UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CAMDEN VICINAGE

ASTRAZENECA LP and ASTRAZENECA AB,

Plaintiffs,

v.

BREATH LIMITED,

Defendant.

ASTRAZENECA LP and ASTRAZENECA AB,

Plaintiffs,

v.

APOTEX, INC. and APOTEX CORP.,

Defendants.

ASTRAZENECA LP and ASTRAZENECA AB,

Plaintiffs,

v.

SANDOZ, INC.,

Defendant.

ASTRAZENECA LP and ASTRAZENECA AB,

Plaintiffs,

v.

WATSON LABORATORIES, INC.

Defendant.

Consolidated Civil Action
No. 08-1512 (RMB/AMD)

REDACTED OPINION

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BUMB, UNITED STATES DISTRICT JUDGE:

Plaintiffs AstraZeneca LP and AstraZeneca AB ("AstraZeneca") bring this consolidated action for patent infringement against the defendants, Breath Limited, Watson Laboratories, Inc. (collectively, "Breath/Watson"), Sandoz, Inc. ("Sandoz", and together with Breath/Watson, "Defendants"), Apotex Corp., and Apotex, Inc. (collectively, "Apotex"). Because the facts and long history of this case are well-known to the parties, the Court recites them only briefly here.

I. BACKGROUND

This case involves AstraZeneca's invention of a once-daily inhaled corticosteroid under the name PULMICORT RESPULES®. Three patents were initially at issue: U.S. Patent No. 6,598,603 (the "'603 Patent"); U.S. Patent No. 6,899,099 (the "'099 Patent"); and U.S. Patent No. 7, 524,834 (the "'834 Patent").[1]

This Court previously found, and was affirmed on appeal, that the '603 Patent was rendered invalid as obvious. AstraZeneca LP v. Breath Ltd., 542 F. App'x 971, 978-81 (Fed. Cir. 2013). The '099 Patent claims also have been rendered invalid. AstraZeneca LP v. Breath Ltd., No. 08-1512, 2013 WL

[1] A related patent, U.S. Patent No. 6,392,036, directed to the inventive heat sterilization process was not the focus of the parties.

2404167 (D.N.J. May 31, 2013). Only the '834 Patent remains for this Court's consideration. AstraZeneca, 542 F. App'x at 975-78 (reversing this Court's claim construction and finding of non-infringement, and remanding for further proceedings).

The '834 Patent is entitled "STERILE POWDERS AND METHODS FOR PRODUCING THE SAME." Claims 1 and 50, the claims at issue, teach a powder and suspension, respectively, comprising a "micronized powder composition." Specifically, Claim 1 recites:

> A pharmaceutically acceptable, micronized powder composition at least 98.5% by weight of which is pure budesonide or an ester, acetal or salt thereof, wherein the composition meets the criteria of sterility according to the US Pharmacopoeia [sic] 23/NF18, 1995, pages 1686-1690 and 1963-1975.

'834 Patent col.11 ll.48-52 (emphasis added). Claim 50 recites:

> A pharmaceutically acceptable suspension consisting of a micronized powder composition at least 98.5% by weight of which is pure budesonide or an ester, acetal or salt thereof, suspended in an aqueous solution, wherein the suspension meets the criteria of sterility according to the US Pharmacopoeia [sic] 23/NF18, 1995, pages 1686-1690 and 1963-1975.

'834 Patent col.13 ll.55-60 (emphasis added).[2]

After the Markman hearing, this Court construed "micronized powder composition" as a product-by-process claim, to mean "heat-sterilized finely divided dry particles." See

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[2] The dependent claims - claims 2 and 51 - include the additional limitation that 98.5% of the "micronized powder composition" is pure budesonide. '834 Patent col.11 ll.53-54 & col.13 ll.61-63.

AstraZeneca, 2013 WL 2404167, at *43. Following a lengthy bench trial, the Court found that claims 50 and 51 were not infringed by Apotex and Sandoz and claims 1, 2, 50 and 51 were not infringed by Breath/Watson. Id. at *43-47. AstraZeneca appealed on several grounds, including the Court's claim construction.

On appeal, AstraZeneca clarified which claims were product-by-process claims and which claims "were not so limited" during prosecution. See AstraZeneca, 542 F. App'x at 977. AstraZeneca also advanced the new argument that there was a distinction between sterile and "sterilization."[3] Id. at 978. On that record, the Federal Circuit reversed this Court's claim construction, construing the disputed term to mean "finely divided dry particles" without requiring any particular process for sterilizing the particles. Id. at 976-77 ("At most, the specification is confusing with respect to whether it limits only the disclosed process to a specific form of sterilization

[3] On appeal, "AstraZeneca explained that a powder can be 'sterile' without ever having been 'sterilized,' but that a 'sterilized' powder must have undergone a sterilization process." 542 F. App'x at 977. During the bench trial, however, AstraZeneca took the position that "[p]ersons in the field understand that a product that purports to be sterile must have been subjected to a sterilization test . . . a sterilization process and then handled aseptically so as to maintain that sterility during the manufacturing process." See Trial Tr. 42:3-9.

or both the process and the disclosed product to a specific form of sterilization. However, that confusion leaves available an interpretation of the patent that the products, as opposed to the processes, are not limited to any particular form of sterilization. Accordingly, we cannot conclude that AstraZeneca disclaimed non-heat sterilized micronized powder compositions based on the specification."). The Federal Circuit remanded the case under the new claim construction for further proceedings before this Court.

II. PRELIMINARY INJUNCTION

On remand, AstraZeneca seeks a preliminary injunction to prevent Defendants from launching their generic versions of PULMICORT RESPULES®. Defendants Breath/Watson and Sandoz oppose the motion, resurrecting several invalidity arguments made during the original bench trial. Apotex does not oppose the request for a preliminary injunction as long as a sufficient bond is posted. Thus, the Court addresses only the arguments made by Defendants Breath/Watson and Sandoz. [See Docket No. 907]. During the bench trial, the Court heard testimony regarding Defendants' invalidity challenges but declined to exercise jurisdiction over Defendants' invalidity counterclaims because it had found - erroneously - non-infringement of the '834 Patent based upon its claim construction. On remand, however, these counterclaims have been reinstated. [See Docket

Nos. 927, 931 and 932]. Specifically, Defendants assert that the '834 Patent is invalid: (1) for failure to comply with the written description requirement; (2) for lack of enablement; and (3) for obviousness. The Court addresses each of these challenges below.

As an initial matter, the parties disagree as to whether discovery should be opened on remand. Defendants argue that the broad claim construction that now governs was a "game changer." Up until the Federal Circuit's decision, the parties had focused their litigation efforts on the heat sterilized particles produced by dry heat sterilization. The record speaks for itself. Nonetheless, AstraZeneca argues that the invalidity challenge remains the same, i.e., that a product process claim can still be rendered invalid by prior art dealing with products made through a different process. Although this is a correct statement of the law, AstraZeneca misses the point. The trial before this Court focused almost entirely on the heat sterilization process, with an emphasis on the prior art that addressed other non-heat sterilization processes. AstraZeneca distinguished those processes from its allegedly innovative heat sterilization process. In the end, the Court construed the claims as products requiring a heat sterilization process.

On appeal, AstraZeneca criticized this Court for failing to afford it the opportunity to address the Court's claim

construction as explained in its final Opinion. See Sandoz Oral Argument Presentation, at 7 ("For the first time ever, and after the trial had concluded, the district court explained, [and expanded] its [claim] construction . . . . AstraZeneca had no opportunity to submit evidence after receiving this expanded construction." (quoting AstraZeneca Opening Appeal Brief at 10)). Having felt it was denied the opportunity to submit evidence after receiving what it asserted to be a newly-explained construction by this Court, AstraZeneca can hardly have a basis to object when Defendants now echo the same refrain of unfairness. In short, the Court finds that the Federal Circuit's change in the claim construction was a "game changer," and the Court will reopen the record to permit discovery on the invalidity defenses. See Asyst Techs., Inc. v. Emtrak, Inc., 544 F.3d 1310, 1317 (Fed. Cir. 2008); Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d 1342, 1357 (Fed. Cir. 1998).

A. Standard

In determining whether to issue a preliminary injunction, the Court should consider the following four factors: (1) the likelihood of the patentee's success on the merits; (2) irreparable harm if the injunction is not granted; (3) the balance of hardships between the parties; and (4) the public interest. AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042, 1049 (Fed. Cir. 2010); Abbott Labs. v. Andrx Pharms., Inc., 473 F.3d

1196, 1200-01 (Fed. Cir. 2007). "These factors, taken individually, are not dispositive; rather, the district court must weigh and measure each factor against the other factors and against the form and magnitude of the relief requested." Hybritech, Inc. v. Abbott Labs., 849 F.2d 1446, 1451 (Fed. Cir. 1988). However, the moving party cannot be granted a preliminary injunction unless it establishes *both* of the first two factors, i.e., likelihood of success on the merits and irreparable harm. See Amazon.com, Inc. v. Barnesandnoble.com, Inc., 239 F.3d 1343, 1350 (Fed. Cir. 2001); Reebok Inter. Ltd. v. J. Baker, Inc., 32 F.3d 1552, 1556 (Fed. Cir. 1994) (citing Hybritech, 849 F.2d at 1451, 1456). The Court discusses each factor in turn below.

1. Likelihood of Success on the Merits

A "patent holder must establish a likelihood of success on the merits both with respect to validity of its patent and with respect to infringement of its patent." Hybritech, 849 F.2d at 1451. Thus, AstraZeneca must show that, in light of the presumptions and burdens that will inhere at a trial on the merits, it will likely prove infringement and the patent will also likely withstand any validity challenges. If Defendants raise a "substantial question" of validity, the preliminary injunction should not issue. Abbott Labs. v. Andrx Pharms., Inc., 452 F.3d 1331, 1335 n.2 (Fed. Cir. 2006). "Vulnerability

is the issue at the preliminary injunction stage, while validity is the issue at trial." Amazon.com, Inc., 239 F.3d at 1359.

Here, none of the Defendants appear to contest infringement, and indeed Breath/Watson and Sandoz concede that the broad claim construction encompasses their products. Accord Sandoz Opp. Br., Docket No. 908, at 1; Breath/Watson Opp. Br., Docket No. 911, at 21.[4] Accordingly, the Court now turns to the Defendants' invalidity arguments.

a. Written Description

Defendants first contend that the '834 Patent is invalid for failure to comply with the written description requirement.[5] Pursuant to 35 U.S.C. § 112, a patentee must provide a written description that allows a person of ordinary skill in the art ("POSA") to recognize that the patentee invented what is claimed. See Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). "The purpose of this provision is to ensure that the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the

[4] Although Apotex maintains that it does not infringe the '834 Patent, it does not oppose the preliminary injunction.

[5] AstraZeneca argues that this Court's previous ruling that all Defendants had waived this defense should continue to control here. [See Docket No. 601]. Because this Court rejects the defense at the preliminary injunction stage for the reasons set forth herein, the Court need not address whether the defense was waived.

[invention] as described in the patent specification." Reiffin v. Microsoft Corp., 214 F.3d 1342, 1345 (Fed. Cir. 2010).

In order to satisfy the written description test, the application must "reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." Ariad Pharms., 598 F.3d at 1351; Centocor Ortho Biotech, Inc. v. Abbott Labs, 636 F.3d 1341, 1348 (Fed. Cir. 2011). The "level of detail required . . . varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology." Ariad Pharms., 598 F.3d at 1351.

Defendant Sandoz argues that the '834 Patent does not disclose any sterile budesonide suspension that includes nonsterile budesonide. Specifically, Sandoz argues an ingredient-based written description defense - that the claims fail to disclose the ingredients that are expressly required to make the claimed suspension. The "micronized powder composition" includes both sterile and nonsterile budesonide powder. The Patent, however, does not disclose nonsterile budesonide powder as an ingredient. Thus, Sandoz argues, the Patent fails to disclose the full scope of the ingredients required by claims 50 and 51 and the suspension defined by those ingredients.

Defendant Breath/Watson argues an unclaimed-method written description defense - that the Patent does not sufficiently convey to a POSA that AstraZeneca was in possession of a product that was made from a non-heat sterilized process. Essentially, Defendants argue the same facts that supported their narrow claim construction (which this Court adopted, but the Federal Circuit rejected) to support their written description challenge:

- the '834 Patent specification does not disclose any sterile budesonide suspensions that include nonsterile budesonide;
- both examples in the Patent involve suspensions with sterile budesonide;
- the inventors describe how to make a sterile suspension with sterilized glucocorticosteroid only;
- sterile budesonide is not interchangeable with nonsterile budesonide;
- the Patent does not disclose what were perceived at the time to be insurmountable agglomeration problems when sterilizing a suspension including nonsterile budesonide;
- AstraZeneca tried to sterilize suspensions made from nonsterile budesonide but failed;
- the specification lacks any mention of a sterile budesonide product made using any non-heat sterilization, including sterile filtration such as that used by Breath/Watson;
- the Patent expressly dissuades a POSA from making a sterile product using methods known in the art; and

- the only viable alternative for sterilizing the micronized budesonide was dry heat sterilization.

See Sandoz Opp. Br. at 8-16; Breath/Watson Opp. Br. at 7-11. Defendants contend that with the broad claim construction AstraZeneca sought and received on appeal, claims 1 and 50 encompass all forms of sterile budesonide suspensions, including non-heat sterilized compositions where sterility was achieved by sterile filtration, like Breath/Watson's product, and suspensions made from nonsterile budesonide achieved , like Sandoz's product. Yet, they contend, the '834 Patent does not convey such inventions.

Now that the Federal Circuit has construed the claims to be product claims, however, the written description requirement does not demand that all methods of making the product, including those followed by Defendants, be described in the specification. Nor does it require that all the ingredients to make the claimed suspension by all methods be set forth. See Amgen Inc. v. Hoeschst Marion Roussel, Inc., 314 F.3d 1313, 1331 (Fed. Cir. 2003). The Federal Circuit expressly found that the specification did not limit the invention to only one method or provide that other methods were outside the invention. AstraZeneca, 542 F. App'x at 977 ("[T]he asserted claims refer merely to a powder or suspension thereof that is sterile, irrespective of how that sterility was achieved."). Thus, in

light of the Circuit's ruling, the '834 Patent cannot be invalidated for failure to describe either a method of achieving sterility that is not itself claimed or the starting ingredients of the sterilization method. See Amgen, 314 F.3d at 1334 ("Because of this lack of clear statements by the patentee limiting the claimed invention . . . we cannot invalidate a patent for failure to describe a method of producing the claimed compositions that is not itself claimed."). As long as the specification describes the product, as now broadly construed, it need not disclose multiple methods of making the product. See Amgen, 314 F.3d at 1334, 1338; see also Research Corp. v. Microsoft Corp., 627 F.3d 859, 873 (Fed. Cir. 2010)("Apparatus claims do not need to recite every method of making the claimed apparatus."); Crown Packaging Tech., Inc. v. Ball Metal Beverage Container Corp., 635 F.3d 1373, 1382 (Fed. Cir. 2011) ("The district court also failed to distinguish in its written description analysis between [the patentee's] only asserted product claim . . . and [the patentee's] method claims . . . .").

In sum, the inventors of the '834 Patent were required to show to a POSA that they had, in fact, obtained a sterile, pharmaceutically acceptable budesonide and pharmaceutically acceptable sterile suspension of budesonide. That, they did. The '834 Patent explains how to make the claimed product in

Columns 3-4, and the claimed suspension in Columns 5-6. Columns 7-10 describe experimental testing validating that the claimed sterile, pharmaceutically acceptable budesonide and suspension thereof had been created. The Patent also expressly shows that the product was sterile according to the U.S. Pharmacopoeia.

In addition, Breath/Watson argues that the '834 Patent specification fails to describe a budesonide composition that meets the criteria of sterility according to both 1995 USP <71> and <1206>. Breath/Watson Opp. Br. at 10 (citing Declaration of Mike Zaccheo ("Zaccheo Decl."), Docket No. 910, ¶¶ 51-56). However, the cross-reference to the U.S. Pharmacopoeia provides sufficient disclosure. Breath/Watson also argues that the '834 Patent fails to provide a written description of a budesonide salt as disclosed in claims 1 and 50. These claims, however, require not a budesonide salt but pure budesonide. See '834 Patent col.11 ll.47-52, col.13 ll.55-60 ("pure budesonide or an ester, acetal or salt thereof").

Accordingly, the Court finds that Defendants have not raised a substantial question as to validity on the written description challenge.

b. Enablement

Defendants Sandoz and Breath/Watson both assert that claims 50 and 51 are invalid for failure to comply with 35 U.S.C. § 112(a) (2012). Pursuant to this statute, a patent must enable

a POSA to make and use the claimed invention without undue experimentation. AK Steel Corp. v. Sollac & Ugine, 344 F.3d 1234, 1244 (Fed. Cir. 2003). Notably, "[t]he enablement requirement is often more indulgent than the written description requirement." Amgen, 314 F.3d at 1334.

Sandoz argues that the specification does not teach a POSA how to make a sterile budesonide suspension using nonsterile budesonide powder. In fact, AstraZeneca was unable to do so, and even disparaged suspensions that included nonsterile budesonide. Sandoz was able to do so,

See Declaration of Russell E. Madsen ("Madsen Decl."), Docket No. 908-10, ¶ 36.

Similarly, Breath/Watson argues that given the now-governing breadth of the claims, the '834 Patent does not teach or give guidance of any kind that would enable a POSA to make the powder composition using sterile filtration. Unlike the low temperature, dry heat process described in the Patent, a sterile budesonide composition made by sterile filtration experienced multiple changes in the physio-chemical properties of the starting budesonide material. Sterile filtration was specifically disparaged. Zaccheo Decl. ¶ 58.[6]

[6] Breath/Watson also argues that the '834 Patent does not enable a POSA to make a budesonide salt or a budesonide composition that meets the criteria of sterility according to 1995 USP<71>

In its "enablement" provision, the Patent Act requires that a patent disclose "the manner and process of making and using [the invention], in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same." 35 U.S.C. § 112(a). However, "[t]he specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without undue experimentation." Amgen, 314 F.3d at 1334.

For product claims, such as those asserted here by virtue of the now-governing broad claim construction, the enablement requirement is satisfied if the specification provides a *single* way to make the claimed product. Invitrogen Corp. v. Clontech Labs, 429 F.3d 1052, 1071 (Fed. Cir. 2005); Amgen, 314 F.3d at 1339 ("the enablement requirement is met if the description enables any mode of making and using the invention"); id. at 1338 ("a product claim is supported by adequate written description and enabling disclosure even if it describes only one method of making the claimed product"); Durel Corp. v. Osram Sylvania, Inc., 256 F.3d 1298, 1306-07 (Fed. Cir. 2001) (same); Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d 1342, 1361 (Fed.

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or <1206>.

Cir. 1998) (same); Engel Indus. v. Lockformer Co., 946 F.2d 1528 (Fed. Cir. 1991) (same).

Defendants do not dispute that the specification enables making sterile, pharmaceutically acceptable budesonide and suspensions thereof. The specification of the '834 Patent teaches a skilled artisan, in detail, how to make sterile, pharmaceutically acceptable budesonide (Columns 3-4) and a sterile budesonide suspension (Columns 5-6). They argue, however, that the Patent does not enable the claims because it does not "teach a person skilled in the art how to make a sterile budesonide suspension made from nonsterile budesonide powder." Sandoz Opp. Br. at 36. Nor, they argue, does it teach or "enable the skilled person to make a sterile budesonide composition made by sterile filtration without changing the physico-chemical properties of the starting material." Breath/Watson Opp. Br. at 22-23. However, much like their written description challenges, Defendants are reiterating their flawed argument that the specification must teach every way to make the claimed product. But the specification need only teach a single method. See Johns Hopkins Univ., 152 F.3d at 1361.

Breath/Watson claims that ALZA Corp. v. Andrx Pharmaceuticals, LLC, 603 F.3d 935 (Fed. Cir. 2010), is "squarely on point," but it is not. ALZA involved a method claim where the patent only disclosed treatment using a

particular method and not the method practiced by the defendants. The issue there was whether the patent enabled both of the claimed methods of treatment. Here, the Federal Circuit has ruled that the '834 Patent is not limited to one method, but to a product. As such, AstraZeneca was not required under Federal Circuit jurisprudence to disclose multiple ways of making the product – a pharmaceutically acceptable, sterile budesonide suspension.

Sandoz argues that AK Steel Corp., 344 F.3d at 1234, in which the Federal Circuit affirmed a finding of non-enablement, contains "very similar" facts to the instant matter. Sandoz Opp. Br. at 19. That case involved patent claims that covered two different steel products, each containing a different kind of aluminum coating. Because the patent enabled only one of the products, the patent was found invalid. The Defendants' other cases are equally inapposite. See Auto Techs. Int'l, Inc. v. BMW, 501 F.3d 1274, 1285 (Fed. Cir. 2007) (claims covered many different products including mechanical and electric sensors, but specification only enabled mechanical sensors); Pharm. Res., Inc. v. Roxane Labs., Inc., 253 F. App'x 26, 30 (Fed. Cir. 2007) (patent claims covered products with a wide range of different surfactants, even though only one surfactant was described). Accordingly, the Court finds that Defendants have not raised a

substantial question as to validity on their enablement challenge.

c. Obviousness

Before this Court undertakes an obviousness analysis, it addresses the ever-shifting arguments made by AstraZeneca. For the first time, AstraZeneca asserts that the term "pharmaceutically acceptable" is limited to a product for inhalation. See AstraZeneca Supp. Br. at 3 (urging Court to construe "pharmaceutically acceptable" to mean "useful as an inhalation drug product"). Nowhere before in the lengthy record did AstraZeneca ever make such an argument. Indeed, from the inception of this case, the parties - including AstraZeneca - took the position that "pharmaceutically acceptable" required no construction and should be accorded its plain meaning. See Joint Claim Construction Chart, Docket No. 93; see also AstraZeneca's Preliminary Claim Constructions to Breath for the '834 Patent, Declaration of Heinz J. Salmen ("Salmen Decl."), Docket No. 975, Ex. 1 at 2 ("'Pharmaceutically acceptable' requires no construction and should be accorded its plain meaning."). Moreover, AstraZeneca never sought to limit the claim language to an inhalation product.

The following illustrates the calculated efforts of AstraZeneca at each stage of the litigation to broaden its claims with each ruling. Before this Court issued its claim

construction, AstraZeneca argued that "pharmaceutically acceptable" needed no construction and "micronized powder composition" meant a "powder composition in which the particle size has been mechanically reduced to form particles having a mass median diameter (MMD) of approximately 20 µm or less." Joint Claim Construction Chart at 16. Yet, both sides' experts were in agreement that particle size above 5 µm was not suitable for an inhalation product.[7] Thus, AstraZeneca's own proposed construction before this Court would not have limited the claim to inhalation products only. On appeal, "pharmaceutically acceptable" was not at issue and the Federal Circuit construed "micronized powder composition" to mean "finely divided dry particles," without limiting the claim to particle size.

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[7] See Trial Tr. 1526:8-12 (Dr. James Agalloco) ("In terms of what this product does in the human, my understanding it has to be **extremely small**. The difference between two and-a-half microns and three microns to the patient is acceptable. That's an acceptable range for this type of a product.") (emphasis added); id. at 2000:13 (Dr. Paul B. Myrdal) ("So we have a relatively narrow particle size range in which to get an aerosol deposited into the lung. It's commonly referred to as about 1 to 5 microns. Now if we go larger and we look at the top state up here, it says 9 to 10 microns . . . it goes to the back of the throat. It's not available for the patient to inhale it. So anything larger than that would not be deposited into the lung. So this is a basic understanding of a person of ordinary skill in the art that, in order to deposit drugs to the lungs, we have to be between this, roughly, 1 to 5 particle size range."); id. at 2139:8-11 (Myrdal) ("So if you have a micronized particle of any steroid in the particle size range that was traditionally used at that time for inhalation therapy, it probably would have been somewhere around 2 to 4 microns.").

AstraZeneca, 542 F. App'x at 975-76. On remand, AstraZeneca now argues that "pharmaceutically acceptable" should be limited to a particle size acceptable for an inhalation product. AstraZeneca's argument is nothing more than an end run around the Federal Circuit's definition. More to the point, it is a furtive attempt to limit the Circuit's binding claim construction, which this Court rejects.

AstraZeneca argues that its product is inventive because it is both pharmaceutically acceptable and meets the criteria for sterility. As AstraZeneca points out these terms capture different meanings.[8] But in making its arguments now, as set forth above, AstraZeneca improperly attempts to interject a new limitation into the claim language. "Pharmaceutically acceptable" means what the parties have always agreed - "acceptable for administration as a pharmaceutical."

Thus, as the case now stands on remand, the following claim analysis applies:

> 1. "A pharmaceutically acceptable, [finely divided dry particles] at least 98.5% by weight . . . wherein the composition meets the criteria of sterility . . . ."

[8] For example, AstraZeneca notes "irradiated budesonide is free of microbes, but the radiation degrades the drug and renders it unusable." AstraZeneca Supp. Br., Docket No. 977, at 3 (citing '834 Patent col.1 ll.62-67). Similarly, the European Pulmicort product was pharmaceutically acceptable although non-sterile. Id.

> 50. "A pharmaceutically acceptable suspension consisting of [finely divided dry particles] at least 98.5% by weight . . . suspended in an aqueous solution, wherein the suspension meets the criteria of sterility . . . ."

'834 Patent col.11 ll.47-52; col.13 ll.55-60.

With this background, the Court turns to Defendants' argument that the prior art or combination of the prior art taught how to make a sterile budesonide that was acceptable for administration as a pharmaceutical and, therefore, claims 1, 2, 50 and 51 of the '834 Patent are invalid as obvious. The obviousness analysis involves four factual inquiries: (1) "'the scope and content of the prior art,'" (2) the "'differences between the prior art and the claims at issue,'" (3) "'the level of ordinary skill in the pertinent art,'" and (4) "'secondary considerations'" of nonobviousness. AstraZeneca, 542 F. App'x at 978 (citing KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 406 (2007)). AstraZeneca urges the Court to turn first to the secondary considerations or objective indicia of non-obviousness factor as a guard against the hindsight consideration that each Defendant ultimately sterilized budesonide through processes that were well-known prior to the invention here. AstraZeneca avers that when, as here, there is a battle of the experts as to obviousness, "the objective indicia provide an unbiased indication regarding the credibility of that evidence." Kinectic Concepts, Inc. v. Smith & Nephew, Inc., 688 F.3d 1342,

1370-71 (Fed. Cir. 2012). The Court thus addresses this factor first.

i. Secondary Considerations

a. Industry Skepticism & Unexpected Results

AstraZeneca argues that the pharmaceutical industry believed that sterilizing budesonide was "impossible." Yet, the only evidence of such belief is AstraZeneca's own publication and the skepticism of one of the inventors. See Trial Tr.[9] 584:21-24, 572-74 (Ms. Cheryl Larrivee-Elkins) ("Q. At that point in time, the November, December 1996 time frame, to your knowledge did anybody at Astra believe that Pulmicort Respules could be sterilized? A. No, not to my knowledge."). Defendants counter that, because the only people who were allegedly skeptical were AstraZeneca's own employees, this factor weighs in favor of obviousness. AstraZeneca's response is two-fold. First, it argues, it is illogical to imply that AstraZeneca would intentionally fail in its attempts to sterilize budesonide using known sterilization methods in order to support its later patent application. Second, AstraZeneca points to statements made by Breath/Watson in one of its later patents, as well as comments made by the FDA, which AstraZeneca

[9] "Trial Tr." refers to the transcripts of the bench trial before this Court.

contends demonstrate that other industry participants shared AstraZeneca's skepticism.

As to AstraZeneca's first argument, it says little regarding the extent of AstraZeneca's efforts using the other known sterilization methods. More importantly, however, as Breath/Watson pointed out at oral argument, the alleged skepticism within AstraZeneca does not appear to have been unanimous. During oral argument, Breath/Watson relied upon DTX 795 for the proposition that European Pulmicort Respules, discussed infra, were sterile. PI H'rg Tr.[10] 38:23-39:9. Although this exhibit was not introduced during the bench trial, it does tend to support Breath/Watson's argument. In fact, according to the exhibit, at least one person within AstraZeneca believed that further data was required to establish that sterilization of budesonide could not be achieved. In a memorandum dated January 17, 1997, P. Alessandro from Regulatory Affairs wrote "[t]he documents do not provide conclusive evidence that the drug substance [budesonide] cannot be sterilized. In fact, in several instances the statements made are not supported by data presented." See DTX 795 at AZ 1358159; see also Trial Tr. 689:6-7 (Elkins) (explaining that U.S. AstraZeneca team felt that it needed more data before it

[10] "PI H'rg Tr." refers to the transcript of the oral argument held on May 9, 2014.

could state to the FDA that it was not feasible to sterilize). Alessandro's memorandum also discusses the well-known sterilization processes: "[m]oist heat sterilization data are lacking particle size distribution results. Simply noting that some large particles are formed is not sufficient;" "[d]ry-heat treatment of drug product at 80° C for 10 minutes leaves many questions unanswered;" and "[t]he data provided for irradiation of the drug product were incomplete."[11] Id. These statements appear to conflict with certain statements of the inventor, Elkins, upon which AstraZeneca heavily relies. Notably, the document AstraZeneca relies upon expresses only an individual opinion: "I don't think we can produce a sterile product!" PTX 515.

As to the second argument, Breath's later patent merely parrots AstraZeneca's own description of the state of the art:

> It is reported in WO 99/25359 (Astra) that long exposure of budesonide to high temperatures leads to agglomeration of the finely divided particles --- the sterilization of budesonide is generally considered by the market to be impossible.

U.S. Patent No. 6,863,865 ("McAffer Patent"), PTX 507, col.4 ll.45-49; see also id. at col.4 ll.62-64. Indeed, during prosecution of the '834 Patent, the Patent Office found:

> Applicant [AstraZeneca] cites McAffer et al (US 6,863,865) as a description of the state of the art

[11] The preceding page in the memorandum, AstraZeneca 1358158, was not produced and may refer to other forms of sterilization.

> with respect to the sterilization of budesonide. McAffer asserts that it allows sterilization of a budesonide suspension 'for which this was previously believed not possible.' It is noted that the basis of McAffer's statement is the report in WO 99/25359 (Astra). This publication is the basis for the instant application. Therefore, Applicant is essentially citing their own specification as an independent description of the state of the art. This is not persuasive.

PTX 611, at Breath 017807. AstraZeneca's attempt to cast the statements in the McAffer Patent as Breath's independent description of the state of the art is therefore unpersuasive.[12] Moreover, the patentee, Ian McAffer, testified at trial that the scientific community, as opposed to the market, did not believe that the sterilization of budesonide was impossible. Trial Tr. 3551:11-3552:9 (McAffer) ("there was a belief in the marketplace, not necessarily the scientific community, that the sterilization of budesonide was generally considered by the market to be impossible").

Similarly, and contrary to AstraZeneca's characterization, there is no evidence that the FDA believed the sterilization of

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[12] At oral argument, AstraZeneca also relied upon two additional statements in the McAffer Patent. Neither one supports a claim of industry skepticism. First, "[k]nown alternative methods for the sterilization of pharmaceuticals are inappropriate for sterilizing suspension formulations of drugs." McAffer Patent col.1 ll.35-37. This statement, however, does not exclude all methods. Second, "[n]o further methods for the sterilization of pharmaceuticals are currently acceptable to regulatory agencies." Id. at col.1 ll.43-45. The FDA had only approved the heat-sterilization method. This is not relevant to an obviousness analysis.

budesonide was "impossible." At most, the record supports the notion that the FDA acknowledged the technical difficulties associated with the sterilization of suspensions - a point Defendants do not dispute.[13] Difficulty, however, does not equate to impossibility. Indeed, the inventor made no such equation. See Trial Tr. 579:8-17 ("difficult" meant that it was unclear if there was a way to sterility). If it were so widely and indisputably accepted that the sterilization of budesonide was impossible as AstraZeneca argues, it is hard to understand why the FDA would ask AstraZeneca to do the impossible.

b. Failure of Others; Long-felt Need

The fact that others tried to solve a known problem but were unable to do so is also an objective indicia of nonobviousness. Long-felt need is closely related to the failure of others and is another indicia. Cyclobenzaprine Hydrochloride Extended Release Capsule Patent Litig., 676 F.3d 1063, 1082-83 (Fed. Cir. 2012). There is insufficient evidence as to this factor. The parties are in agreement that there was a need, although when that need began is not clear. AstraZeneca argues that the need started in the 1980s when it was well-known

[13] PTX 611, at Breath 017897 ("[W]e expect inhalation products to be sterile, although we acknowledge that a suspension presents difficulties . . . it is [AstraZeneca's] burden to make the product sterile or justify why it can't be.").

that deaths were occurring because of contaminated products.[14] In doing so, AstraZeneca relies upon defense expert, Dr. Scott Sutton, who testified: "Q. And the issue was in the 80's and 90's there were contaminated products that were not sterile that were killing people, isn't that correct? A. Yes." Trial Tr. 2524:18-21 (Sutton) (emphasis added).[15] Sutton also testified that in the early to mid-1990s "[the] FDA unofficially started letting everybody know that you better show up with a sterile presentation if you're going to be submitting an inhalant to the FDA because they were tired of this problem." Trial Tr.

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[14] AstraZeneca stated that "[d]ue to recalls of other drugs [since the 1980s], the FDA was moving toward requiring sterilization for solutions and inhaled suspensions." AstraZeneca Br., Docket No. 890, at 20 (citations omitted).

[15] In its Supplemental Brief, AstraZeneca again relies upon Sutton's testimony to argue that "In the 1980s, contaminated inhalation products had caused widely publicized patient deaths, ultimately prompting the FDA to demand that all new inhalation products be manufactured sterile." Supp. Br. at 5. This statement distorts the testimony. At trial, Sutton testified regarding a contaminated product that caused deaths among cystic fibrosis patients in the early 1980s. Trial Tr. 2401:12-2403:17. As a result, it was determined that nonsterile drugs could not contain objectionable organisms and that it was believed that the problem was "solved." Id. It was not until after another problem arose that the FDA "started letting everybody know that you better show up with a sterile presentation," but this occurred in the mid-1990s. Id. Even the inventor who testified does not share AstraZeneca's view. See Trial Tr. 583:4-13 ("Q. Did you have an understanding as to why [the FDA] had that position [i.e., they wanted AstraZeneca to provide a sterile product]? A. So there were recalls of inhalation products **in the previous year or two** to this [November 1996 meeting]." (emphasis added)).

2403:13-17 (Sutton) (emphasis added). Yet, during the bench trial, AstraZeneca took a contrary position, that there was "no documentary evidence corroborating defendants' claims that 'FDA's concerns and intentions concerning sterility requirements' were publicly known prior to 1997." See AstraZeneca's Response to Defendants' Findings of Facts, FF 331, Docket No. 675 (AstraZeneca disputed that "a POSA was aware of FDA's concerns and intentions concerning sterility requirements for aqueous-based inhalation products, whether solutions or suspensions, prior to 1997."). Thus, for AstraZeneca at this time to now back away from that statement and embrace a single phrase from Dr. Sutton's testimony, taken out of context, to suggest there was a two-decade long need is disconcerting. Rather, the evidence before this Court convincingly demonstrated that by the mid-1990s, not before, POSAs were aware of the concerns voiced by the FDA and understood that very soon all aqueous-based inhalants would need to be sterile.

AstraZeneca also argues that its own initial failures as well as the failures experienced by Defendants in sterilizing PULMICORT RESPULES® is indicative of the significant defects in the prior art. However, there is no evidence before the Court as to the who, what and when of these failures. Although evidence of the failure of others is relevant to an obviousness analysis, there must be some understanding of those failures. See

Advanced Display Sys., Inc. v. Kent State Univ., 212 F.3d 1272, 1285 (Fed. Cir. 2000) ("In the present case, [the] deposition furnishes persuasive evidence that the [ ] patent is nonobvious by describing [the] repeated failures to design the claimed invention."). For example, AstraZeneca argues that Breath/Watson's process required numerous and extensive post-filtration steps in order to produce the claimed product.[16] Yet, Dr. Mike Zaccheo opined that a POSA would have known that the addition of an aseptic micronization step to sterile filtration (a well-known process) "would provide the particle size desired for an inhalation powder while maintaining its sterility." Declaration of Robert O. Williams III, PH.D. ("Williams Decl."), Docket No. 923-4, Ex. 6 ("Zaccheo Report") ¶ 62. He stated: "At the very least, this would have been considered routine and obvious to a [POSA] prior to 1997." Id. Zaccheo attested that the same is true for moist heat sterilization. See Zaccheo Report ¶ 67 ("[T]he addition of aseptic micronisation to the moist heat sterilisation and aseptic processing would have been obvious to a person of ordinary skill in the art. (*See, e.g.*, Ex. 16, Akers 1987 at 88 (describing facilities used 'to

[16] One of the documents on which AstraZeneca relies as evidence of Breath/Watson's failures, DTX 475, is a verbatim copy of the "Decision Trees for the Selection of Sterilisation Methods" produced by the European Agency for the Evaluation of Medicinal Products. See Salmen Decl., Ex. 2 at 3.

maintain aseptic conditions for manufacturing processes such as crystallization, ***particle size reduction***, wetting, ***sterilization***, and aseptic dispersion filling and packaging' (emphasis added)) (Breath(Bud) 018391); Ex. 17, Akers 1996 at 620 ('The dried product is aseptically discharged into suitable bulk containers or, alternately, to the milling unit . . . . Milling and blending can be done as separate steps . . . . Mill parts are generally sterilized in place . . . .') (Breath(Bud) 028822); Ex. 23, the '651 patent at col. 21, lines 38-39 (disclosing crystals that are 'sterilely micronized in a sterile micronizer') (Breath(Bud) 028857; Ex. 5, Lachman[17] at 626-27 (disclosing that steam sterilisation could be performed at 100°C on drug products susceptible to thermal degradation at higher temperatures) (Breath(Bud) 025786-87)).").

c. Commercial Success

AstraZeneca avers that PULMICORT RESPULES® has been a "resounding commercial success." AstraZeneca Br. at 22. AstraZeneca's attempt to rely solely on the '834 Patent as a nexus for that success is overstated. Although the FDA would not permit the sales of PULMICORT RESPULES® unless the product was sterilized, regulatory compliance should not automatically translate into a finding of commercial success. See In re

[17] DTX 960.

Oxycontin Antitrust Litig., No. 11-2037, 2014 WL 128013, at *24 (S.D.N.Y. Jan. 14, 2014) ("Purdue emphasizes that the low-ABUK process allowed the Rhodes facility to obtain FDA approval and that Rhodes could not have been successful without FDA approval. The Court cannot equate regulatory compliance with evidence of commercial success."). It is the efficacy of the budesonide molecule that clearly contributed to the success of the product. Cf. Trial Tr. 4439:18-4441:20; see also DTX 716.

ii. The Prior Art

The Court now turns to the remaining factors. An obviousness determination requires that a POSA would have perceived a reasonable expectation of success in making the invention in light of the prior art. See PharmaStem Therapeutics, Inc. v. ViaCell, Inc., 491 F.3d 1342, 1360 (Fed. Cir. 2007). "Obviousness does not require absolute predictability of success. . . . All that is required is a reasonable expectation of success." In re O'Farrell, 853 F.2d 894, 903-04 (Fed. Cir. 1988) (citing In re Longi, 759 F.2d 887, 897 (Fed. Cir. 1985)); see also Bayer Schering Pharma AG v. Barr Labs, Inc., 575 F.3d 1341, 1349, 1351 (Fed. Cir. 2009); Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1364 (Fed. Cir. 2007).

There may also be a motivation to combine the relevant art that need not be explicit, but may be derived from the "combined teachings, knowledge of one of ordinary skill in the art, and

the nature of the problem to be solved as a whole." In re Kahn, 441 F.3d 977, 988 (Fed. Cir. 2006) (quoting In re Kotzab, 217 F.3d 1365, 1370 (Fed. Cir. 2000)).

At the time of the '834 invention, there was a motivation to sterilize all aqueous inhalation products. This motivation came from the FDA. In 1997, the FDA published its Proposed Rules requiring "that all [aqueous-based] inhalation solutions for nebulization be manufactured as sterile." DTX 872, at Breath 018500. Despite the explicit reference only to "solutions" in the Proposed Rules, there is no serious dispute that a POSA understood that the FDA would soon require the sterilization of suspensions. Defendants concede this point, and AstraZeneca, in a reversal of position, does as well. See supra.

In 1997, there were five well-known sterilization methods: (1) radiation sterilization, (2) gas sterilization, (3) steam sterilization, (4) dry heat sterilization, and (5) filtration.[18]

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[18] Defendant Breath/Watson argues that the prior art, and specifically Lachman, clearly taught "how to make sterile products via sterilization and/or aseptic processing." Breath/Watson Supp. Br., Docket No. 974, at 3-4 (citing DTX 960, at Breath 025783-96; 1995 USP <1211>). Not only does Lachman set forth several known sterilization methods, e.g. moist and dry heat, but it also contemplates the need to modify the sterilization process to account for the characteristics of the product sought to be sterilized and provides suggested modifications. See, e.g., Lachman, at Breath 025779, 025784. Significantly, Lachman notes "sterility in the absolute sense cannot be shown to have been achieved, but rather can be

Defendants argue that the prior art combined with AstraZeneca's European PULMICORT RESPULES® taught how to make a sterile budesonide product. The PULMICORT RESPULES® product that AstraZeneca sold in Europe was identical to the product claimed in the '834 Patent except that it was not subject to a sterilization process.[19] Trial Tr. 177:2-6, 179:11-21, 2785:19-2786:5, 2786:24-2787:15, 3245:21-3246:6. Defendants rely upon several prior art references discussed below.

U.S. Patent No. 6,187,765 to Harris (Claims 1 and 2) (Claims 50 and 51)

Defendants contend that Harris provides a step-by-step procedure much like the FDA's 1994 Inspection Guide[20] of how a

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approached with an increasing probability of success as a sterilization process is improved." Id. at Breath 025779. This would seem to suggest that certain "routine steps" for modifying the processes existed and thus appears to support Defendants' obviousness argument.

[19] This fact is acknowledged in the International Patient Package Leaflet ("IPPL"), which discloses Pulmicort® suspension for nebulization. See DTX 751. In particular, the PULMICORT RESPULES® product is a pharmaceutically acceptable suspension consisting of a micronized powder composition. See, e.g., Trial Tr. 803:23-804:18, 649:3-651:8. Also of significance, the '834 Patent acknowledges that PULMICORT RESPULES® nebulizing suspension was known in the art. '834 Patent col.2 ll.40-44.

[20] The 1994 FDA Inspection Guide discloses a sterile filtration process that the FDA recommended as the usual technique for manufacturing sterile pharmaceutical powders. That process includes the following steps:

1. The substance is dissolved in a solvent, which is then sterilized by a filtration process;
2. The sterile drug substance undergoes aseptic precipitation or crystallization;

POSA would manufacture a pharmaceutically acceptable, water-insoluble corticosteroid similar to mometasone. DTX 971 col.1 ll.16-26, col.2 ll.9-15, col.8 ll.3-34. Example 1 of Harris is directed to a method of preparing a sterile mometasone furoate using a sterile filtration process, one of the five well-known sterilization processes. Id. at col.6 ll.26-62. Example 2 teaches how to create a sterile suspension using the sterile mometasone of Example 1. Id. at col.6 l.65 to col.7 l.40.[21] Harris thus discloses a nebulized aqueous suspension of a micronized corticosteroid for use in treating disorders of the lower airway. Id. at col.1 ll.37-42.

According to Dr. Jeanne Moldenhauer, an expert for Defendants Sandoz and Breath/Watson,[22] a POSA would understand

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3. The resulting sterile substance undergoes aseptic isolation by centrifugation or filtration; and

4. The sterile substance then undergoes aseptic drying, milling and blending.

DTX 1000, at Breath 029003.

[21] Harris also acknowledges "[m]ethods are known for reducing particle sizes into the micrometer range, including mechanical milling, application of ultrasonic energy and other techniques. Mechanical milling frequently generates high surface temperatures on the particles, and this is undesirable for mometasone furoate monohydrate which tends to lose some part of its hydration under the influence of high temperatures. Ultrasonic techniques are quite slow in their action, generally requiring very long processing times, but are capable of producing acceptable suspensions." DTX 971 col.5 ll.56-65.

[22] Defendants did not present Dr. Moldenhauer as an expert during the bench trial.

that the sterile powder and suspension in these examples would meet the criteria of sterility in the 1995 USP. Declaration of Jeanne Moldenhauer ("Moldenhauer Decl."), Docket No. 908-22, ¶ 152. Hence, according to Dr. Moldenhauer, because mometasone and budesonide are both glucocorticosteroids, and because Harris mentions budesonide and suspensions, a POSA would have been motivated to use the sterile filtration process to create a sterile version of European Pulmicort with a reasonable expectation of success. See Moldenhauer Decl. ¶¶ 104, 106, 107, 153.

AstraZeneca contends that Harris, filed on October 9, 1997, is not prior art because AstraZeneca's invention, which is the subject of the '834 Patent, was reduced to practice prior to Harris. During the trial, AstraZeneca introduced a Rule 131 Declaration to support an earlier invention date.[23] See PTX 611, at Breath 017807 ("The declaration filed on November 1, 2007 under 37 C.F.R. 1.131 is sufficient to overcome the Harris . . .

[23] Under Rule 131, "[w]hen any claim of an application . . . is rejected, the applicant or patent owner . . . may submit an appropriate oath or declaration to establish invention of the subject matter of the rejected claim prior to the effective date of the reference or activity on which the rejection is based." 37 C.F.R. § 1.131. Notably, "[t]he PTO examines an applicant's affidavit for compliance with [Rule 131], but the PTO does not otherwise investigate the applicant's assertions about his invention date." Spectralytics, Inc. v. Cordis Corp., 576 F. Supp. 2d 1030, 1043 (D. Minn. 2008), aff'd, 485 F. App'x 437 (Fed. Cir. 2012).

reference."). Defendants argue that the Rule 131 Declaration is deficient because there was no competent evidence introduced, beyond the inventor's testimony, which demonstrated that AstraZeneca's invention passed the criteria of sterility according to 1995 USP. In sum, Defendants take issue with the data submitted as part of the Rule 131 Declaration. Elkins did, in fact, testify that in May-July 1997, AstraZeneca manufactured many PULMICORT RESPULES® that met the criteria of sterility set forth in the 1995 USP. Trial Tr. 638:12-25 (Elkins). Dr. George Zhanel, however, testified that none of the tests were conducted on an aqueous suspension of the micronized budesonide. Trial Tr. 4320:11-24 (Zhanel). At oral argument, AstraZeneca highlighted PTX 401, a document that on its face refers to "Budesonide Nebulizing Suspension" and a test date of June 24, 1997. AstraZeneca represents that the code 0403.037 on the face of the document is AstraZeneca's internal procedure for the USP sterility test. See PI H'rg Tr. 139:1-13; see also AstraZeneca Oral Argument Presentation, at AZ 122. However, no testimonial evidence was presented regarding this issue. See Trial Tr. 642:3-8.

AstraZeneca also contends that sterile filtration followed by aseptic micronization to produce a pharmaceutically acceptable product would never have been tried because it would have required at least five steps. Yet, there was little

evidence, if any, regarding what these steps entailed, and whether they were routine or complex. Defendants contend that, although there were well-known difficulties with suspensions, aseptic preparation was the most common method of sterile drug manufacture. While the record will need to be further developed, it does appear that the '834 Patent is vulnerable to a validity challenge in light of Harris.

U.S. Patent No. 5,858,998 to Leuschner (Claims 50 and 51)

Defendants also assert an obviousness invalidity argument based on the combination of European Pulmicort and Leuschner. The Leuschner patent discloses sterile pharmaceutical compositions, both solutions and suspensions, containing corticosteroids, including budesonide, for the treatment of hepatic diseases. Moldenhauer Decl., Ex. 33 ("Leuschner") col.1 ll.15-19. Example 3 explicitly deals with a budesonide solution. According to Dr. Moldenhauer, even though Leuschner calls the formulation a "solution," it is created using an Ultraturrax, a device that makes a suspension. Moldenhauer Decl. ¶ 54. AstraZeneca disputed this at oral argument. PI H'rg Tr. 99:10-16. Leuschner states that the resulting solution (suspension) is sterilized for 20 minutes at 121°. According to Dr. Moldenhauer, a POSA would understand that Leuschner teaches that this sterilized suspension meets the sterility criteria of the USP. See Moldenhauer Decl. ¶ 161.

AstraZeneca apparently concedes that moist heat sterilization produces a sterile product, AstraZeneca Supp. Br. at 3 (citing '834 Patent col.1 ll.35-41, 50-53), but challenges the conclusion of Dr. Moldenhauer, contending that she failed to address the "pharmaceutically acceptable" claim requirement. Leuschner discloses moist heat sterilization, and the evidence at trial established the problems associated with this process, i.e., the method leads to an unacceptable change in particle size. Defendant Sandoz acknowledges the agglomeration problem, but states that it addressed the problem

in order to create a pharmaceutically acceptable product. Defendants, however, have not explained whether a POSA would have had a reasonable expectation of success in addressing the agglomeration issue through moist heat sterilization and

prior to the '834 Patent.[24] Thus, further development of the record on this point is necessary.

U.S. Patent No. 5,407,926 to Clark (Claims 50 and 51)

Defendants also rely on Clark, which discloses sterile pharmaceutical compositions containing glucocorticosteroids, such as budesonide. See DTX 160 col.1 ll.20-24. To sterilize

[24] AstraZeneca accuses Sandoz of admitting to using

See AstraZeneca's Reply, at 21. The Court does not understand Sandoz to be making such admission.

the corticosteroid, Clark recommends dry heat or ethylene oxide. DTX 160 col.7 ll.12-13. According to Dr. Moldenhauer, a POSA would have been motivated to use these methods to create a sterile version of European Pulmicort. Moldenhauer Decl. ¶ 142-143. AstraZeneca argues, however, that the trial evidence established that ethylene oxide sterilization does not produce a pharmaceutically acceptable product because it leaves toxic residue in the case of ethylene oxide and degrades the budesonide in the case of dry heat. The Court agrees that Defendants have failed to explain how a POSA would have understood that a combination of the European Pulmicort and the processes disclosed in Clark would lead to the claimed pharmaceutically acceptable sterile budesonide suspension.[25]

U.S. Patent No. 5,192,528 to Radhakrishnan (Claims 1 and 2)

The Radhakrishnan Patent teaches a sterile, corticosteroid composition that can be sterilized by filtration. Moldenhauer Decl., Ex. 40 col.4 ll.7-24, col.5 ll.45-48, col.6 ll.9-19. According to Dr. Moldenhauer, the '528 Patent discloses "an aqueous suspension of sized liposomes containing budesonide . . ., which is aerosolized under conditions producing particle sizes favoring deposition in the respiratory tract for treating a lung condition or disease . . . ."

[25] The same is true for the U.S. Patent No. 3,962,430 to O'Neill.

Moldenhauer Decl. ¶ 114. Moreover, the Patent "teaches the necessity for particles smaller than 10 μm for effective delivery to the respiratory tract." Id. Thus, Dr. Moldenhauer states that in her opinion the '528 Patent discloses "a sterile, budesonide composition with a particle size under 10 μmm (i.e., 'micronized') intended for nebulized treatment of respiratory diseases." Id.

AstraZeneca relies upon Dr. Williams' testimony that the patent offers no guidance to a POSA on how to make a liposomal budesonide. Indeed, Williams is not aware of any inhaled liposome formulations that have been approved for treating respiratory disease. Williams Decl. ¶ 66. At trial, the Court heard considerable testimony that addressed the complexity and problems inherent in creating liposomal formulations. Thus, Williams' testimony that a POSA would not have been motivated to attempt a liposomal formulation to sterilize budesonide and would not expect success from such an approach seems persuasive.

Overall, Defendants have indeed raised questions regarding the invalidity of the '834 Patent based on obviousness. With respect to claims 1, 2, 50 and 51, AstraZeneca argued before the PTO, not that it was impossible to produce a sterile product through all other sterilization processes, but that all known processes other than dry heat sterilization did not produce a pharmaceutically acceptable product. By not expressly

disavowing those processes it criticized, however, as the Federal Circuit held, AstraZeneca inoculated itself against a process limitation claim construction. But now, with a broad governing claim construction, all sterilization processes become quite relevant. The question that remains is whether a POSA would have had a reasonable expectation of using well-known solutions to these traditional processes to produce a pharmaceutically acceptable product that met the criteria of sterility. If a POSA understood that there were routine solutions available to implement a prior art (or combinations thereof) process to achieve a pharmaceutically acceptable sterilized budesonide or suspension thereof (a product), then the claims are obvious.

B. CONCLUSION

Because the record as to Defendants' obviousness argument is contested and will need to be further developed, as discussed above, the Court will consolidate the hearing on the motion for a preliminary injunction with the trial on the merits.[26] See,

[26] At the oral argument on the preliminary injunction, the Court solicited the parties' views on whether it should consolidate the hearing with the trial on the merits. Only Breath/Watson opposed the consolidation, arguing that any further delay would prejudice Watson, which is prepared to launch, and that a bond cannot compensate Watson for the generic product that is nearing its expiration. [See Docket No. 971 at 2]. The Court disagrees for substantially the same reasons it relied upon in previously enjoining Defendants. To the extent the state of the record has materially changed since the Federal Circuit's decision

e.g., Warner Chilcott Labs v. Mylan Pharm., 451 F. App'x 935, 939-40 (Fed. Cir. 2011). Likewise, in light of the need for further proceedings, the Court need not address the other preliminary injunction factors at this time.

An accompanying Order will issue.

s/Renée Marie Bumb
RENÉE MARIE BUMB
United States District Judge

Dated: June 4, 2014

regarding the bond amount, Breath/Watson is free to present new arguments limited to those changes at the appropriate time.