IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

IN RE BENDAMUSTINE CONSOLIDATED CASES	)	Civil Action No. 13-2046-GMS **CONSOLIDATED**

ORDER CONSTRUING THE TERMS OF U.S. PATENT NOS. 8,436,190; 8,609,863; 8,791,270; 8,445,524; 8,669,279; 8,883,836

The court having considered the submissions of the parties and having heard oral argument on the matter—IT IS HEREBY ORDERED, ADJUDGED, and DECREED that, as used in the asserted claims of U.S. Patent Nos. 8,436,190 ("the '190 Patent"); 8,609,863 ("the '863 Patent"); 8,791,270 ("the '270 Patent"); 8,445,524 ("the '524 Patent"); 8,669,279 ("the '279 Patent"); and 8,883,836 ("the '836 Patent"):

The '524 Patent

1. The term "solid form of bendamustine hydrochloride, designated as bendamustine hydrochloride Form 1" is construed to mean "anhydrous crystal form of bendamustine hydrochloride that can be distinguished from other forms by its X-ray powder diffraction pattern."[1]

2. The terms:

[1] Drawing on statements in the prosecution history, the defendants would construe the term to require a limitation that Form 1 compounds do not contain *any* water. *See Biogen Idec, Inc. v. GlaxoSmithKline LLC*, 713 F.3d 1090, 1095 (Fed. Cir. 2013). The court, however, agrees with the plaintiff that the prosecution history statements explaining that Form 1 does not "contain" or "include" water refer to the crystal structure of Form 1—*i.e.*, Form 1 is not a hydrate. (*See e.g.*, D.I. 153 at JA002585, ¶ 7 ("[B]endamustine hydrochloride Form 1 crystal structure does not include any water molecules, that is, Form 1 is not a hydrate.").) The court is wary of including a limitation that could be read broader than what was originally disclaimed during prosecution. Thus, the court construes the term to include a limitation that is "consistent with the scope of the claimed surrender": Form 1 is "anhydrous." *See Biogen*, 713 F.3d at 1095. Such a limitation is undisputed by both parties and is in line with the teachings of the specification.

- "an X-ray powder diffraction pattern comprising the following reflections: 8.3, 16.8, and 18.5±0.2 degrees 2θ";
- "an X-ray powder diffraction pattern further comprising the following reflections: 14.0, 22.0, 22.9, 25.1, and 28.3±0.2 degrees 2θ"; and
- "an X-ray powder diffraction pattern additionally including, but not limited to, a reflection at 14.0±0.2 degrees 2θ"

are construed to mean:

- "an X-ray powder diffraction pattern including, but not limited to, reflections at 8.3, 16.8 and 18.5 ±0.2 degrees 2θ";
- "X-ray powder diffraction pattern additionally including, but not limited to, the following reflections: 14.0, 22.0, 22.89, 25.1 and 28.3 ±0.2 degrees 2θ"; and
- "X-ray powder diffraction pattern additionally including, but not limited to, a reflection at 14.0±0.2 degrees 2θ,"

respectively.[2]

The '190 Patent

3. The term "tertiary-butyl alcohol" is construed to have its plain and ordinary meaning.[3]

---

[2] The court declines to import additional limitations into these grouped terms and gives "comprising" its traditional meaning in the art. *See Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501 (Fed. Cir. 1997) ("'Comprising' is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim."); MPEP § 2111.03 ("The transitional term 'comprising,' which is synonymous with 'including,' 'containing,' or 'characterized by,' is inclusive or open-ended and does not exclude additional, unrecited elements or method steps."). The defendants' proposal would require that the identified reflection "peaks" be freestanding and not overlapping with peaks of other forms. This limitation, however, conflicts with data in the specification, which shows that *individual* peaks of one form may also be present in other forms. *See* '524 Patent, col. 5 l. 51–col. 9 l. 34. It is the entire set of reflections—the signature *pattern*—that is unique to each form.

The defendants point to a statement in the prosecution history discussing previous versions of the claim language in question: "[The claims] provide a listing of XRPD peaks that are particularly characteristic of Form 1. These claims include peaks that are free-standing and do not overlap with any of the other disclosed forms of bendamustine." (D.I. 153 at JA002580.) But this statement does not require that *each* of the individual peaks be unique; rather, the entire reflection profile must "*include* peaks that are free-standing and do not overlap." (*Id.* (emphasis added).) Thus, this statement confirms that the overall pattern is the focus, and not any single reflection angle. It certainly is not unambiguous evidence of disclaimer. *See Omega Eng'g, Inc, v. Raytek Corp.*, 334 F.3d 1314, 1325–26 (Fed. Cir. 2003) ("[F]or prosecution disclaimer to attach, our precedent requires that the alleged disavowing actions or statements made during prosecution be both clear and unmistakable.").

[3] "As a general proposition, a limitation that does not exist in a claim should not be read into that claim." *Biovail Corp. Int'l v. Andrx Pharm., Inc.*, 239 F.3d 1297, 1301 (Fed. Cir. 2001). Defendant Innopharma, Inc.

4. The term "pharmaceutical composition" is construed to mean "a composition that is made under conditions such that it is suitable for administration to humans."[4]

5. As used in the phrase "containing not more than about 0.5% bendamustine ethyl ester," the term "0.5%" is construed to mean "0.5 area percent relative to the amount of bendamustine as determined by, *e.g.*, HPLC."[5]

("Innopharma") seeks to import a host of limitations into this straightforward claim term. The intrinsic record does not support doing so.

Each of the proposed limitations, Innopharma argues, captures the inventive "magic" of having tertiary-butyl alcohol ("TBA") in the claimed invention. (D.I. 327 at 60.) But as the plaintiff correctly points out, goals of the invention are not to be imported as claims, absent further evidence of disclaimer. *See Intel Corp. v. ITC*, 946 F.2d 821, 836 (Fed. Cir. 1991). First, Innopharma would require a process limitation that TBA is "separately added," to rule out the possibility that TBA is present as residue from an upstream process. The court disagrees that the specification and prosecution history statements "clearly and unmistakably" evidence that such a process limitation is required. *See Sanofi-Aventis U.S. LLC v. Sandoz, Inc.*, 345 F. App'x 594, 597 (Fed. Cir. 2009). Second, Innopharma would require an amount or concentration limitation. The court once again sees inadequate language of disclaimer, and notes also that reading in an amount limitation would result in a claim differentiation problem in the dependent claims, which recite explicit concentration limitations. *See* '190 Patent, claims 2, 3, 5 & 6. Claims terms should be construed so as not to create redundancies. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1324–25 (Fed. Cir. 2005). The patent drafters and the examiner knew how to include amount limitations, had that been a condition of patentability.

Finally, Innopharma would require a limitation that TBA "materially alters the solubility of bendamustine in water." As already stated, a stated *goal* of the invention or its elements need not be limiting. Moreover, such a limitation has no definite or ascertainable metrics—indeed the proposed phrase is never used in the intrinsic record. Unsurprisingly, the court disfavors a construction that injects considerable ambiguity into a term that has a readily understandable meaning.

[4] "Although words in a claim are generally given their ordinary and customary meaning, a patentee may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or file history." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). The drafters clearly defined "pharmaceutical composition" in the specification, and therefore their lexicography guides the court's construction. '190 Patent, col. 10 ll. 53–55. The plaintiff's proposal includes an additional clause identifying a non-exhaustive list of embodiments meeting this definition. While this clause is also taken from the specification, the court is not persuaded that naming particular embodiments—even acknowledging that they are non-exhaustive—adds anything to the construction. Defendant Accord Healthcare Inc. ("Accord") proposes a construction that ignores the explicit definition in the specification. The court sees no justification for straying from this well-accepted canon of construction.

[5] The parties agree that the meaning of "area percent of bendamustine" is defined in the patent specification: "the amount of a specified degradant, e.g., HP1, relative to the amount of bendamustine as determined, *e.g.*, by HPLC." '190 Patent, col. 11 ll. 57–60. The parties disagree, however, as to whether the percentage figure in the claim term refers to area percent of bendamustine. The court finds that it does.

The definition of "area percent of bendamustine" confirms that it is used to measure *degradants*. Although only HP1 is specifically identified in the definition, bendamustine ethylester is also a degradant. The court sees no reason to measure only HP1 in terms of area percent of bendamustine, while using a different methodology for bendamustine ethylester. Indeed, the specification supports measuring bendamustine ethylester as an area percent of bendamustine: "the amount of bendamustine ethylester produced during lyophilization from about 0 to 24 hours does not exceed about *0.5% (area percent bendamustine)*." '190 Patent, col. 6 ll. 11–13 (emphasis added).

The court is not persuaded by the defendants' contention that they advocate for the plain meaning. A percentage is a ratio of two quantities that must be defined—it has no standalone meaning. The defendants are unable to cite anything in the intrinsic record in support of their view.

The '863 Patent

6. The term "trace amount of tertiary-butyl alcohol" is construed to mean a "non-zero amount tertiary-butyl alcohol that is equal to or below recommended levels for pharmaceutical products."[6]

7. The term "stable lyophilized preparation" is construed to mean "solid material obtained by freezedrying having sufficient stability to have utility as a pharmaceutical product."[7]

The '270 Patent

8. The court declines to construe "amount of HP1 measured at time zero after reconstitution" at this time.[8]

---

[6] The specification states: "'trace amount of an organic solvent' means an amount of solvent that is equal to or below recommended levels for pharmaceutical products . . . ." '863 Patent, col. 11 ll. 61–63. As explained above, "the inventor's lexicography governs." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005). The defendants seek to include an additional limitation—taken from the following sentence in the specification—that a trace amount must be "detectable." '863 Patent, col. 11 ll. 66–67 ("The lower limit is the lowest amount that can be detected.").

While the court is sensitive to the defendants' position, the proposed limitation injects ambiguity and uncertainty into the construction. Detectability is a variable parameter, changing over time and under different conditions. The specification makes no further mention of detection. The court's inclusion of "non-zero" clarifies that an *amount* is a physical quantity. In the court's view, this addresses the defendants' concern without adding unnecessary vagueness. (*See* D.I. 125 at 24 ("Undetectable is not an amount; it is a phantom or an inference. Yet this is inconsistent with the fact that there must be an 'amount' of TBA, as required by the claim language.").

Ultimately, the court does not necessarily read the disputed follow-on sentence as a limitation, as the defendants contend. Rather, it appears to emphasize the broad scope of "trace amount." The court is reluctant to shoehorn an amorphous limitation into the construction, when it is not apparent that the language was indeed intended to be limiting.

[7] The court's construction combines the commonly understood meaning of lyophilization—*i.e.*, freezedrying—with the explicit definition found in the specification. Defendant Innopharma seeks to include additional limitations concerning an amount of TBA. In other words, Innopharma seeks to overcome the presumptions both that "the inventor's lexicography governs" and that limitations from the specification should not be imported into the claims. *See Phillips*, 415 F.3d at 1316, 1323. The intrinsic evidence does not support a departure from these presumptions.

[8] "A determination that a claim term 'needs no construction' or has the 'plain and ordinary meaning' may be inadequate when a term has more than one 'ordinary' meaning or when reliance on a term's 'ordinary' meaning does not resolve the parties' dispute." *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1361 (Fed. Cir. 2008). As explained during the hearing, the court is convinced that extrinsic evidence is necessary to determine how one skilled in the art would understand "at time zero." (D.I. 110–11.) The court will hear testimony on this issue at trial.

9. The term "bendamustine degradants" is construed to mean "chemical compounds resulting from a change in chemical structure of bendamustine."[9]

10. The term "containing less than or equal to 4.0% (area percent of bendamustine) of bendamustine degradants" is construed to mean "containing less than or equal to 4.0% of total chemical compounds resulting from a change in chemical structure of bendamustine, relative to the amount of bendamustine as determined, *e.g.*, by HPLC."[10]

11. The term "pharmaceutical composition" is construed to mean "a composition that is made under conditions such that it is suitable for administration to humans."[11]

12. The terms "lyophilized preparation" and "lyophilized composition" are construed to mean "freezedried preparation" and "freezedried composition," respectively.[12]

The '279 & '836 Patents

13. The term "an X-ray powder diffraction pattern comprising the following reflections: 7.9, 15.5, and 26.1±0.2 degrees 2θ" is construed to mean "an X-ray powder

---

[9] The court's construction comes from the explicit definition of "degrades," found in the specification: "By 'degraded' is meant that the active has undergone a change in chemical structure." '270 Patent, col 9 ll. 56–57. As emphasized repeatedly, the court will adopt "special definition[s]" that are "clearly stated in the patent specification or file history." *See Vitronics*, 90 F.3d at 1582. The defendants seek to limit the ambit of possible degradants to four specific compounds: monohydroxy bendamustine (*i.e.*, HP1), bendamustine dimer, bendamustine ethylester, and BM1DCE (Formula V). Although the four named degradants figure prominently in the specification, the court does not see adequate disclaiming language to limit the claim term in such a fashion. Moreover, several claims reference HP1 in particular. Thus, the drafters knew how to specify individual degradants, had that been the intent. Without more, the court will not infer a disclaimer of claim scope.

[10] The court agrees with the plaintiff that the proper construction of this term is simply the combination of the agreed-upon construction of "area percent of bendamustine," (D.I. 317), and the construction of "bendamustine degradants," outlined above. Innopharma is the only defendant seeking an alternative construction. The intrinsic record does not support the importation of Innopharma's additional limitations. *Flo Healthcare Solutions, LLC v. Kappos*, 697 F.3d 1367, 1375 (Fed. Cir. 2012) ("[I]t is not proper to import from the patent's written description limitations that are not found in the claims themselves.").

[11] The court's construction of this term is the same as outlined in the context of the '190 Patent. *See supra* note 4.

[12] The court's construction of these terms simply imports the plain meaning of lyophilization—*i.e*, freezedrying. Only Innopharma seeks an additional limitation requiring an added alcohol that "materially alters the solubility of bendamustine." Innopharma does not seek further construction of these terms (rather, their analogs) in the context of the '524, '279, and '836 Patents. (D.I. 349.) The court does not see sufficient evidence of disclaimer to warrant a different construction for the '270 Patent.

diffraction pattern including, but not limited to, reflections at 7.9, 15.5, and 26.1±0.2 degrees 2θ."[13]

Dated: June 3, 2015

UNITED STATES DISTRICT JUDGE

[13] The court's construction is consistent with those of similar terms in the '524 Patent. *See supra* note 2. The court agrees with the plaintiff that defendants' proposed construction—which requires that the reflection peaks be produced from Form 3—is redundant. The claims already explain that the reflection peak profile is produced by Form 3 bendamustine hydrochloride. Repetition of this requirement only serves to confuse.