

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PAR PHARMACEUTICAL, INC.,
PAR STERILE PRODUCTS, LLC,
and ENDO PAR INNOVATION
COMPANY, LLC,

Plaintiffs,

v.

EAGLE PHARMACEUTICALS
INC.,

Defendant.

Civil Action No. 18-0823-CFC-JLH

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Martin J. Black, Sharon K. Gagliardi, Brian M. Goldberg, Daniel Roberts,
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MEMORANDUM OPINION

August 31, 2021
Wilmington, Delaware



COLM F. CONNOLLY
CHIEF JUDGE

Plaintiffs Par Pharmaceutical, Inc., Par Sterile Products, LLC, and Endo Par Innovation Company, LLC (collectively, Par) have sued Defendant Eagle Pharmaceuticals Inc. for infringement of two patents: U.S. Patent Nos. 9,744,209 (the #209 patent) and 9,750,785 (the #785 patent). Par alleges that Eagle's submission to the Food and Drug Administration (FDA) of an Abbreviated New Drug Application (ANDA) for approval to market generic versions of Par's Vasostrict[®] drug product constitutes infringement of the asserted patents pursuant to § 271(e)(2)(A) of the Patent Act, 35 U.S.C. § 100, *et seq.* Eagle has alleged in counterclaims that the asserted patents are invalid and unenforceable.

In July 2021, I held a three-day bench trial. As required by Federal Rule of Civil Procedure 52(a)(1), I have set forth separately below my findings of fact and conclusions of law. Because I conclude that Par failed to prove by a preponderance of the evidence that Eagle's ANDA product will infringe the asserted patents, I need not and do not address Eagle's counterclaims.

I. THE STATUTORY AND REGULATORY FRAMEWORK

The ANDA procedures out of which this case arise were established by FDA regulations promulgated pursuant to the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 301 *et seq.*, and specifically by the so-called Hatch-Waxman

Amendments to the FDCA. Justice Kagan provided in *Caraco Pharmaceutical Laboratories, Ltd. v. Novo Nordisk A/S*, 566 U.S. 399 (2012) this helpful summary of the provisions of the Amendments and the FDA regulations that bear on this case:

The FDA regulates the manufacture, sale, and labeling of prescription drugs under a complex statutory scheme. To begin at the beginning: When a brand manufacturer wishes to market a novel drug, it must submit a new drug application (NDA) to the FDA for approval. The NDA must include, among other things, a statement of the drug's components, scientific data showing that the drug is safe and effective, and proposed labeling describing the uses for which the drug may be marketed. The FDA may approve a brand-name drug for multiple methods of use—either to treat different conditions or to treat the same condition in different ways.

Once the FDA has approved a brand manufacturer's drug, another company may seek permission to market a generic version pursuant to legislation known as the Hatch–Waxman Amendments. Those amendments allow a generic competitor to file an abbreviated new drug application (ANDA) piggy-backing on the brand's NDA. Rather than providing independent evidence of safety and efficacy, the typical ANDA shows that the generic drug has the same active ingredients as, and is biologically equivalent to, the brand-name drug. As we have previously recognized, this process is designed to speed the introduction of low-cost generic drugs to market.

Because the FDA cannot authorize a generic drug that would infringe a patent, the timing of an ANDA's approval depends on the scope and duration of the patents covering the brand-name drug. Those patents come in different varieties. One type protects the drug compound itself. Another kind . . . gives the brand manufacturer

exclusive rights over a particular method of using the drug. In some circumstances, a brand manufacturer may hold such a method-of-use patent even after its patent on the drug compound has expired.

To facilitate the approval of generic drugs as soon as patents allow, the Hatch–Waxman Amendments and FDA regulations direct brand manufacturers to file information about their patents. The statute mandates that a brand submit in its NDA the patent number and the expiration date of any patent which claims the drug for which the brand submitted the NDA or which claims a method of using such drug. And the regulations issued under that statute require that, once an NDA is approved, the brand provide a description of any method-of-use patent it holds. That description is known as a use code, and the brand submits it on FDA Form 3542. . . . [T]he FDA does not attempt to verify the accuracy of the use codes that brand manufacturers supply. It simply publishes the codes, along with the corresponding patent numbers and expiration dates, in a fat, brightly hued volume called the Orange Book (less colorfully but more officially denominated Approved Drug Products With Therapeutic Equivalence Evaluations).

After consulting the Orange Book, a company filing an ANDA must assure the FDA that its proposed generic drug will not infringe the brand’s patents. When no patents are listed in the Orange Book or all listed patents have expired (or will expire prior to the ANDA’s approval), the generic manufacturer simply certifies to that effect. Otherwise, the applicant has two possible ways to obtain approval.

One option is to submit a so-called section viii statement, which asserts that the generic manufacturer will market the drug for one or more methods of use not covered by the brand’s patents. A section viii statement is typically used when the brand’s patent on the drug compound has expired and the brand holds patents on only some approved methods of using the drug. If the ANDA

applicant follows this route, it will propose labeling for the generic drug that “carves out” from the brand’s approved label the still-patented methods of use. The FDA may approve such a modified label as an exception to the usual rule that a generic drug must bear the same label as the brand-name product. FDA acceptance of the carve-out label allows the generic company to place its drug on the market (assuming the ANDA meets other requirements), but only for a subset of approved uses—*i.e.*, those not covered by the brand’s patents.

* * * *

The generic manufacturer’s second option is to file a so-called paragraph IV certification, which states that a listed patent “is invalid or will not be infringed by the manufacture, use, or sale of the generic drug.” 21 U.S.C. § 355(j)(2)(A)(vii)(IV). A generic manufacturer will typically take this path in either of two situations: if it wants to market the drug for all uses, rather than carving out those still allegedly under patent; or if it discovers, as described above, that any carve-out label it is willing to adopt cannot avoid the brand’s use code. Filing a paragraph IV certification means provoking litigation. The patent statute treats such a filing as itself an act of infringement, which gives the brand an immediate right to sue [under] 35 U.S.C. § 271(e)(2)(A). Assuming the brand does so, the FDA generally may not approve the ANDA until 30 months pass or the court finds the patent invalid or not infringed. Accordingly, the paragraph IV process is likely to keep the generic drug off the market for a lengthy period, but may eventually enable the generic company to market its drug for all approved uses.

566 U.S. at 404–08 (irrelevant citations and internal quotation marks omitted).

II. FINDINGS OF FACT

A. Vasostrict® and the Asserted Patents

1. Vasostrict® is an injection product used to increase blood pressure in adults with vasodilatory shock. D.I. 268-1 ¶ 7. Vasostrict® works because its active ingredient—vasopressin—causes contraction of vascular and other smooth muscle cells. D.I. 268-1 ¶ 6.

2. In September 2012, JHP Pharmaceuticals, LLC filed with the FDA an NDA for approval to manufacture and sell Vasostrict®. D.I. 268-1 ¶ 7. In February 2014, while that NDA was pending before the FDA, Par Pharmaceutical Companies, Inc. acquired JHP, which subsequently changed its name to Par Sterile Products, LLC. D.I. 268-1 ¶ 8. Two months later, the FDA approved the Vasostrict® NDA, and in November 2014 Par began selling Vasostrict®. D.I. 268-1 ¶ 9.

3. Par listed the #209 and #785 patents in the Orange Book for Vasostrict®. D.I. 268-1 ¶ 34. The #785 patent is directed to specified vasopressin compositions and the #209 patent is directed to methods of increasing blood pressure using such compositions. Both patents require that the vasopressin compositions have a pH of between 3.7 and 3.9.

4. Claim 1 of the #785 patent recites:

A pharmaceutical composition comprising, in a unit dosage form, from about 0.01 mg/mL to about 0.07

mg/mL of vasopressin or a pharmaceutically-acceptable salt thereof, wherein the unit dosage form further comprises impurities that are present in an amount of 0.9% to 1.7%, wherein the impurities have from about 85% to about 100% sequence homology to SEQ ID NO.: 1, and *wherein the unit dosage form has a pH of 3.7-3.9.*

Claim 1 of the #785 patent (emphasis added). Claims 5 and 8 of the #785 patent depend from claim 1.

5. Claim 1 of the #209 patent recites:

A method of increasing blood pressure in a human in need thereof, the method comprising administering to the human a unit dosage form, wherein

the unit dosage form comprises from about 0.01 mg/mL to about 0.07 mg/mL of vasopressin or a pharmaceutically acceptable salt thereof, wherein:

the unit dosage form has a pH of 3.7-3.9;

the unit dosage form further comprises impurities that are present in an amount of 0.9% - 1.7%, wherein the impurities have from about 85% to about 100% sequence homology to SEQ ID NO.: 1;

the administration provides to the human from about 0.01 units of vasopressin or the pharmaceutically-acceptable salt thereof per minute to about 0.1 units of vasopressin or the pharmaceutically-acceptable salt thereof per minute; and

the human is hypotensive.

Claim 1 of the #209 patent (emphasis added). Claims 4, 5, and 7 of the #209 patent depend from claim 1.

6. pH is a measurement of the acidity or basicity of an aqueous solution.

Tr. 200:20–201:8.

B. The Artisan of Ordinary Skill

7. “A court construing a patent claim seeks to accord a claim the meaning it would have to a person of ordinary skill in the art at the time of the invention.” *Innova/Pure Water, Inc. v. Safari Water Filtration Sys.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004). The parties offered at trial competing but similar definitions of the artisan of ordinary skill to whom the asserted patents are directed. Both parties stated that their positions “would not change if the Court were to adopt the other side’s definition” of a skilled artisan. D.I. 290 ¶ 462; D.I. 284 ¶ 45. Accordingly, I will adopt Par’s proposal that an artisan of ordinary skill

would have a Master’s, Pharm.D., or Ph.D. in the field of pharmaceutical sciences or a related discipline and several years of experience in the development of pharmaceutical dosage forms. [An artisan of ordinary skill] may also have less formal education and a greater amo[unt] of experience. Further, [an artisan of ordinary skill] would have had access to and would have worked in collaboration with persons who have several years of experience in the formulation of drug products as well as other professionals in the drug development field, such as pharmacologists, chemists, biologists, or clinicians.

D.I. 284 ¶ 45.

8. The parties agree that an artisan of ordinary skill would round pH readings to the nearest tenth decimal and that, therefore, the pH limitation of the

asserted claims—i.e., the requirement that the pharmaceutical composition in the #785 patent and the unit dosage form in the #209 patent have a pH between 3.7 and 3.9—is met when the pH is greater than or equal to 3.65 and less than or equal to 3.94. D.I. 290 ¶ 323.

C. Eagle’s ANDA and its ANDA Product

9. In January 2018, Eagle filed its ANDA for approval to manufacture and sell a generic version of Vasostriect[®] before the asserted patents expire. D.I. 268-1 ¶ 40.

10. Eagle’s ANDA includes a paragraph IV certification that states Eagle’s belief that the asserted patents are invalid or will not be infringed by the commercial manufacture, use, or sale of Eagle’s proposed ANDA product. D.I. 268-1 ¶ 41.

11. Eagle’s ANDA contains specifications that define, among other things, the acceptable pH ranges of Eagle’s ANDA product at different stages of the product’s manufacturing process and during its shelf life. Tr. 349:5–350:2; DTX-327 at 1. Eagle’s ANDA seeks approval for a product with a shelf life of 24 months at a refrigerated storage temperature of 2–8 °C. D.I. 268-1 ¶ 43.

12. Eagle represented in its ANDA that both the “release [pH] specification” and the “stability [pH] specification” of its ANDA product are 3.4–

3.6. DTX-678 at 2 (stating that the “Release Specification” for pH is “3.4 – 3.6” and that the “Stability Specification” for pH is “[s]ame as release”).

13. Like Eagle’s ANDA, the parties throughout the trial used the terms “release specification” and “stability specification.” Par maintained at trial that the definitions of these terms are matters of fact, Tr. 32:20–22, but Par’s counsel also told me during trial that both terms had a “regulatory definition,” Tr. 32:20–33:12.

14. Neither Par nor Eagle sought to introduce at trial expert testimony about FDA procedures or regulations.

15. The parties agree, and I find, that the FDA’s definition of “release specification” is set forth in 21 C.F.R. § 211.165. Section 211.165(a) provides that “[f]or each batch of [a] drug product, there shall be appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release.” The parties did not cite and I was unable to find an FDA regulation or provision in the FDCA that defines “release.” But § 211.165 is titled “Testing and release *for distribution*.” 21 C.F.R. § 211.165 (emphasis added). And the FDA’s definitions of “batch number” and “manufacturing, processing, packing, or holding” make clear that “release for distribution” means release in final packaged form for distribution for consumption by patients. *See* 21 C.F.R. § 210.3(b)(11) (defining “batch number” as “any distinctive combination of letters, numbers, or

symbols, or any combination of them, from which the complete history of *the manufacture, processing, packing, holding, and distribution* of a batch or lot of drug product or other material can be determined”) (emphasis added); 21 C.F.R. § 210.3(b)(12) (defining “[m]anufacture, processing, packing, or holding of a drug product” as “include[ing] packaging and labeling operations, testing, and quality control of drug products”). Thus, I find that the release pH specification in Eagle’s ANDA means the pH specification for its ANDA product immediately prior to the product’s release for distribution.

16. Par and Eagle agree, and I find, that Eagle’s ANDA product cannot lawfully be released for distribution unless, at the time of the release, the product has a pH of between 3.4 and 3.6 (i.e., before rounding, between 3.35 and 3.64).

17. The parties agree, and I find, that “stability specification” means “the combination of physical, chemical, biological, and microbiological tests and acceptance criteria that a drug product should meet throughout its shelf-life.” D.I. 284 ¶ 84; D.I. 276 at 2. The FDA defines “acceptance criteria” as “the product specifications and acceptance/rejection criteria, such as acceptable quality level and unacceptable quality level, with an associated sampling plan, that are necessary for making a decision to accept or reject a lot or batch (or any other convenient subgroups of manufactured units).” 21 C.F.R. § 210.3(b)(20). Based on these definitions and the stability pH specification set forth in Eagle’s ANDA, I

find that Eagle's ANDA product cannot not lawfully be distributed for use and would not be approved for distribution by the FDA unless, at all periods during the product's shelf life, the product's pH is between 3.4 and 3.6 (i.e., before rounding, between 3.35 and 3.64). Thus, to comply with its ANDA specifications, Eagle's generic version of Vasostriect® must have a pH of 3.4 to 3.6 at the time of its release for distribution and for its entire shelf life.

18. Eagle has manufactured to date 17 batches of its ANDA product. D.I. 268-1 ¶ 44; Tr. 151:2–8. The batches are numbered SVA001 through SVA017. It is undisputed that two batches (SVA010 and SVA015) were rejected by Eagle for reasons unrelated to any of the disputed issues in this case. The parties did not adduce at trial evidence of the pH data for those batches.

19. Batches SVA001 through SVA003 (referred to as the “registration batches”) were manufactured in March 2017 to evaluate the stability of Eagle's ANDA product. D.I. 268-1 ¶ 45; Tr. 179:3–14, 220:19–221:3, 351:8–19. At the time of their manufacture, the registration batches had release and stability pH specifications of 2.5–4.5. DTX-323 at 12–13; Tr. 375:15–20, 263:17–21. But after the asserted patents were published in June 2017, Eagle narrowed the release and stability pH specifications for its ANDA Product to 3.4–3.6. DTX-327 at 1; Tr. 375:21–23, 264:20–24.

20. Batches SVA004 through SVA006 (referred to as “characterization batches”) were manufactured in March and April 2019. D.I. 268-1 ¶ 46; Tr. 352:2–9. The characterization batches were manufactured “in accordance with the manufacturing process used for the registration batches.” D.I. 268-1 ¶ 47; DTX-331 at 20. Eagle placed samples from Batches SVA001 through SAV006 into stability studies to evaluate whether these batches would remain in-specification over their shelf lives. Tr. 353:18–354:10; DTX-331 at 4, 20. To do this evaluation, Eagle performed three distinct stability studies, storing the samples at: (1) room temperature for 12 months; (2) refrigerated temperature for 24 months; and (3) refrigerated temperature for a period of time (12 months for the registration batches and 21 months for the characterization batches), followed by room temperature for a period of time (12 months for the registration batches and 7.5 months for the characterization batches). DTX-331 at 4–7, 20–23; *see also* DTX-727 at 4–7, 20–23; PTX-1427 at 4–7, 20–23; Tr. 353:18–354:10. Par has based its infringement arguments solely on the studies that evaluated stability at a refrigerated temperature for 24 months. *See* D.I. 283 at 1 (“Eagle’s ANDA product has a drift problem: when stored in refrigerated conditions, its pH tends to rise.”); D.I. 283 at 3 (“[T]he pH [of the ANDA product] tends to rise over time when stored in refrigerated conditions.”); D.I. 284 ¶¶ 107–116 (analyzing only the

pH data from the refrigerated stability studies). Thus, unless otherwise noted, the following references to pH data refer to refrigerated pH data.

21. During the stability study of SVA001, Eagle recorded a pH level of 3.69 (which rounds to 3.7) at the 24-month mark—i.e., at the very end of SVA001’s a shelf life. DTX-331 at 9; DTX-727 at 9; *see also* DDX7-1; DTX-993 at 1; Tr. 357:19–358:2. All other pH measurements for SVA001 and all pH measurements for Eagle’s other registration and characterization batches remained within the stability specification of 3.4–3.6 for the duration of those batches’ shelf lives. Tr. 357:3–358:10; *see also* DDX7-1; DTX-993. After an investigation into the lone out-of-specification result for SVA001, “[t]he root cause . . . was determined to be [that] batch SVA001 was released at the upper limit of the pH specification” at a pH of 3.64. DTX-331 at 9; DTX-727 at 9; Tr. 362:2–10.

22. In response to the single out-of-specification pH test result for SVA001, Eagle “optimized” its manufacturing process “to assure tighter control of pH.” DTX-331 at 9; DTX-727 at 9; PTX-1433 at 9; Tr. 362:11–20. To achieve this optimization, Eagle made three adjustments to its manufacturing process. First, Eagle narrowed the specified pH range for its pH adjustment step—i.e., the step where Eagle adds acid to its ANDA product to achieve its desired pH. The pH range for this step for the pre-optimization batches had been 3.4–3.6 with a target of 3.5. For the post-optimization batches, Eagle changed the specified pH range to

3.42–3.49 with a target of 3.45. *Compare* DTX-323 at 5 *with* DTX-323 at 10, 16; *see also* DTX-324 at 25; Tr. 363:15–24, 371:14–72:2. Second, Eagle added a new pH stabilization step after the pH adjustment step to ensure pH uniformity. Tr. 366:22–67:1. The pH stabilization step requires mixing the solution for no less than 20 minutes, and then pulling samples from the mixing vessel to measure pH at ten-minute intervals. DTX-323 at 10, 16; DTX-324 at 27; Tr. 365:7–13, 372:3–8. Each pH measurement taken during the pH stabilization step must be within 0.03 pH units of the preceding measurement, DTX-323 at 10, 16; DTX-324 at 27; Tr. 365:23–366:2, and the pH measurement taken at the end of the stabilization step must be between 3.42 and 3.50, DTX-323 at 10, 16; DTX-324 at 27; Tr. 365:21–22, 372:9–13. Third, Eagle narrowed the in-process pH specifications for the pH measurements taken immediately before and after a filtration step from 2.5–4.5 (for the pre-optimization batches) to 3.42–3.54 (for the post-optimization batches). DTX-323 at 12–13; Tr. 373:12–374:2.

23. Eagle stated in its ANDA that these process and specification modifications “were implemented to provide greater assurance [that] all future . . . batches will remain within the proposed stability specifications through the end of shelf life (24 months) for all labeled storage conditions.” DTX-331 at 24; DTX-727 at 25; *see also* DTX-133 at 21 (Eagle stating to the FDA that the process and specification modifications were designed to “ensure the pH remains

within the established [pH] range during finished product manufacturing and through the proposed shelf life”).

24. Eagle represented in its ANDA that it will use its optimized manufacturing process to manufacture its ANDA product. *See generally* DTX-324; *see also* DTX-133 at 21; Tr. 364:12–18, 466:18–467:4.

25. Every batch of Eagle’s ANDA product manufactured after SVA006 (i.e., batches SVA007 through SVA017) has been manufactured using Eagle’s new, optimized process.

26. The pH measurements for the first six batches of Eagle’s ANDA product (i.e., the pre-optimization batches) and batches SVA007 through SVA017 (i.e., the post-optimization batches) are summarized in Appendix Table 1.

27. Par argues that the post-optimization batches’ data “show a tendency for pH to rise between final in-process testing and release testing, by as much as 0.07 pH units, such that batches made at a pH within the latest in-process specification (up to 3.54) can rise to at least pH 3.61 by the time of release.” D.I. 283 at 5. Par also argues that pH stability data for the “optimized” batches shows that pH continues to “drift” after release, by as much as 0.06 pH units. D.I. 283 at 5. But the data do not establish that Eagle’s ANDA product has the “drift problem” Par claims; instead, the pH data establish that it is more likely than not that Eagle’s ANDA product will not meet the 3.7–3.9 pH range claimed in the

asserted patents. The data show that Eagle has taken approximately 200 pH stability measurements since March 2017. DTX-993 at 1, 5, 7, 9. Only one of those pH stability measurements (for batch SVA001) was outside of Eagle’s ANDA stability specification and within the range of the pH limitation claimed in the asserted patents. DDX7-1; DTX-993 at 1, 5, 7, 9; Tr. 357:11–358:22. And on every occasion that a pH measurement was taken since Eagle optimized its manufacturing process, the pH measurement has been within the stability pH specification in Eagle’s ANDA and outside the pH limitation claimed in the asserted patents.

28. Eagle’s optimized manufacturing process achieved its goal of assuring a tighter control over pH. As shown in the table below, the optimized process enabled Eagle to maintain (1) a pH of around 3.50 during manufacturing and release and (2) a stability pH of around 3.50 during refrigerated storage.

	<i>Pre-Filtration</i>	<i>Post-Filtration</i>	<i>Release</i>	<i>Refrigerated Stability</i>
Pre-Optimization Batches (SVA001–SVA006)	3.5–3.7	3.5–3.7	3.53–3.64	3.39–3.75
Post-Optimization Batches (SVA007–SVA017)	3.48–3.53	3.44–3.50	3.45–3.57	3.46–3.55

DTX-993; Tr. 360:6–13, 361:2–16. The fact that none of the pH measurements for the post-optimization batches approach the top end of Eagle’s release specification (3.64) is telling, because the “root cause” of SVA001’s out-of-specification (and infringing) pH measurement “was determined to be [the fact that] batch SVA001

was released at the upper limit of the pH specification.” DTX-331 at 9; DTX-727 at 9; Tr. 362:2–10.

29. Par is correct that pH measurements for the tested batches varied over the course of the batches’ shelf lives. But this variability does not make it more likely than not that Eagle’s ANDA product will meet the claimed pH limitation. I make this finding for two reasons. First, contrary to Par’s suggestion, the stability pH data for individual batches do not show a steady and inevitable creep (i.e., drift) to higher pH values. Instead, the data show minor fluctuations in pH over a batch’s shelf life. Moreover, these fluctuations do not reveal any discernible trend. Sometimes the pH value increases between measurements; sometimes it decreases. Second, the pH fluctuations observed over the shelf lives of the post-optimization batches, as Par’s expert admitted, are “in the neighborhood of . . . [0].05 and generally located around 3.50–3.52.” Tr. 295:18–296:2, 358:11–22, 360:6–13, 361:2–16, 377:21–378:3. It follows that the pH measurements for Eagle’s ANDA product will be between 3.45 (that is, 3.50 minus 0.05) and 3.57 (that is, 3.52 plus 0.05) at the time of their release and over their shelf lives.

30. Par has not demonstrated by a preponderance of the evidence that Eagle believes it is not bound by its representation to the FDA that it will use its optimized manufacturing process to manufacture its ANDA product. Nor has Par demonstrated by a preponderance of the evidence that Eagle will use a

manufacturing process other than its optimized manufacturing process to manufacture its ANDA product. Par argues that “Eagle has steadfastly refused to lower its release pH specification below 3.6 (3.64 rounded),” D.I. 283 at 19, and appears to suggest that I can infer from that “refusal” an intent to use a manufacturing process other than Eagle’s optimized process, *see* D.I. 283 at 19 (“Eagle’s refusal to [lower its release pH specification] speaks volumes about its true intent—it clearly wishes to reserve the right to sell products that, at the time of release, have a pH of 3.60 or higher, presumably because it knows that products made at the upper end of its in-process pH specification can drift into that range by the time of release testing.”). But Par adduced no evidence at trial from which it could be inferred that the FDA (or any other entity) *asked* Eagle to lower its release pH specification, let alone that Eagle refused to comply with such a request. It also makes sense that the FDA would not make such a request, since Eagle represented to the FDA that it would use the optimized process and since the data for the optimized process shared by Eagle with the FDA demonstrate that that process results in products that comply with both the ANDA’s release pH specification and its stability pH specification.

31. I find therefore as a matter of fact that even if Eagle’s ANDA product were not required as a matter of law to maintain the stability pH specification set forth in Eagle’s ANDA, because Eagle will have to use the optimized

manufacturing process it committed to in its ANDA, the product Eagle will manufacture and sell will not have a pH that would drift into the range of the pH limitation claimed in the asserted patents.

32. Par has not demonstrated by a preponderance of the evidence that a generic version of Vasostrict® manufactured according to Eagle's optimized process will have a pH that does not meet the stability pH specification. The pH measurement data adduced at trial demonstrates that if Eagle uses its optimized process to manufacture its ANDA product, the product will have a pH that meets the ANDA's stability pH specification.

33. Par adduced at trial no evidence from which it could be reasonably inferred that Eagle believes it is not legally bound by the stability pH specification in its ANDA.

34. Par has not demonstrated by a preponderance of the evidence that Eagle will distribute a generic version of Vasostrict® that does not meet the stability pH specification in its ANDA.

III. LEGAL STANDARDS FOR INFRINGEMENT

Analyzing infringement involves two steps. The first step is to construe disputed patent terms consistently with how they would be understood by an artisan of ordinary skill. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc). The second step is to determine whether the accused products or

methods infringe the patent, by comparing those products or methods to the construed claims. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). The first step in the infringement analysis is a question of law; the second is a question of fact. *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1565 (Fed. Cir. 1997). A patentee bears the burden of proving infringement by a preponderance of the evidence. *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 758 (Fed. Cir. 1984).¹

As noted above, § 271(e)(2)(A) of the Patent Act defines the filing of an ANDA with a paragraph IV certification as an act of infringement. That definition “create[s] case or controversy jurisdiction to enable a court to promptly resolve any dispute concerning infringement and validity” of patents listed in the Orange Book. *Glaxo*, 110 F.3d at 1569. “Notwithstanding this defined act of infringement, a district court’s inquiry in a suit brought under § 271(e)(2) is the same as it is in any other infringement suit, *viz.*, whether the patent in question is ‘invalid or *will not be infringed* by the manufacture, use, or sale of the drug for which the [ANDA] is

¹ Par alleges that Eagle’s manufacture and sale of its ANDA product will directly infringe and induce the infringement of the asserted patents. Because I find that Eagle’s ANDA product does not infringe the asserted patents, Par’s theory of induced infringement necessarily fails. See *Epcon Gas Sys., Inc. v. Bauer Compressors, Inc.*, 279 F.3d 1022, 1033 (Fed. Cir. 2002). (“[T]here can be no inducement of infringement without direct infringement by some party.”).

submitted.” *Id.* (italics in the original) (underline added) (quoting 21 U.S.C. § 355(j)(2)(A)(vii)(IV)). Thus, “the ultimate infringement question is determined by traditional patent law principles and, if a product that an ANDA applicant is asking the FDA to approve for sale falls within the scope of an issued patent, a judgment of infringement must necessarily ensue.” *Sunovion Pharms., Inc. v. Teva Pharms. USA, Inc.*, 731 F.3d 1271, 1278 (Fed. Cir. 2013). By the same token, if the product that an ANDA applicant is asking the FDA to approve falls outside the scope of an asserted patent, a judgment of noninfringement must follow. In short, “[w]hat [the ANDA applicant] has asked the FDA to approve as a regulatory matter is the subject matter that determines whether infringement will occur.” *Id.* at 1278.

The infringement analysis in an ANDA case is most straightforward when the ANDA’s specification directly addresses the elements of the asserted claims that are at issue. “Because drug manufacturers are bound by strict statutory provisions to sell only those products that comport with the ANDA’s description of the drug, an ANDA specification defining a proposed generic drug in a manner that directly addresses the issue of infringement will control the infringement inquiry.” *Abbott Lab’ys v. TorPharm, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002). As the Federal Circuit explained in *Bayer AG v. Elan Pharmaceutical Research Corp.*, 212 F.3d 1241 (Fed. Cir. 2000):

[i]f any of the statements in [the ANDA’s] specification are false, [the ANDA filer] is subject to civil penalties and

the withdrawal of the approval of its drug. Additionally, if [the ANDA filer] introduces a drug into interstate commerce without complying with the approval requirements of 21 U.S.C. § 355, it is subject to various additional penalties, including an injunction, criminal sanctions, seizure of the unapproved drug, and debarment of its corporation and individual officials from submitting or assisting in the submission of an ANDA in the future. [The ANDA filer] also would be subject to criminal prosecution for making false statements to the FDA under 18 U.S.C. § 1001, conspiring to defraud the United States under 18 U.S.C. § 371, and obstructing proceedings before a federal agency under 18 U.S.C. § 1501. If [the ANDA filer] changes its ANDA, it must file the changes with the FDA, and if the changes are to the drug's specification, [the ANDA filer] must obtain approval for the changes before they can be made.

Id. at 1249–50 (citations omitted). Because of these statutory and regulatory requirements and the consequences that flow from failing to abide by them, courts “cannot assume that [an ANDA filer] will not act in full compliance with its representations to the FDA.” *In re Brimonidine Patent Litigation*, 643 F.3d 1366, 1378 (Fed. Cir. 2011).

This principle that an ANDA filer is bound by the representations and specifications in its ANDA is central to the infringement inquiry. And if an ANDA specification describes a product that either necessarily infringes an asserted patent or necessarily does not infringe the patent, the specification dictates the outcome of the infringement analysis. *See Ferring B.V. v. Watson Lab'ys, Inc.-Florida*, 764 F.3d 1401, 1409 (Fed. Cir. 2014) (“In some cases, the ANDA

specification directly resolves the infringement question because it defines a proposed generic product in a manner that either meets the limitations of an asserted patent claim or is outside the scope of such a claim.”); *Elan*, 212 F.3d at 1249 (finding that an ANDA specification that clearly defined a noninfringing product “mandate[d] a finding of no literal infringement”).

IV. DISCUSSION

Par brought this infringement action pursuant to § 271(e)(2)(A) based on Eagle’s paragraph IV certification. It has asserted claims 1, 4, 5, and 7 of the #209 patent and claims 1, 5, and 8 of the #785 patent. All the asserted claims require vasopressin compositions with a pH of 3.7 to 3.9. The parties did not ask me to construe this pH limitation and therefore it is understood to have its plain and ordinary meaning. *Phillips*, 415 F.3d at 1312.

Eagle stipulated before trial that its ANDA product infringes every limitation of the asserted claims except for the pH limitation. D.I. 268 ¶ 58; D.I. 251 at 1. Thus, Par’s infringement case turns on whether Eagle’s ANDA product is more likely than not to have a pH between 3.7 and 3.9.

I have already determined as a matter of fact that to comply with its ANDA specifications, Eagle’s generic version of Vasostrict® must have a pH of 3.4 to 3.6 at the time of its release for distribution and for its entire shelf life. Accordingly, the ANDA product Eagle is asking the FDA to approve cannot have at the time of

its release or at any time during its shelf life a pH between 3.7 and 3.9, and therefore a judgment of noninfringement “must necessarily ensue.” *Sunovion Pharms.*, 731 F.3d at 1278. In other words, Eagle’s ANDA’s release and stability pH specifications define its proposed generic product in a manner that directly addresses the issue of infringement raised by Par; and therefore the ANDA “controls the infringement inquiry” and requires a judgment of noninfringement.

Par argues that “[t]wo undisputed facts compel a finding of infringement.”

D.I. 283 at 1. In Par’s words:

First, Eagle’s ANDA product has a drift problem: when stored in refrigerated conditions, its pH tends to rise. This is true even for batches made using Eagle’s supposedly “optimized” manufacturing process.

Second, per its release specification, Eagle seeks authority to release products into the marketplace with pH values up to 3.64, such that if those products drift upward just 0.01 pH unit—and the data shows they would drift far further—Eagle’s products would rise into Par’s claimed pH range.

These facts, taken together, mean that Eagle is seeking authority to sell products that would more likely than not infringe Par’s patents. That is Hatch-Waxman Act infringement.

D.I. 283 at 1.

These alleged facts, however, are neither undisputed nor correct. With respect to the first alleged fact, as explained above, the pH measurements taken from Eagle’s batches negate Par’s claims that Eagle’s ANDA product has a “drift

problem.” Par’s second alleged fact makes too much of too little. It is true that Eagle’s ANDA product’s release pH specification, if read in isolation, allows for a pH range of between 3.4 and 3.6; and it is true that a pH of 3.64 would meet that specification. But the release specification is not the only specification in Eagle’s ANDA; and it is not accurate to say that Eagle “seeks authority to release products into the marketplace with pH values up to 3.64.” Rather, Eagle seeks authority to release products into the marketplace that satisfy *both* the release pH specification *and* the stability pH specification, and thus it seeks authority to distribute products that have a pH of between 3.4 and 3.6 from the time of their release for distribution *through the entirety of the products’ shelf lives*.

Par argues that the “release specification is the gatekeeper for what Eagle will or will not be authorized to sell and thereby defines the scope of its authority under the ANDA.” D.I. 283 at 1. But it is the entirety of Eagle’s ANDA, not a single specification in the ANDA, that “defines the scope of [Eagle’s] authority under the ANDA.” Par wants me to assume that Eagle will comply with the ANDA’s release pH specification but not comply with its stability pH specification. It insists that “the stability specification is not a legal bar to finding infringement.” D.I. 283 at 24. But unequivocal binding precedent holds otherwise. As the Federal Circuit held in *In re Brimonidine*, courts “cannot assume that [an ANDA filer] will not act in *full compliance* with its representations to the

FDA.” 643 F.3d at 1378 (emphasis added). And as the court stated in *Abbott Laboratories*, “an ANDA specification defining a proposed generic drug in a manner that directly addresses the issue of infringement will control the infringement inquiry.” 300 F.3d at 1373.

This case is virtually on all fours with *In re Brimonidine*. As here, the asserted patent in *In re Brimonidine* had a pH limitation that did not overlap with the release and stability pH specifications in the ANDA in question. Specifically, the asserted claims in *In re Brimonidine* required a pH of 7.0 or greater, while the ANDA specified a release and stability pH between 6.5 and 6.7. 643 F.3d at 1376–77. Relying on testing data from the defendant’s ANDA, the district court found that the proposed drug product’s pH would fall over its shelf life and that, therefore, the defendant would need to manufacture the product with a pH of 7.0 or above to achieve a pH of between 6.5 and 6.7 over the drug’s shelf life. *Id.* Based on that finding, the district court entered a judgment of infringement against the defendant. The Federal Circuit reversed. In doing so, it cited the language quoted above from *Abbott* that the ANDA “control[s]” the infringement analysis and noted that the ANDA unambiguously defined a noninfringing product. *Id.* at 1377–78.

The ANDA in this case similarly defines a noninfringing product. And following the Federal Circuit’s lead in *In re Brimonidine*, I reject Par’s attempt to

use testing data to support a finding that Eagle would violate the binding representations it made to the FDA in its ANDA.²

But even if I were to consider that data, it would not change the outcome of this case. I have already found as a factual matter that Par failed to demonstrate by a preponderance of the evidence that Eagle believes it is not bound by either its ANDA stability pH specification or its representation to the FDA that it will use its optimized process to manufacture its ANDA product. Par similarly failed to demonstrate by a preponderance of the evidence that Eagle will use a

² In support of its position that I can consider such data, Par cites passages from *Abbott Laboratories* and *Tyco Healthcare Group LP v. Mutual Pharmaceutical Co.*, 762 F.3d 1338 (Fed. Cir. 2014). See *Abbott*, 300 F.3d at 1373 (“It is also possible, at least in theory, that other evidence may directly contradict the clear representations of the ANDA and create a dispute of material fact regarding the identity of the compound that is likely to be sold following FDA approval.”); *Tyco Healthcare*, 762 F.3d at 1344 (“The question addressed in *Elan* and similar cases is whether the product that the ANDA applicant will likely market if its application is approved will infringe. That can occur in spite of the ANDA specification if, for example, the ANDA is based on faulty testing or screening procedures.”) (citations omitted); *id.* (“[W]e agree with Tyco that it is not unreasonable for a patent owner to allege infringement under section 271(e)(2)(A) if the patent owner has evidence that the as-marketed commercial ANDA product will infringe, even though the hypothetical product specified in the ANDA could not infringe.”). I have spent more hours than my caseload affords trying without success to reconcile these passages with the unequivocal holdings from the Federal Circuit cases I have cited above. I also wonder whether a district court has the necessary expertise or constitutional authority to decide either while an ANDA is pending before the FDA or after the FDA has approved the ANDA that the ANDA applicant employed faulty testing or screening procedures.

manufacturing process other than its optimized process to manufacture its ANDA product. And finally, Par has failed to demonstrate by a preponderance of the evidence that a generic version of Vasostriect[®] manufactured according to Eagle's optimized process will have a pH that does not meet its ANDA's stability pH specification. Because of those failures, Par failed to establish by a preponderance of the evidence that Eagle would distribute a generic version of Vasostriect[®] that does not meet the 3.4–3.6 stability pH specification in its ANDA; and therefore, necessarily, Par failed to prove by a preponderance of the evidence that Eagle's ANDA product will infringe the 3.7–3.9 pH limitation in the asserted claims. At most, Par proved at trial that *if* Eagle were not bound by its stability pH specification and its representation to use its optimized manufacturing process then Eagle *could* use a different manufacturing process that *could* result in a drug product with a pH that meets the pH limitation in the asserted claims. Proof of that *possibility* is insufficient to sustain a finding of infringement under § 271(e)(2). *See Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1364 (Fed. Cir. 2003) (“Section 271(e)(2) does not encompass ‘speculative’ claims of infringement.”).

V. CONCLUSION

For the reasons discussed above, I find that Eagle does not infringe claims 1,

4, 5, and 7 of the #209 patent and claims 1, 5, and 8 of the #785 patent.³

The Court will issue an Order directing the parties to submit a proposed order by which the Court may enter final judgment consistent with this Opinion.

³ On page 30 of its posttrial brief, Par stated: “For similar reasons, Par is entitled to a declaration of infringement under § 271(a) and (b).” D.I. 283 at 30. It did not elaborate. Having concluded that Par failed to prove by a preponderance of the evidence that Eagle infringed the asserted patents, I will deny its application for a declaratory judgment of infringement under § 271(a) and (b).

APPENDIX TABLE 1

Batch	Pre-Filter	Post-Filter	Release			1M	3M	6M	9M	12M	18M	24M
SVA001 U	3.7	3.6	3.64			–	3.44	3.61	3.64	3.58	3.61	3.69, 3.75, 3.68
SVA001 I						3.6	3.6	3.62	3.64	3.57	3.61	3.61
SVA002 U	3.5	3.5	3.53			–	3.39	3.53	3.57	3.52	3.52	3.55
SVA002 I						3.5	3.5	3.53	3.56	3.51	3.52	3.57
SVA003 U	3.7	3.7	3.60			–	3.46	3.59	3.60	3.59	3.58	3.59
SVA003 I						3.6	3.6	3.59	3.63	3.60	3.58	3.62
SVA004 U	3.6	-	3.6			3.6	3.6	3.55	3.60	3.58	3.60	3.56
SVA004 I						3.6	3.6	3.56	3.61	3.58	3.61	3.57
SVA005 U	3.6	3.6	3.6			3.5	3.6	3.6	3.57	3.56	3.54	3.55
SVA005 I						3.5	3.6	3.6	3.57	3.55	3.56	3.56
SVA006 U	3.6	3.6	3.6			3.6	3.6	3.6	3.61	3.58	3.55	3.60
SVA006 I						3.6	3.6	3.6	3.61	3.59	3.53	3.59
SVA007 U	3.50, 3.51	3.50	3.50			3.48	3.51	3.55	3.51	3.51	3.46	–
SVA007 I						3.54	3.51	3.51	3.52	3.51	3.49	–
SVA008 U	3.49	3.48	3.52			3.51	3.51	3.53	3.53	3.51	3.53	–
SVA008 I						3.49	3.51	3.53	3.53	3.51	3.51	–
SVA009 U	3.48	3.48	3.48			3.52	3.52	3.50	3.50	3.52	3.52	–
SVA009 I						3.50	3.53	3.52	3.51	3.54	3.53	–
SVA011 I	3.50	3.50	3.54	3.56	3.57	3.49	3.48	3.48	–	–	–	–
			3.51	3.49	3.47							
SVA012 I	3.49	3.44	3.45	3.48	3.50	3.51	3.51	3.52	–	–	–	–
SVA013 I	3.53	3.49	3.48	3.50	3.48	3.53	3.54	3.53	–	–	–	–
SVA014	3.53	3.49	3.49									
SVA016	3.52	3.50	3.49									
SVA017	3.53	3.50	3.47									

Notes on Appendix Table 1

- Data for Appendix Table 1 were taken from DDX7-1 and DTX-993.
- Samples were stored in both upright and inverted positions, denoted with a “U” or “I”, respectively, following the batch names. Storage orientation does not affect the pH of Eagle’s ANDA product. Tr. 316:1–9.
- Three pH measurements were recorded for SVA001 at the 24-month mark because the initial pH measurement was out-of-specification. Tr. 357:19–358:2.
- SVA011 through SVA013 were manufactured to validate the overall manufacturing process by measuring the pH of the ANDA product at various stages of the filling process (i.e., at the beginning, middle, and end). Tr. 154:1–20. SVA011 I has six (as opposed to three) pH measurements because the measurements were inadvertently repeated. Tr. 158:12–160:10, 162:17–20.