IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

LEO PHARMA A/S, LEO LABORATORIES LIMITED, AND LEO PHARMA, INC., Plaintiffs, v. ACTAVIS LABORATORIES UT, INC., AND ACTAVIS, INC., Defendants.	)	Civil Action No. 16-333-JFB-SRF Civil Action No. 18-402-JFB-SRF **UNDER SEAL**
LEO PHARMA A/S, LEO LABORATORIES LIMITED, AND LEO PHARMA, INC., Plaintiffs, v. PERRIGO UK FINCO LIMITED PARTNERSHIP AND PERRIGO COMPANY, Defendants.	)	Civil Action No. 16-430-JFB-SRF Civil Action No. 18-401-JFB-SRF **UNDER SEAL**

REPORT AND RECOMMENDATION

I. INTRODUCTION

In these patent infringement actions filed under the Hatch-Waxman Act by plaintiffs LEO Pharma A/S ("LEO Pharma"), LEO Laboratories Limited ("LEO Labs"), and LEO Pharma, Inc. ("LEO, Inc.") (collectively, "LEO") against defendants Actavis Laboratories UT, Inc. and Actavis, Inc. (together, "Actavis"), and Perrigo UK Finco Limited Partnership and Perrigo Company (together, "Perrigo"), LEO alleges infringement of numerous patents directed to LEO's Picato® drug. Against Actavis in Civil Action No. 16-333-JFB-SRF, LEO filed a second

amended complaint alleging infringement of United States Patent Nos. 7,410,656 ("the '656 patent"), 8,278,292 ("the '292 patent"),[1] 8,372,827 ("the '827 patent"), 8,372,828 ("the '828 patent"), 8,377,919 ("the '919 patent"), 8,536,163 ("the '163 patent"), 8,716,271 ("the '271 patent"), 8,735,375 ("the '375 patent"), 9,676,698 ("the '698 patent"), and 9,416,084 ("the '084 patent"). (C.A. No. 16-333-JFB-SRF, D.I. 73) Against Actavis in Civil Action No. 18-402-JFB-SRF, LEO filed a complaint alleging infringement of the '292 patent and United States Patent Nos. 9,820,959 ("the '959 patent"), 9,933,428 ("the '428 patent"), and 9,833,429 ("the '429 patent"). (C.A. No. 18-402-JFB-SRF, D.I. 2) Against Perrigo in Civil Action No. 16-430-JFB-SRF, LEO filed a first amended complaint alleging infringement of United States Patent Nos. 6,787,161 ("the '161 patent") and 6,844,013 ("the '013 patent), as well as the '656 patent, the '292 patent, the '827 patent, the '828 patent, the '919 patent, the '163 patent, the '271 patent, the '375 patent, the '698 patent, and the '084 patent. (C.A. No. 16-430-JFB-SRF, D.I. 99) Against Perrigo in Civil Action No. 18-401-JFB-SRF, LEO filed a complaint alleging infringement of the '292 patent, the '959 patent, the '428 patent, and the '429 patent. (C.A. No. 18-401-JFB-SRF, D.I. 2)

Presently before the court is the matter of claim construction. This decision sets forth the court's recommendations of constructions for the disputed claim terms discussed in the briefing and at the *Markman* hearing held on May 2, 2018.

[1] The '292 patent is the ultimate parent of the '428 and '429 patents, and shares a specification with those patents.

II. BACKGROUND

A. Parties

LEO is the holder of New Drug Application ("NDA") No. 202833 for ingenol mebutate gel, 0.015% and 0.05%, which was approved by the FDA on January 23, 2012. (D.I. 73 at ¶ 13)[2] LEO markets the drug under the trade name Picato®. (*Id.*) The active pharmaceutical ingredient ("API") in Picato® is ingenol mebutate, or ingenol-3-angelate. (*Id.* at ¶ 14)

Actavis manufactures and sells generic copies of branded pharmaceutical products throughout the United States. (*Id.* at ¶ 6) Actavis has submitted two Abbreviated New Drug Applications ("ANDA") to the FDA for approval of a generic version of Picato®: ANDA No. 208807 and ANDA No. 209086. (*Id.* at ¶¶ 32-33)

Perrigo manufactures and sells generic copies of branded pharmaceutical products. Perrigo has submitted two ANDAs to the FDA for approval of a generic version of Picato®: ANDA No. 209018 and ANDA No. 209019. (*Id.* at ¶¶ 45-46)

B. Technology of the Brown Patents

The Brown Patents[3] share a common specification and name as inventors Marc Barry Brown, Michael Edwards Crothers, and Tahir Nazir. The Brown Patents are directed to topical skin cancer treatments. Specifically, the '292 patent, entitled "Therapeutic Compositions," claims pharmaceutically acceptable formulations of ingenol-3-angelate combined with pharmaceutical solvents and excipients to achieve a stable form. ('292 patent, col. 1:60-67)

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[2] All references to docket entries in this ruling will reflect the docket in Civil Action No. 16-333-JFB-SRF, unless otherwise noted.

[3] The Brown patents include the '292 patent, the '827 patent, the '828 patent, the '919 patent, the '163 patent, the '271 patent, and the '375 patent. (D.I. 142, Ex. A at 3) The '292 patent is the only originally-asserted Brown patent still asserted against defendants. (D.I. 249 at 1-2) The other Brown Patents originally asserted against defendants have been dropped.

On December 6, 2017, LEO filed complaints in Civil Action Nos. 17-1752-JFB-SRF and 17-1753-JFB-SRF, alleging infringement of the '959 patent, the '428 patent, and the '429 patent (collectively, the "New Brown Patents"). The New Brown Patents are members of the Brown Patent family that had not yet been issued at the time the original complaints in the 2016 actions were filed. Like the Brown Patents, the New Brown Patents disclose pharmaceutical formulations of ingenol-3-angelate.

On March 14, 2018, LEO filed complaints in Civil Action Nos. 18-401-JFB-SRF and 18-402-JFB-SRF, alleging infringement of the '292 patent, the '959 patent, the '428 patent, and the '429 patent. In April 2018, the court entered stipulations dismissing Civil Action Nos. 17-1752-JFB-SRF and 17-1753-JFB-SRF without prejudice and consolidating Civil Action Nos. 18-401-JFB-SRF and 18-402-JFB-SRF with Civil Action Nos. 16-333-JFB-SRF and 16-430-JFB-SRF. (C.A. No. 16-333-JFB-SRF, D.I. 289; C.A. No. 16-430-JFB-SRF, D.I. 252)

III. LEGAL STANDARD

Construing the claims of a patent presents a question of law, although subsidiary fact finding is sometimes necessary. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 837-38 (2015) (citing *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 977-78 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370, 388-90 (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). "[T]here is no magic formula or catechism for conducting claim construction." *Id.* at 1324. Instead, the court may attach the appropriate weight to appropriate sources "in light of the statutes and policies that inform patent law." *Id.*

The words of the claims "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." *Phillips*, 415 F.3d 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); *see also Eon Corp. IP Holdings v. Silver Spring Networks, Inc.*, 815 F.3d 1314, 1320 (Fed. Cir. 2016). Claim terms are typically used consistently throughout the patent, and "usage of a term in one claim can often illuminate the meaning of the same term in other claims." *Phillips*, 415 F.3d at 1314 (observing that "[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 . . . .").

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) (citing *Ecolab Inc. v. Paraclipse, Inc.*, 285 F.3d 1362, 1375 (Fed. Cir. 2002).

Other intrinsic evidence, including 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). "[T]he 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 (citing *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002)). 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." *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). The specification "is not a substitute for, nor can it be used to rewrite, the chosen claim language." *SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004).

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 also "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 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.* ("[C]onclusory, unsupported assertions by experts as to the definition of a claim term are not useful to a court."). 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). 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).

IV. CONSTRUCTION OF DISPUTED TERMS

A. "pharmaceutically acceptable solvent" ('428 patent, claims 25, 30, 31; '429 patent, claims 5, 10, 24)[4]

LEO	Defendants	Court
"solvent suitable for use in a pharmaceutical formulation"	"aprotic solvent suitable for use in a pharmaceutical formulation, which is distinct from the penetration enhancer"	"solvent suitable for use in a pharmaceutical formulation"

I recommend that the court adopt LEO's proposed construction, in accordance with the intrinsic evidence. The parties agree that a pharmaceutically acceptable solvent must be suitable for use in a pharmaceutical formulation. (D.I. 249 at 5; D.I. 250 at 3) The parties' dispute is related to: (1) whether the term is limited to an aprotic solvent,[5] and (2) whether the solvent must be distinct from the claimed penetration enhancer.

1. Aprotic solvent

Defendants' proposal to limit the disputed term to aprotic solvents is not sufficiently supported by the specification. The parties do not dispute that a solvent may be either protic or aprotic. (5/2/18 Tr. at 7:2-5; 38:11-17) The disputed claim language does not expressly limit the term to a specific type of solvent. ('292 patent, col. 53:23-31) The specification's use of the terms "protic" and "aprotic" to further describe various solvents indicates that the patentee could have incorporated the word "aprotic" into the claim language itself if the patentee intended to limit the term in the manner proposed by defendants. (*Id.* at col. 2:7-18)

[4] The term "pharmaceutically acceptable solvent" also appears in the independent claims of the '292 patent and, as a result, the court's construction of this term shall apply equally to the '292 patent. *See Aventis Pharms. Inc. v. Amino Chems. Ltd.*, 715 F.3d 1363, 1380 (Fed. Cir. 2013).
[5] There is no dispute that benzyl alcohol is an aprotic solvent in the context of the New Brown Patents. (D.I. 251, Ex. 4 at 259:10-14; D.I. 280, Ex. 9; Ex. 10 at 4)

Moreover, the specification discloses examples of ingenol-3-angelate achieving stability in protic solvents. Specifically, Table 3 of the '292 patent discloses "Phosphate buffer pH 4.5" and "Ammonium buffer pH 4.5" as protic solvents in which ingenol-3-angelate remained stable. ('292 patent, col. 13:12-53) Example 1 of the '292 patent also demonstrates that ingenol-3-angelate "was shown to be stable in . . . phosphate buffer pH 4.5 and ammonium buffer (pH 4.5)."[6] (*Id.*, col. 9:15-20) Although the specification acknowledges that "ingenol angelate is generally susceptible to rearrangement in protic solvents," which "is undesirable in a pharmaceutical formulation," the examples identified in Example 1 and Table 3 demonstrate that stability may be achieved in certain cases when using a protic solvent. (*Id.*, col. 2:9-13)

Defendants allege that the invention was intended to resolve the problem of rearrangement of ingenol angelate, which is known to occur with dissolution of ingenol angelate in protic solvents. (D.I. 279 at 3, 7) Defendants cite case authorities holding that disavowal may exist "[w]here the general summary or description of the invention describes a feature of the invention . . . and criticizes other products," and a "patentee's choice of preferred embodiments can shed light on the intended scope of the claims." *AstraZeneca AB, Aktiebolaget Hassle, KBI-E, Inc. v. Mutual Pharm. Co., Inc.*, 384 F.3d 1333, 1340 (Fed. Cir. 2004). However, the specification proposes a solution to the disadvantages posed by protic solvents, explaining that the rearrangement "can be minimized if a small amount of acid or acidic buffer . . . is added." ('292 patent, col. 3:18-22) The specification's proposed solution to the problem of

[6] Although the pH level of 4.5 falls outside the preferred pH range between 3 and 4, counsel for LEO noted that the patent teaches obtaining the preferred pH by adding an acid to a solvent, regardless of whether the solvent is aprotic or protic. (5/2/18 Tr. at 18:4-12; 24:21-25:2) The specification explains that "rearrangement is likely to occur at above a pH of about 4.5," further supporting LEO's position that a protic solvent with a pH of 4.5 may be stable, and the pH range of 3 to 4 represents a preferred embodiment. ('292 patent, col. 2:35-38)

rearrangement posed by protic solvents,[7] viewed in combination with examples showing the use of protic solvents in solutions achieving the requisite stability benchmarks, illustrate that the inventors did not disavow the use of protic solvents in the New Brown Patents.

The abstract of the '292 patent, which specifies that ingenol angelate "can be stabilized by dissolving [ingenol angelate] in an aprotic solvent in the presence of an acidic buffer," is read by defendants to suggest that the inventors intended to limit the scope of the claims to aprotic solvents. *See Hill-Rom Co., Inc. v. Kinetic Concepts, Inc.*, 209 F.3d 1337, 1341 (Fed. Cir. 2000) (concluding that courts, unlike examiners, may look to the abstract to determine the scope of the invention). However, the permissive language of the abstract leaves room for the possibility that ingenol angelate can also be stabilized in solvents which are not aprotic. (5/2/18 Tr. at 25:9-20; 26:15-24; 40:7-10) Moreover, the law is well-established that "the specification as a whole must be considered." *Cubist Pharms., Inc. v. Hospira, Inc.*, 805 F.3d 1112, 1118 (Fed. Cir. 2015). For the reasons previously discussed, the specification in its entirety does not preclude the use of a protic solvent in a stable formulation. The specification's delineation between solvents, aprotic solvents, and protic solvents would not be necessary if the only solvents encompassed by the claimed invention were aprotic. *See Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1368 (Fed. Cir. 2012).

The prosecution history provides further support for LEO's proposed construction because it reveals that the original application limited the claims to aprotic solvents, and the "aprotic" limitation was subsequently removed by amendment during prosecution. (D.I. 252,

[7] The specification also describes circumstances in which aprotic solvents can lead to disadvantageous rearrangement, establishing that the problem of rearrangement is not unique to protic solvents. ('292 patent, col. 2:14-18) ("In aprotic solvents . . . dissolution can take some considerable time and this, together with the temperatures required, can also lead to rearrangement to an extent above acceptable levels.")

Ex. 5 at LEO_PCT01164395; Ex. 6 at LEO_PCT01164488) The law is well-established that courts may not generally read back into the claims limitations which were included in the original application, but were removed during prosecution of the application. *United States v. Telectronics, Inc.*, 857 F.2d 778, 783 (Fed. Cir. 1988) (citing *Kistler Instrumente AG v. United States*, 628 F.2d 1303, 1308 (Ct. Cl. 1980)). In the present case, the applicant originally included an "aprotic" solvent in the claim language, but deleted the "aprotic" limitation from the claims. The examiner ultimately allowed the claims without rejecting the deleted limitation.[8] *See* Notice of Allowance (Oct. 3, 2017). Consequently, it would be improper to read the "aprotic" limitation back into the claimed solvent. *See Laryngeal Mask Co. Ltd. v. Ambu*, 618 F.3d 1367, 1372-73 (Fed. Cir. 2010); *see also 3M Innovative Properties Co. v. Avery Dennison Corp.*, 350 F.3d 1365, 1372 (Fed. Cir. 2003) (concluding that a broadening claim amendment made during the prosecution history supported a plain-meaning construction of the claim without a sequential-embossment limitation).

Moreover, the parties did not seek construction of "pharmaceutically acceptable solvent" during the previous claim construction proceeding, which encompassed the parent '292 patent. The court's scheduling order requires the parties to "identify, during the claim construction phase of the case, any claim language that will have a meaning to a person of ordinary skill in the art that differs from the ordinary meaning. Any language not so identified will be construed according to its ordinary meaning." (D.I. 20 at 5 n.5) The parties also stipulated that terms not identified for construction during the first claim construction proceeding "do not require construction by the Court." (D.I. 142 at 2) The court cannot properly construe the term in the

[8] The Manual of Patent Examining Procedure provides a basis for rejection under 35 U.S.C. § 112(a) and (b) if a claim "omits matter disclosed to be essential to the invention as described in the specification, or in other statements of record." MPEP § 2163 at § I.B, ¶ 3.

'428 and '429 patents in accordance with defendants' proposed construction, while maintaining the identical term's plain and ordinary meaning in the '292 patent.

The cases cited by defendants in support of their proposed "aprotic" limitation are distinguishable. In *Edgewell Personal Care Brands, LLC v. Albaad Massuot Yitzhak, Ltd.*, the court concluded that an amendment of the term "maximum of three petals" to "plurality of petals" did not substantially alter the meaning of the term because the patentee offered no explanation for why the changes were made. C.A. No. 15-1188-RGA, 2017 WL 1900736, at *7-8 (D. Del. May 9, 2017). The specification consistently referred to the "maximum of three petals" language in describing the scope of the invention and the superiority of this particular design over the prior art. *Id.* The court concluded that the emphasis on the "three petal or less" design throughout the specification constituted a clear disavowal of embodiments containing more than three petals. *Id.* at *6. In contrast, the specification of the '292 patent identifies examples of protic solvents capable of achieving the requisite stability, and proposes a solution to the problem of rearrangement that generally occurs when protic solvents are used.

In *Edwards Lifesciences LLC v. Cook Inc.*, the inventors deleted the word "intraluminal," which modified "graft," from the claim language during prosecution to presumably broaden the claim language. 582 F.3d 1322, 1330-31 (Fed. Cir. 2009). However, the Federal Circuit declined to construe the claim language more broadly because the accompanying remarks by the inventors during prosecution stated that the claim "defines an intraluminal graft," suggesting that no broadening of the claim language was intended. *Id.* at 1331. This case is distinguishable from the circumstances presently before the court because the inventors of the New Brown Patents did not expressly identify an intention to maintain the narrower scope of the claim language despite the removal of the "aprotic" limitation from the amended claim language.

2. Penetration enhancer

Defendants' proposal to limit the disputed term to a solvent distinct from the claimed penetration enhancer likewise does not find adequate support in the intrinsic record. The specification illustrates that substances such as propylene glycol may serve as both a penetration enhancer and a solvent. ('292 patent, col. 8:32-36; col. 9:58-10:19, Table 3) Likewise, the specification identifies DMSO as both a penetration enhancer and a solvent. ('292 patent, col. 13:56-63) Nothing in the specification or the claim language expressly bars a substance from serving as both a penetration enhancer and a solvent, so long as the substance is capable of satisfying both of the claimed functions. Defendants' proposed construction would read these examples out of the claim language.

This reading of the claim language does not violate the doctrine of claim differentiation. Independent claim 1 of the '428 patent requires the dissolution of ingenol angelate in a pharmaceutically acceptable solvent, while dependent claim 8 of the '428 patent incorporates the formulation of claim 1, with the added limitation of "further comprising a penetration enhancer." ('428 patent, col. 55:20-28; col. 55:46-47) The fact that a single substance may be capable of satisfying both the "solvent" and "penetration enhancer" limitations does not alter the fact that those terms remain separate requirements, both of which must be satisfied. *See Applied Med. Res. Corp. v. U.S. Surgical Corp.*, 448 F.3d 1324, 1333 n.3 (Fed. Cir. 2006) ("[T]he use of two terms in a claim requires that they connote different *meanings*, not that they necessarily refer to two different *structures.*"); *see also Retractable Techs., Inc. v. Becton, Dickinson & Co.*, 653 F.3d 1296, 1303-04 (Fed. Cir. 2011) (concluding that "needle holder" and "retainer member" need not be separately molded pieces where the specifications disclose a method of forming them as an integral structure in the first instance); *Powell v. Home Depot U.S.A., Inc.*, 663 F.3d

1221, 1231-32 (Fed. Cir. 2011) (holding that a single structure in an accused product could meet both the "cutting box" and "dust collection structure" limitations of the asserted claim). Defendants' proposed limitation would preclude the use of substances that can perform both functions, even if those substances satisfy the express limitations of the claim language. There is no support for such an exclusion of dual-purpose substances in the intrinsic record.

The court's recommended construction is not inconsistent with case authorities construing the language "further comprising" to signify a separate, additional modification because a single substance, such as propylene glycol or polyethylene glycol, may be capable of performing the separate functions of a solvent and a penetration enhancer. In *HTC Corp. v. IPCom GmbH & Co., KG*, the Federal Circuit indicated that the use of "further comprising" in the claim language would signify additional modification of a claim element. 667 F.3d 1270, 1275 (Fed. Cir. 2012). In contrast, the present dispute does not involve appropriate modifiers, and instead requires resolution of whether a single substance may satisfy more than one claim limitation. ('292 patent, col. 8:32-36; col. 9:58-10:19, Table 3) In *Purdue Pharms. L.P. v. Actavis Elizabeth LLC*, the court concluded that one ingredient could not serve more than one purpose in the same composition. 2015 WL 5032650, at *14 (D.N.J. Aug. 25, 2015). However, in that case, the court found insufficient evidence to establish that tartrate was intended to serve dual functions in the claim even if it could act as a buffering agent. In the present case, the '292 patent specification contains express examples of various substances serving as a solvent and/or as a penetration enhancer.

The same is true of independent claim 1 of the '429 patent, which requires a formulation comprising ingenol angelate, a penetration enhancer, a gelling agent, an acidifying agent, and a pharmaceutically acceptable solvent. ('429 patent, col. 54:26-32) Although each of these

elements is required in accordance with the claim language, nothing in the claim language or specification requires that each element be satisfied by a different substance. Because nothing in the intrinsic record suggests an intention to limit the claim terms in this manner, the court declines to recommend adoption of defendants' proposed construction.

Defendants cite claim 1 of another patent from the Brown family, U.S. Patent No. 9,603,822 ("the '822 patent"), which requires mixing a penetration enhancer with a mixture comprising a pharmaceutically acceptable solvent, among other ingredients. (D.I. 249 at 10) However, the '822 patent claims a process, as opposed to the formulation claims of the asserted patents in the present case. The Federal Circuit has rejected efforts to impose process limitations on formulation claims. *See Vanguard Prods. Corp. v. Parker Hannifin Corp.*, 234 F.3d 1370, 1372 (Fed. Cir. 2000); *Merck Sharp & Dohme Corp. v. Xellia Pharms. ApS*, C.A. No. 14-199-RGA, 2015 WL 82386, at *4 (D. Del. Jan. 6, 2015). Moreover, nothing in the '822 patent prohibits the pharmaceutically acceptable solvent from also acting as a penetration enhancer.

B. "penetration enhancer" ('959 patent, claim 15; '429 patent, claims 5, 10, 24)

LEO	Defendants	Court
"a substance that is capable of enhancing penetration of a drug across the stratum corneum"	"an agent that increases the rate of penetration of the active ingredient across the skin, which is distinct from the pharmaceutically acceptable solvent"	"a substance that is capable of enhancing penetration of a drug across the stratum corneum"

I recommend that the court adopt LEO's proposed construction of the disputed term. For the reasons previously discussed at § IV.A.2, *supra*, the intrinsic evidence does not support defendants' proposed requirement that the penetration enhancer must be distinct from the pharmaceutically acceptable solvent. In accordance with the intrinsic record, a person of

ordinary skill in the art would understand that a "penetration enhancer" enhances penetration across the stratum corneum.

When discussing the use of penetration enhancers, the specification of the '292 patent explains that ingenol-3-angelate "diffuses across the stratum corneum (which forms the main barrier for the diffusion of most drugs) at detectable levels." ('292 patent, col. 14:11-13) The examples in the specification describing the effect of penetration enhancers such as Captisol® and DMSO uniformly describe the diffusion of ingenol-3-angelate across the stratum corneum, as opposed to the skin. (*Id.*, col. 11:5-13) Moreover, the testing data summarized in the specification details the process of separating the stratum corneum from the remaining layers of the skin to test the effectiveness of various penetration enhancers. (*Id.*, col. 11:53-12:47) Because the stratum corneum "forms the main barrier for the diffusion of most drugs," a person of ordinary skill would understand that the goal of the penetration enhancer is particularly directed to penetrating the stratum corneum. (*Id.*, col. 14:11-13)

The parties agree that this recommendation is not inconsistent with the court's previous construction of the term "across the skin" in the '919 patent.[9] (D.I. 203 at 29-30; 5/2/18 Tr. at 82:2-16; 90:8-91:2) The court's December 28, 2017 Report and Recommendation expressly acknowledges that "[w]hen the patentee sought to describe the diffusion of ingenol-3-angelate across the stratum corneum in the specification, the patentee expressly identified the stratum corneum." (*Id.* at 29) As previously discussed, the specification's discussion of penetration enhancers uniformly identifies their effect on the stratum corneum, as opposed to their effect on

[9] Defendants acknowledge that "the dispute [regarding 'across the skin'] is not material in the context of construing 'penetration enhancer,'" (D.I. 279 at 18 n.12), and LEO agrees that "the issues are independent; Plaintiffs' construction of 'penetration enhancer' would not itself modify the interpretation of 'the skin,'" (D.I. 276 at 20).

the skin more broadly. Consequently, I recommend that the court adopt LEO's proposed construction of the term "penetration enhancer."

V. CONCLUSION

For the reasons set forth above, I recommend that the court construe disputed terms as follows:

Claim Term	Recommended Construction
"pharmaceutically acceptable solvent"	"solvent suitable for use in a pharmaceutical formulation"
"penetration enhancer"	"a substance that is capable of enhancing penetration of a drug across the stratum corneum"

Given that the court has relied upon material that technically remains under seal, the court is releasing this Report and Recommendation under seal, pending review by the parties. In the unlikely event that the parties believe that certain material in this Report and Recommendation should be redacted, the parties should jointly submit a proposed redacted version by no later than **June 19, 2018**. The court will subsequently issue a publicly available version of its Report and Recommendation.

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 fourteen (14) days after being served with a copy of this Report and Recommendation. Fed. R. Civ. P. 72(b)(2). The objections and responses to the objections are limited to ten (10) pages each. 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 Sincavage v. Barnhart*, 171 F. App'x 924, 925 n.1 (3d Cir. 2006); *Henderson v. Carlson*, 812 F.2d 874, 878-79 (3d Cir. 1987).

The parties are directed to the court's Standing Order For Objections Filed Under Fed. R. Civ. P. 72, dated October 9, 2013, a copy of which is available on the court's website, http://www.ded.uscourts.gov.

Dated: June 5, 2018

Sherry R. Fallon
UNITED STATES MAGISTRATE JUDGE