IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

ICEUTICA PTY LTD, et al.	*	
Plaintiffs	*	
vs.	*	CIVIL ACTION NO. MJG-17-0394
LUPIN LIMITED, et al.	*	
Defendants	*	

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MEMORANDUM AND ORDER RE: SUMMARY JUDGMENT

The Court has before it Defendants Lupin Limited and Lupin Pharmaceuticals, Inc.'s Motion for Summary Judgment and Request for Hearing [ECF No. 44] regarding Plaintiffs iCeutica Pty Ltd. and Iroko Pharmaceuticals, LLC's claims of patent infringement of United States Patent Nos. 9,526,734 and 9,649,318. The Court has considered the materials and has had the benefit of the arguments of counsel.

I. BACKGROUND

In 2015, Co-Plaintiff Iroko Pharmaceuticals, LLC ("Iroko") gained approval from the United States Food and Drug Administration ("FDA") for its New Drug Application ("NDA") for 5 milligram ("mg") and 10 mg formulations of the drug meloxicam[1] which it markets under the VIVLODEX® trademark. The NDA lists

[1] Meloxicam is a nonsteroidal anti-inflammatory drug ("NSAID") used to manage osteoarthritis pain. '734 Patent at 1:24-48.

United States Patent Nos. 9,526,734 ("the '734 patent") and 9,649,318 ("the '318 patent")(collectively, "the Patents-in-Suit") in FDA's publicly available Orange Book[2] as covering VIVLODEX® by at least one claim in each patent.

The Patents-in-Suit are owned by the Co-Plaintiff iCeutica Pty Ltd. ("iCeutica") which exclusively licenses the patents to Iroko (Iroko and iCeutica collectively referred to as "Plaintiffs").

On August 4, 2016, Defendants Lupin Limited and Lupin Pharmaceuticals, Inc. ("Lupin") filed an Abbreviated New Drug Application ("ANDA") seeking FDA approval for a generic version of VIVLODEX®. Lupin sent the Plaintiffs a Paragraph IV Certification letter stating that it had filed an ANDA and that it intended to commercially manufacture, use, import, offer for sale, or sell its generic version before the expiration of the '734 and '318 patents.[3] The letter asserted that the Patents-in-Suit are invalid and/or would not be infringed by Lupin's product. Lupin contends that it does not infringe on any claims — literally or through the doctrine of equivalents — and that Plaintiffs are barred from arguing doctrine of equivalents

[2] NDA applicants are required to list patents covering the NDA's drug in the public "Approved Drug Products with Therapeutic Equivalence Evaluations" database (commonly known as the "Orange Book"). 21 U.S.C. § 355(b)(1)(G).

[3] Applicants are required to make such assertions if they intend to market their product before expiration of the NDA's listed patents. CFR 314.94(a)(12)(i)(A)(4).

infringement because of prosecution history estoppel. Defs.' Mem. in Supp. of Mot. for Summ. J. 1-3, ECF No. 45.

Plaintiffs contend that Lupin's product directly infringes on all claims of the '734 and '318 patent—either literally or through the doctrine of equivalents—and that the prosecution history does not estop it from arguing doctrine of equivalents. Pls.' Init. Discl. of Infring. Cont., ECF No. 45-2. In its Amended Complaint, Plaintiffs also argue that Lupin will indirectly infringe by inducing doctors to prescribe (and patients to take) the allegedly infringing product. Pls.' Am. Compl. ¶¶ 57-114, ECF No. 42.

A. The Invention

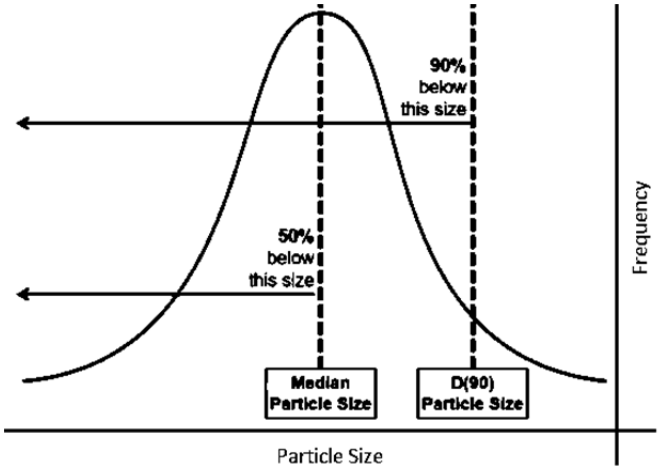
The alleged invention pertains to formulations of meloxicam (5 mg and 10 mg formulations) that are milled to meet a specified nanoparticulate size distribution profile.[4] '734 Patent 2:7-14. A specified single unit dose allegedly has desirable pharmacokinetic properties[5] and provides effective pain relief to patients suffering from osteoarthritis while exposing patients to a "relatively low[er]" amount of meloxicam than other products on the market. Id.

[4] The drug particles are ground down until the diameter of the particles reaches the desired nanomolecular size (10^-9 meters).
[5] Pharmacokinetic data describes the concentration of the drug absorbed in the bloodstream over a period of time.

The claim limitations at issue for purposes of Lupin's motion for summary judgment are limitations on the particle size of meloxicam. The particle size of powdered drugs is reported as a distribution of values reflective of the varying size of particles in a given sample ("particle size distribution"). The particle size distribution of the alleged invention is defined by two parameters:

> (1) the median particle size ("D(0.5)"), referring to "the particle size that divides the population in half such that 50% of the population is greater or less than this size"; and
> (2) the D(0.9) value, referring to the particle size below which 90% of the population of particles falls.

'734 patent 13:11-24 (emphasis added).



Each independent claim in the '734 and '318 patents is limited by meloxicam particle size expressed in terms of

nanometers ("nm").[6] A representative claim[7] from each patent is set forth below, with relevant limitations highlighted:

Independent Claim 1 of '734 patent:

> 1. A capsule form of a pharmaceutical composition comprising 5 mg of meloxicam having a median particle size, on a volume basis, between 100 nm and 500 nm and a D(0.9) that is between 1200 nm and 3000 nm, wherein a single capsule, upon oral administration to a population of healthy adults in the fasted state, provides a mean plasma AUC (0-∞) of 7500-20000 h*ng/ml and a mean plasma Cmax of 350-950 ng/ml, wherein the dissolution rate is such that, when the capsule is tested using USP Apparatus 1 (baskets) set to rotation speed of 100 RPM in 500 mL of pH 6.1 phosphate buffer with 0.1% sodium lauryl sulfate (SLS) at 37° C.+0.5° C., at least 80% of the meloxicam dissolves in 10 minutes or less, wherein a single capsule is effective for treating osteoarthritis pain.

'734 patent 25:33-46 (emphasis added).

Independent Claim 1 of '318 patent:

> 1. A capsule form of a pharmaceutical composition comprising 5 mg of meloxicam having a median particle size, on a volume basis, between 100nm and 1000 nm, wherein a single dose, upon oral administration to a population of healthy adults in the fasted state, provides a mean plasma AUC (0-∞) of 7500-20000 h*ng/ml and a mean plasma Cmax of 350-950 ng/ml, wherein the D(0.9) of the particles of meloxicam is less than 4000 nm

[6] Thereby, every claim in the '734 and '318 patents is limited by meloxicam particle size.

[7] The claimed particle size distribution is the same for every independent claim in the '734 patent. The claimed particle size distribution is also the same (although different from the '734 patent) for every individual claim in the '318 patent.

> and greater than 1200 nm, and wherein the dissolution rate is such that, when tested using USP Apparatus 1 (baskets) set to rotation speed of 100 RPM in 500 mL of pH 6.1 phosphate buffer with 0.1% sodium laurel sulfate (SLS) at 37° C.±0.5° C., at least 80% of the meloxicam dissolves in 10 minutes or less.

'318 patent 25:33-45 (emphasis added).

The bounds of particle size distribution claimed in the patents are as follows:

Patent	Claimed D(0.5) Range	Claimed D(0.9) Range
'734 Claims	100-500 nm	1200-3000 nm
'318 Claims	100-1000 nm	1200-4000 nm

The shared specification[8] repeatedly states that "[t]he particles of meloxicam have a median particle size, on a volume average basis, between 100 nm and 5000 nm. In various cases: the D(0.9) of the particles of meloxicam is less than 3000 nm." '734 patent 2:32-38.[9] The specification also states:

> In some embodiments, the D90 of the particle size distribution, as measured on a particle volume basis, is selected from the group consisting of less than or equal, 4000 nm, 3000 nm, 2000 nm, 1900 nm, 1800 nm, 1700nm, 1600nm, 1500nm, 1400nm, 1300nm, 1200 nm, 1100 nm, or 1000 nm and, in some cases, greater than 900 nm.

Id. at 5:60-67, 7:28-42.

[8] The '318 Patent was filed as a continuation on the '734 patent and shares an identical specification.
[9] See also '734 patent 3:14-18, 4:41-44, 5:19-23.

Furthermore, the specification provides two examples of meloxicam formulations with a defined particle size distribution:

'734 and '318 Specification Examples	**D(0.5)**	**D(0.9)**
Attrited Blend A	260 nm	1945 nm
Attrited Blend B	242 nm	1768 nm

Id. at 20:1-15.

B. Lupin's ANDA Product

In its ANDA application, Lupin specifies that the generic products it intends to market will have a D(0.9) of less than 800 nm. See Lupin's ANDA LMELOX0000554, ECF No. 45-3. In batch records submitted to the FDA in support of the ANDA application, the D(0.5) and D(0.9) measured in samples had the following values:

Lupin's Batch #	**D(0.5)**	**D(0.9)**
H590610	200 nm	393 nm
H590639	204 nm	404 nm
H590653	204 nm	419 nm

Id. at LMELOX0000605, LMELOX0026597, LMELOX0026616-21, LMELOX0026597.

Lupin also tested one of its test batches (the H590653 batch with a D(0.5) of 204 nm and a D(0.9) of 419)) against a batch having a D(0.9) of 1048 nm ("the H690053 batch"). Lupin argued that the pharmacokinetic results were equivalent and concluded that it would not need to control the D(0.5) value if

it were able to control the D(0.9) value. Id. at LMELOX0026598-9.

II. SUMMARY JUDGMENT STANDARD

A motion for summary judgment shall be granted if the pleadings and supporting documents "show[] that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a).

The well-established principles pertinent to summary judgment motions can be distilled to a simple statement: The Court may look at the evidence presented in regard to a motion for summary judgment through the non-movant's rose-colored glasses, but must view it realistically. After so doing, the essential question is whether a reasonable fact finder could return a verdict for the non-movant or whether the movant would, at trial, be entitled to judgment as a matter of law. See, e.g., Celotex Corp. v. Catrett, 477 U.S. 317, 322-3 (1986); Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248 (1986); Shealy v. Winston, 929 F.2d 1009, 1012 (4th Cir. 1991). Thus, in order to defeat a motion for summary judgment, "the party opposing the motion must present evidence of specific facts from which the finder of fact could reasonably find for him or her."

Mackey v. Shalala, 43 F. Supp. 2d 559, 564 (D. Md. 1999) (emphasis added).

When evaluating a motion for summary judgment, the Court must bear in mind that the "summary judgment procedure is properly regarded not as a disfavored procedural shortcut, but rather as an integral part of the Federal Rules as a whole, which are designed 'to secure the just, speedy and inexpensive determination of every action.'" Celotex, 477 U.S. at 327 (quoting Rule 1 of the Federal Rules of Civil Procedure).

III. INFRINGEMENT STANDARDS

While submitting an ANDA constitutes an artificial act of patent infringement for purposes of moving infringement and invalidity challenges forward in time, the patentee must still prove infringement by a preponderance of the evidence. Spectrum Pharm., Inc. v. Sandoz Inc., 802 F.3d 1326, 1336 (Fed. Cir. 2015); see also Glaxo, Inc v. Novopharm Ltd., 110 F.3d 1562, 1567-9 (Fed. Cir. 1997)(finding that the infringement analysis focuses on comparing the asserted patent claims against the ANDA product that is likely to be sold following FDA approval).

A determination of patent infringement requires a two-step analysis. Akzo Nobel Coatings, Inc. v. Dow Chem. Co., 811 F.3d 1334, 1339 (Fed. Cir. 2016). First, the court construes the

asserted claims,[10] and second, it compares the properly construed claims to the accused product. Id. Step one, claim construction, is a question of law. Markman v. Westview Instruments, Inc., 52 F.3d 967, 970-71 (Fed. Cir. 1995)(en banc), aff'd, 517 U.S. 370 (1996). Step two, comparison of the asserted claims to the accused product, requires a determination that every claim limitation or its equivalent is found in the accused product. Warner-Jenkinson Co. v. Hilton Davis Chem. Co., 520 U.S. 17, 29 (1997).

Whether there is infringement, either literally or under the doctrine of equivalents, is a question of fact. Akzo, 811 F.3d at 1339. "As such, it is amenable to summary judgment when no reasonable factfinder could find that the accused product contains every claim limitation or its equivalent." Id.

A. Literal infringement

"To establish literal infringement, every limitation set forth in a claim must be found in an accused product, exactly." Advanced Steel Recovery, LLC v. X-Body Equip., Inc., 808 F.3d 1313, 1319 (Fed. Cir. 2015)(quoting Southwall Techs., Inc. v. Cardinal IG Co., 54 F.3d 1570, 1575 (Fed. Cir. 1995)).

[10] See the Memorandum and Order Re: Claim Construction issued herewith.

B. Infringement by the Doctrine of Equivalents

1. The Doctrine

Where literal infringement of a claim element is not found, infringement under the doctrine of equivalents ("DOE") may be found where the "accused product or process contain[s] elements identical or equivalent to each claimed element of the patented invention." Warner-Jenkinson, 520 U.S. at 40.

"[A]n element in the accused device is equivalent to a claim limitation if it performs substantially the same function in substantially the same way to obtain substantially the same result." Voda v. Cordis Corp., 536 F.3d 1311, 1326 (Fed. Cir. 2008). An equivalence determination is normally reserved for a factfinder. Sage Products, Inc. v. Devon Indus., Inc., 126 F.3d 1420, 1423 (Fed. Cir. 1997).

2. Prosecution History Estoppel

The doctrine of prosecution history estoppel may bar a patentee from alleging that subject matter surrendered during patent prosecution infringes on the claimed invention through DOE. Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 535 U.S. 722, 739-40 (2002)("Festo VIII"). Prosecution history estoppel "hold[s] the inventor to the representations made during the application process and to the inferences that may reasonably be drawn." Id. at 737-8. It can occur in one of two

ways: "(1) [when an applicant makes] a narrowing amendment to the claim ('amendment-based estoppel'); or (2)[when the applicant surrenders] claim scope through argument to the patent examiner ('argument-based estoppel')." Voda, 536 F.3d at 1326. Determination of prosecution history estoppel presents a question of law to be determined by the court, not a jury. Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 344 F.3d 1359, 1368 (Fed. Cir. 2003)(en banc)("Festo X"); see also Biagro Western Sales, Inc v. Grow More, Inc., 423 F.3d 1296, 1302 (Fed. Cir. 2005)(holding that rebutting the presumption of surrender of subject matter through prosecution history estoppel may involve factual determinations, but those factual issues may be decided by the Court).

a. Amendment-Based Estoppel

If an applicant voluntarily surrenders subject matter through a narrowing amendment in order to satisfy any requirement of the Patent Act and is unable to explain the reason for the amendment, a presumption is raised that bars equivalents for the added limitations. Festo VIII, 535 U.S. at 740. The patentee "bear[s] the burden of showing that the amendment does not surrender the equivalent in question." Id. In order to overcome the presumption that prosecution history

estoppel bars a finding of equivalence, the patentee is required show that:

> 1) an alleged equivalent would have been unforeseeable at the time of the amendment and thus beyond a fair interpretation of what was surrendered;
>
> . . . .
>
> 2) the rationale underlying the narrowing amendment [bore] no more than a tangential relation to the equivalent in question; or
>
> . . . .
>
> 3) [there is] some other reason suggesting that the patentee could not reasonably be expected to have described the insubstantial substitute in question.

Festo X, 344 F.3d at 1369-70 (emphasis added).

The tangential relation exception may be satisfied if the "reason for the narrowing amendment was peripheral, or not directly relevant, to the alleged equivalent." Id. at 1369. "Although there is no hard-and-fast test for what is and what is not a tangential relation, it is clear that an amendment made to avoid prior art that contains the equivalent in question is not tangential." Intervet Inc. v. Merial Ltd., 617 F.3d 1282, 1291 (Fed. Cir. 2010)(citing Pioneer Magnetics, Inc. v. Micro Linear Corp., 330 F.3d 1352, 1357 (Fed. Cir. 2003).

b. Argument-Based Estoppel

To invoke argument-based estoppel, "the prosecution history must evince a clear and unmistakable surrender of subject matter." Deering Precision Instruments, L.L.C. v. Vector Distribution Sys., Inc., 347 F.3d 1314, 1326 (Fed. Cir. 2003). "The relevant inquiry is whether a competitor would reasonably believe that the applicant had surrendered the relevant subject matter." Conoco, Inc. v. Energy & Envtl. Intern., L.C., 460 F.3d 1349, 1364 (Fed. Cir. 2006)(citations omitted).

IV. DISCUSSION

Plaintiffs contend that Lupin infringes on the '734 and '318 patents through the doctrine of equivalents (for particle size limitations) and literally (for all other limitations). Pls.' Opp'n. to Defs.' Mot. for Summ. J. 1, ECF No. 59. In its Motion for Summary Judgment, Lupin contends that its ANDA products do not literally infringe on Plaintiffs' patents, that Plaintiffs are estopped from arguing the doctrine of equivalents in light of the prosecution history, and that it is entitled to summary judgment as a matter of law. Defs.' Mot. for Summ. J., ECF No. 44.

A. Lupin's Products do not Literally Infringe

Lupin's ANDA products would not literally infringe on the '734 and '318 claims because the product's particle size distribution would not fall within the claimed ranges. Defs.' Mem. 1-3, ECF No. 45. The '734 patent claims a D(0.5) of 100-500 nm and a D(0.9) of 1200-3000 nm. The '318 patent claims a D(0.5) of 100-1000 nm and a D(0.9) of 1200-4000 nm.

Lupin does not specify a D(0.5) requirement in its ANDA and even asserts that "additional control on d(10) and d(50) is not required once we have control on d(90) values." Lupin's ANDA LMELOX0026598, ECF No. 45-3. Evidence from batch records shows D(0.5) values of 200 nm, 204 nm, and 204 nm in three separate batches. Because Lupin used D(0.5) values of roughly 200 nm and has not specified any other limitations, the Court can presume that Lupin's ANDA product will likely fall within the claimed D(0.5) range of 100-500 nm.

However, Lupin's ANDA product needs a D(0.9) of less than 800 nm for FDA approval. Lupin's ANDA LMELOX0000554, ECF No. 45-3. Any D(0.9) value below 800 nm will fall outside of the minimum claimed value of 1200 nm.

The Plaintiffs concede that Lupin's product would not literally infringe the D(0.9) limitation but maintain that every other claim limitation in the independent claims is literally met. Pls.' Init. Discl. Ex. A 1,10, Ex. B 3,10, ECF No. 45-2.

Because the D(0.9) of Lupin's products does not fall within the claimed range of 1200-3000 nm (or 1200-4000 nm), the Court holds that a reasonable factfinder could not find that Lupin's products will contain every limitation in the '734 and '318 patent claims.

B. Prosecution History Estoppel Bars Plaintiffs from Arguing Doctrine of Equivalents

The Plaintiffs allege that Lupin's ANDA products will infringe the D(0.9) limitation by virtue of the doctrine of equivalents. Id. Plaintiffs contend that a D(0.9) below 800 nm will perform substantially the same function, in substantially the same way, to achieve substantially the same result as the D(0.9) of the claimed amount because of the allegedly broad distribution between the D(0.5) and the D(0.9). Pls.' Opp'n. 19, ECF No. 59.

Lupin contends that Plaintiffs are barred from arguing the doctrine of equivalents because of prosecution history estoppel. Defs.' Mem. 1, ECF No. 45. Lupin argues that Plaintiffs surrendered D(0.9) values below 1200 nm during prosecution of the patent. Id. Without a doctrine of equivalents argument, Lupin contends that its ANDA product would not infringe on the patent claims and that they are entitled to judgment as a matter of law. Id.

The Court finds, by clear and convincing evidence, that Plaintiffs are estopped from arguing that Lupin's ANDA products would infringe on the '734 and '318 patent claims through the doctrine of equivalents because the applicant surrendered any particle size distributions with a D(0.9) below 1200 nm during prosecution through both amendment-based and argument-based estoppel.

1. Prosecution History of '734 and '318 Patents

a. '734 Prosecution History

The prosecution history shows that the '734 patent claimed a D(0.9) value of "less than 3000 nm" in the original application, indicating a range of 0-3000 nm.[11] '734 File History ICTMELOX00000124, ECF No. 44-5. The '734 patent also claimed a D(0.5) range of 100-5000 nm in the original application. Id.

The Examiner rejected the claims in a Non-Final Office Action as obvious (pursuant to 35 U.S.C. § 103) in view of a published Patent Cooperation Treaty ("PCT") application, WO 2005/002542 ("Cooper"). Id. at ICTMELOX00003995-4000. The Examiner argued that Cooper teaches nanoparticulate meloxicam formulations that have a D(0.5) below 2000 nm and a D(0.9) of

[11] The '318 patent was prosecuted separately and at a later time but underwent substantially the same analysis (through narrowing amendments and arguments) as the '734 patent. Therefore, the '318 prosecution history may be referred to interchangeably with the '734 prosecution history.

2000 nm. Id. Cooper's meloxicam formulation also teaches oral dosage forms and desirable pharmacokinetic properties compared to conventional meloxicam formulations. Id.

In a Response to the rejection, the applicant amended the D(0.5) to 100-3000 nm and the D(0.9) to 900-3000 nm. Id. at ICTMELOX00004099-103.

In subsequent responses and interviews with the Examiner, the applicant argued that the claimed D(0.9) value of 900 nm allowed for a much broader distribution between the claimed D(0.5) range, compared to the narrow distribution taught by Cooper. Id. at ICTMELOX00004190, 7. The distribution between D(0.5) and D(0.9) taught by Cooper is exemplified in the following chart which appears as Table 2 in Cooper's specification:

Cooper's Formulations (different stabilizers)	**D(0.5)(nm)**	**D(0.9)(nm)**
PLURONIC® F68	110	226
PLURONIC® F108	108	219
KOLLIDON® 12 PF	90	125
KOLLIDON® 17 PF	95	135
Polysorbate 80	227	322
Sodium Deoxycholate	101	198
Lecithin	169	271
Lysozyme	89	117

Cooper 43:1-4. The applicant argued that a broader particle size distribution (than the roughly 100 nm distribution taught by Cooper's examples) was required to achieve the other claim

limitations (such as desirable pharmacokinetic data). '734 File History ICTMELOX00004190, 97. The applicant even argued that:

> As can be seen from [Table 2 in Cooper], the D90 is very close to the D50 in all cases, and the D90 is below 300 nm. This indicates that nearly all of the particles, on a volume basis are quite small. The present claims, in contrast, require a much larger D90, at least 900 nm. The meloxicam in the formulations described in the present specification have a D90 that is above 900 nm (see description of attrited blends on pages 27-28). Thus, the size characteristics of the meloxicam used by Cooper differs substantially from that of the present claims and from that of the formulations described in the present application.

'318 File History ICTMELOX00004379, ECF No. 44-6 (emphasis added).

The Examiner still upheld the rejection over Cooper in a second Non-Final Office Action. Id. at ICTMELOX00004165-71.

Finally, the claims were further amended to a D(0.5) of 100-500 nm and a D(0.9) of 1200-3000 nm. In an Examiner Interview Summary, the Examiner noted that the amended ranges would "still adequately describe a broader particle size distribution, wherein the D(0.9) is distinct from the median particle size, which was not taught or contemplated by the prior art teachings of Cooper" and would be "commensurate in scope with the data provided in the specification." Id. at ICTMELOX00004211.

The Examiner allowed the claims after the applicant agreed to the amendments. Id. at ICTMELOX00004202-10. In the Reasons for Allowance, the Examiner further explained:

> Cooper also exemplifies particles wherein the D50 for each particle is close to its D90, indicating a narrow particle size distribution. However, instant independent claims 1 and 13 as amended required a much broader particle size distribution, wherein the median particle size (D50) is 100-500 nm, while the D90 is 1200-3000 nm.

Id. at ICTMELOX00004209 (emphasis added). The applicant concurred with the Examiner's explanation. Id. at ICTMELOX00004226.

b. '318 Prosecution History

The '318 patent underwent a similar prosecution as the '734 patent. However, the examiner allowed the claims with a D(0.5) of 100-1000 nm and a D(0.9) of 1200-4000 nm. '318 File History at ICTMELOX00004447. The upper bounds for the D(0.5) and D(0.9) are higher than those of the '734 patent. The prosecution history does not reveal a reason for why the upper bounds of the D(0.5) were allowed to remain at 1000 nm (as opposed to 500 nm as amended in the '734 patent).

The following chart summarizes the narrowing amendments made for the '734 and '318 patents:

Patent No.	**'734**		**'318**	
	D(0.5)(nm)	**D(0.9)(nm)**	**D(0.5)(nm)**	**D(0.9)(nm)**
Original	100-5000	0-3000	100-5000	0-3000
1st Amend.	100-3000	900-3000	100-1000	900-4000
Allowed Amend.	100-500	1200-3000	100-1000	1200-4000

2. Amendment-Based Estoppel Bars DOE

a. '734 Patent

The Plaintiffs clearly narrowed its D(0.5) and D(0.9) values through amendments during prosecution. These amendments were made to overcome a § 103 rejection over Cooper. Therefore, a presumption is raised that bars a DOE argument for any product with a D(0.5) greater than 500 nm and a D(0.9) below 1200 nm. The equivalent in question (Lupin's ANDA product) would have a D(0.5) of roughly 200 nm[12] and a D(0.9) of less than 800 nm, falling below the claimed 1200 nm threshold. The Plaintiffs have the burden of rebutting the presumption and may do so by showing that the rationale for surrendering values less than 1200 nm is

[12] Lupin argued to the FDA in a response to an Information Request that it would not be necessary to control the D(0.5) value if they were able to control the D(0.9) value. Lupin's ANDA LMELOX0026597-9, ECF No. 45-3. However, the D(0.5) value will have to fall somewhere between 0-800 nm (with a D(0.9)below 800 nm), and batch samples indicate D(0.5) values of about 200 nm.

only tangentially related to the equivalent in question. Plaintiffs have not done so.

Plaintiffs argue that the amendments were made to demonstrate a broader particle size distribution between D(0.5) and D(0.9) over Cooper's. Pls.' Opp'n. 1-2, ECF No. 59 (emphasis added). It further argues that the distribution is only tangentially related to Lupin's D(0.9) of below 800 nm. Id. Even if viewing the prosecution history in a light most favorable to the Plaintiffs and accepting its argument that the reason for the narrowing amendments was to demonstrate a broad particle size distribution, the Plaintiffs have not rebutted the presumption barring a DOE argument. Lupin's D(0.9) value of less than 800 nm is not merely tangentially related to the reason for narrowing the amendments. In fact, it is quite relevant.

The breadth of particle size distribution is defined by two parameters: the D(0.5) and the D(0.9) values. The Examiner explained that the D(0.9) value was ultimately amended to a minimum of 1200 nm for two reasons: (1) to demonstrate a broader particle size distribution [than Cooper's] that was (2) "commensurate in scope with the data provided in the specification." Id. at ICTMELOX00004211.

While the examiner did not issue a formal § 112 rejection for lack of support in the specification, the Examiner clearly required the patentee to amend the D(0.9) value from 900 nm to

1200 nm (and the D(0.5) from 100-1000 nm to 100-500 nm) so that the claims were "commensurate in scope with the data provided in the specification." Id. The Examiner quite generously allowed the D(0.9) value to remain at 1200 nm while the only two examples supported by data in the Plaintiffs' specification had D(0.9) values of 1945 nm and 1768 nm (compared to D(0.5) values of 260 nm and 240 nm). '734 patent 20:1-15 (emphasis added).

Moreover, the Examiner required the patentee to amend its D(0.9) value from 0 nm to 1200 nm (even after amending to 900 nm) in order to distinguish the D(0.9) value from the D(0.5) value so that the claimed particle size distribution was sufficiently broad to overcome the narrower distribution taught by Cooper. Based on the data provided in the specification and the narrow distribution taught by Cooper, the Examiner concluded that a particle size distribution is sufficiently broad only if the D(0.5) is 100-500 nm and the D(0.9) is 1200-3000 nm. This indicates that any D(0.9) value less than 1200 nm is too close to the claimed D(0.5) value of 100-500 nm (indicating a particle size distribution too narrow to overcome Cooper) and too low to be supported by the data in the specification.

Plaintiffs argue that if it did surrender any territory, it was the D(0.5) range of 89-277 nm and the D(0.9) of 119-322 nm as taught by Cooper. Pls.' Opp'n. 32, ECF No. 59. This argument is not supported by the prosecution history. If this were the

case, the applicant could have claimed a D(0.9) range of 322-3000 nm. Instead, Plaintiffs attempted to claim a minimum D(0.9) of 900 nm, which was rejected, and were forced to claim a minimum D(0.9) of 1200 nm in order to gain allowance. 734 File History ICTMELOX00004211, ECF No. 44-5.

Plaintiffs cannot now allege that Lupin's ANDA product will also have a sufficiently broad particle size distribution profile with a D(0.9) value below 800 nm and a D(0.5) of roughly 200 nm. The Plaintiffs surrendered this territory through narrowing amendments during prosecution. The Examiner expressly concluded that in order to demonstrate a broad distribution profile (to overcome Cooper) that was commensurate in scope with the data provided in the specification, the applicant had to narrow the D(0.5) to 100-500 nm and the D(0.9) to 1200-3000 nm through amendments. '734 File History ICTMELOX00004211, ECF No. 44-5. The Examiner allowed the claims only under these conditions.

During the motions hearing, the Plaintiffs also cited Eli Lilly and Co. v. Dr. Reddy's Labs., LTD, et al., No. 1:16-cv-00308-TWP-MPB, slip op. at *6-7 (S.D. Ind. Dec. 14, 2017) to support its argument that the tangential relation exception applies. Mot. for Summ. J. Hr. 77:15-79:10, Dec. 18, 2017. However, this case is not binding precedent on this Court and merely provides an example of when the tangential relation

exception may be appropriate. In Eli Lilly, a claim for a broad class of pharmaceutical compounds (antifolates) was limited to a specific salt form of a particular antifolate compound (pemetrexed disodium) through amendments during prosecution to overcome a reference that taught the broader class of antifolates. Id. The alleged equivalent was a different salt form of pemetrexed (pemetrexed ditromethamine). Id. The Court held that the amendment was merely tangential to the equivalent because the amendment was made to limit the invention to the active pemetrexed ingredient (from a broader class of drugs), and the specific salt form of pemetrexed was not relevant. Id.

The present case is distinguishable from Eli Lilly because the amendments to the '734 patent were made to narrow the ranges for D(0.5) and D(0.9) to specific values in order to demonstrate a broader particle size distribution over the prior art. The narrowed D(0.5) and D(0.9) values define the scope of the amendment. The alleged equivalent directly relates to the amendments because Lupin's ANDA products would have a narrower particle size distribution profile that falls within the surrendered territory. Any variation of D(0.5) and D(0.9) values outside of the specific ranges allowed by the Examiner would contradict the purpose for the amendment. The amendments in the present case did not limit the claims from a broader genus of drugs to a specific species as in Eli Lilly.

The Court concludes that Plaintiffs have not rebutted the presumption (through the tangential relation exception) that Plaintiffs have surrendered D(0.9) values of less than 1200 nm, and Plaintiffs are thus barred from arguing that Lupin's products will infringe through doctrine of equivalents for the '734 patent.

b. '318 Patent

The '318 patent claims were amended from a D(0.5) of 0-5000 nm and a D(0.9) of 0-4000 nm to final allowed values of a D(0.5) of 100-1000 nm and a D(0.9) of 1200-4000 nm. The '318 patent underwent a substantially similar prosecution history to that of the '734 patent except that the allowed maximum D(0.5) value is 1000 nm (as opposed to 500 nm in the '734 patent), and the maximum D(0.9) value is 4000 nm (as opposed to 3000 nm in the '734 patent).

As allowed by the examiner, the '318 patent conceivably permits a much narrower particle size distribution profile (with a maximum D(0.5) of 1000 nm and a minimum D(0.9) of 1200 nm).[13] However, based on the '734 prosecution history and lack of explanation by the applicant in the '318 prosecution history, it

[13] Theoretically, the D(0.5) could be as high as 1000 nm with a D(0.9) as low as 1200 nm, resulting in a 200 nm particle size distribution between the D(0.5) and D(0.9). The minimum particle size distribution in the '734 patent is 700 nm (with a maximum D(0.5) of 500 nm and a D(0.9) of 1200 nm).

is reasonable for the Court to conclude that the Examiner allowed the maximum D(0.5) value to remain at 1000 nm (instead of 500 nm as in the '734 patent) because the D(0.9) value was also raised to 4000 nm (from 3000 nm as in the '734 patent). It is reasonable to conclude that the higher D(0.5) values corresponded to the higher D(0.9) values.[14] The Court is entitled to make such factual determinations regarding prosecution history estoppel. Festo X, 344 F.3d at 1368; see also Biagro Western Sales, 423 F.3d at 1302.

Therefore, the same presumptions of surrendered territory are raised as in the '734 patent, and the same analysis for rejecting the tangential relation exception applies for the '318 patent.

3. Argument-Based Estoppel Also Bars DOE

The prosecution history clearly and convincingly shows that Plaintiffs surrendered D(0.9) values below 1200 nm through arguments to the Examiner for the Patents-in-Suit such that a

[14] In light of the prosecution history, the Court is not willing to conclude that any claimed D(0.5) value can correspond to any claimed D(0.9) value to produce the necessary particle size distribution, particularly for the '318 patent. The Examiner expressly rejected claims with narrower particle size distributions in the '734 prosecution history and allowed higher D(0.5) values in the '318 patent when the maximum D(0.9) was also raised.

competitor would reasonably believe that the subject matter had been surrendered.

For many of the same reasons discussed above, the applicant repeatedly argued to the Examiner that its invention required a higher D(0.9) value in order to demonstrate a broader particle size distribution than Cooper's. The applicant also repeatedly insisted that the D(0.9) must be at least 900 nm. Most notably during prosecution of the '318 patent, the applicant argued:

> As can be seen from [Table 2 in Cooper], the D90 is very close to the D50 in all cases, and the D90 is below 300 nm. This indicates that nearly all of the particles, on a volume basis are quite small. The present claims, in contrast, require a much larger D90, at least 900 nm. The meloxicam in the formulations described in the present specification have a D90 that is above 900 nm (see description of attrited blends on pages 27-28). Thus, the size characteristics of the meloxicam used by Cooper differs substantially from that of the present claims and from that of the formulations described in the present application.

'318 File History ICTMELOX00004379, ECF No. 44-6. (emphasis added). When referring to Cooper's D(0.9) below 300 nm, the applicant used strong language to argue that its D(0.9) "require[s] a much larger D90" that is "at least 900 nm." Id. (emphasis added). The Examiner relied on these assertions when allowing the patent, stating (in the '734 patent prosecution) that "claims 1 and 13 as amended require a much broader particle size distribution [than Cooper], wherein the median particle

size (D50) is 100-500 nm, while the D90 is 1200-3000 nm." '734 File History, ICTMELOX00004209, ECF No. 44-5. The applicant expressly agreed to the Examiner's statements in responding to the Notice of Allowance. Id. at ICTMELOX00004226.

Furthermore, after the applicant amended the D(0.9) to 900 nm, the examiner issued a 35 U.S.C. § 112 rejection for failure to comply with a written description requirement. '318 File History ICTMELOX00004397-8, ECF No. 44-6. The rejection stemmed from the interpretation of the misspelled word, "greater," in the following paragraph of the specification:

> In some embodiments, the D90 of the particle size distribution, as measured on a particle volume basis, is selected from the group consisting of less than or equal, 4000 nm, 3000 nm, 2000 nm, 1900 nm, 1800 nm, 1700nm, 1600nm, 1500nm, 1400nm, 1300nm, 1200 nm, 1100 nm, or 1000 nm and, in some cases, greter [sic] than 900 nm.

Id. (emphasis added). In response, the applicant argued that "[t]he first part of the sentence lists a variety of upper limits for the D90" and "[t]he last part of the sentence provides a lower limit for the D90, 'greater than 900 nm.'" Id. at ICTMELOX00004426. The applicant reiterated that "it is clear from the context that the paragraph[]... provide[s] a lower limit for the D90 (greater than 900 nm)." Id. at ICTMELOX00004428.

While the § 112 rejection merely pertained to the misspelling of the word "greater" and its interpretation, the applicant made a clear and unmistakable argument that the lower limit for the D(0.9) is 900 nm. This shows that values below 900 nm were surrendered and never supported in the specification and further supports the applicant's previous arguments to the examiner that a D(0.9) of greater than 900 nm is required to establish a broad particle size distribution.

The applicant had every opportunity during prosecution to better define the breadth of particle size distribution between D(0.5) and D(0.9). It might have been better to express the claim in terms of a percentage or specific difference between D(0.5) and D(0.9) while not specifying the exact D(0.9) values. Lack of data for support clearly made it difficult to do so. However, in fact the applicant clearly and unmistakably argued that D(0.9) values were required to be at least 900 nm (and ultimately 1200 nm).

Through its arguments during prosecution, the applicant clearly and unmistakably surrendered D(0.9) values below 1200 nm (and below 900 nm) in order to establish a broader particle size distribution profile consistent with data provided in the specification. A competitor would reasonably believe that the claims do not encompass D(0.9) values below 1200 nm because D(0.9) values below 1200 nm would conceivably be too small to

generate the broad particle size distribution allegedly required to produce the claimed pharmacokinetic effects. Therefore, the Court finds that Plaintiffs are also barred from alleging infringement through the doctrine of equivalence because of argument-based estoppel.

C. Lupin is Entitled to Summary Judgment

The Plaintiffs concede that Lupin's ANDA products would not literally infringe on either the '734 or '318 patent claims.

In order to prove infringement through equivalents, the Plaintiffs allege that a genuine dispute of material fact exists regarding the Examiner's comments and the reason for allowing the amended claims in the '734 and '318 patents. Pls.' Opp'n. 22, ECF No. 59. However, prosecution history estoppel is a question of law for the Court to decide, including factual determinations related to rebutting prosecution history estoppel. Festo X, 344 F.3d at 1368; see also Biagro Western Sales, 423 F.3d at 1302.

Even when viewing the prosecution history in a light most favorable to the Plaintiffs, the Plaintiffs are, as a matter of law, barred from alleging infringement through the doctrine of equivalents because of both amendment-based and argument-based prosecution history estoppel.

Because the Plaintiffs cannot prove literal infringement of the '734 and '318 patents and are barred from proving infringement through the doctrine of equivalents, the Court finds that there are no remaining genuine issues of material fact, and Lupin is entitled to judgment as a matter of law.

V. CONCLUSION

For the foregoing reasons:

1. Defendant Lupin's Motion for Summary Judgment [ECF No. 44] is GRANTED.

2. Judgment shall be entered in favor of Defendants and against Plaintiffs, dismissing all claims of the First Amended Complaint [ECF No. 42]. All counterclaims shall be DISMISSED AS MOOT.

3. Judgment shall be entered by separate Order.

SO ORDERED, on Thursday, February 1, 2018.

/s/
Marvin J. Garbis
United States District Judge