafter, Actavis filed an Abbreviated New Drug Application ("ANDA") with the FDA in order to seek approval to market a generic version of Noxafil®. *See* 21 U.S.C. § 355(j)(1). Accordingly, pursuant to 21 U.S.C. §

355(j)(5)(B)(iii), Merck initiated this suit against Actavis because Actavis' request to market the generic version of Noxafil® is done prior to the expiration of the '151 patent.

As noted in the Joint Claim Construction, the parties dispute the meaning of the following claim terms recited in claim 12 of the '151 patent —"pharmaceutical[] composition," and "pharmaceutically acceptable carrier" (collectively "disputed claim terms").

On May 2, 2017, pursuant to L. Pat. R. 4.6, the Court held a *Markman* hearing to define the aforementioned two claim terms. These terms are construed below.

BACKGROUND

The '151 patent is generally directed to the synthesis and clinical use of antifungal compound posaconazole, which is used for treating and/or preventing fungal infections. (*See* Abstract of the '151 patent). The '151 patent filed on June 2, 1995, as Application No. 460,752, is a continuation-in-part of an application filed under the Patent Cooperation Treaty ("PCT"). The PCT application is a continuation-in-part of another application filed on December 21, 1993. As such, the potential effective filing date of the '151 patent is December 21, 1993. The '151 patent discloses antifungal compounds of formula I and pharmaceutical compositions, which are expected to exhibit anti-allergic, anti-inflammatory and immunomodulating activities. The pharmaceutical composition contains a fungicidally effective amount of other antifungal compounds such as cell wall active compound. (*Id.* at col. 56, ll. 40-67).

The '151 patent further discloses that pharmaceutical compositions are formulated by combining the compound of formula I or an equivalent amount of a pharmaceutically acceptable salt of compound I *with* a suitable, inert, pharmaceutically acceptable carrier or diluent. Examples of suitable pharmaceutical compositions include solid or liquid compositions for oral

administration such as tablets, capsules, pills, powders, granules, solutions, suppositories, troches, lozenges, suspensions or emulsions. (*Id.* at col. 57, ll. 40-50).

Further, the '151 patent discloses that a solid carrier can be one or more substances which may act as diluents, flavoring agents, solubilizers, lubricants, suspending agents, binders or tablet disintegrating agents, or as an encapsulating material. The carrier can also be a finely divided solid which is in admixture with the finely divided active compound. In a tablet form, for example, the active compound is mixed with the carrier that has the necessary binding properties. The carrier is added in suitable proportions such that the tablet is compacted in the desired shape and size. (*Id.* at col. 57, ll. 45-55).

During prosecution of the patent application of the '151 patent, the examiner rejected the claimed subject matter. Applicant amended the then pending claims to include claim term "in vivo" to differentiate over the cited art. (*See* Image File Wrapper of the '151 patent, Applicant's Arguments/Remarks Made in an Amendment, filed May 24, 1996). This amendment was made in response to patent examiner's rejection mailed on November 22, 1995. Additionally, arguments against the obviousness rejection under 35 U.S.C. § 103 were also made. (*Id.*)

After mailing a final rejection on August 21, 1996, the examiner conducted a personal interview with the Applicant's representative. During the personal interview, the enablement rejection under pre-AIA ("America Invents Act") 35 U.S.C. § 112, first paragraph, was discussed, and the Applicants agreed to provide an affidavit demonstrating that enablement exists for use of "in vivo" esters. (*See* Examiner Interview Summary Record mailed on December 19, 1996).

Accordingly, the Applicant filed a response to the outstanding Office action with a declaration from Dr. Ashit K. Ganguly, a co-inventor of the '151 patent. In its response, the Applicant essentially argued that based on the specification one skilled in the art would be able to

readily determine which of the ester compounds would be soluble or suspendible in a pharmaceutically acceptable aqueous media. (*See* Applicant's Arguments/Remarks filed on January 29, 1997; *citing* Declaration of Dr. Ganguly at ¶ 17).

Further, Applicants noted that they are "amending claim 17 of this application to cover a preferred embodiment, and to recite that such esters of the compounds of the claimed invention have a solubility in a pharmaceutically acceptable media of at least about 1 to about 50 mg/ml." (*Id.* at 6). Thereafter, on February 7, 1997, a notice of allowance was mailed by the patent examiner, which was later followed by a corrected notice of allowance on February 27, 1997. No reasons for allowance in-particular were provided by the patent examiner when issuing the notice of allowance.

LEGAL STANDARD

"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) (en banc) (quoting *Innova/Pure Water Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004)). Claim construction determines the correct claim scope, and is a determination exclusively for the court as a matter of law. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 978-79 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). The focus in construing disputed terms in claim language "is on the objective test of what one of ordinary skill in the art at the time of the invention would have understood the term[s] to mean." *Id.* at 986.

To determine the meaning of the claims, courts start by considering the intrinsic evidence. *Phillips*, 415 F.3d at 1313; *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 861 (Fed. Cir. 2004); *Bell Atl. Network Servs., Inc. v. Covad Comms. Group, Inc.*, 262 F.3d 1258, 1267 (Fed. Cir.

2001). The intrinsic evidence includes the claims themselves, the specification, and the prosecution history. *Phillips*, 415 F.3d at 1314; *C.R. Bard, Inc.*, 388 F.3d at 861.

The claims themselves provide substantial guidance in determining the meaning of particular claim terms. *Phillips*, 415 F.3d at 1314. First, the context in which a term is used in the asserted claim can be very instructive. *Id.* Other asserted or non-asserted claims can aid in determining the claim's meaning because claim terms are normally used consistently throughout a patent. *Id.* Differences among claims can also assist in understanding a term's meaning. *Id.* For example, when a dependent claim adds a limitation, there is a presumption that the independent claim does not include that limitation. *Id.* at 1314-15.

"[C]laims 'must be read in view of the specification of which they are a part.'" *Id.* at 1315 (quoting *Markman*, 52 F.3d at 979). "[T]he 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.'" *Id.* (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). This is true because a patentee may define his own terms, give a claim term a different meaning than the term would otherwise possess, or disclaim or disavow the claim scope. *Id.* at 1316. In these circumstances, the inventor's lexicography governs. *Id.* The specification may also resolve the meaning of ambiguous claim terms "where the ordinary and accustomed meaning of the words used in the claims lack sufficient clarity to permit the scope of the claim to be ascertained from the words alone." *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1325 (Fed. Cir. 2002). But, "[a]lthough the specification may aid the court in interpreting the meaning of disputed claim language, particular embodiments and examples appearing in the specification will not generally be read into the claims." *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998) (quoting *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560,

1571 (Fed. Cir. 1988)); *also see Phillips*, 415 F.3d at 1323 ("although the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments.").

The prosecution history is another tool to supply the proper context for claim construction. It "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 that it would otherwise be." *Phillips*, 415 F.3d at 1317.

"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. Although extrinsic evidence can be useful, it is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" *Phillips*, 415 F.3d at 1317 (quoting *C.R. Bard, Inc.*, 388 F.3d at 862).

Dictionaries and treatises may aid a court in understanding the underlying technology and the manner in which one skilled in the art might use claim terms, but dictionaries and treatises may provide definitions that are too broad or may not be indicative of how the term is used in the patent. *Id.* at 1318. Similarly, expert testimony may aid a court in understanding the underlying technology and determining the particular meaning of a term in the pertinent field, but an expert's conclusory, unsupported assertions as to a term's definition are entirely unhelpful to a court. *Id.*

Generally, extrinsic evidence is "less reliable than the patent and its prosecution history in determining how to read claim terms." *Id.* The Supreme Court recently explained the role of extrinsic evidence in claim construction:

> In some cases, however, 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. . . . In cases where those subsidiary facts are in dispute, courts will need to make subsidiary factual findings about that extrinsic evidence. These are the "evidentiary underpinnings" of claim construction that we discussed in *Markman*, and this subsidiary fact finding must be reviewed for clear error on appeal.

Teva Pharm. USA, Inc. v. Sandoz, Inc., 135 S.Ct. 831, 841 (2015).

Overall, in construing the claims, "[t]he judge's task is not to decide which of the adversaries is correct. Instead, the judge must independently assess the claims, the specification, and if necessary the prosecution history and relevant extrinsic evidence, and declare the meaning of the claims." *Exxon Chem. Patents, Inc. v. Lubrizol Corp.*, 64 F.3d 1553, 1556 (Fed. Cir. 1995).

ANALYSIS

With the above standard in mind, the Court construes the following claim terms that the parties submitted before the Court—(i) "pharmaceutical[] composition," and (ii) "pharmaceutically acceptable carrier," as recited in claim 12 of the '151 patent.

Claim 12 of the '151 patent states,

> "A **pharmaceutically composition** for treating or preventing a fungal infection comprising an antifungally effective amount of the compound of claim 11 together with a **pharmaceutically acceptable carrier** therefor."

The Court notes that claim 12 is a dependent claim because it refers back to another claim, namely independent claim 11.[1]

[1] *See* Manual of Patent Examining Procedure ("MPEP"), Section 1824, 6.4(a) ("Any claim which includes all the features of one or more other claims (claim in dependent form, hereinafter referred to as "dependent claim") shall do so by a reference, if possible at the beginning, to the other claim or claims and shall then state the additional features claimed.").

1. "Pharmaceutical[] composition"

Merck's Proposed Construction	Actavis's Proposed Construction
"A formulation of a pharmacologically active ingredient prepared outside an organism and adapted for any mode of administration to that organism"	Plain meaning, which means "A composition of matter that includes a drug substance."

As a preliminary matter, the Court notes that the preamble of claim 12 recites "pharmaceutically composition." However, the parties have agreed that this is a typographical error, and it should be corrected to read as "pharmaceutical composition." (*See* Def.'s Opening Br. at 1, fn. 2; D.I. 55)[2].

Actavis argues that this Court should refrain from construing the aforementioned term because it is a preamble, which generally does not contain any patentable weight unlike the body of the claim. (*See* Def.'s Opening Br. at 5-6, D.I. 55; *also see* Transcript of May 2, 2017 *Markman* hearing ("Trans.") at 53:19—54:3). In support, Actavis relies on *SourceOne Global Partners, LLC v. KGK Synergize, Inc.*, No. 08-7403, 2010 WL 2232944, at *4 (N.D. Ill. June 3, 2010) ("'pharmaceutical composition,' merely introduce the claim" and do "not have their own independent significant"), and *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1375-76 (Fed. Cir. 2001) ("[a] method for treating a cancer patient," merely stated the intended

[2] Based on a review of the Image File Wrapper of the '151 patent, there was no Certificate of Correction made of record pursuant to either 37 C.F.R. 1.322 (Certificate of correction of Office mistake) or 37 C.F.R. 1.323 (Certificate of correction of Applicant's mistake). Granted, district courts have long had the power to fix obvious drafting mistakes where no certificate of correction has been issued. *See I.T.S. Rubber Co. v. Essex Rubber Co.*, 272 U.S. 429, 442 (1926); *also see Novo Industries L.P. v. Micro Molds Corp.*, 350 F.3d 1348, 1354 (Fed. Cir. 2003). "[A] district court can [correct a patent] only if (1) the correction is not subject to reasonable debate based on consideration of the claim language and the specification and (2) the prosecution history does not suggest a different interpretation of the claims." *Novo Industries L.P.*, 350 F.3d at 1354. However, it is the patent holder who has the primary responsibility of ensuring that the patent is "precise enough to afford clear notice of what is claimed, thereby apprising the public of what is still open to them. Otherwise there would be a zone of uncertainty […]." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S.Ct. 2120, 2129 (2014). Since there is no dispute over the correction, the Court agrees it was a "typo."

use or purpose of the invention, and did not limit the scope of the claim). (*See* Def.'s Opening Br. at 5-6; *also see* Trans. at 61: 3-24 and 62:8—63:10).

The Court does not find Actavis' arguments persuasive because the cases relied upon, *SourceOne Global* and *Bristol-Myers Squibb*, are not analogous to the case at hand. In both, *SourceOne Global* and *Bristol-Myers Squibb*, the claim terms analyzed by the Courts were recited in independent claims and not in dependent claims, which is the situation in the instant case. Unlike, "[a] pharmaceutical composition," in *SourceOne Global*, or "[a] method for treating a cancer patient," in *Bristol-Myers Squibb*, the claim term "pharmaceutical composition" to be construed here is recited in a dependent claim. By definition, a dependent claim is a claim which includes *all* the features of one or more other claims which it references. (*See* supra fn. 1). As such, the preamble of claim 12 in the instant case is distinguishable from the preambles of claim terms construed in *SourceOne Global* and *Bristol-Myers Squibb*.

The "preamble" of a claim is the introductory portion of the claim that describes the invention in more general terms than the rest of the claim, typically appearing before the transition term "comprising". *Nexans Inc. v. General Cable Technologies Corp.*, 630 F.Supp.2d 499, 506 (E.D. Pa. 2008). The determination of whether a preamble limits a claim is made on a case-by-case basis in light of the facts in each case. As such, there are some principles but no precise standard to define when a preamble should be construed as a claim limitation. *Corning Glass Works v. Sumitomo Elec., U.S.A. Inc.*, 868 F.2d 1251, 1257 (Fed. Cir. 1989). There is a presumption against reading preamble language as a claim limitation "where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use of the invention" or "to give context for what is being described in the body of the claim." *Symantec Corp. v. Computer Assocs. Int'l, Inc.*, 522 F.3d 1279, 1288 (Fed. Cir. 2008).

However, "[i]f the claim preamble, when read in the context of the entire claim, recites limitation of the claim, or, if the claim preamble is 'necessary to give life, meaning, and vitality' to the claim, then the claim preamble should be construed as if in the balance of the claim." *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305-1306 (Fed. Cir. 1999); *also see In re: Cruciferous Sprout Litigation*, 301 F.3d 1343, 1347 (Fed. Cir. 2002). Additionally, where there is a "[c]lear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art may indicate that the preamble is a claim limitation because the preamble is used to define the claimed invention." *In re: Cruciferous Sprout Litigation*, 301 F.3d at 1347; *also see Metabolite Labs., Inc. v. Corp. of Am. Holdings*, 370 F.3d 1354, 1358-62 (Fed. Cir. 2004).

Here, as noted above, claim 12 depends from claim 11. As such, claim 12 includes all the features of claim 11. Claim 12 is a product claim as it includes 'an effective amount of the compound represented by the formula of claim 11 and a pharmaceutically acceptable carrier.' In claim 11, there is no reference that the compound must be of "pharmaceutical" quality. Claim 12 requires same. As such, the term "pharmaceutical composition" recites a structural limitation and carries patentable weight. It is evident that the '151 patent is directed not only towards antifungal compounds, but also towards pharmaceutical compositions, that are fit for safe use. (*See* Abstract and col. 56, ll. 40-67 of the '151 patent; *see Corning Glass*, 868 F.2d at 1256).

Now, assuming *arguendo*, that if the Court adopts Actavis' arguments that the "pharmaceutical composition" does not carry any patentable weight and should not be construed as a claim limitation, then such an interpretation would render claim 12 meaningless and run afoul of pre-AIA 35 U.S.C. § 112, fourth paragraph.[3]

[3] *See* 35 U.S.C. § 112, fourth paragraph ("a claim in dependent form shall contain a reference to a claim previously set forth and then specify a *further limitation* of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers."

By rendering the preamble of claim 12 to be merely an introductory statement, claim 12 would then essentially read, "an antifungally effective amount of the compound of claim 11 together with a pharmaceutically acceptable carrier therefor." Granted claim 12 would remain a dependent claim of claim 11 as it references back to claim 11. However, claim 12 would then essentially include the 'compound' and the 'pharmaceutically acceptable carrier,' as separate components, without further limiting the subject matter of claim 11 (i.e., the compound).

The introduction of 'pharmaceutically acceptable carrier' in claim 12 does not further limit the 'compound' of claim 11 because it is a new feature that is independent of the compound. This is evidenced by some of the other claims recited in the '151 patent. For example, dependent claims 2-7 of the '151 patent further limit the compound of claim 1 by adding structure to the 'ester group convertible in vivo into OH' of the compound recited in claim 1. That is, the 'ester group convertible in vivo into OH' being "a polyether ester, a phosphate estate, a sulfate ester, a heterocyclic ester, an alkanoate ester, an alkenoate ester, an amino acid ester or an acid ester," as recited in claim 2. Unlike claims 2-7, the 'pharmaceutically acceptable carrier' in claim 12 does not further limit the compound of claim 11. Instead, it is introduced as a new feature that is not present in the compound itself. As such, by grouping the 'compound' of claim 11 with a 'pharmaceutically acceptable carrier,' results in a new component—a pharmaceutical composition—that is different from the compound itself.

Accordingly, the Court finds that when considering the entirety of the '151 patent and claim 12, the term "pharmaceutical composition" carries patentable weight as it ties together the compound of 11 *with* a carrier; thereby being 'necessary to give life, meaning, and vitality' to claim 12. *Pitney Bowes, Inc.*, 182 F.3d at 1305-1306.

Next, the Court will construe the claim term "pharmaceutical composition." Generally, claim terms are "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." *Phillips*, 415 F.3d at 1303.

Here, the parties dispute as to the meaning of the aforementioned term. Merck proposes that this term means—(i) a formulation of a pharmacologically active ingredient, (ii) that is prepared outside an organism, and (iii) is adapted for any mode of administration to that organism. (*See* Pl.'s Opening Br. at 7; D.I. 56). Dr. Vladimir R. Muzykantov ("Dr. Muzykantov), on behalf of Actavis, has provided a declaration in which he provides reasons as to why the aforementioned interpretation should not be adopted. (See Declaration of Muzykantov ("Decl. of Muzykantov") at ¶ 1; D.I. 65-1). The reasons he provides are as follows—(1) pharmaceutical composition" is not the same as "formulation" because formulation connotes both a process and a product produced by that process; whereas, a pharmaceutical composition connotes a product only. (Decl. of Muzykantov at ¶ 29); (2) Dr. Muzykantov notes that including "a pharmaceutically active ingredient prepared outside the organism" in construing the aforementioned term would result in excluding pharmacological agents, whose delivery and effect in the body depend on the biological factors encountered by drugs and their carriers after administration. In support, Dr. Muzykantov cites to prodrugs such as nitroglycerin (e.g., a pharmaceutical composition) that do not become pharmaceutically active until after being dissolved in the body. (*Id.* at ¶¶ 30-31; *also see* Trans. at 85:6—86:13); and (3) Dr. Muzykantov notes that excluding compositions prepared inside an organism would not be considered by a skilled person of art in construing the aforementioned term because the composition prepared outside the body may contain a pharmacologically active or

inactive agent that undergoes an enzymatic transformation to become a pharmaceutically active agent inside the body. (*Id.* at ¶ 32).

Dr. Roland E. Dolle, a medicinal chemist, testified on behalf of Merck during the *Markman* hearing. Dr. Dolle testified that he has used the term "pharmaceutical composition" hundreds of times in the context of clinical candidates, and its plain and ordinary meaning has not changed for nearly eighty (80) years since it was introduced in the Federal Food Drug and Cosmetic Act. (*See* Trans. at 114:3-20). Dr. Dolle noted that when referring to compositions for administration, one skilled in the art would refer to drug formulations prepared outside a human body, which include drug substances that have been combined with other molecules to render them suitable for administration. Formulation being the pharmaceutical compound mixed with other chemicals which are excipients or vehicles to produce a product that is suitably administered. (*Id.* at 115:1-19). Further, Dr. Dolle noted that "pharmaceutical composition" and "pharmaceutical formulation" are synonymous terms in their plain meaning. (*Id.* at 118:10-18).

As such, there is a dispute as to the plain and ordinary meaning of the term "pharmaceutical composition." Because the ordinary meaning is "often not immediately apparent, and because patentees frequently use terms idiosyncratically," the Court looks to "the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." *Phillips*, 415 F.3d at 1303.

The Court notes that the intrinsic evidence clearly indicates what constitutes "pharmaceutical composition." For example, col. 57, ll. 40-50 disclose that "[s]uch [pharmaceutical] compositions are formulated by combining the compound of formula I […] with

a suitable, inert, pharmaceutically acceptable carrier or diluent." As such, the pharmaceutical composition is a combination of a formula and a carrier.

Further, the Court recognizes that the '151 patent discloses the different forms that the pharmaceutical compositions can take (i.e., solid, liquid, or topical), and as such, would require conscious, intentional activity of a human being. This, thereby, excludes generation of the pharmaceutical compositions through internal, psychological process—a proposition advanced by Actavis. For example, col. 57 and col. 58 of the '151 patent disclose various methods of forming the pharmaceutical composition, and the different forms that can be embodied therein. From the disclosure of the '151 patent, it is evident that the inventors intended to formulate the pharmaceutical composition in a physical environment that was under their control.

However, the Court does take issue in-part with Merck's claim construction. In particular, phrases "prepared outside an organism" and "adapted for any mode of administration to that organism." With respect to "prepared outside an organism," the Court notes that the term "formulation," in terms of pharmaceutical formulation, inherently suggests being prepared in a physical environment, outside an organism.[4] As such, using the term "formulation" renders the terms "prepared outside an organism" superfluous. Lastly, with respect to "adapted for any mode of administration to that organism," the Court recognizes that there are different ways of administering the pharmaceutical composition. However, the foregoing phrase does not define the scope of what constitutes the term "pharmaceutical composition." Instead, it pertains to the intended use of the pharmaceutical composition.

[4] *See* Medical-Dictionary, "formulation." ("a pharmacological substance prepared according to a formula."), *available at* http://medical-dictionary.thefreedictionary.com/Pharmaceutical+formulation (last visited June 26, 2017).

Accordingly, the Court defines the term "pharmaceutical composition" to mean "formulation of at least one active ingredient with a substance or collection of substances capable of being combined with the at least one active ingredient."

2. "Pharmaceutically acceptable carrier"

Merck's Proposed Construction	Actavis's Proposed Construction
"An inert, non-cellular, non-toxic substance or collection of substances that serve(s) as a vehicle for delivery of a pharmacologically active ingredient."	Plain meaning, which means "A substance that functions as a carrier for a drug substance, e.g., helps facilitate storage or shipment of a drug substance; introduction of the drug substance into an organism; and/or delivery or regulation of activity of a drug substance within an organism, and is not intolerably toxic."

Initially, the Court notes that during the *Markman* hearing, Merck conceded that the terms "inert" and "non-cellular" from their proposed definition could be removed, without departing from the proposed meaning of the term "pharmaceutically acceptable carrier." (*See* Trans. at 34:5-13, 71:9-24). As such, Merck proposes the following definition for the aforementioned term, "[a] non-toxic substance or collection of substances that serve(s) as a vehicle for delivery of a pharmacologically active ingredient."

Actavis argues that Merck's claim construction of "pharmaceutically acceptable carrier" should not be adopted by the Court because—(i) it improperly imports a limitation from the specification, (ii) uses vague terms, such as "non-toxic," that result in more confusion, and (iii) it imports a process limitation into the claim. (*See* Def.'s Opening Br. at 11; D.I. 55). In particular, Actavis asserts that the term "non-toxic" adds further ambiguity to the term "pharmaceutically acceptable carrier" because itself would require additional defining. (*Id.* at 13).

The term "pharmaceutically acceptable carrier" essentially consists of two separate terms—(i) "pharmaceutically acceptable," and (ii) "carrier." The second term, "carrier" being

"pharmaceutically acceptable." In addition to "carrier," the specification of the '151 patent also uses the term "pharmaceutically acceptable" with respect salts, acids, esters, bases and topical carrier.

Merck asserts that common sense dictates that the aforementioned term be interpreted to mean a carrier that is suitable for administration to a human being or other mammal without triggering an adverse immune reaction in a subject. (*See* Pl.'s Opening Br. at 11; D.I. 56)

With respect to "pharmaceutically acceptable," Merck cites to col. 5, ll.48-57 of the U.S. Patent No. 5,440,056, ("the '056 patent"). The '056 patent defines "pharmaceutically acceptable" as "within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response and the like, and are commensurate with a reasonable benefit/risk ratio." And, further the '056 patent defines "pharmaceutically acceptable carrier" as "a non-toxic, inert solid, semi-solid or liquid filler, diluent, encapsulating material or formulation auxially of any type." (*Id.* at 11-12). The '056 patent was filed on March 9, 1994, and issued into a patent on August 8, 1995. The '056 patent is assigned to Abbott Laboratories.

The Court notes that the '056 patent is not cited or incorporated by reference in the '151 patent. The two patents do not share the same inventive entity or the same assignee. However, the '056 patent, filed before the '151 patent, is generally directed to the same technical arts as the '151 patent is it is directed towards plant-derived chemotherapeutic compounds for the treatment of cancers and leukemia. (*See* the '056 patent at col. 1, ll. 10-20 and col. 2, ll. 50-55). As such, one skilled in the art may reasonably rely on the '056 patent to determine the ordinary and customary meaning of a claim term. *See CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366-1367 (Fed. Cir. 2002) ("a claim term will not carry its ordinary meaning if the intrinsic evidence shows

that the patentee distinguished that term from prior art"); *also see* MPEP 2173.01, I. "Interpreting the Claims" ("The ordinary and customary meaning of a term may be evidenced by a variety of sources, including the words of the claims themselves, the specification, drawings, and prior art.")

During the *Markman* hearing, there was much disagreement between the parties as to what constitutes "non-toxic." Dr. Muzykantov, on behalf of Actavis, testified that there is no such thing as "non-toxic," and everything depends on the dose, route administration, and the status of the patient—i.e., any preexisting conditions. (*See* Trans. at 89:17-21, 90:2-10 ("[e]ven sterile water would be toxic if you inject it sufficient amount [intravenously]. So, yes, there are things which are toxic at one route of administration and purely benign with another route."). Whereas, Dr. Dolle, on behalf of Merck, testified that when a drug is formulated with a carrier, it is formulated in a way that the product will not cause undue toxicity. Such that the amount of toxicity would be acceptable to the patient. (*Id.* at 125:6-15). However, Dr. Dolle did note that "all compounds are toxic at some dose," including sterile water "in [an] extraordinary dose[.]" (*Id.* at 127:22—128:7).

In an effort to eliminate any ambiguity of what constitutes "non-toxic," Merck's counsel proposed another construction in lieu of non-toxic to mean, "not unacceptably toxic under anticipated exposure conditions." Dr. Muzykantov testified this to be "much better." (*See* Trans. at 98:2-6).

The Court finds that the term "non-toxic" itself creates more ambiguity than clarity to the term "pharmaceutically acceptable." The Court recognizes and appreciates that the composition or the drug being administered to a patient, under anticipated exposure conditions, should aid in patient's therapy, and not in-turn cause anaphylaxis with the patient's immune system. However, the intrinsic and extrinsic evidence fails to establish a definition for the term "non-toxic." Accordingly, the Court determines that one skilled in the art may construe the term

"pharmaceutically acceptable" to mean "suitable for use in contact with the tissues of mammals for purposes of a therapeutic treatment in the mammals under anticipated exposure conditions."

As to the second part of the aforementioned term, "carrier," the '151 patent discloses that the carrier is combined with the salt of compound I to form a pharmaceutical composition. The different forms that the pharmaceutical composition can take are—oral, topical or vaginal administration, or by inhalation. (*See* the '151 patent, col. 57, ll. 40-45). The carrier can be a solid. A solid carrier can be one or more substances, which allows it to act as, for example, diluents, flavoring agents, solubilizers, or lubricants. In powder form, the carrier is a "finely divided solid which is admixture with the finely divided active compound." (*Id.* at col. 57, ll. 50-55). Whereas, in the tablet form, the active compound is mixed with carrier having the necessary "binding properties in suitable proportions and compacted in the shape and size desired." (*Id.* at col. 57, ll. 55-57).

Accordingly, based on the intrinsic evidence, the Court determines the term "carrier" to mean, "a substance or collection of substances capable of being combined with an active ingredient." As such, the term "pharmaceutically acceptable carrier" is construed as—"substance or collection of substances capable of being combined with an active ingredient that is suitable for use in contact with the tissues of mammals for purposes of a therapeutic treatment in the mammals under anticipated exposure conditions."

ORDER

IT IS on this 27th day of June, 2017,

ORDERED that "pharmaceutical composition," recited in claim 12 of the U.S. Patent No. 5,661,151 ("the '151 patent"), means "formulation of at least one active ingredient with a substance or collection of substances capable of being combined with the at least one active ingredient;" and it is further

ORDERED that "pharmaceutically acceptable carrier," recited in claim 12 of the '151 patent, means "substance or collection of substances capable of being combined with an active ingredient that is suitable for use in contact with the tissues of mammals for purposes of a therapeutic treatment in the mammals under anticipated exposure conditions."

s/Peter G. Sheridan
PETER G. SHERIDAN, U.S.D.J.