SENJU PHARMACEUTICAL CO., LTD. et al v. LUPIN, LTD. et al Doc. 107

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

SENJU PHARMACEUTICAL CO., LTD., BAUSCH & LOMB, INC., BAUSCH AND LOMB PHARMA HOLDINGS CORP., Plaintiffs, v. LUPIN LTD., LUPIN PHARMACEUTICALS, INC., Defendants.	HONORABLE JEROME B. SIMANDLE Civil Action Nos. 14-667 (JBS/KMW) 14-4149 (JBS/KMW) 14-5144 (JBS/KMW) 15-335 (JBS/KMW) 14-6893 (JBS/KMW) 15-3240 (JBS/KMW) **MARKMAN OPINION**
SENJU PHARMACEUTICAL CO., LTD., BAUSCH & LOMB, INC., BAUSCH & LOMB PHARMA HOLDINGS CORP., Plaintiffs, v. LUPIN LTD., LUPIN PHARMACEUTICALS, INC., Defendants.	
SENJU PHARMACEUTICAL CO., LTD., BAUSCH & LOMB, INC., BAUSCH & LOMB PHARMA HOLDINGS CORP., Plaintiffs, v. LUPIN LTD., LUPIN PHARMACEUTICALS, INC., Defendants.	
SENJU PHARMACEUTICAL CO., LTD., BAUSCH & LOMB INCORPORATED, BAUSCH & LOMB PHARMA HOLDINGS CORP., Plaintiffs, v. LUPIN, LTD., LUPIN PHARMACEUTICALS, INC., Defendants.	

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SENJU PHARMACEUTICAL CO., LTD., BAUSCH & LOMB, INC., BAUSCH & LOMB PHARMA HOLDINGS CORP.,
Plaintiffs,
v.

INNOPHARMA LICENSING, INC., INNOPHARMA LICENSING, LLC, INNOPHARMA, INC., INNOPHARMA, LLC,
Defendants.

SENJU PHARMACEUTICAL CO., LTD., BAUSCH & LOMB INCORPORATED, BAUSCH & LOMB PHARMA HOLDINGS CORP.,
Plaintiffs,
v.

INNOPHARMA LICENSING, INC., INNOPHARMA LICENSING, LLC, INNOPHARMA, INC., INNOPHARMA, LLC,
Defendants.

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SIMANDLE, Chief Judge:

I. INTRODUCTION

Plaintiffs Senju Pharmaceutical Co., Ltd., Bausch & Lomb Inc., and Bausch & Lomb Pharma Holdings Corp. (collectively, "Plaintiffs") brought these various patent infringement actions

under the Hatch-Waxman Act, 35 U.S.C. §§ 271, 281, against Defendants Lupin, Ltd., Lupin Pharmaceuticals, Inc., Innopharma Licensing, Inc., Innopharma Licensing, LLC, Innopharma, Inc., and Innopharma, LLC (collectively, "Defendants") concerning Defendants' submissions of abbreviated new drug applications ("ANDAs") seeking FDA approval to market a generic version of Plaintiffs' drug Prolensa®, which is used to treat patients who have undergone cataract surgery. Plaintiffs allege that Defendants' ANDA submissions infringe the various patents covering Plaintiffs' Prolensa® product: U.S. Patent Nos. 8,129,431 ("the '431 patent"), 8,669,290 ("the '290 patent"), 8,754,131 ("the '131 patent"), 8,871,813 ("the '813 patent"), and 8,927,606 ("the '606 patent") (collectively, the "patents-in-suit").

Before the Court is the parties' request for claim construction of three disputed terms in these patent infringement actions:[1]

1. "**in an amount sufficient to stabilize said first component,**" as it appears in asserted claim 1 of the

[1] The parties initially disputed a fourth term, "EDTA sodium salt" and "sodium edetate" (which the parties agree are equivalent terms), in their Markman briefs, but subsequently stipulated to a joint proposed construction of the two terms. (See, e.g., Stip. [Docket Item 102], Senju Pharm. Co. Ltd. v. Lupin, LTD., Civ. No. 14-667.) The Court will therefore adopt the parties' construction and construe "EDTA sodium salt" and "sodium edetate" to mean "A sodium salt of ethylenediaminetetraacetic acid. This phrase encompasses, for example, the disodium salt of ethylenediaminetetraacetic acid."

'290 patent, claim 1 of the '131 patent, claim 1 of the '813 patent, and claim 1 of the 606 patent; and **"stable,"** as it appears in asserted claims 1, 7, 8, 10, 13, 14, 19, 20, 22, 25 of the '290 patent, claims 1, 6, 7, 9, 12, 13, 18-22, 24 of the '131 patent, claims 1, 7, 9, 13, 19-21 of the '813 patent, claims 1, 9, 11, 12, 18, 19, 25, 26 of the '606 patent.

2. **"consisting essentially of"** and **"consists essentially of,"**[2] as they appear in asserted claims 1 and 18 of the '431 patent, claims 1, 7, and 13 of the '813 patent, claims 7, 13, 19, and 25 of the '290 patent, claims 6, 12, 18, and 24 of the '131 patent, and claims 9, 18, and 25 of the '606 patent;

3. **"satisfies the preservative efficacy standard of US Pharmacopoeia as follows: viable cell counts of bacteria (S. aureus, P. aeruginosa) 24 hours and 7 days after inoculation decrease to not more than 1/10 and not more than 1/1000, respectively, and thereafter, the cell count levels off or decreases; and viable cell count of fungi (C. albicans, A. niger) 14 days after inoculation decreases to not more than 1/10, and thereafter, the cell count keeps the same level as that of 14 days after inoculation,"** as it appears in asserted claims 25-29 of the '131 patent.

For the reasons that follow, the Court construes the disputed phrases as follows:[3]

Term	Court's Construction
"in an amount sufficient to stabilize said first component" and **"stable"**	"in an amount sufficient to stabilize said first component" means "an amount sufficient to confer sufficient resistance to

[2] The parties agree that "consisting essentially of" and "consists essentially of" have the same meaning. (See Def. Opening Claim Constr. Br. at 24 n.8.)

[3] The Court held a Markman hearing on November 2, 2015, and considered the lengthy Markman submissions by the parties, which included thousands of pages of exhibits, along with declarations from Plaintiffs' experts, Dr. Robert O. Williams, Ph.D. and Dr. Thomas K. Green, Ph.D., and Defendants' expert, Dr. Jayne Lawrence, Ph.D.

	degradation to be formulated and maintained for ophthalmic use," and "stable" means "having sufficient resistance to degradation and having sufficient preservative efficacy to be formulated and maintained for ophthalmic use"
"consisting essentially of" and **"consists essentially of"**	Includes the listed ingredients and additional unlisted ingredients so long as they do not materially affect the basic and novel characteristics of the claimed preparations. May include additional active ingredients that do not materially affect the basic and novel properties of the claimed preparation.
"satisfies the preservative efficacy standard of US Pharmacopoeia as follows: viable cell counts of bacteria (S. aureus, P. aeruginosa) 24 hours and 7 days after inoculation decrease to not more than 1/10 and not more than 1/1000, respectively, and thereafter, the cell count levels off or decreases; and viable cell count of fungi (C. albicans, A. niger) 14 days after inoculation decreases to not more than 1/10, and thereafter, the cell count keeps the same level as that of 14 days after inoculation"	"satisfies the preservative efficacy standard of EP-criteria B of the European Pharmacopoeia as follows: viable cell counts of bacteria (S. aureus, P. aeruginosa) 24 hours and 7 days after inoculation . . ."

II. BACKGROUND

A. Factual and Procedural Background[4]

Plaintiff holds the patents for novel formulations of bromfenac, an active ingredient in Plaintiff's drug Prolensa®, which has been approved by the Food and Drug Administration (hereinafter, the "FDA") for the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery. The patents at issue in this case, namely, the '431 patent, the '290 patent, the '131 patent, the '813 patent, and the '606 patent, together disclose and claim an ophthalmic bromfenac formulation which contains (1) bromfenac and (2) tyloxapol, a non-ionic surfactant, and methods of using these formulations to treat ocular pain and inflammation.

The '431, '290, '131, '813, and '606 patents all share essentially the same specification, and all claim an "Aqueous Liquid Preparation Containing 2-Amino-3-(4-Bromobenzoyl)Phenylacetic Acid." (See, e.g., '431 patent, Pl. Opening Claim Constr. Br. Ex. 1.)[5] 2-Amino-3-(4-bromobenzoyl)phenylacetic acid is the chemical name of

[4] For purposes of the pending Markman determination, the Court need not retrace the detailed factual and procedural history of these complex infringement actions, and writes primarily for the parties.

[5] Because the parties acknowledge that the five patents have the same specifications (see Pl. Opening Claim Constr. Br. at 1 n.2; Def. Opening Claim Constr. Br. at 2 n.2), the Court only cites to one illustrative specification, unless otherwise indicated.

bromfenac, which is a non-steroidal anti-inflammatory drug ("NSAID") that is used to treat inflammatory diseases of the anterior or posterior segment of the eye. (See, e.g., '431 patent at 1:24-45.) The patents-in-suit claim the addition of tyloxapol to an aqueous liquid preparation of bromfenac. The addition of tyloxapol stabilizes the solution within a pH range that is non-irritating to the eyes, and inhibits the deterioration of the preservative effect of a widely-used preservative, benzalkonium choride, allowing for a longer shelf life.[6] (Id. at 2:35-47.)

The claims in the '431, '290, '131, and '813 patents are directed to the new formulation of bromfenac. Independent claim 1 of the '431 patent, for example, states:

> 1. An aqueous liquid preparation consisting essentially of the following two components, wherein the first component is 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, wherein the hydrate is at least one selected from a 1/2 hydrate, 1 hydrate, and 3/2 hydrate and the second component is tyloxapol, wherein said liquid preparation is formulated for ophthalmic administration, and wherein when a quaternary ammonium compound is included in said liquid preparation, the quaternary ammonium compound is benzalkonium chloride.

[6] Benzalkonium chloride is widely used as a preservative in ophthalmic solutions, but has generally been considered incompatible with NSAIDs such as bromfenac, because it "lose[s] [its] ability to function as [it] forms complexes with the charged drug compounds." ('431 patent at 1:63-2:3.)

('431 patent at 11:66-12:9.) The independent claims of the '290, '131, and '813 patents contain similar language. Claim 1 of the '290 patent, for example, replaces the phrase "consisting essentially of" with "comprising," specifies that the first component is the "sole pharmaceutical active ingredient contained in the preparation," and adds limitations that tyloxapol be present "in an amount sufficient to stabilize said first component," and that the aqueous liquid preparation be "stable." ('290 patent, Pl. Opening Claim Constr. Br. Ex. 2, at 12:2-12.) The '131 patent is a division of the '290 patent, and claim 1 adds the additional limitation that the first component, the "sole pharmaceutical active ingredient contained in the preparation," "is present in the preparation at a concentration from about 0.05 w/v % to about 0.2 w/v %." ('131 patent, Pl. Opening Claim Constr. Br. Ex. 3.) The '813 patent is a division of the '290 patent and claim 1 specifies an aqueous liquid preparation that consists essentially of five components – the first two already specified, plus boric acid, sodium tetraborate, and water. ('813 patent, Pl. Opening Claim Constr. Br. Ex. 4.)

The '606 patent is directed to a method for treating an inflammatory disease of the eye, by administering a composition comprising bromfenac and tyloxapol to the eye "at a dose and a

frequency effective to treat said inflammatory disease." ('606 patent, Pl. Opening Claim Constr. Br. Ex. 5, at 11:30-31.)

Beginning in late 2013, Defendants began to send Notice Letters to Plaintiffs, pursuant to 21 U.S.C. § 355(j)(2)(B)(ii), informing Plaintiffs that Defendants have submitted ANDAs with the FDA with Paragraph IV certifications on the patents-at-issue to seek approval to manufacture and sell generic bromfenac ophthalmic solution prior to the expiration of the '431, '290, '131, '813, and '606 patents. The certifications notified Plaintiffs that their patents were "invalid, unenforceable, and/or will not be infringed" by Defendants' product. (See Pl. Opening Claim Constr. Br. Exs. 8-16.)

Plaintiffs filed the first patent infringement action before this Court on January 31, 2014, see Senju Pharm. Co., Ltd. v. Lupin, Ltd., Civ. No. 14-667 (JBS/KMW) (filed January 31, 2014), and the five other related cases followed. See Senju Pharm. Co., Ltd. v. Lupin, Ltd., Civ. No. 14-4149 (JBS/KMW) (filed June 26, 2014); Senju Pharm. Co., Ltd. v. Lupin, Ltd., Civ. No. 14-5144 (JBS/KMW) (filed Aug. 15, 2014); Senju Pharm. Co., Ltd. v. Innopharma Licensing, Inc., Civ. No. 14-6893 (JBS/KMW) (filed Nov. 3, 2014); Senju Pharm. Co., Ltd. v. Lupin, Ltd., Civ. No. 15-335 (JBS/KMW) (filed Jan. 16, 2015); Senju

Pharm. Co., Ltd. v. Innopharma Licensing, Inc., Civ. No. 15-3240 (JBS/KMW) (filed May 8, 2015).[7]

III. CLAIM CONSTRUCTION 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) (internal quotations omitted). Claim construction is a matter of law to be determined solely by the court, Markman v. Westview Instruments, Inc., 517 U.S. 370, 372 (1996), and the Court need not follow the parties' proposed constructions. See Marine Polymer Techs., Inc. v. HemCon, Inc., 672 F.3d 1350, 1359 n.4 (Fed. Cir. 2012) (en banc).

In construing a claim term, the Court looks first to the intrinsic evidence, "including the claims themselves, the specification, and the prosecution history of the patent." Sunovion Pharm., Inc. v. Teva Pharm. USA, Inc., 731 F.3d 1271, 1276 (Fed. Cir. 2013) (citing Phillips, 415 F.3d at 1315–17;

[7] Defendants have also filed several petitions against Plaintiffs for inter partes review ("IPR") before the Patent Trial and Appeal Board ("PTAB") seeking a ruling on the validity of the patents-in-suit. See Inter Partes Review of U.S. Patent No. 8,669,290, IPR2015-00902 (filed by Innopharma); Inter Partes Review of U.S. Patent No. 8,129,431, IPR2015-00903 (Innopharma); Inter Partes Review of U.S. Patent No. 8,754,131, IPR2015-01097 (Lupin); Inter Partes Review of U.S. Patent No. 8,669,290, IPR2015-01099 (Lupin); Inter Partes Review of U.S. Patent No. 8,927,606, IPR2015-01100 (Lupin); Inter Partes Review of U.S. Patent No. 8,871,813, IPR2015-01105 (Lupin).

Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996)). The words of a claim are generally "given their plain and ordinary meanings," Golden Bridge Tech., Inc. v. Apple, Inc., 758 F.3d 1362, 1365 (Fed. Cir. 2014), 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," read in the context of the entire patent. Phillips, 415 F.3d at 1312-13 (internal quotations omitted).

The claims themselves provide "substantial guidance as to the meaning of particular claim terms." Id. at 1314; see also ACTV, Inc. v. Walt Disney Co., 346 F.3d 1082, 1088 (Fed. Cir. 2003) ("[T]he context of the surrounding words of the claim also must be considered in determining the ordinary and customary meaning of those terms"). The specification is also "highly relevant to the claim construction analysis" and it is "entirely appropriate for a court, when conducting claim construction, to rely heavily on the written description for guidance as to the meaning of the claims." Phillips, 415 F.3d at 1315, 1316-17. Finally, the court will consider the patent's prosecution history – "the complete record of the proceedings before the PTO . . . includ[ing] the prior art cited during the examination of the patent." Id. at 1317. Although the prosecution history is "less useful for claim construction purposes," it may inform the meaning of a claim term "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.

If the intrinsic evidence fails to disclose the meaning of a term, the Court may examine extrinsic evidence – all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises – to determine the meaning of particular terminology to those of skill in the art of the invention. Id. at 1318. The Court of Appeals for the Federal Circuit, however, cautions against "heavy reliance" upon extrinsic sources divorced from the intrinsic evidence because it "risks transforming the meaning of the claim term to the artisan into the meaning of the term in the abstract," and out of the context of the specification. Id. at 1321.

"The 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.'" Shire Dev., LLC v. Watson Pharms., Inc., 746 F.3d 1326, 1330 (Fed. Cir. 2014) (quoting Phillips, 415 F.3d at 1316).

IV. DISCUSSION

A. "in an amount sufficient to stabilize said first component" and "stable"[8]

Plaintiffs' Construction	Defendants' Construction	Court's Construction
"in an amount sufficient to stabilize said first component" means "an amount sufficient to confer sufficient resistance to degradation to be formulated and maintained for ophthalmic use," and "stable" means "having sufficient resistance to degradation and having sufficient preservative efficacy to be formulated and maintained for ophthalmic use"	Indefinite (i.e., the claim, even read in light of the specification and the prosecution history, fails to inform, with reasonable certainty, those skilled in the art concerning the scope of the invention)	"in an amount sufficient to stabilize said first component" means "an amount sufficient to confer sufficient resistance to degradation to be formulated and maintained for ophthalmic use," and "stable" means "having sufficient resistance to degradation and having sufficient preservative efficacy to be formulated and maintained for ophthalmic use"

The term "stable" is used in the context of "stable liquid preparation" or "stable aqueous liquid preparation" to describe the patented product. The phrase "in an amount sufficient to stabilize said first component" describes the amount of the ingredient tyloxapol in the patented product to stabilize the

[8] As stated above, these disputed phrases appear in asserted claims 1, 7, 8, 10, 13, 14, 19, 20, 22, 25 of the '290 patent, claims 1, 6, 7, 9, 12, 13, 18-22, 24 of the '131 patent, claims 1, 7, 9, 13, 19-21 of the '813 patent, claims 1, 9, 11, 12, 18, 19, 25, 26 of the '606 patent.

active ingredient bromfenac from degradation. Claim 1 of the '290 patent illustrates how these terms are used:

> A stable aqueous liquid preparation comprising (a) a first component; and (b) a second component, . . . the first component is the sole pharmaceutical active ingredient contained in the preparation;[9] the second component is tyloxapol and is present in said liquid preparation in an amount sufficient to stabilize said first component; and wherein said stable liquid preparation is formulated for ophthalmic administration.

('290 patent, Pl. Opening Claim Constr. Br. Ex. 2, at 12:2-12.)

Plaintiffs argue that "in an amount sufficient to stabilize said first component" refers specifically to tyloxapol's effect on bromfenac, and means "an amount sufficient to confer sufficient resistance to degradation to be formulated and maintained for ophthalmic use." They argue that the word "stable," by contrast, modifies the patented product as a whole, and refers to "having sufficient resistance to degradation *and* having sufficient preservative efficacy to be formulated and maintained for ophthalmic use." (Pl. Opening Claim Constr. Br. at 18-19) (emphasis added). Plaintiffs cite to cases in which courts have construed "stable" and "stabilizing" to mean "resistant to decomposition," or that the "active pharmaceutical ingredient does not decompose substantially such that that the

[9] The "first component" refers to 2-amino-3-(4-bromobenzoyl)phenylacetic acid [bromfenac], or a pharmacologically acceptable salt thereof or a hydrate thereof. ('290 patent, at 12:4-6.)

formulation has a pharmaceutically acceptable shelf life." (Id. at 19-20 (quoting Cadence Pharm., Inc. v. Paddock Labs. Inc., 886 F. Supp. 2d 445, 452 (D. Del. 2012) and Rohm & Haas Co. v. Lonza Inc., 997 F. Supp. 635, 638 (E.D. Pa. 1998)).) Plaintiffs also point to the specification for support, noting that the three experimental examples illustrate the preservative efficacy of the patented product, and the ability of tyloxapol to make the composition stable for eye drops. (Id. at 20-21; see also Pl. Resp. Br. at 10-15.)

Defendants contend that the terms "stable" and "stabilized" are indefinite because they can refer to many different attributes in the context of an ophthalmic preparation, such as chemical stability or physical stability. They also argue that since the experimental examples in the specification do not define the boundary between "stable" and unstable, there is no way to know what does or does not fall within the meaning of the terms "stable" or "stabilize[d]." (Def. Opening Claim Constr. Br. at 18-23; Def Resp. Br. at 2-10.)

Title 35 U.S.C. § 112 requires that every patent's specification "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112 ¶ 2

(2006).[10] "A claim fails to satisfy this statutory requirement and is thus invalid for indefiniteness if its language, when read in light of the specification and the prosecution history, 'fail[s] to inform, with reasonable certainty, those skilled in the art about the scope of the invention.'" Media Rights Techs., Inc., 800 F.3d 1366, 1371 (Fed. Cir. 2015) (quoting Nautilus, Inc. v. Biosig Instruments, Inc., 134 S. Ct. 2120, 2124 (2014)). The indefiniteness inquiry is governed by the same principles that govern claim construction, and the Court must therefore evaluate the disputed term in light of the patent's claim, specification, and prosecution history. Nautilus, 134 S. Ct. at 2128; Interval Licensing LLC v. AOL, Inc., 766 F.3d 1364, 1370 (Fed. Cir. 2014).

The Supreme Court recently articulated a new test in Nautilus and explained that the definiteness standard calls for a "delicate balance": it "must allow for a modicum of uncertainty," but must also be "precise enough to afford clear notice of what is claimed." Id. A claim may prove indefinite if its language "might mean several different things and no informed and confident choice is available among the contending

[10] Paragraph 2 of 35 U.S.C. § 112 was replaced by § 112(b) when the Leahy–Smith America Invents Act ("AIA"), Pub.L. No. 112–29, 125 Stat. 284 (2011) took effect on September 16, 2012. Because the application resulting in the asserted patent was filed before that date, the Court refers to the pre-AIA version of 35 U.S.C. § 112.

definitions." Id. at 2130 n.8. "[W]here different approaches to measurements are involved," "the patent and prosecution history must disclose a single known approach or establish that, where multiple known approaches exist, a person having ordinary skill in the art would know which approach to select." Dow Chem. Co v. Nova Chems. Corp (Canada), ___ F.3d ____, 2015 WL 5060947, at *6 (Fed. Cir. Aug. 28, 2015) (citation omitted); see also Teva Pharms. USA, Inc. v. Sandoz, Inc., 789 F.3d 1335 (Fed. Cir. 2015); see also Markman Opinion at 33, Otsuka Pharm. Co., Ltd. v. Torrent Pharma Inc., Civ. No. 14-1078 (D.N.J. Nov. 16, 2015).

As required by the principles of claim construction, the Court looks first at the intrinsic evidence to determine whether an ordinary skilled person would understand, with reasonable certainty, the scope of the terms "stable" and "in an amount sufficient to stabilize said first component." Because the claims themselves provide no explanation of the terms, the Court turns to the specification and prosecution history.

Here, Plaintiff cites to the experimental examples in the specification. Specifically, Experimental Examples 1 and 2, entitled "Stability Test of Sodium 2-amino-3-(4-bromobenzoyl)phenylacetate," test the rate of degradation of bromfenac in solutions containing various concentrations of tyloxapol. Solutions in both Examples were stored at 60° C for four weeks, but at a pH of 7.0 in Example 1 and a pH of around

8.15 in Example 2. (’290 patent, 7:10-63; 8:11-52.)[11] Example 1 was used by the Patent Examiner in his Notice of Allowance to credit the finding that tyloxapol has an “unexpected stabilizing effect on an aqueous solution of bromfenac in comparison to polysorbate 80.” (Notice of Allowance, Pl. Opening Claim Constr. Br. Ex. 49, at 9.) In Example 1, a solution containing 0.15 w/v% tyloxapol showed 73.8% remaining rate of bromfenac, while a solution containing 0.02 w/v% tyloxapol showed 89.6% remaining rate of bromfenac. In Example 2, at a pH of 8.15, the remaining rate of bromfenac after four weeks in all three solutions containing various levels of tyloxapol was over 90%. Based on this data, the specification concludes that “those compositions have sufficient stability for eye drops.” (’290 patent, 8:50-51.) Thus, the phrase “in an amount sufficient to stabilize said first component,” which refers specifically to tyloxapol’s effect on bromfenac, is explained by the Examples above, which illustrate the concentration of tyloxapol that would create an ophthalmically-acceptable solution which prevents the degradation of the active ingredient bromfenac. A skilled person would know from reading the specification that a solution containing tyloxapol would be considered chemically stable when

[11] The experimental examples appear in the specification of all five patents. For simplicity, the Court cites only to the ’290 patent.

it shows a remaining rate of bromfenac of over 90% under the conditions indicated. Put another way, a preparation that meets or exceeds that rate under the same testing conditions would have "sufficient stability for eye drops," i.e., be sufficiently resistant to degradation to be formulated and maintained for ophthalmic use.

The specification also suggests that the term "stable," which, as noted above, modifies the composition as a whole, includes an additional dimension. Example 3 shows that two bromfenac preparations containing different amounts of tyloxapol sufficiently controls microbial growth in the preparation to meet European Pharmacopoeia-Criteria B standards for a long shelf life. Example 3 demonstrates that in addition to being resistant to chemical degradation, the tyloxapol compositions also satisfy preservative efficacy standards for ophthalmic use.[12]

Particularly with the benefit of Experimental Examples that illustrate the exact testing conditions and results at which the solution would be acceptable for ophthalmic use, the Court finds

[12] Indeed, expert for Defendants, Dr. Jayne Lawrence, testified at deposition that a person of ordinary skill in the art would make an aqueous liquid preparation of claim 25 of the '131 patent by producing a variety of formulations to their preferred specification and then "test those formulations with respect to stability which would include, but not totally be, preservative stability." (Pl. Resp. Br. Ex. 3 [Docket Item 101-4], at 110:19-111:5; see also id. at 110:6-10.)

that the terms “stable” and “in an amount sufficient to stabilize said first component” are not indefinite.

Defendants argue that 90% is not a clear benchmark because the word “stable” is also used to describe compositions in Experimental Example 1 containing less than 90% retention rate. (Def. Opening Claim Constr. Br. at 20-21.) But Experimental Example 1 merely shows the relative stabilizing effect of tyloxapol. The specification notes that “[bromfenac] in each eye drop was stable in the order of tyloxapol-containing preparation>polyoxyl 40 stearate-containing preparation>polysorbate 80-containing preparation” and that a preparation containing 0.02 w/v% of tyloxapol “is more stable than [a preparation] containing 0.15 w/v% of tyloxapol.” Notably, Example 1 does not conclude, as Example 2 does with solutions over 90%, that the 73.8% and 89.6% solutions have “sufficient stability for eye drops.” The Patent Examiner used Experimental Example 1 to show only that tyloxapol has an “unexpected stabilizing effect on an aqueous solution of bromfenac in comparison to polysorbate 80.” (Def. Opening Claim Constr. Br. Ex. R, at 9.) Thus, contrary to Defendants’ contention, the phrase “in an amount sufficient to stabilize said first component” is most aptly described by Example 2, and may be defined by a bromfenac retention rate of above approximately 90% at the specified conditions.

Defendants nonetheless insist that the term must be indefinite because Plaintiffs have not defined the "necessary" condition for stability – the *minimum* percentage rate of bromfenac after four weeks below which the solution would not be considered stable. (Def. Opening Claim Constr. Br. at 20 (arguing that the 90% retention rate is described only as a sufficient, not necessary, property to qualify as 'stable.'").) The Court disagrees. Even assuming that the 90% rate does not provide a lower boundary, the patents explicitly use the phrase "sufficient to stabilize." The phrase itself makes clear that the patentee did not intend to define an absolute minimum boundary. It would be contrary to the plain meaning of the term to construe the phrase "sufficient to stabilize" as indefinite because the patent does not specify what is "necessary to stabilize."

Nor does the fact that the patent does not identify a particular stability range or attribute (e.g., chemical stability versus physical stability) render the terms indefinite. Even after Nautilus, the Federal Circuit has recognized that "a patent which defines a claim phrase through examples may satisfy the definiteness requirement." Interval Licensing LLC v. AOL, Inc., 766 F.3d 1364, 1373 (Fed. Cir. 2004). In this case, the specification identifies, with detailed experimental illustrations, a particular method for determining

resistance to chemical degradation and preservative efficacy;[13] describes how the testing was carried out; and provides a precise numerical measurement or standard that serves as a benchmark for what would be considered acceptable for pharmaceutical use for eye drops. Thus, the patent not only provides an exemplary value, it identifies – by way of the illustrative experiments – the exact attributes that are being measured. Given this context, a person of ordinary skill in the art would be able to understand with reasonable certainty the meaning and scope of the term "stable." The law does not require more. See, e.g., Nautilus, 134 S. Ct. at 2129 ("[T]he certainty which the law requires in patents is not greater than is reasonable, having regard to their subject-matter.") (citation and quotations omitted).[14]

For the reasons above, the Court finds that the terms "stable" and "in an amount sufficient to stabilize said first component" are sufficiently definite. "Stable" means "having

[13] Defendants admit that the specification "identifies a test to use to assess stability." (Def. Opening Claim Constr. Br. at 21.)

[14] The Court also does not agree that the experiment description "lacks critical details about the conditions of storage." (Def. Opening Claim Constr. Br. at 20.) On the contrary, the Experimental Examples describe the testing conditions in detail: eye drop solutions containing specified ingredients were filled in a polypropylene container and preserved at 60º C for four weeks, and the remaining percentage rate of bromfenac in each of the solutions was obtained "by correcting moisture vaporization from the container." ('290 patent, 7:10-63; 8:11-52.)

sufficient resistance to degradation and having sufficient preservative efficacy to be formulated and maintained for ophthalmic use," and "in an amount sufficient to stabilize" means "an amount sufficient to confer sufficient resistance to degradation to be formulated and maintained for ophthalmic use."

B. "consisting essentially of" and "consists essentially of"[15]

Plaintiffs' Construction	Defendants' Construction	Court's Construction
Includes the listed ingredients and additional unlisted ingredients so long as they do not materially affect the basic and novel characteristics of the claimed preparations.		
These phrases exclude, for instance, any other active ingredient besides the bromfenac active ingredient recited in the claims.	May include additional active ingredients that do not materially affect the basic and novel properties of the claimed preparation.	May include additional active ingredients that do not materially affect the basic and novel properties of the claimed preparation.

The transitional phrases "consisting essentially of" and "consists essentially of" are used in the claims to preface the ingredients in the claimed invention. For example, claim 1 of the '813 patent states that the invention claimed is "[a] stable aqueous liquid preparation consisting essentially of: (a) a first component; (b) a second component, . . . (c) boric acid;

[15] As noted above, this disputed phrase appears in asserted claims 1 and 18 of the '431 patent, claims 1, 7, and 13 of the '813 patent, claims 7, 13, 19, and 25 of the '290 patent, claims 6, 12, 18, and 24 of the '131 patent, and claims 9, 18, and 25 of the '606 patent.

(d) sodium tetraborate; and (e) water; . . . .” (’813 patent, Pl. Opening Claim Constr. Br. Ex. 4, at 11:30-35.)

The parties do not dispute that the phrases “consisting essentially of” and “consists essentially of” are equivalent, and they agree on its well-recognized legal meaning: the claim encompasses only the listed ingredients and other unlisted ingredients “that do not materially affect the basic and novel properties of the invention.” PPG Indus. v. Guardian Indus. Corp., 156 F.3d 1351, 1354 (Fed. Cir. 1998). The parties depart, however, over whether the unspecified ingredients may include active ingredients.

Plaintiffs contend that, based on the prosecution history and extrinsic evidence such as Dr. Williams’ expert testimony, the phrase excludes any other active ingredient besides bromfenac, which is already listed. (Pl. Opening Claim Constr. Br. at 24-27; Pl. Resp. Br. 15-17.) Defendants, on the other hand, argue that active ingredients may be included among the unspecified materials, as long as they “do not materially affect the basic and novel properties of the invention.” They argue that the specification in the ’290 patent reinforces this interpretation, and that nothing in the prosecution history supports adding the additional limitation that Plaintiffs seek to introduce into the phrase. (Def. Opening Claim Constr. Br. at 24-26; Def. Resp. Br. 10-15.)

The Court agrees with Defendants that the phrase "consists essentially of" may include unlisted active ingredients. As explained above, and as both parties agree, the meaning of the phrase is well-settled, and a person of ordinary skill in the art would know that it includes the recited ingredients and may include other ingredients which "do not materially affect the basic and novel properties of the invention.'" Yoon Ja Kim v. Earthgrains Co., 451 Fed. App'x 922, 925 (Fed. Cir. 2011) (quoting PPG Indus., 156 F.3d at 1354). Notably, the definition makes no distinction between active or inactive ingredients. The only limitation placed on the unlisted ingredients that may be included is that they "do[] not materially affect the characteristics of the invention." Water Techs. Corp. v. Calco, Ltd., 850 F.2d 660, 666 (Fed. Cir. 1988). Thus, logically, so long as an active ingredient does not materially affect the basic and novel properties of the invention, it may be included. Plaintiffs' proposed construction, which excludes *all* additional active ingredients (even those that do not materially affect the purpose of the invention) is plainly unsupported by the definition they themselves advance. See ResQNet.com, Inc. v. Lansa, Inc., 346 F.3d 1374, 1378 (Fed. Cir. 2003) ("[N]ormal rules of usage suggest a 'heavy presumption' that claim terms carry their accustomed meaning in the relevant community at the

relevant time." (quoting CCS Fitness, Inc. v. Brunswick Corp., 288 F.3d 1359, 1366 (Fed. Cir. 2002))).

Plaintiff could have "provide[d] its own definition for the terms used in its patent claim, including the transition phrase 'consisting essentially of.'" PPG Indus., 156 F.3d at 1355. But nothing in the specification indicates that the patentee intended to limit the transitional phrase to inactive ingredients, or deviate from its well-settled legal meaning. On the contrary, the specification to the '290 patent states that "[s]o long as the purpose of the present invention is achieved, other same or different kind of active ingredients may be appropriately added." ('290 patent, Pl. Opening Claim Constr. Br. Ex. 3.) The specification therefore explicitly contemplates the addition of other active ingredients to the invention without altering the invention's purpose, and the Court finds this evidence highly relevant. See Phillips v. AWH Corp., 415 F.3d 1303, 1321 (Fed. Cir. 2005) (holding that the specification "'is the single best guide to the meaning of a disputed term' and . . . 'acts as a dictionary when it . . . defines terms by implication.'" (quoting Vitronics Corp. v. Conceptronics, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996))); see also Ericsson, Inc. v. D-Link Sys., Inc., 773 F.3d 1201, 1218 (Fed. Cir. 2014) (reiterating that the specification is "usually dispositive") (citing Phillips, 415 F.3d at 1318).

Although the prosecution history may limit the scope of the claims if the "alleged disavowing actions or statements made during prosecution [are] both clear and unmistakable," Omega Eng'g, Inc. v. Raytek Corp., 334 F.3d 1314, 1326 (Fed. Cir. 2003), that is not the case here. The Court finds no persuasive "clear and unmistakable" language in the prosecution history that narrows the settled meaning of the phrase at issue.[16]

In light of the above, the Court holds that "consists essentially of" and "consisting essentially of" have the following construction: Includes the listed ingredients and additional unlisted ingredients so long as they do not materially affect the basic and novel characteristics of the

[16] Plaintiffs point to the fact that during prosecution, they sought to distinguish from Gamache et al. because Gamache included an active ingredient, an IB/ID agonist, which would be excluded in the present invention by the phrase "consisting essentially of." (Pl. Opening Claim Constr. Br. at 25.) But this evidence provides no support for Plaintiffs, since they themselves explained in their submission that the "IB/ID agonist of the Gamache composition would affect the basic novel properties of the claimed preparation." (Pl. Opening Claim Constr. Br. Ex. 50, at 14.) The position the patent applicants took during prosecution does not rule out the possibility that "consisting essentially of" may include active ingredients that do *not* affect the claimed invention's basic novel properties. Plaintiffs' argument about the Cagle reference is equally unpersuasive. Cagle disclosed an additional active ingredient but the Examiner nonetheless accepted the applicant's claims over the Cagle prior art. The Examiner gave no explanation why it was doing so, and there is no "clear and unmistakable" language indicating that the decision was because the Examiner understood the phrase "consisting essentially of" to exclude all other active ingredients.

claimed preparations, and may include additional active ingredients that do not materially affect the basic and novel properties of the claimed preparation.

C. "satisfies the preservative efficacy standard of US Pharmacopoeia as follows: viable cell counts of bacteria (S. aureus, P. aeruginosa) 24 hours and 7 days after inoculation decreases to not more than 1/10 and not more than 1/1000, respectively, and thereafter, the cell count levels off or decreases; and viable cell count of fungi (C. albicans, A. niger) 14 days after inoculation decreases to not more than 1/10, and thereafter, the cell count keeps the same level as that of 14 days after inoculation"

Plaintiffs' Construction	Defendants' Construction	Court's Construction
"satisfies EP-criteria B, which is viable cell counts of bacteria (S. aureus, P. aeruginosa) 24 hours and 7 days . . ."	Indefinite (i.e., the claim, even read in light of the specification and the prosecution history, fails to inform, with reasonable certainty, those skilled in the art concerning the scope of the invention)	"satisfies EP-criteria B, which is viable cell counts of bacteria (S. aureus, P. aeruginosa) 24 hours and 7 days . . ."

In the '131 patent, the asserted claims 25-29 each disclose a product comprised of one of the "aqueous liquid preparation[s]" specified in an earlier claim (claims 1, 4, 7, 9, and 13, respectively), wherein the aqueous liquid preparation further "satisfies the preservative efficacy standard of US Pharmacopoeia as follows: viable cell counts of bacteria (S. aureus, P. aeruginosa) 24 hours and 7 days after inoculation

decreases to not more than 1/10 and not more than 1/1000, respectively, and thereafter, the cell count levels off or decreases; and viable cell count of fungi (C. albicans, A. niger) 14 days after inoculation decreases to not more than 1/10, and thereafter, the cell count keeps the same level as that of 14 days after inoculation."[17] ('131 patent, Pl. Opening Claim Constr. Br. Ex. 3, at 14:15-15:4 (emphasis added).)

Although the phrase references the US Pharmacopoeia, the recited preservative efficacy standard actually reflects the preservative efficacy standard of EP-criteria B of the European Pharmacopoeia. The US Pharmacopoeia and European Pharmacopoeia standards are not identical, though they are similar. (See Declaration of Jayne Lawrence, Ph.D. in Supp. of Def. Opening Claim Constr. Br. ("Lawrence Decl."), ¶¶ 75-76.)

Plaintiffs argue that this phrase contains an error that is readily apparent to a person of ordinary skill in the art, and should be corrected by replacing "US Pharmacopoeia" with "EP-criteria B," so that the recited bacterial and fungi counts accurately reflect the preservative efficacy standard of the European Pharmacopoeia. (Pl. Opening Claim Constr. Br. at 27-29.) Defendants contend that the claim as written is indefinite, because a person of ordinary skill in the art would not

[17] The disputed phrase appears only in asserted claims 25-29 of the '131 patent.

understand which criteria should be satisfied. They urge the Court to refrain from rewriting the claim to correct the error, arguing that a claim must be construed as written, even if it creates a nonsensical result. (Def. Opening Claim Constr. Br. at 27-29; Def. Resp. Br. at 28-33 (citing Chef Am., Inc. v. Lamb-Weston, Inc., 358 F.3d 1371, 1374 (Fed. Cir. 2004)).)

"It is well-settled law that, in a patent infringement suit, a district court may correct an obvious error in a patent claim." CBT Flint Partners, LLC v. Return Path, Inc., 654 F.3d 1353, 1358 (Fed. Cir. 2011). An error may be corrected only if, based upon a review of the claim language and specification, "the correction is not subject to reasonable debate," and "the prosecution history does not suggest a different interpretation of the claims." Novo Indus., L.P. v. Micro Molds Corp., 350 F.3d 1348, 1357 (Fed. Cir. 2003).

Here, the citation to US Pharmacopoeia instead of EP-criteria B of the European Pharmacopeia for the preservative efficacy standard is an obvious error when examined in light of the related patents and the overall prosecution history. In Experimental Example 3, the results of the "Preservative Effect Test" are compared only to the European Pharmacopoeia standards, and the specification for the '131 patent makes no mention of US Pharmacopoeia standards at all. The bacteria and fungi cell counts recited in claims 25-29 are reprinted in Experimental

Example 3 in the specification, which identifies those standards as EP-criteria B of the European Pharmacopoeia. The only other patents-in-suit to include a preservative efficacy standard in their claims, the ’290 patent and ’606 patent, recite those same bacteria and fungi cell counts and likewise match them to “EP-criteria B of the European Pharmacopoeia.” (’290 patent, claims 26-30; ’606 patent, claims 28-30.) The US Pharmacopoeia is not mentioned in *any* of the related patents. Moreover, the prosecution history of the ’131 patent does not suggest a different interpretation. Claims 25-29 were added in an amendment in their current form and were allowed without any amendment or correction.

Accordingly, the Court will construe the ’131 patent in a manner consistent with the related patents-in-suit and prosecution history, and will replace “US Pharmacopoeia” with “EP-criteria B of the European Pharmacopoeia” in claims 25-29.

V. CONCLUSION

An accompanying Order will be entered.

November 17, 2015
Date

s/ Jerome B. Simandle
JEROME B. SIMANDLE
Chief U.S. District Judge