IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF WEST VIRGINIA

DEY, L. P. and DEY, INC.,

Plaintiffs,

v. **// CIVIL ACTION NO. 1:09CV87**
(Judge Keeley)

TEVA PARENTERAL MEDICINES, INC.,
TEVA PHARMACEUTICALS USA, INC., and
TEVA PHARMACEUTICAL INDUSTRIES, LTD.,

Defendants.

FINDINGS OF FACT AND CONCLUSIONS OF LAW GRANTING JUDGMENT IN FAVOR OF THE PLAINTIFFS, DEY L.P. AND DEY, INC.

I. INTRODUCTION

The plaintiffs, Dey, L.P. and Dey Inc. (collectively "Dey"), have asserted eight causes of action against the defendants, Teva Parenteral Medicines, Inc., Teva Pharmaceuticals USA, Inc., and Teva Pharmaceutical Industries, Ltd.(collectively "Teva") regarding Teva's infringement of four of Dey's patents associated with the drug Perforomist®.[1] (Dkt. No. 1). On July 17, 2013, the Court granted partial summary judgment in favor of Dey on the issue of infringement, finding that the product described in Teva's Abbreviated New Drug Application ("ANDA") infringes claims 1 and 65 of the 6,667,344 Patent ("the '344 Patent"). (Dkt. No. 211). Teva

[1]These four patents include: 6,667,344 ("the '344 Patent"), 6,814,953 ("the '953 Patent"), 7,348,362 ("the '362 Patent"), and 7,462,645 ("the '645 Patent") (collectively, the "patents-in-suit").

contends that infringement is warranted in this instance because the patents-in-suit are invalid on a number of grounds.

Between July 29, 2013 and August 6, 2013, the Court conducted a bench trial on Teva's invalidity defenses of anticipation, obviousness, and enablement. In lieu of closing arguments, the parties submitted post-trial memoranda. All briefing concluded on October 29, 2013.

On the basis of the record and the applicable law, the Court issues the following findings of fact and conclusions of law pursuant to Fed. R. Civ. P. 52,[2] and concludes that Teva has failed to meet its burden of proving by clear and convincing evidence the invalidity of the patents-in-suit.

II. THE RECORD AND RELEVANT PROCEEDINGS

A. PROCEDURAL HISTORY

In a letter dated May 12, 2009, Teva, the world's largest manufacturer of generic drugs, notified Dey that it had filed an ANDA seeking United States Food and Drug Administration ("FDA") approval to market a generic version of Perforomist®. Pursuant to

[2]To the extent that any findings of fact may be deemed conclusions of law, they shall also be considered conclusions of law; to the extent that any conclusions of law may be deemed findings of fact. Miller v. Fenton, 474 U.S. 104, 113-14, 106 S.Ct. 445, 88 L.Ed.2d 405 (1985).

21 U.S.C. § 355(j)(2)(A)(vii)(IV), Teva also filed a Paragraph IV certification with the FDA, alleging that the four patents issued to Dey for Perforomist® are invalid, unenforceable, and not infringed by Teva's manufacture or sale of the proposed generic drug product.

Dey responded to Teva's ANDA by filing this action pursuant to the Hatch-Waxman Act, which "gives a drug patent owner the right to bring an action for infringement upon the filing of a paragraph IV certification." Bristol-Myers Squibb Co. v. Royce Laboratories, Inc., 69 F.3d 1130, 1135 (Fed. Cir. 1995) (citing 35 U.S.C. § 271(e)(2)(A)). When a branded manufacturer files suit pursuant to that right within 45 days of notice of the Paragraph IV certification, as was the case here,[3] the litigation automatically stays the generic's entry to the market. 21 U.S.C. § 355(j)(5)(B)(iii).

The purpose of the Hatch Waxman Act, then, is to shift risks between the patent holder and generic manufacturer, allowing the generic manufacturer to challenge the validity of a patent without risking damages from infringement. More importantly, for purposes of this trial, this structure allows the parties to try the dueling

[3]Dey filed suit 42 days after receiving notice of Teva's ANDA.

issues of patent infringement and invalidity in one action. Ark. Carpenters Health & Welfare Fund v. Bayer AG, 544 F.3d 1323, 1338 (Fed. Cir. 2008).

B. Claim Construction

Following extensive briefing and a claim construction hearing, the Court issued a Memorandum Opinion and Order Construing Patent Claims, (dkt. no. 99), which construed the patent claims at issue to the extent the parties disputed the meaning of claim terms. For the purposes of this trial, that Memorandum Opinion and Order "define[s] the invention to which the patentee is entitled the right to exclude." Phillips v. AWH Corp., 415 F.3d 1303, 1312 (Fed. Cir. 2005).

C. Infringement

On September 21, 2012, Dey moved for partial summary judgment on the issue of infringement. (Dkt. No. 159). Following a hearing, the Court granted the motion, (dkt. no 211), which Teva did not appeal. Thus, the only issue remaining is whether Teva has established, by clear and convincing evidence, that the patents-in-suit are invalid.

D. Expert and Other Witnesses

1. Dr. Peter Barnes

Dr. Peter Barnes, a witness proffered by Dey, is an expert in the field of respiratory disease research. He received a BM, BCh (MD equivalent) degree from the University of Oxford in 1972. He also received a Medical Research degree and later a Doctorate in Science from the University of Oxford.

Dr. Barnes is currently President-Elect of the European Respiratory Society. Since 1987, he has been Professor of Thoracic Medicine at the National Heart and Lung Institute, Head of Respiratory Medicine at Imperial College, London, and honorary Consultant Physician at Royal Brompton Hospital.

Since 1978, Dr. Barnes has focused his research on cellular and molecular mechanisms of asthma and COPD. He has published over 1,000 articles in peer reviewed journals and has written, edited or co-edited over 1000 articles on the topics of asthma, COPD and pulmonary pharmacology. In addition to his research work and medical practice, Dr. Barnes has consulted with several pharmaceutical companies involved in the development and marketing of drugs for the treatment of asthma and COPD. (Dkt. No. 201).

2. Dr. Jayne Hastedt

Dr. Jayne Hastedt testified for Dey as an expert in the field of pharmaceutical compositions. Dr. Hastedt received an Associate in Science degree in Chemical Engineering from Waterbury State Technical College in 1980, and a Bachelor of Arts degree in Biochemistry from Western Connecticut State University. She also received a Master in Science and later a Ph.D. in Pharmaceutics from the University of Wisconsin-Madison School of Pharmacy.

Dr. Hastedt is currently CEO and Co-Founder of JDP Pharma Consulting, LLC. She also serves as an Adjunct Professor at the Thomas J. Long School of Pharmacy and Health Sciences at the University of the Pacific. Previously, she worked as a Research Investigator and Researching Leader in the Pharmaceutics Department at Glaxo Research Institute. She also held positions as Product Development Manager, Director of ChemPharm Management, and Senior Director for West Coast ChemPharm while working for ALZA Corporation, a Johnson & Johnson Company.

Dr. Hastedt has lectured on dissolution and diffusion at the University of North Carolina School of Pharmacy and California Polytechnic State University. She has also served as a reviewer for various pharmaceutical journals.

3. Dr. Imtiaz Chaudry

Dr. Imtiaz Chaudry is one of the named inventors on the patents-in-suit. He received his Master in Science degree from the Philadelphia College of Pharmacy and Science and his Ph.D. in Pharmacy from St. John's University. He is also a licensed pharmacist.

Dr. Chaudry is currently Senior Vice President of Scientific Affairs at Dey, where he leads a research group charged with developing new drug compounds for the company's future branded products line. Dr. Chaudry has been employed by Dey since 1999. Prior to joining Dey, he was Vice President of Pharmaceutical Development at Schering-Plough Research Institute, where he worked for over two decades.

Dr. Chaudry has published over 20 articles in peer reviewed scientific journals. He has served on the University of Kansas, Drug Delivery Center, Scientific Advisory Board, and was a member of the Board of Governors of the Controlled Release Society for Bioactive Materials. (Dkt. No. 201).

4. Dr. Steve Wald

Dr. Steve Wald is a former employee of Sepracor, Inc. ("Sepracor"), where he worked from 1985-2009. Dr. Wald received a

Master in Science degree from the University of California, Berkeley, and a Bachelor of Science degree in Chemical Engineering from Cornell University.

While at Sepracor, Dr. Wald served as Senior Vice President of Chemistry & Pharmaceutical Sciences and also of Commercial and Technical Operations. Notably, for purposes of the scope of this litigation, Dr. Wald oversaw the development of the product Brovana®, including Sepracor's Transactions with Automated Liquid Packaging ("ALP"), during his time at Sepracor.

5. Dr. Leslie Hendeles

Dr. Leslie Hendeles is an expert witness proffered by Teva in the field of inhalation solutions. Dr. Hendeles received a Doctor of Pharmacy degree from the University of Southern California in 1969. He currently is a professor in the College of Pharmacy and in the Department of Pediatrics at the University of Florida. He also is a practicing Clinical Pharmacist at the University of Florida's Pediatric Pulmonary Clinic.

Dr. Hendeles has taught, researched, and made recommendations to physicians about inhalation solutions for over thirty years. He has also conducted clinical trials and published extensively regarding pharmaceutical formulations for bronchoconstriction. He is a consultant to the Pulmonary/Allergy Drugs Division of the

Center for Drug Evaluation and Research at the U.S. Food and Drug Administration where he assists in evaluating the safety and effectiveness of drugs used to treat pulmonary and allergic diseases.

In the last five years, Dr. Hendeles has conducted at least ten clinical trials relating to the treatment of asthma and cystic fibrosis. He is currently conducting a study to determine the bioequivalence of formoterol delivered by novalizer and aerolizer devices. (Dkt. No. 201).

6. Dr. Paul B. Myrdal

Dr. Paul B. Myrdal was proffered by Teva as an expert in the field of inhalation drug delivery techniques and technologies. He received a Bachelor of Science degree in Molecular and Cellular Biology from the University of Arizona in 1989, and a Ph.D. in Pharmaceutical Chemistry from the University of Arizona in 1994. Currently, he is an Associate Professor in Pharmaceutics at the University of Arizona. Prior to that, from 2000-2006, he served as an Assistant Professor in Pharmaceutics at that university.

Dr. Myrdal's research at Arizona includes the understanding of the chemistry and product performance of HFA-based metered dose inhalers, the development of topical formulations for skin cancer, formulation of poorly soluble compounds and evaluation of oral

bioavailability, preclinical testing of nebulized agents for the chemoprevention of lung cancer, and traditional preformulation and formulation activities.

From 1995-2000, Dr. Myrdal worked at 3M Pharmaceuticals, where he was involved in the development of conventional and novel inhalation delivery techniques and the preformulation and formulation of new chemical entities for pulmonary delivery. He has also served as a consultant for the pharmaceutical industry on various preformulation, formulation, and related drug delivery techniques.

III. FINDINGS OF FACT

A. Dey's Development of Perforomist

Through the process of developing Perforomist®, Dey invented, patented, and sold a unique inhalation solution for the treatment of chronic obstructive pulmonary disease ("COPD"). Perforomist® embodies the attributes of long-term stability and a ready to use unit dose of a long-acting beta agonist ("LABA") suitable for nebulization. To date, Perforomist® and a formerly infringing but now licensed competitor, Brovana®, are the only LABAs approved in the United States for treatment of COPD by nebulization. (Tr.944:8-17 (Hendeles).)

Dey's goal in developing Perforomist was to become "a leader in the area of nebulization. [Dey's] strong view was that there [was] an

unmet need as far as bringing new medications in COPD for nebulization." (Tr. 47:22-25 (Chaudry).) Dey recognized that a significant segment of the COPD population, namely elderly patients, had trouble using the dry powder inhaler ("DPI") and metered dose inhaler ("MDI") treatments then available, as these required coordinating inhalation with manipulation–precisely the abilities many elderly patients lacked.

Dey came to identify formoterol, a LABA, as a "good opportunity for developing [a] nebulization product." (Tr. 48:20-49:3 (Chaudry), 254:22-255:3 (Barnes).) Formoterol was first discovered as an effective bronchodilator, and patented (U.S. Patent No. 3,994,974 ("Murakami")) in the 1970s. (Tr. 54:2-5 (Chaudry).) Formoterol quickly became widely used outside the United States. At the time Dey began its development program in 1999, however, "there [were] no formoterol product[s] for nebulization anywhere in the world," and no formoterol products whatsoever in the United States. (TX 269; Tr. 57:14-19 (Chaudry); TX 1, 7:37-46.)

From the start, Dey's scientists faced the challenge of the instability of formoterol in aqueous solutions. Two of those scientists, Drs. Partha Banerjee and Imtiaz Chaudry, leaders of the formoterol inhalation solution project at Dey, knew that formoterol was "prone to degradation by hydrolysis." (Tr. 58:5-15, 146:20-147:1

(Chaudry).) A search of the leading formoterol literature at the time confirmed formoterol's aqueous instability. (Tr. 58:16-25, 60:23-61:7, 78:25-79:7 (Chaudry).)

For example, U.S. Patent No. 6,040,344 ("Gao") taught that "because of the problematic stability" of formoterol "in aqueous solutions," a formulation of formoterol in "citrate buffered saline, buffered to pH 5 . . . is not attractive for long term storage." (TX 15, 20:1-6.) Dey scientists understood from this that "formoterol in an aqueous[,] or water-based[,] solution is not adapt[ed] or appropriate for long-term storage." (Tr. 66:25-67:10 (Chaudry).)

The Gao Patent also referred to U.S. Provisional Application 60/061,363 (later issued as U.S. Patent No. 6,161,536 ("Redmon")), which stated that formoterol is "not sufficiently stable in an aqueous environment to provide a practical shelf life for the aqueous formulation" and suggested instead to "make up the [formoterol] solution immediately before use." (TX 17, 1:53-55, 62-64; TX 612 (Redmon PCT publication).) The Dey scientists thus learned that it would not be feasible to "mix the [aqueous] solution and the [formoterol] dry-powder and then keep it in that form for periods of weeks or months before using it." (Tr. 69:6-11 (Chaudry).)

According to U.S. Patent No. 6,150,418 ("Hochrainer"), "formoterol cannot be stored in a sufficiently stable manner in a

solution to guarantee the pharmaceutical quality of the formulation over lengthy periods of time." (TX 13, 1:30-35.) On the contrary, Hochrainer taught an "active substance concentrate" that could be stored and then "converted by dilution into a therapeutically effective formulation" to be used "within a few minutes or possibly a few seconds." (TX 13, 1: 62-67, 5:21-26.) From this, the Dey team came to understand that when formoterol is present in water, "a very highly concentrated solution or a suspension" is necessary to "have reasonable stability for a longer storage." (Tr. 69:24-70:8 (Chaudry).)

Due to the technical challenges they faced, Drs. Chaudry and Banerjee "were highly skeptical that a stable, aqueous-based nebulized formulation, . . . c[ould] be developed." (Tr. 78:25-79:3; 82:9-12, 189:11-14 (Chaudry).) They were not aware of any "ready fixes" that would result in a stable, ready-to-use aqueous solution. (Tr. 79:8-12 (Chaudry).) Furthermore, they were not confident that, even if they could identify a solution composition that would maximize formoterol's stability, it would have sufficient stability to be use effectively. (Tr. 89:2-4, 90:13-21, 91:2-16, 93:21-25 (Chaudry).)

In August 1999, Dey began to test "the amount of formoterol in a solution and also be able to test the breakdown products" of

formoterol (Tr. 83:7-14, 85:23-25 (Chaudry)). The Dey team used these test results to generate pH-solubility and stability data for formoterol. (TX 61) They determined the solubility at pH 3, 4, 5, and 7 (TX 254), which surprisingly was "more than adequate solubility in water to develop a nebulization product." (Tr. 96:1-4, 10-20 (Chaudry).) Dey also discovered that formoterol was most stable at pH 5. (TX 254; Tr. 98:15-17, 99:17-23 (Chaudry); TX 293.1(discussing later experiments confirming maximum stability between pH 4.8 and 5.1).)

Based on these experiments, Dr. Stephan Pham, a scientist who joined Dey in 2000 (Tr. 99:3-10 (Chaudry)), determined that formoterol degradation was likely affected by solution pH, buffer concentration, and ionic strength, but the "extent of the individual effects" remained to be determined. (TX 69). The team also "knew by [September 2000] what other ingredients [they] would like to use and [had in] mind a core formulation" for further refinement. (Tr. 100:2-13 (Chaudry).) Dr. Pham focused on formulations containing 5, 10, and 20 mM citrate, acetate, and phosphate buffers, to control pH, and sodium chloride, to control ionic strength. (TX 80).

Dr. Pham's experiments illustrated that "buffer concentration had no appreciable effect on [formoterol stability] in pH region 4.6 – 5.6," but did have a significant effect within other pH ranges. (TX

293.1; TX 80; Tr. 103:5-8 (Chaudry).) The effect of buffer concentration was a subject other researchers had failed to address. Ultimately, Dey selected a buffer concentration of 20 mM to ensure that the pH did not drift upward over time, as had occurred with lower buffer concentrations. (TX 293.1; Tr. 103:21-104:24 (Chaudry).) Dr. Pham also determined that the sodium chloride concentration necessary for isotonicity "would have a minimal effect on the [formoterol fumarate] stability" in a buffered pH 5 solution. (TX 293.1; TX 80; Tr. 105:11-22 (Chaudry).)

Dr. Pham also tested the stability of a version of Dey's "core formulation" (5 mM acetate buffer at pH 5.2, with an ionic strength of 0.05), and employed Arrhenius kinetics to project its shelf life. (See, TX 80). Contrary to expectations, by November, 2000 Dey had discovered that this formulation had an estimated shelf life (90% of the initial formoterol remaining) of about six years at 5°C and about eight months at 25°C (approximately room temperature). (TX 72; TX 293.1).

After confirming the stability of the core formulation, Dey then began to refine it. The scientists chose a formulation containing a citrate at pH 5 (TX 80) and, ultimately, a 20 mM citrate buffer concentration. (Tr. 112:3-14 (Chaudry).) Later, based on clinical studies conducted in 2003, Dey chose a formoterol dose that was

similar to the standard dose of Foradil® (Tr. 112:15-25, 164:14-22 (Chaudry)), a formoterol DPI product approved by the FDA in February of 2001. (Tr. 55:16-18 (Chaudry); Tr. 841:17-19 (Hendeles).)

Dey had never considered refrigeration, by itself, to be a viable strategy, and its tests confirmed this suspicion. (TX 12; Tr. 117:18-119:5, 198:2-10 (Chaudry).) Dey's testing of formoterol in water showed that, after six months of storage at 5°C, only 91% of the initial formoterol remained. (TX 12; Tr. 117:18-119:5 (Chaudry) (extrapolating to 18 to 20% degradation after one year).) After six months at room temperature, only 80% formoterol remained. (TX 12; Tr. 117:18-119:5 (Chaudry) (interpolating to 3 to 4% degradation after one month).) This was not sufficient for Dey; it wanted to create a formoterol product with "a shelf life of 24 months at [a] long-term storage condition, including 3 months at room temperature after dispensing" from the pharmacy. (TX 293.1; Tr. 195:13- 20 (Chaudry).) Formoterol in water satisfied neither of these requirements. After a year at 5°C (predicted 18-20% degradation), plus a month at room temperature (3-4% degradation), formoterol in water would degrade at least 20 percent (Tr. 117:18-119:5, 198:2-10 (Chaudry)), if not more. Reflecting long-term storage needs, Dey's patents require that at least 80% formoterol remain after consecutive storage conditions of

"one year at 5°C refrigeration and one month at room temperature." (Tr. 118:4-8 (Chaudry); e.g., TX 1, claim 3.)

The stable, ready-to-use formoterol inhalation solution that Dey invented is now marketed as Perforomist®. Perforomist® is indicated for "[l]ong term, twice daily (morning and evening) administration in the maintenance treatment of bronchoconstriction" in patients with COPD. (TX 49; Tr. 1197:2-9 (Graybill); Tr. 1007:21-24 (Hendeles).) Each vial of Perforomist® contains 2mL of 10 µg/mL formoterol fumarate in "an isotonic, sterile aqueous solution containing sodium chloride, pH adjusted to 5.0 with citric acid and sodium citrate." (TX 49). The drug is refrigerated at a temperature between 2-8°C before being sold to the consumer. (TX 49; Tr. 154:1-6; 163:9-15 (Chaundry).) Once sold, it is expected that Perforomist® may be successfully stored at room temperature (25°C) for up to three months. Id.

B. The Patents-In-Suit

The parties have stipulated[4] that the proposed generic product described in Teva's ANDA infringes four of Dey's patents. (TX 871). The first two patents, the '344 and '953 Patents, entitled

[4]The stipulation is a result of Teva's failure to appeal from the Court's July 17, 2013 partial summary judgment ruling, in which the Court held that Teva's ANDA infringes the patents-in-suit.

"Bronchodilating Compositions and Methods" (the "First Family" patents), derive from provisional U.S. patent application 60/284,606 and share essentially identical specifications. The '362 and '645 Patents, entitled "Bronchodilating Beta-Agonist Compositions and Methods" (the "Second Family" patents), derive from provisional U.S. patent application 60/486,386. They too share essentially identical specifications that closely resemble those of the First Family patents.

All four patents-in-suit claim aqueous compositions of formoterol that allow the compositions to remain suitable for direct administration by nebulization during long-term storage. They also cover methods for using these compositions to treat broncho-constrictive disorders:

- The '344 Patent claims pharmaceutical compositions of formoterol that are stable during long term storage and suitable for direct administration (TX 1; Tr. 225:25-226:2 (Barnes));
- The '953 Patent claims methods of administering such compositions for the treatment of bronchoconstrictive disorders (TX 4; Tr. 226:3-4 (Barnes));

- The '362 Patent claims various "unit dose" formulations of formoterol and methods of using the same. (TX 7; Tr. 226:5-6 (Barnes)); and
- The '645 Patent claims methods for treating bronchoconstriction, including COPD, using such "unit dose" formulations of formoterol (TX 9; Tr. 226:7-9(Barnes)).

Because of terminal disclaimers, all four patents will expire on June 22, 2021. (TX 49).

C. Prosecution of the Patents-In-Suit

During the prosecution of the four patents-in-suit, examiners at the U.S. Patent and Trademark Office ("PTO") considered a number of prior art references (Tr. 232:1-3 (Barnes)), including, but not limited to:

- Murakami (TX 5; TX 8 at DEY-TV0008942; TX 10 at DEYTV0009176);
- Gao (TX 2 at DEY-TV0000141-142; TX 5 at DEY-TV0004549; TX 8 at DEYTV0004814, '8937-940, '943, '974-978, '9032-035, '049-051; TX 10 at DEYTV0009173-174, '177);
- Redmon (TX 2 at DEY-TV0000141-142, '3997; TX 5 at DEY-TV0004479, '550; TX 8 at DEY-TV0009032-035, '049-051; TX 10 at DEY-TV0009177);

- Hochrainer (TX 2 at DEY-TV0000082, '141-142, '3988-991, '929-939; TX 5 atDEY-TV0004473-479, '550, '735-737, '747-748; TX 8 at DEY-TV0004814, '8937-940, '943, '974-978, '9032-035, '049-051; TX 10 at DEY-TV0009173-74, '177); and
- PCT Publication No. WO 01/78745 ("Gavin," TX 95) (TX 2 at DEY-TV0003999; TX 5 at DEY-TV0004551; TX 8 at DEY-TV0008945; TX 10 at DEY-TV0009179).

The two First Family patents later underwent reexamination, during which the examiner also considered the following references:

- a publication by Whelan et al. ("Whelan," TX 568) (TX 3 at DEY-TV1729971-984, DEY-TV1730194-197, '202-03, '211-213, '687, '1971; TX 6 at DEY-TV1733992-4005, '353-356, '362-363, '375-377, '544, '769); and
- a publication by Puigbó et al. ("Puigbó," TX 625) (TX 3 at DEY-TV1732956; TX 6 at DEY-TV1735005).

After considering these references during Dey's four patent prosecutions and two reexaminations, the PTO issued the four patents-in-suit and confirmed the patentability of the claims of the two First Family patents. (Tr. 947:20-23 (Hendeles).) During reexamination, the examiner provided a "Statement of Reasons for Patentability and/or Confirmation," which set forth the reasons why these references did not pose an obstacle to patentability:

> [T]he prior art of Maesen, Wade, Remington, Gao, Murakami, Whelan, Hochrainer, Redm[o]n, and Lachman fail to teach or fairly suggest either alone or in combination an aqueous solution of formoterol or its derivative in a pharmaceutical composition that is stable during long term storage and is administered by nebulization as claimed. In addition, the instant independent claims require that the pharmaceutical composition of formoterol is at a concentration effective for bronchodilation by nebulization and suitable for direct administration to a subject in need of bronchodilation without propellant and without dilution of the composition (claim 1) or is in a unit dosage form of formoterol (claim 89 and claim 114) or a unit dosage form comprising [R,Rformoterol] (claim 118) with a concentration corresponding to about 5 µg/mL to about 50 µg/mL that is administered by nebulization without dilution for bronchodilation. Moreover, the prior art recognized that increasing the concentration of a stable formulation of formoterol would likely preserve or improve stability, but decreasing its concentration was unpredictable, and likely would lead to instability.

(TX 3 at DEY-TV1731971 ('344 Patent); TX 6 at DEY-TV1734769 ('953 Patent; Tr. 233:5-20 (Barnes).)

IV. STANDARD OF LAW

A defendant "in any action involving...infringement of a patent" may plead as an affirmative defense that the asserted patent is invalid. 35 U.S.C. § 282 (b)(2)-3. Because "[a] patent shall be presumed valid," "[t]he burden of establishing invalidity...rest[s] on the party asserting such invalidity." 35 U.S.C. § 282(a). A defendant asserting patent invalidity must establish that the patent is invalid by clear and convincing

evidence. Microsoft Corp. v. i4i Ltd., 131 S.Ct. 2238, 2242 (2011).

Invalidity may be established under either 35 U.S.C. § 102 or § 103. Section 102 denies the granting of a patent when the invention cannot be considered new in light of the prior art. This situation arises either when the prior art discloses each and every limitation of the claimed invention (§ 102(a) ("anticipation")), or when the invention was subject to a commercial sale more than one year prior to the filing of the patent application (§ 102(b) ("on-sale bar")). Section 103, by contrast, denies patentability if the claimed invention, though new, was nevertheless obvious to a person of ordinary skill in the art(§ 103(a)("obviousness")).

V. LEGAL ANALYSIS

Teva argues that the patents-in-suit are invalid under the doctrines of anticipation, obviousness, and enablement. First, it contends that the Asserted Claims were anticipated by the Murakami and Gao Patents, as well as Sepracor's transactions with ALP. Next, it argues that the Asserted Claims were obvious in light of the prior art. Finally, it contends that the Asserted Claims fail to enable a person of ordinary skill in the art to practice the invention without undue experimentation. The Court turns now to the application of these doctrines in this case.

A. Anticipation

1. Standard of Law

In order for a patentee to obtain a valid patent, its invention must be novel. 35 U.S.C. § 102. "Invalidity based on lack of novelty (often called 'anticipation') requires that the same invention, including each element and limitation of the claims, was known or used by others before it was invented by the patentee." Hoover Grp. Inc. v. Custom Metalcraft Inc., 66 F.3d 299, 302 (Fed. Cir. 1996). A patent thus is invalid for anticipation if "a single prior art reference discloses each and every limitation of the claimed invention." Schering Corp. v. Geneva Pharm., Inc., 339 F.3d 1373, 1377 (Fed. Cir. 2003).

A prior art reference will anticipate the patent claim if it either expressly or inherently discloses each claim limitation. Id. at 1379. To establish inherent anticipation, a defendant must prove, by clear and convincing evidence, that a claim limitation not disclosed by the anticipating reference will still be present when the prior art is practiced as taught in that reference. Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043, 1047-48 (Fed Cir. 1995). "Inherent anticipation requires that the missing descriptive material is 'necessarily present,' not merely probably or possibly

present" in the anticipating reference. Trintec Indus., Inc. v. Top-USA Corp., 295 F.3d 1292, 1295 (Fed. Cir. 2002).

Anticipation also requires that the prior patent "be enabling, such that one of the ordinary skill in the art could practice the invention without undue experimentation." Novo Nordisk Pharm., Inc. v. Bio-Tech Gen. Corp., 424 F.3d 1347, 1355 (Fed. Cir. 2005). "A claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." Elan Pharm., Inc. v. Mayo Found. for Med. Educ. Research, 346 F.3d 1051, 1054 (Fed Cir. 2003).

Finally, anticipation is a question of fact. SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1343 (2005).

2. Findings of Fact and Conclusions of Law

a. The Murakami Patent

Teva argues that Murakami discloses claims 3, 34, and 40 of the '344 Patent, claims 76, 106, 112, and 160 of the '953 Patent, claims 1, 2, 6, 8, 9, and 12 of the '362 Patent, and claims 2 and 6 of the '645 Patent, and, therefore, these claims are invalid for anticipation. According to Teva, Murakami teaches a formoterol composition with the same ingredients and proportions as the claimed compositions. (Dkt. No. 249). Further, Teva argues that

Murakami teaches a person of ordinary skill in the art to formulate an inhalation solution of formoterol. Id. Dey disputes this, asserting that Murakami does not disclose the compositional and stability elements of the Asserted Claims, nor does it enable a person of ordinary skill in the art to formulate an inhalation solution of formoterol. (Dkt. No. 250).

After careful consideration of these arguments, the Court concludes that the Murakami Patent does not anticipate the Asserted Claims. In November, 1976, more than a year before the '344, '953, and '645 Patents were filed, Murakami (TX 16) was issued to Yomanouchi Pharmaceutical Co. Ltd., and therefore is prior art for purposes of § 102(b). The PTO considered the Murakami Patent during the prosecution of the '344, '953, and '654 Patents, and allowed them over Murakami. (Tr. 947:20-23 (Hendeles).) Although the PTO's decision with respect to anticipation is not binding on this Court, it is material evidence that the Court "must consider in determining whether the party asserting invalidity has met its statutory burden by clear and convincing evidence." Fromson v. Advance Offset Plate, Inc., 755 F.2d 1549, 1555 (Fed. Cir. 1985).

Murakami claims a set of compounds, including the formoterol molecule, from a family of molecules that it describes as effective bronchodilating agents. (TX 16, 1:54-57, 38:33-66; Tr. 233:21-

234:6 (Barnes).) The claimed set comprises a large number of compounds and contains examples of how to synthesize specific compounds, including formoterol. (TX 16, 17:13-37:52; Tr. 238:5-7 (Barnes), 585:7-586:7; 587:3-588:4 (Myrdal).)

Murakami states that the compounds it describes may be administered in various ways, including "orally," "subcutaneously, intramuscularly, or intravenously as injections" or "in the form of aerosols as inhalations." (TX 16, 7:65-8:3). Importantly, however, the patent only discloses three pharmaceutical formulations of the claimed compounds. Those formulations are designated as either "injectable," "for injection," or tablets. (Tr. 234:11-10, 237:24-238:12 (Barnes).)

Although the parties agree that Murakami is prior art to the '344, '953, and '654 Patents, they disagree as to whether it discloses all of the limitations of the Asserted Claims, and whether it enables a person of ordinary skill in the art to formulate an inhalation solution of formoterol. The Court therefore turns next to this issue.

1) The Murakami Patent's Disclosures of the Compositional Elements of the Asserted Claims

Murakami discloses injectable solutions containing a hydroxyl analogue, a molecule structurally similar to formoterol. It does

not, however, disclose an aqueous formulation that either contains formoterol or is suitable for inhalation by nebulization, both of which are components of every Asserted Claim. (Tr. 780:6-16 (Hendeles).)

Teva characterizes Murakami as teaching "aqueous formoterol formulations," even though its own experts admitted that the Murakami formulations do not contain formoterol. (Tr. 588:5-9, 589:8-14 (Myrdal), 982:19-21 (Hendeles).) Teva attempts to classify the hydroxyl analogue contained in Murakami as a derivative of formoterol. Notably, however, while the hydroxyl analogue is structurally similar to formoterol, it was not prepared, synthesized, or derived from formoterol. (TX 16, 11:12-12:41, 19:47-68).

Teva dismisses this critical defect, arguing that, because Murakami describes a molecule similar to formoterol, a formulator could have chosen to swap formoterol with the molecule that was used, and the new formulation then would have anticipated the Asserted Claims. As Dey pointedly notes, however, the law does not allow for a mix and match approach to anticipation. Rather, the identical invention must be described in the prior art reference in order for an anticipation defense to be successful. See Sanofi-Synthelabo v. Apotex, Inc., 550 F.3d 1075, 1083-84 (Fed. Cir. 2008)

("The anticipating reference must clearly and unequivocally disclose the claimed invention or direct those skilled in the art to the invention without any need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference."). Thus, Teva has failed to establish, by clear and convincing evidence, that the compositional elements of the Asserted Claims are inherently disclosed by Murakami. Glaxo, 52 F.3d at 1043.

2) The Murakami Patent's Disclosures of the Stability Elements of the Asserted Claims

Unlike a majority of the Asserted Claims, Murakami does not disclose any specific stability limitations.[5] To overcome this gap, Teva relies on the opinion of Dr. Myrdal that the experiments performed by Dr. Robert O. Williams in 2009, which examined the long-term stability of a formulation similar to Murakami, establish that Murakami inherently discloses a stability limitation. Unfortunately for Teva, Dr. Myrdal acknowledged during his testimony that the composition tested by Dr. Williams cannot be found anywhere in the Murakami Patent. (Tr. 593:18-19).

[5] Only eight of the twenty-eight Asserted Claims do not recite a specific stability limitation: claims 4, 6, 8, 12, and 15 of the '362 Patent and claims 6, 8, and 9 of the '645 Patent.

Furthermore, unlike Murakami's formulation, Dr. Williams's formulation was oxygen free, a fact that could have significantly influenced the formulation's stability. (Tr. 696:2-7 (Myrdal).) Hence, Dr. Myrdal's opinions of Murakami's stability, based as they are on Dr. Williams's experiments, are merely speculative and inadequate to establish, by clear and convincing evidence, that a stability limitation is inherently disclosed by Murakami. Glaxo, 52 F.3d at 1043.

3) Enablement

In order to anticipate the Asserted Claims, Murakami must also enable a person of ordinary skill in the art to practice the invention without undue experimentation. Novo Nordisk Pharm., 424 F.3d at 1347. "Whether a prior art reference is enabling is a matter of law based upon underlying factual findings." Id.

When a prior art patent is asserted as evidence of an invalidity defense, as is the case here, the Court must presume that the prior art patent is enabling, and the patentee has the burden of overcoming that presumption. Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1355 (Fed Cir. 2003). If the patentee satisfies that burden by setting forth "evidence of nonenablement that a trial court finds persuasive, the trial court

must then exclude that prior art patent in any anticipation inquiry." Id.

Dey argues that the Murakami Patent does not enable a person of ordinary skill in the art to practice the Asserted Claims without undue experimentation because nothing in the patent indicates that an injectable formulation could be derived from its components. Teva asserts in response that Murakami teaches an inhalable solution by explaining that the compounds it discloses can be delivered as aerosols.

As Dr. Barnes testified, however, this explanation was part of a disclosure listing "every conceivable way of giving a drug to a human," and could not possibly be sufficient to teach one of ordinary skill how to make a solution of formoterol by nebulization without undue experimentation. (Tr. 235:24-236:3 (Barnes).). Thus, it is not clear that a person of ordinary skill in the art would understand from Murakami how to create a solution suitable for nebulization.

Further, an anticipating reference must also enable a person of ordinary skill in the art to practice the *invention* without undue experimentation. Impax Labs., Inc. v. Aventis Pharm. Inc., 545 F.3d 1312, 1314-16 (Fed. Cir. 2008). Thus, even if Teva were able to prove that Murakami's disclosure of an injectable solution

enables nebulizer solutions, it must also teach a person of ordinary skill in the art to formulate a solution that 1) contains formoterol, and 2) achieves long-term stability. Nothing in the Murakami Patent indicates that a person of ordinary skill in the art would be able to make these deductions, considering the patent discloses different compositional and stability elements from the Asserted Claims.

4) Conclusion

The Murakami Patent does not disclose, either expressly or inherently, every required limitation of claims 3, 34, and 40 of the '344 Patent; claims 76, 106, 112, and 160 of the '953 Patent; claims 1, 2, 6, 8, 9, and 12 of the '362 Patent; and claims 2 and 6 of the '645 Patent. Nor does it enable a person of ordinary skill in the art to formulate an inhalation solution of formoterol. Thus, the Murakami Patent does not "disclose each and every limitation" of the Asserted Claims, and therefore does not anticipate and invalidate these claims. Schering, 339 F.3d 1377.

b. The Gao Patent

Teva next argues that, because the Gao Patent discloses all of the elements of claims 3 and 34 of the '344 Patent, and claims 75 and 106 of the '953 Patent, these claims are invalid for

anticipation. (Dkt. No. 249). It asserts that, consistent with the Asserted Claims, Gao contains a formoterol concentration suitable for broncholization by nebulization without prior dilution. Further, Teva argues that the formulation described in Gao has the same inherent stability, shelf life, degradation rate, and short term storage ability as the claimed composition. Id. Dey contends that the Gao Patent differs from the Asserted Claims in critical ways–namely, in its compositional and stability elements–thus preventing anticipation. (Dkt. No. 250). Dey has the better argument.

The Gao Patent was issued to Sepracor in March of 2000. Since it issued more than a year before the First Family patents were filed on April 17, 2001, it is prior art for purposes of § 102(b). The PTO considered the Gao Patent during the prosecution of the First Family patents, and allowed these patents over it. (Tr. 947:20-23 (Hendeles).)

The Gao Patent describes a salt form of the optically pure formoterol compound called "arformoterol," along with the compositions containing it. (TX 15, 20:33-59). The patent also specifies methods of preparing the compound. (TX 14, 1:11-14). Gao's focus is stereochemical separation. It teaches "an approach to long-term storage of dosage forms for aqueous aerosols," which

is described in a co-pending patent application known as the Redmon Patent. (TX 15, 20:6:10).

The Redmon Patent does not teach stable aqueous formulations, but instead describes a method for "preparing aerosols of water-sensitive medicaments" using a pharmaceutical kit consisting of a two-chambered device (TX 17 at DEY-TV0177979). One chamber, which is "substantially water-impermeable," holds a solid-state matrix form of the medicament and a carrier material, while the second container holds a "sufficient quantity of an aqueous vehicle to dissolve the matrix network within fifteen seconds." (TX 17, 2:13-20). According to Redmon, this two-chamber solution was necessary because, while "water is the only vehicle that can reasonably be employed in nebulization, the medicament is itself not sufficiently stable in an aqueous environment to provide a practical shelf life for the aqueous formulation." (TX 17, 1:52-55). The parties agree that the Gao Patent is prior art to the First Family Patents, but disagree as to whether it discloses all of the limitations of claims 3 and 34 of the '344 Patent and claims 75 and 106 of the '953 Patent.

1) The Gao Patent's Disclosures of the Compositional Elements of the Asserted Claims

i) Concentration

Gao's formulation has an arformoterol free base concentration of 139 µ/mL. (Tr. 473:14-23 (Myrdal), 813:18-20 (Hendeles).). The formoterol concentration in the Gao formulation thus exceeds 50 µ/mL, which is the highest formoterol concentration disclosed in any Asserted Claim specifying a concentration.

Despite Gao's high formoterol concentration, Teva asserts that, based on Dr. Barnes's testimony, the drug is still "effective for bronchodilation by nebulization" and "suitable for direct administration by nebulizer without dilution." (Dkt. No. 249). However, Dr. Barnes did not testify that 139 µg/mL is suitable for direct administration by nebulizer without dilution; rather, he noted that 200 µg/mL was described in, but not within the scope of, the '344 Patent. (Tr. 320:6-22). Further, he specifically stated that a 139 µg/mL concentration would be "too high" for the long term treatment of COPD. (Tr. 315:24-316:2, 320:2-5 (Barnes).)

Dr. Barnes's testimony that a 139 µg/mL formoterol concentration is too high for the long-term treatment of COPD is consistent with the distinction drawn by Dey during the reexamination of the First Family patents. At the reexamination,

Dey overcame an anticipation objection based on Gao by arguing that the formulation in Dey's claims did not encompass concentrations of 139 µg/mL and up. (TX 3 at Dey-TV1730555 (n.14).) Thus, as a matter of law, this distinction defines "suitable for direct administration" for these patents as being limited to concentrations below 139 µg/mL. See SanDisk Corp. v. Memorex Prods., Inc., 415 F.3d 1278, 1286 (Fed. Cir. 2005) ("When the patentee makes clear and unmistakable prosecution arguments limiting the meaning of a claim term in order to overcome a rejection, the courts limit the relevant claim term to exclude te disclaimed matter.").

ii) Buffer Concentration, Ionic Strength, and Salinity

Gao fails to disclose any specific buffer concentration, ionic strength, or salinity. (Tr. 699:13-25, 700:17-22 (Myrdal), 977:17-19 (Hendeles), 1418:3-10 (Hastedt).). Thus, it does not anticipate any claim reciting a specific buffer concentration, including claim 74 of the '344 Patent and claim 136 of the '953 Patent, which both recite a buffer concentration of "about 20mM," or any of the Asserted Claims of the '362 or '645 Patents, which provide a buffer concentration range. Further, it does not anticipate claim 34 of the '344 Patent and claim 106 of the '953 Patent, which recite

iconic strengths of .05 to .16, or claim 116 of the '344 Patent, and claim 163 of the '953 Patent, which require isotonic saline solution.

iii) Dosage

The formulation disclosed in Gao is not suitable for a single unit dosage. (Tr. 977:9-16 (Hendeles).) Thus, Gao does not anticipate claims 104 and 116 of the '344 Patent, claims 160 and 163 of the '953 Patent, and each of the Asserted Claims of the '362 and '645 Patents, all of which require a single unit dose.

2) The Gao Patent's Disclosures of the Stability Elements of the Asserted Claims

Unlike a majority of the Asserted Claims;[6] Gao does not disclose any specific stability limitations. Rather, it describes a formulation that has "problematic stability" and is "not attractive for long term storage." (TX 15, 20:1-6).

Teva attempts to overcome this defect by arguing that the Gao formulation "inherently" meets the stability requirements of the Asserted Claims. (Dkt. No. 249). Its argument relies on the opinion expressed by Dr. Hendeles that, based on his examination of Dr. Williams's experimental report, Gao inherently met the stability

[6]See *Supra* Note 6.

requirements of the Asserted Claims. (Tr. 856:11-15, 1009:9-1010:7 (Hendeles).).

Dr. Hendeles, however, failed to note that the formulation tested by Dr. Williams was his own invention, not Gao's. Although Dr. Williams created a drug with a citrate buffer concentration of 5 and 50mM, Gao does not teach any specific buffer concentration. Thus, it is likely that Gao's formulation and the formulation of Dr. Williams have different stabilities. (Tr. 699:13-17, 700:1-5, 700:17-22 (Myrdal), 1431:22-1433:22 (Hastedt).) Dr. Williams's test results therefore cannot definitively predict Gao's actual stability. Accordingly, Gao does not anticipate any of the Asserted Claims that contain stability limitations.

3) Conclusion

Because the Gao Patent does not "disclose every limitation" of claims 3 and 34 of the '344 Patent, or claims 76 and 106 of the '953 Patent, it does not anticipate and therefore invalidate these claims. Schering, 339 F.3d at 1377.

c. Sepracor Transaction

Teva contends that the Asserted Claims are invalidated by the on-sale bar of 35 U.S.C. § 102 (b), due to Sepracor's transactions with ALP. (Dkt. No. 249). Dey, however, argues that Teva has

failed to establish, by clear and convincing evidence, that the elements of the on-sale bar have been met in this case. (Dkt. No. 254). Dey's arguments are the most persuasive.

1) Factual Background

From the late 1990s until the early 2000s, the pharmaceutical company, Sepracor, developed Brovana®, a drug containing arformoterol in an aqueous solution.[7] (Tr. 1328:15-19 (Wald).) In the course of developing Brovana®, Sepracor discovered a way to manufacture arformoterol, the stereochemically pure active ingredient in formoterol. (Tr. 1340:7-23 (Wald).)

[7] Apart from this action, Dey has successfully prosecuted claims of infringement of the patents-in-suit against Sepracor based on its marketing of Brovana®. Dey, Inc. v. Sepracor, Inc., 847 F.Supp.2d 541, 547 (S.D.N.Y. 2012). On March 1, 2012, the United States District Court for the Southern District of New York granted Sepracor's motion for partial summary judgment, finding that the patents-in-suit were invalid under the on-sale bar of 35 U.S.C. § 102(b) based on Sepracor's use of Dey's invention in clinical trials more than one year before Dey's filing of the second family patents. Id.

In May of 2013, the Federal Circuit held that Brovana® infringed Dey's valid Perforomist® patents. Dey, Inc. v. Sepracor, Inc., 715 Fed. Cir. 1351 (Fed. Cir. 2013). Following the Federal Circuit's decision, Sepracor stipulated to the infringement and validity of Dey's patents, and the district court entered a final judgment reflecting this. (TX. 864). Sepracor continues to market Brovana® pursuant to a licensing agreement with Dey, and Teva does not dispute that Brovana® infringes the patents-in-suit. (Tr. 516:11-12).

Sepracor outsourced the preparation of several test batches of a packaged aqueous solution containing the arformoterol it owned and manufactured to a "contract packager," ALP. Sepracor contracted with ALP to utilize their packaging service because Sepracor did not own the necessary "blow-fill-seal" packaging equipment. Throughout their various transactions, Sepracor provided ALP with the arformoterol it had manufactured, together with precise specifications for the formulation ALP was to mix and package. ALP then prepared the product according to Sepracor's specifications. Sepracor paid ALP for providing its services, labor, and expertise in mixing and packaging the formulations. (Tr. 1342:17-25, 1345:2-5 (Wald).)

In total, ALP prepared the following three formulations for Sepracor:

1) Lot No. 02797A: 100 µg/mL arformoterol concentration, packaged with 15 mL citrate buffered saline solution in 20 mL bottle. Manufactured in November of 1997;

2) Lot No. 01799B: 96 µg/mL arformoterol concentration, packaged in 7 mL citrate buffered saline solution in 20 mL bottle. Manufactured in July of 1999; and

3) Lot No. 03501A: 15 µg/2 mL arformoterol concentration, packaged in 2 mL citrate buffered saline solution in 2 mL vials. Manufactured in July of 2001.

(TX 509). Sepracor used the Lots packaged by ALP exclusively in its clinical trials of Brovana®. (Tr. 1342:17-25, 1345:2-5 (Wald).)

2) Standard of Law

Patent law denies a patent to an inventor who applies for a patent more than one year after making an attempt to profit from his invention by putting it on sale. 35 U.S.C. § 102(b); Atlanta Attachment Co. v. Leggett & Platt, Inc., 516 F.3d 1361, 1365 (Fed. Cir. 2008). An invention is so barred from patenting when it was both the subject of a commercial offer or sale before the critical date and also ready for patenting at the time of offer. Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 67, 199 S.Ct. 304, 311-12 (1998). Furthermore, "the court should determine whether the subject of the barring activity met each of the limitations of the claim, and thus was an embodiment of the claimed invention." Atlanta Attachment Co., 516 F.3d at 1365.

The overriding concern of the on-sale bar is that an inventor may attempt to commercialize his invention beyond the statutory term. Netscape Commc'ns. Corp. v. Konrad, 295 F.3d 1315, 1323 (Fed. Cir. 2002). The on-sale bar, thus, seeks to prevent an inventor

from extending his monopoly by the expedient of first commercially selling his offer for a time and then later applying for a patent.

An inventor who seeks to perfect his discovery through experimentation, however, may conduct extensive testing without losing his right to a patent, even if such testing occurs in the public eye. Netscape, 295 F.3d at 1323. The law has long recognized a distinction between experimental usage and commercial exploitation of an invention. "While any attempt to use [an invention] for profit...would deprive the inventor of his right to a patent," and inventor's use "by way of experiment," does not bar patentability. Atlanta Attachment Co., 516 F.3d at 1365. Thus, the Court must consider "whether the suspect activities were experiments as opposed to an attempt to profit from the invention, that is, whether the primary purpose of the offers and sales was to conduct experimentation." Allen Eng'g Corp. v. Bartell Indus., 299 F.3d 1336, 1354 (Fed. Cir. 2002).

3) Analysis

i) Commercial Offer for Sale

As noted, the on-sale bar only applies if an invention was subject to a prior "commercial offer for sale." To meet this requirement, the offer must be sufficiently definite such that

another party could make a binding contract by simple acceptance, assuming consideration. Netscape, 295 F.3d at 1323. In determining such definiteness, the Court must review the language of the proposal in accordance with the principles of general contract law. Id.

Contract law distinguishes between sales for commercial versus experimental purposes. Id. While "[a]ny attempt to use [an invention] for profit ... would deprive the inventor of his right to a patent," an inventor's use "by way of experiment" does not bar patentability. Elizabeth v. Am. Nicholson Pavement Co., 97 U.S. 126, 137 (1877). Thus, the Court must determine whether the "sale" of the Sepracor Lots to ALP was done for experimental, rather than commercial, purposes.

Dey contends that the transactions between Sepracor and ALP were purely experimental. (Dkt. No. 250). Teva responds that Dey has failed to establish that the on-sale bar is not applicable in this instance. (Dkt. No. 253).

As described by Dey, the arrangement between Sepracor and ALP was a "contract for services," not the sale of a product. (Tr. 1345:5 (Wald).) Pursuant to Sepracor's contract with ALP, Sepracor would provide, among other things, active and excipient raw materials, along with "complete product and packaging

specifications," while ALP would provide, among other things, "blow/fill/seal machinery and associated support equipment," "in-process testing," and "finished product testing," it being "understood that [ALP] is a packager pursuant to [Sepracor's] specifications." (TX 436; TX 449.1; TX 488.1). Further, ALP made "no warranties, express or implied, as to the efficacy of the packaged product." Id. The Lots were then used exclusively by Sepracor for its clinical trials. (Tr. 1353:5-9 (Wald).) This evidence establishes that the primary purpose of Sepracor's transaction with ALP was experimental, not commercial.

Teva contends that there is no "supplier exception" to the on-sale bar. (Dkt. No. 249). Teva's argument misapprehends the issue. Dey never attempted to argue that the on-sale bar is inapplicable because ALP was merely a "supplier" to Sepracor. In the contrary, consistent with the case law, Dey's argument has always been that there was no "sale," because ALP merely served as a contract "packager," and the packaged Lots were only used for experimental purposes. (TX 436; TX 449:1, TX 448.1). Consistent with Dey's arguments, the evidence adduced at trial failed to establish that the transaction between Sepracor and ALP constituted a "commercial sale."

ii) Sale of the Invention

The on-sale bar requires that there be a sale of the entire claimed invention. 35 U.S.C. § 102(b). Here, even if the contract between ALP and Sepracor could be construed as a "commercial sale," the contract did not embody all the elements of the "invention" claimed in Dey's patents. It is undisputed that, at no time, did Sepracor surrender ownership to ALP of the active ingredient, formoterol, which is an element of every Asserted Claim. As a result, ALP never sold the complete "invention" to Sepracor. Sepracor owned the core component–formoterol–of the solutions ALP packaged at Sepracor's request.

The Federal Circuit allows inventors, such as Sepracor, to "request another entity's services in developing products embodying the invention without triggering the on-sale bar." Trading Techs. Int'l, Inc. v. eSpeed, Inc., 595 F.3d 1340, 1361-62 (Fed. Cir. 2010). To hold otherwise would disadvantage small pharmaceutical companies who "fairly common[ly]" outsource mixing and packaging "because of [the] capital investment and specialized knowledge required to operate the machinery." (Tr. 1332:20-23 (Wald).) Therefore, Teva has failed to establish, by clear and convincing evidence, that there was a "commercial sale" of Dey's "invention."

iii) Public Nature of the Sale

The on-sale bar also requires that the sale of an invention be public. The bar is not triggered when a third party, unaffiliated with the inventor, sells a non-public invention in a manner that does not give the public access to the transaction. W.L. Gore & Assos., Inc. v. Garlok, Inc., 721 F.2d 1540, 1550 (Fed. Cir. 1983). This is because such sales neither create an expectation that an unpatented invention is in the public domain nor constitute pre-application commercial exploitation of an invention by the inventor–the policies that the on-sale bar attempts to further. Id.

Here, it is uncontested that Dey was not a party to the transaction between ALP and Sepracor. Thus, the on-sale bar is not triggered by the parties' private transaction. Id.

iv) Timing of the Transaction

The on-sale bar only applies to inventions sold one year prior to the application for a patent. Atlanta Attachment Co. v. Leggett & Platt, Inc., 516 F.3d 1361, 1365 (Fed. Cir. 2008). The parties do not dispute that the 3501 Lot was packaged by ALP in July, 2001. (TX 509). It is also undisputed that the provisional application for the First Family patents was not filed until April 17, 2001. Thus, ALP packaged and transferred the 3501 Lots only after the

provisional application was filed for the First Family patents; therefore, the transfer of the 3501 Lots cannot invalidate those patents.

v) Composition of the Sepracor Lots

The on-sale bar invalidates a patent under § 102(b) only if the subject of the barring activity practiced every limitation of the Asserted Claims. ResQNet.com v. Lansa, Inc., 594 F.3d 860, 866-67 (Fed. Cir. 2010). Dey contends that two of the three Sepracor Lots, Lots 2797A and 1799B, fail to practice one or more limitations of the Asserted Claims. In its response, Teva asserts that Dey has misconstrued the true composition of the Sepracor Lots.

(a). Unit Dosage

Lots 2797A and 1799B were packaged and transferred to Sepracor in large volumes (15 mL and 7 mL quantities, respectively). Accordingly, the Lots were not packaged as "unit doses," or in a "quantity that is [to be] taken or administered at one time," as is required by several of the Asserted Claims.[8] (Tr. 1378:21-1379:8 (Wald), 977:9-16 (Hendeles).)

[8]The following claims require unit doses: claims 65, 104, and 116 of the '344 Patent; claims 160 and 163 of the '953 Patent; and each Asserted Claim of the '342 and '645 Patents.

Teva attempts to overcome this gap by claiming that the Lots were eventually apportioned into unit doses when they were used in clinical trials. (Dkt. No. 249). However, the fact that the Lots had the potential to be apportioned into unit doses after they were "sold" is irrelevant to a determination of whether the Lots "as sold" anticipated the Asserted Claims. A court must analyze the composition of the potentially anticipating formulation at the time of its sale. Schaltech Inc. v. Retec/Tetra, L.L.C., 178 F.3d 1378, 1383 (Fed. Cir. 1999). Here, Lots 2797A and 1799B were not packaged as unit doses at the time of sale, and thus, do not anticipate the Asserted Claims that require packaging as unit doses.

(b). Stability

Unlike the Asserted Claims, Lots 2797A and 1799B did not disclose stability limitations. Although Dr. Myrdal made certain projections of stability based on Sepracor data concerning the shelf life of the Sepracor Lots, he failed to conduct any analysis of how much formoterol would remain in the formulation after one year. Thus, his findings fail to establish whether the Lots exhibit long-term stability. (Tr. 704:1-706:21 (Myrdal).)

To overcome this defect, Teva contends that, because the Lots have "all of the components of the composition of the Asserted

Claims," they must have the same "inherent stability." (Dkt. No. 249). However, as discussed earlier, because the compositions of the Lots are not identical to the Asserted Claims, positing that they exhibit the same "inherent stability" is speculative. Lots 2797A and 1799B therefore do not anticipate the Asserted Claims that disclose stability elements.

(c). Concentration

It is uncontested that the concentration of 2797A and 1799B was 100 µg/mL and 96 µg/mL, respectively. These Lots, therefore, are too highly concentrated to fall within any of the specific concentration ranges recited by several of the Asserted Claims, none of which exceeds 50 µg/mL. (Tr. 708 2-10 (Myrdal)). Thus, these Lots cannot anticipate claims 40, 104, and 116 of the '344 Patent, claims 112, 160, and 163 of the '953 Patent, and each Asserted Claim of the '362 and '645 Patents.

4) Conclusion

The Sepracor Lots were not subject to a commercial sale in the one year prior to the time Dey applied for its patents. Further, the Lots differ in composition from the Asserted Claims. Consequently, the Asserted Claims are not invalidated by the on-sale bar of 35 U.S.C. § 102(b).

d. Conclusion as to the Defense of Anticipation

Because there is no clear and convincing evidence that the prior art discloses each and every limitation of the claimed invention, the Asserted Claims are not invalid for anticipation.

B. Obviousness

1. Standard of Law

A patent will be invalid pursuant to 35 U.S.C. § 103 when "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." OSRAM Sylvania, Inc. v. Am. Induction Techs., Inc., 701 F.3d 698, 706-07 (Fed Cir. 2013). "Generally, a party seeking to invalidate a patent as obvious must demonstrate by clear and convincing evidence that a skilled artisan would have been motivated to combine the teaching of the prior art references to achieve the claimed invention, and that the skilled artisan would have had the reasonable expectation of success in doing so." Id. "The Supreme Court has warned, however, that while an analysis of any teaching, suggestion, or motivation to combine known elements is useful to an obviousness analysis, the overall obviousness

inquiry must be expansive and flexible." Id. at 707 (citing KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 415, 127 S.Ct. 1727, 167 L.E.2d 705 (2007)). The concern with granting patents in spite of obviousness is that doing so would allow parties to obtain a monopoly over inventions already known in a given field, discouraging innovation. KSR Int'l Co., 550 U.S. at 416.

A claim must have been nonobvious "at the time the invention was made." 35 U.S. § 103(a). A court therefore must avoid the use of hindsight in this analysis and go beyond "simply retracing the path of the inventor." Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc., 520 F.3d 1358, 1364 (Fed. Cir. 2008).

In Graham v. John Deere Co. of Kansas City, 383 U.S. 1, 17-18, 86 S. Ct. 684, 694-95 (1966), the Supreme Court of the United States established the following four-part test for determining obviousness:

> Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is to be determined. Such secondary considerations as commercial success, long felt but unresolved needs, failures of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.

Any analysis of obviousness therefore must include a consideration of secondary, objective indicia. Power Integrations, Inc. v. Fairchild Semiconductor Int'l, Inc., 711 F.3d 1348, 1368 (Fed. Cir. 2013). These considerations include "copying, long felt but unresolved need, failure of others, commercial success, unexpected results created by the claimed invention, licenses showing industry respect for the invention, and skepticism of skilled artisans before the invention." Id.

"The ultimate judgment of obviousness is a legal determination." KSR Int'l Co., 550 U.S. at 417. However, the obviousness inquiry also involves factual determinations within the framework of the Graham factors. Sakaraida v. Ag. Pro, Inc., 425 U.S. 273, 280, 96 S.Ct. 1532 (1976).

2. Findings of Fact and Conclusions of Law

The Court begins its obviousness analysis with a discussion of the Graham factors. 383 U.S. at 17-18.

a. Scope and Content of the Prior Art

It is undisputed that the Murakami and Gao Patents, as well as the Puigbó (TX 635) and Gavin (TX 95) articles, are part of the relevant prior art for the patents-in-in suit. As discussed earlier, the parties agree that Murakami and Gao are prior art to

the Asserted Claims. Murakami discloses a set of bronchodilating agents. (TX 16, 1:54-57, 38:33-66; Tr. 233:21-234:6 (Barnes).) The claimed set comprises a large number of compounds and contains examples of how to synthesize specific compounds, including formoterol. (TX 16, 17:13-37:52; Tr. 238:5-7 (Barnes), 585:7-586:7; 587:3-588:4 (Myrdal).) Further, Murakami Example 34 discloses an injectable formulation containing a hydroxyl analogue, a molecule structurally similar to formoterol.

Gao discloses an aqueous formulation of formoterol. It relates to optically pure isomers of formoterol and teaches an aqueous aerosol formulation for nebulization that is "quite suitable for short term use" but "not attractive for long term storage" at room temperature. (TX 15).

The parties further agree that the Puigbó and Gavin articles are prior art to the Asserted Claims. Both articles discuss experiments related to the treatment of respiratory diseases and were considered by the PTO during the prosecution of the patents-in-suit. (Tr. 947-20-23 (Hendeles).)

The Puigbó article was published in 2000 and is prior art to the Second Family patents. It describes experiments by Dr. A. Perez Puigbó to treat asthma exacerbations by administering unit doses of formoterol fumarate by nebulization. (TX 625). Puigbó

discloses dissolving a single dose of dry Foradil® formoterol fumarate powder in 2 mL of 0.9% sterile saline solution. Id. The pH of the Puigbó composition was 5.5 and the concentration was approximately 6 µg/mL. Id.

The Gavin article was published in October, 2001 and is prior art to the Second Family patents. (TX 95). It describes compositions for treating respiratory diseases. In pertinent part, Gavin discloses formoterol (in combination with fluticasone) in an aqueous nebulizer formulation that includes polysorbate 20 and sorbitan monolaurate. Id.

The parties disagree as to whether the Sepracor Lots are part of the prior art. Teva argues that they are prior art because their compositions are virtually the same in scope as the compositions in Dey's patents. (Dkt. No. 249). Dey contends that the Sepracor Lots cannot be prior art because they were not sold or publicly disclosed. (Dkt. No. 254).

As the Court has already concluded, the Sepracor Lots were not "on-sale" within the meaning of § 102(b), and, thus, are not considered prior art under either § 102 or § 103. Further, even if the Lots had been "on sale," and therefore considered prior art under § 102, their non-public status would still prevent them from being relevant under § 103. In re Newell, 891 F.2d 899, 901 (Fed.

Cir. 1989). Obviousness is concerned with public knowledge–what a person of ordinary skill in the art would actually know based on the prior art. Id. Such a person would not be aware of non-public materials, such as the Lots that ALP confidentially delivered to Sepracor.

b. Differences Between the Prior Art and the Claims at Issue

Unlike the Asserted Claims, Murakami does not disclose an aqueous formulation that either contains formoterol or is suitable for inhalation by nebulization, nor does it contain any stability limitations. While Gao does teach an aqueous solution of formoterol, it does not disclose a formulation with long-term stability, but rather describes a formulation with problematic stability. It also fails to disclose any specific buffer concentration, ionic strength, or salinity, and it also describes a formulation not suitable for single unit dosage.

Furthermore, unlike the Asserted Claims, it is undisputed that the Gavin article fails to disclose the pH or the stability of the experimental formulation. (Tr. 252:16-18 (Barnes).) Similarly, the Puigbó article does not discuss stability. (Tr. 248:21-250:7 (Barnes).) That Puigbó does describe a process of administering the formoterol solution immediately after preparation only aids the

conclusion that the authors believed the solution would not exhibit long-term stability. (TX 625).

c. Level of Skill in the Art

The parties agree that a person of ordinary skill in the art for purposes of this action would have either an advanced degree in pharmacy or a graduate degree in pharmaceutics, along with several years of experience with pharmaceutical formulations, including basic formulation principles, pharmacology, and/or the treatment of pulmonary diseases. (Tr. 439:19-440:3, 751:15-25.)

The Federal Circuit has established a "teaching, suggestion, or motivation" test ("TSM test") to determine whether, in light of the prior art, an invention would have been obvious to a person of ordinary skill in the art. The TSM test provides that a claim will be rendered obvious only if there is "some motivation or suggestion to combine the prior art teachings" in either the prior art, the nature of the problem, or the knowledge of a person of ordinary skill in the art. Al-Site Corp. v. VSI Int'l, Inc., 174 F.3d 1308, 1323-24 (Fed. Cir. 1999). The fact that all of the elements of a claimed invention were part of the prior art does not automatically render an invention obvious, since many inventions build on knowledge that is already known. KSR Int'l Co., 127 S.Ct. at 1727. Thus, there must have been some inherent motivation to combine the

elements as done in the claimed invention in order for that invention to be invalid for obviousness. Id.

In KSR, the Supreme Court explained that the TSM test should not be reduced to a rigid formula. 127 S.Ct. At 1741. An "obvious analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." Id. A court may also consider "interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue." Id. at 1740-41.

Thus, there need not be an explicit statement in the prior art itself suggesting the invention in order for the prior art to render the invention obvious. Rather, an issue in the relevant field present at the time of the creation of the invention can serve as a motivation to combine prior art elements. Id. at 1742. Furthermore, when an invention involves a combination of elements already known in the prior art, that invention is obvious unless

"the improvement is more than the predictable use of prior art elements according to their established functions. Id. at 1741.

Likewise, if a combination would have been obvious to try at the time of the invention, that invention could be rendered obvious by the prior art. Id. However, if the prior art teaches against combining the known elements, then an invention that successfully combines those elements is likely nonobvious. United States v. Adams, 383 U.S. 39, 50-51, 86 S.Ct. 708, 15 L.Ed.2d 572 (1966).

1) Combining the Prior Art References

Teva contends that, while no single prior art reference may have rendered Dey's invention obvious, a combination of those various references did. (Dkt. No. 249). Specifically, it argues that, through combining the following prior art disclosures, Dey's invention is rendered obvious:

- Gao discloses concentrations of formoterol "effective for bronchodilation" and formulations that could be used in a nebulizer;
- Murakami discloses "formoterol";
- Murakami discloses "sterile" solutions;
- Murakami, in Example 34, used a citrate buffer to generate a pH of 4 to 6 and Gao uses a citrate buffer to achieve a pH of 5; and

- Other drugs have been "formulated for single dose administration."

Id.

The fact that certain features are disclosed in the prior art, however, is insufficient to establish that a claimed invention is obvious. Connell v. Sears, Roebuck & Co., 722 F.2d 1542, 1549 (Fed. Cir. 1983). It is common to find elements of a claimed invention in the prior art. The test is "whether the claimed invention as a whole, in light of all the teachings of the references in their entireties, would have been obvious to one of ordinary skill at the time the invention was made." Id.

Here, there is no evidence that any combination of the prior art would indicate that an aqueous formulation of formoterol with long-term stability was possible. From formoterol's discovery in the 1970s until Dey's development of Perforomist®, the primary method of maintaining formoterol's stability was "keeping the powder dry." (TX 15, 20:3-6). Gao restates the conventional wisdom–that formoterol's stability in aqueous solution is "problematic" and "not attractive for long term storage." Id.

Gao and Redmon suggested a two-chamber storage system that keeps the solid drug dry and separate from the aqueous solution until immediately prior to use in order to effectively store

formoterol. (TX 15, 20:6-10; TX 17, 1:62-664, 2:12-62). Similarly, Puigbó suggests dissolving a dry powder formulation of formoterol in saline solution and administering it via nebulization immediately after the solution is prepared. (TX 625 at 74; Tr. 249:4-22 (Barnes), 624:8-11, 626:2-6 (Myrdal), 999:20-1000:2 (Henedeles).)

Thus, a person of ordinary skill reading the prior art in combination would understand that, to administer formoterol via nebulization, a user should keep the powder dry until just before use. That person would not understand that an aqueous formoterol solution could exhibit long-term stability. (Tr. 978:15-2, 1000:3-6 (Hendeles).) Therefore, there was no explicit motivation to combine the teachings set forth in the prior art, because those teachings taught against the elements Dey used to create its invention. KSR, 127 S.Ct. at 1738-39.

Furthermore, even if the elements of each Asserted Claim could be found somewhere in the prior art, any attack on the obviousness of Teva's invention would be entirely hindsight driven and therefore "legally incorrect." McGinley v. Franklin Sports, Inc., 262 F.3d 1339, 1351 (Fed. Cir. 2001). A person of skill reviewing the prior art would not have had a reasonable expectation that a ready-to-use, stable formoterol formulation drawing upon those

elements could be successfully made. The fact that the prior art taught compositional elements used to solve different problems that, in hindsight, turned out to be part of Dey's ultimate solution is not evidence that the solution was obvious. Cheese Sys., Inc. v. Tetra Pak Cheese & Powder Sys., Inc., 725 F.3d 1341, 1352 (Fed. Cir. 2013). ("Obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fir the parameters of the patented invention."). Rather, only if, without the benefit of hindsight, "a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so," Procter & Gamble Co. v. Teva Pharm. USA, Inc., 566 F.3d 989, 994 (Fed Cir. 2009), could a showing of obviousness be made. Teva has not established this by clear and convincing evidence.

2) Use of Standard Techniques

Relying on Dr. Myrdal's testimony, Teva also contends that the Asserted Claims are obvious because Dey's scientists used standard techniques in formulating their invention. (Dkt. No. 249). At trial, Dr. Myrdal opined that Dey did nothing more than apply "first principles" and "standard techniques" while doing "routine

testing." (Tr. 584:10-15.) He further testified that any invention arrived at in the same way would be considered obvious. Id.

Patent law, however, rejects the idea that novel inventions only arise from novel techniques. The process by which an invention was created is irrelevant to the analysis of its patentability. "Patentability shall not be negated by the manner in which the invention was made." 35 U.S.C. § 103(a). Thus, contrary to Teva's contentions, the use of routine techniques do not render an invention obvious. In re Yates, 663 F.2d 1054, 1056 n.4 (C.C.P.A. 1981)("[T]he emphasis upon routine experimentation is contrary to the last sentence of section 103."). Dey was therefore free to utilize standard, routine techniques in creating its invention without risking its patentability.

Furthermore, even though Dey's scientists admitted to using routine techniques known in the scientific community, Dey did not seek out a patent based on the use of those routine techniques, but rather sought a patent based on formulations shaped by the results of those tests. As described above, those results were neither known nor predictable. (Tr. 90:18-21, 91:2-9, 125:2-127:18 (Chaudry).)

3) Patenting Variations of the Prior Art

Finally, Teva argues that Dey's invention is obvious because its scientists merely patented minor variations of formulations Dey had discerned in the prior art based on their discovery of an "inherent" property (long-term stability) of those previously known formulations. (Tr. 1550:3-1555:6). Again, Teva relies on Dr. Myrdal's analysis of Dr. Williams's experiments, and his opinion that the "stability of the asserted claims would have been inherent property of the [prior art] compositions" such that these compositions "would have had the same stability and met the limitations of the [asserted] claims." (Tr. 434:3-11).

To the extent Teva is arguing that, based on Dr. Myrdal's analysis of Dr. Williams's testing, the formulations tested by Williams in 2009 inherently possessed the stability requirements of the Asserted Claims, this argument is irrelevant to a determination of whether those claims are obvious. Obviousness is concerned only with public knowledge, what a person of ordinary skill in the art would know based on the prior art. Newell, 891 F.2d at 901 ("A retrospective view of inherency is not a substitute for some teaching or suggestion which supports the selection and use of the various elements in the particular claimed combination."); 2-5 Chisum on Patents § 5.03[3][a][i][A] (2013 ed.) ("An inherent

feature may be relied upon to establish obviousness only if the inherency would have been obvious to one of ordinary skill in the art: 'Inherency and obviousness are distinct concepts.'" (quoting Kloster Speedsteel AB v. Crucible Inc., 793 F.2d 1565, 1576 (Fed. Cir. 1986) (subsequently overruled on other grounds))). Thus, such data is not relevant to an assessment of whether the Asserted Claims were obvious; it was generated in 2009, and would not have been part of the knowledge of a person of ordinary skill in the art at the time Dey applied for its patents.

Moreover, as discussed above, the claimed formulations are too different from those in the prior art to argue effectively that the Asserted Claims possess the same "inherent" stability as those prior art formulations. To date, there is no reliable source of information about the stability of the actual Gao or Murakami formulations. (Tr. 186:12-14 (Chaudry).) Furthermore, Dey never attempted to test their stabilities. Instead, it undertook an independent and lengthy scientific process to identify the claimed formulations. Id. Thus, Teva has failed to establish that the Asserted Claims merely claim "inherent" properties obvious to a person of ordinary skill in the art.

In summary, there is no clear and convincing evidence that a person of ordinary skill in the art at the relevant time would have

had the teaching, skill, or motivation to combine the prior art elements and create the claimed invention.

d. Secondary Considerations

Dey argues that secondary considerations of commercial success, satisfying a long felt need, and copying further illustrate the nonobviousness of the patents-in-suit. (Dkt. No. 250). Teva asserts that Dey failed to provide sufficient evidence to establish that objective indicia support a finding of nonobviousness. (Dkt. No. 253). Dey's arguments are more persuasive.

The Federal Circuit requires that, in addition to assessing the prior art, a court must examine evidence of "secondary considerations" of nonobviousness, if such evidence is available. Spectralytics, Inc. v. Cordis Corp., 649 F.3d 1336, 1344 (Fed. Cir. 2011). These considerations include "commercial success, long-felt but unresolved need, failure of others, and copying." Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc., 807 F.2d 955, 960 (Fed. Cir. 1986).

Such objective indicia "can be the most probative evidence of nonobviousness in the record, and enable the court to avert the trap of hindsight." Crocs, Inc. v. ITC, 598 F.3d 1294, 1310 (Fed. Cir. 2010). This is because the evidence "reflect[s] the

contemporary view of the invention by competitors and the marketplace," Spectralytics, 649 F.3d at 1344, and as such, is less susceptible to hindsight analysis.

The Court now examines each of the objective considerations raised by the parties.

1) Commercial Success

Initially, Dey contends that Perforomist® has been a commercial success due to its significant sales and profitability. (Dkt. No. 250). Teva asserts that, contrary to Dey's contentions, Perforomist® has actually been a commercial failure with meager sales growth. (Dkt. No. 253).

Since its launch, Perforomist® has experienced stable sales growth. Between the years of 2007-2012, it generated $278 million in profits, and Dey projects that net sales of Perforomist® will reach $1 billion throughout the life of the product. (Tr. 1166:10-16 (Graybill).) Teva argues that these numbers illustrate that Perforomist® was a commercial disappointment, since the profits did not meet the company's initial expectations.[9] (Dkt. No. 249).

[9] Dey initially invested 47.6 million dollars in the Perforomist® project, and originally projected that it would break even with costs and profits by early 2011, however, it took until late 2012 to do so. (Tr. 1068:4-1069:4).

Commercial success is not automatically negated by the early issuance of overly optimistic internal projections. Allergan Inc. v. Apotex, Inc., No. 1:10-CV-681, 2013 U.S. Dist. LEXIS 13987 at *35-36 (M.D.N.C. Jan. 24, 2013). Looking at the numbers objectively, it is apparent that Perforomist® has been a commercial success. The product "is in the top deciles, the top quarter of well-performing drugs in the marketplace," and achieves a compound annual growth rate of 50%. (Tr. 1233:1-23, 1236:11-1237:5 (Rausser).)

Moreover, the fact that Teva has so vigorously attempted to launch a generic of Perforomist® may be considered a testament to its commercial success. As another court overseeing an ANDA case against Teva recently observed, "if the patented drug were not a commercial success, at least to some degree, generic manufacturers would have little interest in offering their own versions of the drug." Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc., 923 F.Supp.2d 602, 677 (D. Del. 2013). The same rationale applies here.

The commercial success of Perforomist® is a testament to the nonobviousness of the invention, since that success may be attributed to the specific features claimed in Dey's patents. "A *prima facie* case of nexus is made when the patentee shows both that

there is commercial success, and that the product that is commercially successful is the invention disclosed and claimed in the patent." Crocs, Inc. v. Int'l Trade Comm'n, 598 F.3d 1294, 1310-11 (Fed Cir. 2010).

Perforomist® has not been successful merely because it is manufactured by Dey or because of Dey's marketing efforts. Rather, Perforomist® has achieved commercial success because it is an easy to use, non-DPI nebulizer formulation suitable for long term storage–the exact features for which Dey sought patent protection. This is illustrated by the fact that COPD patients have shown a preference for Perforomist® and are willing to pay a premium for the easy to use product. Medicare reimbursement, as Teva concedes, also favors Perforomist®.

Thus, Dey has made a clear showing of the commercial success of its product, which Teva has failed to successfully rebut. Performist's® commercial success supports the conclusion that Dey's invention was not obvious.

2) Long-Felt, Unresolved Need

Dey asserts that the creation of Perforomist® satisfied a long-felt, unresolved need for a non-DPI inhalation formulation of formoterol. (Dkt. No. 250). Teva argues that the needs of COPD

patients were effectively served by the MDI and DPI products already in the marketplace. (Dkt. No. 253).

Prior to the launch of Perforomist®, there were no non-DPI inhalation formulations of formoterol available for commercial sale. Rather, when Dey applied for its patents, the only inhalable formoterol product approved for sale in the United States was Foradil®, a DPI formulation. (Tr. 228:8-24; 254:8-255:3; 256:1-8 (Barnes)). From this, Teva concludes that COPD patients were not in need of a product such as Perforomist. (Dkt. No. 24).

The need for a non-DPI inhalation formulation stemmed from the fact that many COPD patients lack the ability to effectively use DPIs, which require strength and cognitive skills to coordinate inhalation with manipulation of the devices. (Tr. 254:8-256:8 (Barnes), 47:22-48:10 (Chaundry)). In addition, DPIs require individuals to take a deep and forceful breath to deliver the drug to their lungs, which is the precise physical ability many COPD patients lack. (Tr. 222:15-223:7 (Barnes)). Nebulizers, however, avoid the inherent problems of DPIs, because they do not require coordination of actions while in use. Individuals need only breathe normally into the nebulizer in order to take their medication.

In 2001, the time when Dey applied for its first patent, the need for a non-DPI inhalation formulation was unmet. Several non-

nebulizer formulations were considered, marketed, and often abandoned. These included oral products, such as those marketed by Yamanouchi; DPI products, such as Foradil®; and an MDI product that required refrigeration. Thus, no other company had satisfied the need for a non-DPI inhalation formulation until Dey introduced Perforomist® into the market. (Tr. 228:8-24 (Barnes)).

The existence of the need for an easy to use inhalation formulation is confirmed by the fact that physicians frequently prescribe Perforomist® to COPD patients. (Tr. 945:11-23 (Hendeles).) Additionally, insurance companies widely include Perforomist® on formularies, indicating that "the product is deemed valuable in having medical benefit to the patient." (Tr. 1168:3-1169:1) (stating that approximately 86% of insured lives have formulary plans including Perforomist®)(Graybill); (Tr. 1192:16-19) (Perforomist® appears on the most preferred tier for non-generic drugs in approximately 40% of formularies) (Graybill); (Tr. 954:6-958:7 (Hendeles)). Had there been no need for Perforomist®, it would be difficult to explain these statistics. In the Court's opinion, this history establishes that Dey's invention was not obvious prior to its inception.

3) Copying

Dey argues that Teva's decision to copy the exact composition of Perforomist® illustrates that its invention was not obvious. (Dkt. No. 250). According to Teva, however, it was required to copy Perforomist® in order to obtain approval of its ANDA. (Dkt. No. 253).

Teva undisputably copied Dey's invention in its ANDA. "That . . . a large corporation with many engineers on its staff[] did not copy [the prior art], but found it necessary to copy the . . . claims in suit, is equally strong evidence of nonobviousness." Panduit Corp. v. Dennison Mfg. Co., 774 F.2d 1082, 1099 (Fed. Cir. 1985). Teva's assertion that the Hatch Waxman Act requires ANDA applicants to copy an already patented invention in order to be relieved from the Act's clinical safety requirements is unavailing.

Teva faced no requirement to copy Perforomist® in order to obtain approval of its ANDA. The Hatch Waxman Act only requires that an ANDA applicant copy certain attributes of an already approved product in order to be relieved from the Act's clinical safety trial requirements. Namely, the Act only requires that the applicant copy an approved drug's 1)active ingredient (*e.g.*, Formoterol), 2) its route of administration (*e.g.*, Oral

Inhalation), and 3) its strength (*e.g.*, 0.02 mg/2 ml). 21 U.S.C. 355j(2)(A)(ii)(I).

The Act does not require TEVA to copy Perforomist's® "inactive ingredients" or "excipients", which, here, are the features of Perforomist® that make aqueous formoterol suitable for long-term use. In fact, Teva's own experts agreed that "in showing bioequivalence [and thereby obtaining ANDA approval], you don't have to use the same excipients that the brand uses in formulating the generic product." (TX 1017, 38:13-16 (D'Abreu-Hayling)). Thus, Teva could have developed its own solution using different excipients, but instead chose to reverse engineer Dey's formulation based on Dey's patents. This provides a strong indication that the prior art provided Teva with no obvious alternative to Dey's invention.

e. Conclusion as to the Defense of Obviousness

There is no clear and convincing evidence that the scope and the content of the prior art included the motivation and capability to invent the patents-in-suit. Thus, the Asserted Claims are not invalid due to obviousness.

C. Enablement

1. Standard of Law

A patent is invalid if it violates the enablement clause of 35 U.S.C. § 112. Section 112 demands that the patent enable others to replicate it. Id. Thus, a valid patent must disclose enough detail to enable a person of ordinary skill in the art to practice the invention "without undue experimentation at the time of filing." Alza Corp. v. Andrx Pharms., LLC, 603 F.3d 935, 939 (Fed. Cir. 2010). The key word is 'undue,' not 'experimentation.' Id. Accordingly, patents need not be exact blueprints for commercial production of a product.

2. Findings of Fact and Conclusions of Law

Teva challenges whether the First Family patents "teach those in the art enough that they can make and use the invention without undue" experimentation.[10] Amgen Inc. v. Hoeschst Marion Roussel, Inc., 314 F.3d 1313, 1335 (Fed. Cir. 2003). Teva focuses its enablement argument on several claims of the '355 and '953

[10]Teva's main focus at trial was on the defenses of anticipation and obviousness. Its argument regarding the affirmative defense of enablement appears only briefly in its post-trial briefs.

Patents,[11] contending that they do not teach a person of ordinary skill in the art the specific buffers and pH range needed to practice the invention. (Dkt. No. 249).

Teva's argument that the specifications of the First Family patents are non-enabling is unavailing. First, the required level of skill in the art is high. As the Court has determined, a person of ordinary skill in the art is an individual with an advanced degree in Pharmacy with experience in creating pharmaceutical formulations. Secondly, the patents-in-suit provide sufficient guidance that such a skilled artisan could practice the claimed invention. The specifications in the First Family patents disclose experimental data illustrating that formoterol is most stable, and therefore suitable for long-term storage, within the range of pH 4.0 to 6.0. The Patents specify that "[t]he rate constant...at a pH of 3, 4, 5, and 7 is approximately 0.62, 0.11, 0.044, and 0.55, respectively. Therefore, the decomposition of formoterol...is slowest at a pH of about 5.0." (TX 1, 9:24-41). A person of ordinary skill in the art would credit this teaching and have no reason to engage in "undue experimentation" with pH solutions

[11]These claims include claims 3, 34, 40, 65, 74, 104 and 116 of the '344 Patent and claims 76, 106, 112, 136, and 160 of the '953 Patent.

outside this range. The specifications further teach that suitable buffers include citrate, phosphate, and acetate (TX 1, 10:9-13), which are known to control pH within the range of 4.0 to 6.0. (Tr. 581:5-13 (Myrdal).)

Teva also contends that various claims of the First Family Patents are not enabled because their specifications include a list of several buffers, three of which a person of ordinary skill in the art would not consider suitable for buffering an inhalation solution. (Dkt. No. 249). However, only two non-asserted claims include the full list of suitable buffers.[12] All of the Asserted Claims either specify the use of a citrate buffer or do not call for the use of any specific buffer. Thus, Teva's argument that the buffers of the Asserted Claims are not enabled is without merit.

Teva further contends that various claims of the First Family Patents are not enabled because they recite a wide pH range of 2.0 to 8.0, thus preventing a person of ordinary skill in the art from identifying an appropriate pH range for the invention. However, of the claims Teva cites,[13] only one of those claims includes a pH

[12]These claims include claim 11 of the '344 Patent and claim 83 of the '953 Patent.

[13]Id.

limitation,[14] and that claim recites a narrow pH range of 4.0 to 6.0. The rest of the claims do not require a pH limitation, but only solutions that are "suitable for" or "stable during long-term storage."

Thus, based on the above-cited specifications, a person of ordinary skill in the art would be able to conclude, without undue experimentation, that solutions "suitable for long-term storage" would have a pH in the range of 4.0-6.0, and that buffers useful to achieve such a pH would include citrate, acetate, and phosphate.

a. Conclusion as to Defense of Enablement

Teva has not demonstrated by clear and convincing evidence that the patents-in-suit fail the disclosure requirements set forth in 35 U.S.C. § 112.

VI. CONCLUSION

Teva has failed to prove, by clear and convincing evidence, that the Asserted Claims are invalidated by the doctrines of anticipation, obviousness, or enablement. In light of its prior findings of Teva's infringement, the Court **DECLARES** that the making, using, selling, offering to sell, or importing the inhalation product described in ANDA No. 91-141 constitutes

[14]This describes claim 160 of the '953 Patent.

infringement of the patents-in-suit, and **ENJOINS** Teva, its officers, agents, servants and employees, from making, using, offering to sell, selling or importing the inhalation product described in ANDA No. 91-141. The Court also **ORDERS** that the effective date of the products described in ANDA No. 91-141 shall not precede the expiration of the patents-in-suit. Further, the Court **DENIES AS MOOT** all pending motions and **ORDERS** that this case be **DISMISSED WITH PREJUDICE** and be removed from its active docket.

It is so **ORDERED**.

Pursuant to Fed. R. Civ. P. 58, the Court directs the Clerk of Court to enter a separate judgment order and to transmit copies of both orders to counsel of record and all appropriate agencies.

Dated: March 21, 2014.

/s/ Irene M. Keeley
IRENE M. KEELEY
UNITED STATES DISTRICT JUDGE