

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SUN PHARMACEUTICALS INDUSTRIES INC.,

Petitioner

v.

NIVAGEN PHARMACEUTICALS, INC.,

Patent Owner

IPR2025-00893

Patent No. 11,878,076

PATENT OWNER'S PRELIMINARY RESPONSE

LIST OF EXHIBITS

Exhibit	Description
Ex2001	<i>Nivagen, Inc. v. Sun Pharmaceuticals Industries, Inc.</i> , Civil Action No. 2:24-cv-36 (E.D. Tex.) (the “Nivagen lawsuit”), docket sheet (printed on July 18, 2025)
Ex2002	The Nivagen lawsuit, D.I. 37, Docket Control Order (scheduling order)
Ex2003	Sun’s May 8, 2025 Amended Invalidity Contentions served in the Nivagen lawsuit
Ex2004	The Nivagen lawsuit, D.I. 54, Joint Claim Construction and Prehearing Statement
Ex2005	Sun’s Fourth Set of Requests for Production served upon Nivagen in the Nivagen lawsuit
Ex2006	Sun’s Seventh Set of Interrogatories served upon Nivagen in the Nivagen lawsuit
Ex2007	Sun’s Sixth Set of Requests for Admissions served upon Nivagen in the Nivagen lawsuit
Ex2008	Sun’s Motion for Letter Rogatory to Nobelpharma in the Nivagen lawsuit
Ex2009	Nivagen’s third-party subpoena to Blank Rome LLP in the Nivagen lawsuit
Ex2010	Nivagen’s third-party subpoena to Curia Global in the Nivagen lawsuit
Ex2011	A collection of deposition notices in the Nivagen lawsuit
Ex2012	Collection of expert confidentiality undertakings by disclosed experts in the Nivagen lawsuit
Ex2013	An email chain regarding product sample production and the use of the information obtained from the samples in the Nivagen lawsuit

Ex2014	Eastern District of Texas Patent Rule 4-1 disclosures exchanged between the parties on April 10, 2025 (proposed claim terms for construction) in the Nivagen lawsuit
Ex2015	Eastern District of Texas Patent Rule 4-2 disclosures exchanged between the parties on May 1, 2025 (preliminary constructions and extrinsic evidence) in the Nivagen lawsuit
Ex2016	Eastern District of Texas P.R. 4-3(b) disclosure (Declaration of Alexander Klibanov) served by Nivagen upon Sun on May 22, 2025 in the Nivagen lawsuit
Ex2017	A redacted version of Nivagen’s opening claim construction brief filed as D.I. 58 (June 9, 2025) in the Nivagen lawsuit
Ex2018	Sun Pharma’s third-party subpoena to Corbel Capital Partners, served in the Nivagen lawsuit
Ex2019	Emails among litigation counsel regarding a potential <i>Sotera</i> stipulation that includes “commercial embodiments”-based patent invalidity theories
Ex2020	Email chain dated June 3, 2025 among litigation counsel in the Nivagen lawsuit, regarding motion to stay, motion to dismiss or transfer venue, and the IPR Petition
Ex2021	Exhibit B-1 (“’608 Publication”) served by Sun to Nivagen as part of Sun’s May 8, 2025 Amended Invalidity Contentions disclosures, in the Nivagen lawsuit
Ex2022	Exhibit B-2 (“Nobelbar”) served by Sun to Nivagen as part of Sun’s May 8, 2025 Amended Invalidity Contentions disclosures, in the Nivagen lawsuit
Ex2023	Exhibit B-8 (“Hikma/DailyMed”) served by Sun to Nivagen as part of Sun’s May 8, 2025 Amended Invalidity Contentions disclosures, in the Nivagen lawsuit
Ex2024	Hikma/West-Ward press release, found at https://www.hikma.com/media/xybpzxvf/us-brand-launch-press-release-final-26-june-2018.pdf /

Ex2025	National Drug Code Directory search result for “0641-0476”, found at https://dps.fda.gov/ndc/searchresult?selection=finished_product&content=PRODUCTNDC&type=0641-0476
Ex2026	National Drug Code Directory search result for “0641-0477”, found at https://dps.fda.gov/ndc/searchresult?selection=finished_product&content=PRODUCTNDC&type=0641-0477
Ex2027	Sun’s October 22, 2024 Invalidity Contentions served in the Nivagen lawsuit
Ex2028	Declaration of Brent A. Batzer Esq.
Ex2029	Declaration of Alexander M. Klibanov, Ph.D., in Support of Patent Owner’s Preliminary Response (“Klibanov Decl.”)
Ex2030	<i>Curriculum Vitae</i> of Alexander M. Klibanov, Ph.D.

TABLE OF CONTENTS

I. Introduction.....	1
II. Background.....	4
A. The Field of Technology at Issue.....	4
B. The '076 Patent	6
1. The Specification.....	6
2. The Claims.....	7
C. Prosecution of the Applications Resulting in the '076 Patent	8
D. Sun's Prior Art References.....	9
1. PIF (Ex. 1009)	9
2. Parker (Ex. 1012)	11
3. West-Ward (Ex. 1013)	12
4. U.S. Pat. App. Pub. No. 2021/0085608 ("the '608 Publication") (Ex. 1005)..	13
III. Definition of Person of Ordinary Skill in the Art.....	13
IV. Claim Construction.....	14
V. The Petition should be denied because it presents no ground on which petitioner is reasonably likely to prevail.....	15
A. Ground 1 Fails Because Petitioner's Cited Art Does Not Render the Claims of the '076 Patent Obvious.	15
1. A POSA would not be motivated to combine PIF, Parker, and West-Ward with a reasonable expectation of success in achieving the inventions of claim 1	16
a. PIF, Parker, and West-Ward do not disclose all of the limitations of claim 1.....	17
b. A POSA would not be motivated to combine the teachings of PIF, Parker, and West-Ward to arrive at claim 1.	23
c. A POSA would not reasonably expect success in achieving the invention of claim 1.	31
2. PIF, Parker, and West-Ward do not render claims 2–20 obvious for the same reasons as claim 1, as well as others.	32

a. The references do not disclose, and a POSA would not be motivated to obtain, a reconstituted composition with the specifically claimed impurity thresholds with a reasonable expectation of success.....	32
b. The references do not disclose, and a POSA would not be motivated to obtain, an amorphous formulation with the recited stability and impurity levels with a reasonable expectation of success.....	35
B. Grounds 2 & 3 Fail At Least Because They Rely on the '608 Publication, Which Is Not Prior Art to the '076 Patent.	36
1. Sun's imposition of a heightened written description requirement is legally erroneous.....	37
2. The specification of the pre-CIP Applications adequately describes inventive compositions that have crystalline structures.	40
3. The originally filed claims of the pre-CIP applications already disclose inventive compositions that have crystalline structures.	43
4. Sun's legally irrelevant arguments including a disclaimer-type argument regarding crystallinity of the claimed compositions are erroneous and must be disregarded.....	46
5. The specifications of the pre-CIP Applications adequately describe inventive compositions with organic solvents.....	49
6. The originally filed claim 1 of the pre-CIP '881 Application discloses inventive compositions that can contain any amount of residual organic solvent.....	56
7. Because the '076 patent properly claims priority to the '511 Application, Petitioner's anticipation and obviousness arguments necessarily fail.	57
VI. Conclusion	57

TABLE OF AUTHORITIES

Cases

<i>Allergan USA v. MSN Labs. Private Ltd.</i> , 111 F.4th 1358 (Fed. Cir. 2024)	38, 43, 56
<i>Antares Pharma, Inc. v. Medac Pharma Inc.</i> , 771 F.3d 1354 (Fed. Cir. 2014)	54
<i>Apple, Inc. v. Ameranth, Inc.</i> , 842 F.3d 1229 (Fed. Cir. 2016)	45
<i>Ariad Pharms., Inc. v. Eli Lilly & Co.</i> , 598 F.3d 1336 (Fed. Cir. 2010) (en banc)	46, 47, 54, 57
<i>Bausch Health Ireland Ltd. v. Padagis Israel Pharms. Ltd.</i> , 2022 WL 17352334 (D.N.J. Dec. 1, 2022)	25
<i>Cadence Pharms. Inc. v. Exela PharmSci Inc.</i> , 780 F.3d 1364 (Fed. Cir. 2015)	42
<i>CIAS Inc. v. Alliance Gaming Corp.</i> , 504 F.3d 1356 (Fed. Cir. 2007)	38
<i>Computer Docking Station Corp. v. Dell, Inc.</i> , 519 F.3d 1366 (Fed. Cir. 2008)	52
<i>Cordis Corp. v. Medtronic AVE, Inc.</i> , 339 F.3d 1352 (Fed. Cir. 2003)	39
<i>Corephotonics, Ltd. v. Apple Inc.</i> , 84 F.4th 990 (Fed. Cir. 2023)	16
<i>Dealertrack, Inc. v. Huber</i> , 674 F.3d 1315 (Fed. Cir. 2012)	53
<i>Dome Patent L.P. v. Lee</i> , 799 F.3d 1372 (Fed. Cir. 2015)	16
<i>Epistar Corp. v. Int’l Trade Comm’n</i> , 566 F.3d 1321 (Fed. Cir. 2009)	52
<i>Exxon Chemical Patents, Inc. v. Lubrizol Corp.</i> , 64 F.3d 1553 (Fed. Cir. 1995)	45
<i>Flo Healthcare Solutions, LLC v. Kappos</i> , 697 F.3d 1367 (Fed. Cir. 2012)	43
<i>Funai Elec. Co. v. Daewoo Elecs. Corp.</i> , 616 F.3d 1357 (Fed. Cir. 2010)	45
<i>In re Entresto</i> , 125 F.4th 1090 (Fed. Cir. 2025)	38
<i>In re Float’N’Grill LLC</i> , 72 F.4th 1347 (Fed. Cir. 2023)	54
<i>In re Soni</i> , 54 F.3d 746 (Fed. Cir. 1995)	31
<i>In re Xencor, Inc.</i> , 130 F.4th 1350 (Fed. Cir. 2025)	21, 22
<i>Insite Vision Inc. v. Sandoz, Inc.</i> , 783 F.3d 853 (Fed. Cir. 2015)	24, 25

<i>Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.</i> , 821 F.3d 1359 (Fed. Cir. 2016)	16
<i>Lockwood v. Am. Airlines, Inc.</i> , 107 F.3d 1565 (Fed. Cir. 1997)	46
<i>Minnesota Min. & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.</i> , 976 F.2d 1559 (Fed. Cir. 1992)	30
<i>Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH</i> , 139 F.3d 877 (Fed. Cir. 1998)	24
<i>PowerOasis, Inc. v. T-Mobile USA, Inc.</i> , 522 F.3d 1299 (Fed. Cir. 2008)	55
<i>Regeneron Pharms., Inc. v. Mylan Pharms. Inc.</i> , 127 F.4th 896 (Fed. Cir. 2025)	37, 39
<i>Sanofi-Aventis Deutschland GmbH v. Mylan Pharms. Inc.</i> , 66 F.4th 1373 (Fed. Cir. 2023)	15
<i>ScriptPro LLC v. Innovation Assocs.</i> , 833 F.3d 1336 (Fed. Cir. 2016)	42
<i>Teva Branded Pharm. Prods. R&D, Inc. v. Amneal Pharms. of New York, LLC</i> , 124 F.4th 898 (Fed. Cir. 2024)	38
<i>Thorner v. Sony Comput. Entm't Am. LLC</i> , 669 F.3d 1362 (Fed. Cir. 2012)	53
<i>Trading Techs. Int'l, Inc. v. Open E Cry, LLC</i> , 728 F.3d 1309 (Fed. Cir. 2013)	47
<i>Unigene Lab'ys, Inc. v. Apotex, Inc.</i> , 655 F.3d 1352 (Fed. Cir. 2011)	25
<i>Ventana Med. Sys., Inc. v. Biogenex Lab'ys, Inc.</i> , 473 F.3d 1173 (Fed. Cir. 2006)	52
<i>WBIP, LLC v. Kohler Co.</i> , 829 F.3d 1317 (Fed. Cir. 2016)	26
<i>Yeda Rsch. & Dev. Co. v. Abbott GMBH & Co. KG</i> , 837 F.3d 1341 (Fed. Cir. 2016)	41

Statutes

35 U.S.C. § 103(a)	15
35 U.S.C. § 112	38

Other Authorities

83 Fed. Reg. 51340–59 (Oct. 11, 2018)	15
---	----

I. INTRODUCTION

In 2019, Patent Owner Nivagen Pharmaceuticals, Inc. (“Nivagen”), a specialty pharmaceutical company based in Sacramento, California, unexpectedly discovered that it could make a phenobarbital sodium product superior to anything on the market at the time. Phenobarbital sodium was used as an anti-seizure medication, and has been sold in ready-to-inject liquid solution dosage forms for generations—since even before Congress required pharmaceutical companies to file new drug applications. Because phenobarbital can degrade in the presence of water, those liquid formulations often contained certain impurities, including phenylethylacetylurea (“PEAU”), that could be toxic. Advances had been made to reduce the presence of PEAU by limiting the amount of water in the liquid formulation. Yet it was Nivagen scientists who developed a lyophilized (*i.e.*, freeze-dried) phenobarbital sodium powder that presented a dramatically reduced impurity profile that increased the drug’s storage stability and safety beyond what had existed before. Nivagen never had the opportunity to reap the financial gains of its efforts, however, because before Nivagen could commercialize a product, Petitioner Sun Pharmaceutical Industries Inc. (“Sun”), a much larger company, launched Sezaby®, its own lyophilized powder phenobarbital sodium product. Nivagen has sued Sun for patent infringement, and Sun retaliated by filing this IPR.

Sun’s Petition is meritless. The Petition does not present a credible case of

invalidity, either through a three-reference combination or through Sun's attempt to undo the chain of priority on the '076 patent.

First, a POSA would not arrive at the claimed inventions from Sun's three-reference combination of PIF (a description of a 2008-vintage Japanese lyophilized phenobarbital sodium product called Nobelbar), Parker (a 2017 patent application publication describing a "stable" liquid phenobarbital sodium composition that was an improvement upon the "up to 10% PEAU" impurity level for the prior art liquid phenobarbital sodium compositions after two years of storage, but the Parker composition actually still generates significant impurities during storage, *e.g.* up to 0.8% PEAU), and West-Ward (also known as Hikma, a liquid phenobarbital sodium commercial product that predated Parker). Indeed, Sun begins its analysis from an inquiry that improperly presupposes a POSA would be motivated to develop a new lyophilized phenobarbital sodium product with an improved impurity profile. Yet, given advances made in the field as shown in Parker, there was no reason in 2019 for a POSA to even undertake such an endeavor, let alone switch from the Parker formulation to the lyophilization technology, and try to control the specific impurities to specific thresholds claimed in the '076 patent. And as explained below, putting the teachings of the references together does not actually result in a disclosure to a POSA of the claimed inventions.

Second, Sun tries to claim that the inventors believed their inventions to cover

only phenobarbital sodium compositions that were completely amorphous (*i.e.*, non-crystalline) in nature and that were free of organic solvents, and only after becoming aware of Sezaby® broadened their understanding. Sun's claim is belied by the prior applications' specifications and original claims, which, among other things, described compositions that were partially or even majority crystalline compositions, and that included claim limitations specifically directed to amorphous compositions that narrowed broader claims not so limited. And for the solvent issue, Sun cobbles together a few sentences from the specification that discuss organic solvents that are added to the bulk solution (the liquid containing phenobarbital sodium before lyophilization) as a drawback, but they do not limit the scope of the pharmaceutical product invention in any way, and do not preclude the presence of *residual* organic solvents in the lyophilized cake in the claimed product. The residual organic solvents can originate from the active pharmaceutical ingredient phenobarbital sodium itself. In any event, if the written description had clearly and unmistakably disclaimed the use of organic solvents, so too then do the claims—creating parity amongst the two and avoiding the written description failure Sun alleges.

Because the Petition does not show a reasonable likelihood that Petitioner would prevail on their theories of invalidity, the Board should decline to institute.

II. BACKGROUND

A. The Field of Technology at Issue

The dispute here centers on Nivagen’s new lyophilized forms of phenobarbital sodium that are storage-stable and contains very low levels of certain impurities after storage.

Phenobarbital is an old drug; it has been in medical use for more than half a century as a barbiturate that doctors have employed to reduce seizures as an anti-convulsant and to assist in sleep as a sedative or pre-anesthetic. (Ex. 1001, ’076 patent, at 1:40–44; Ex. 1015, Suryanarayanan Decl. ¶ 59). And for nearly as long, phenobarbital or its salt has been formulated for commercial sale in the United States as a liquid solution dosage form. The liquid is then administered to patients either by an intramuscular or intravenous injection. (Ex. 1001, ’076 patent, at 1:44–47).

The liquid formulation has a serious drawback—one that no product development scientists until Nivagen’s had overcome. Through degradation by contact with water (*i.e.*, hydrolysis) or in increased pH, phenobarbital forms certain toxic byproducts, including phenylethylacetylurea or PEAU mentioned above, 2-ethyl-2-phenylmalonamide (“2EPMM”), and alpha-phenylbutyrylguanidine (“PBG”). (*Id.* at 1:51–57). As discussed in more detail below with respect to the Parker reference Sun relies on, before 2015, the PEAU level in a liquid formulation product could be as high as 10%. (Ex. 1012 at [0006]). The Parker formulation

reduced that level to up to 0.8% after storage. (*Id.* at [0029]). PEAU is particularly nasty; although once a commercially available active ingredient used to treat those with severe epilepsy, the FDA withdrew approval because of its unacceptably high risk of disruption of calcium and folate metabolism. (Ex. 1001 at 1:60–2:3).

Although Parker disclosed a liquid formulation of phenobarbital sodium that was “stable” and had decreased amount of PEAU upon storage compared to prior formulations, the PEAU level in Parker, which is up to 0.8% upon storage, is still “undesirable” to the Nivagen inventors. (*Id.* at 2:12-24; Ex. 1012 at [0029]). Furthermore, Parker (or any other references) never discussed an impurity level threshold for 2EPMM or PBG or how to achieve such a low level for these two impurities. The '076 patent inventors identified “a need for a stable Phenobarbital Sodium formulation in a formulation that is storage stable and void or essentially void of degradation impurities upon solubilization in water.” (*Id.* at 2:38-41). The inventor reduced the levels for PEAU, 2EPMM, and PBG, to less than 0.1% and 0.05% upon storage. (*Id.* at claims).

B. The '076 Patent

1. The Specification¹

The inventors of the '076 patent describe and claim storage stable, lyophilized phenobarbital sodium compositions with excellent reconstitution profiles and impurity levels below very low thresholds even under stress storage conditions.

Seeking to solve the problem of undesirable level of impurities, the inventors disclosed “compositions of, methods of producing, and use of a lyophilized Phenobarbital Sodium formulation.” (Ex. 1001 at 2:45-47). “The lyophilized amorphous formulation that was produced resulted in surprising, unexpected and desirable results. The quantity of undesirable and/or toxic degradation impurities that are produced from this formulation are less than those in current commercial products. And the stability of this formulation is superior to that of current commercial products.” (*Id.* at 2:53-59). The levels for PEAU, 2EPMM, and PBG in the lyophilized Phenobarbital Sodium upon storage and reconstitution can be reduced to “0.05% or less” or even below detection. (*Id.* at 4:49-53).

¹ For purposes of this background, Nivagen relies solely on portions of the specification that were submitted as part of the Pre-CIP Applications. That said, the inventions are described in further detail with the inclusion of additional testing and embodiments submitted as part of the U.S. Patent Application No. 17/854,914.

The specification describes the crystallinity of the inventive lyophilized powder in significant detail. For example, a lyophilized powder could be 100% amorphous, but it also could be a mixture of amorphous and non-amorphous (i.e. crystalline) material, in a wide variety of proportions. (*Id.* at 3:1-8). “[T]he inventors also contemplate lyophilized Phenobarbital Sodium.” (*Id.* at 5:11-12 (no requirement on any particular kind of crystallinity or the lack thereof)).

2. The Claims

The claims reflect the key advantages of the phenobarbital sodium compositions that the inventors developed, namely high-purity phenobarbital compositions with storage stability (and in some cases, after reconstitution, certain impurities at levels below specific thresholds), with doses at specific amounts between 65 and 200 mg, and in single-use vials. Independent claim 1 reads:

1. A storage stable pharmaceutical product, comprising:

a single use dose vial, and

a composition comprising a 65 mg dose, a 100 mg dose, a 130 mg dose, or a 200 mg dose of phenobarbital sodium, in the single use dose vial,

wherein the composition is sterile and lyophilized, and

wherein the composition comprises no less than 98% phenobarbital sodium.

Claims 2–4, 6, 14 elaborate on these properties by reciting specified impurity limits under specified storage stability conditions. Claims 5 and 15 further limits the

compositions of Claim 1 (and claims depending on claim 1) to those where the composition is amorphous. Claim 16 limits the dosage to 100 mg.

Independent claim 7 is similar to claim 1 but recites a specified impurity limitation, and its dependent claims 8-13 and 17-20 incorporate limitations similar to those dependent on claim 1.

C. Prosecution of the Applications Resulting in the '076 Patent

On September 20, 2019, Nivagen filed Provisional Patent Application No. 62/903,511 (“the ’511 Application”) with the Patent Office naming Bala Tripura Sundari Chodavarapu, Thirupathi Mangali, Jay Shukla, Anand Shukla, and Dasaradhi Lakkaraju as inventors. (Ex. 1003). The provisional application contains original claim 17, which is directed to a method of reducing formulation of degradation products of Phenobarbital Sodium reconstituted in an aqueous solution, resulting in “stable lyophilized Phenobarbital sodium.” (*Id.* at 32, claim 17).

Thereafter, Nivagen filed U.S. Patent Application No. 17/025,881 (“the ’881 Application”), which contained a substantially identical specification to the ’511 Provisional Application. (Ex. 1004).² The original claim 1 of the ’881 Application reads, “a pharmaceutical composition comprising lyophilized amorphous

² The ’881 Application ultimately issued as U.S. Patent No. 11,406,598.

Phenobarbital Sodium.” (*Id.* at 230, claim 1).

On June 30, 2022, before FDA had approved Sun’s commercial lyophilized phenobarbital sodium product Sezaby®, Nivagen filed U.S. Patent Application No. 17/854,914 (“the ’914 Application”) as a continuation in part. (Ex. 1007). The ’914 Application maintained the substance of the ’881 Application’s specification and added new tables and descriptions of certain experiments. Thereafter, Nivagen filed U.S. Patent Application No. 18/100,804 (the “’804 Application”) as a continuation of the ’914 Application. (Ex. 1002). On January 23, 2024, the Patent Office granted the ’076 Patent from the ’804 Application. (Ex. 1001).

D. Sun’s Prior Art References

1. PIF (Ex. 1009)³

PIF is an English translation of a July 2010 pharmaceutical interview form for a Japanese commercial product, Nobelbar, manufactured by Nobel Pharma. (Ex. 1009, PIF, at 1; Ex. 1010, Bernasch Decl.).

PIF appears to describe a 250 mg for injection lyophilized phenobarbital

³ The Petition claims that a POSA “would have reviewed various Nobelbar regulatory documents, including PIF.” Petition at 14. Sun attached only PIF, however, and should not be permitted to rely on other unspecified Nobelbar-related documents should the Board institute.

formulation that contains in each vial 274 mg of phenobarbital sodium. (Ex. 1009 at 1, 7). PIF discloses that the product contains a relatively high level of impurities that are prone to rapid hydrolysis. (Ex. 1009 at 8 section IV-6 (0.09% of certain “related substances” upon dissolution of the powder in water, which increased to 0.49% after 24 hours); Ex. 2029, Klibanov Decl. at ¶¶ 38, 73). Although PIF states that there was “no change” for “related substances” after various storage durations, PIF does not specify which related substances were tested for or what standard was used to make the “no change” determination. (Ex. 1009 at 7 section IV-5; Ex. 2029 at ¶¶ 39-43, 72, 74). Because the moisture content in the vials did increase during that storage stability testing, a POSA would find this disclosure regarding moisture, and the presence of hydrolysis-prone related substances in the product as shown by the dissolution stability testing, to be in conflict with the “no change” disclosure, unless “no change” could just mean “did not cross a threshold.” (Ex. 2029 at ¶ 42). As PIF otherwise reflects, after dissolution in water or saline solution, the concentration of related substances (which may not be the total impurities present in the product) increased over a 24-hour period to 0.49%. (Ex. 1009 at 5).

Under “additives,” PIF states, “not including,” the meaning of which is unclear. (Ex. 1009 at 7; Ex. 2029 at ¶¶ 35-36). PIF teaches that certain substances such as PEAU “may be introduced as contaminants in the manufacturing process of the bulk drug,” and “related substances” may get into the lyophilized powder from

the rubber stopper of the vial after manufacturing. (Ex. 1009, PIF, at 7, 11). There is no mention of 2EPMM or PBG in PIF. (Ex. 2029 at ¶ 40).

2. Parker (Ex. 1012)

Parker is a patent publication directed to a liquid phenobarbital sodium formulation that purports to be stable, *i.e.*, to “not generate impurities during extended storage.” (Ex. 1012, Parker, at Abstract). Recognizing that hydrolysis was one pathway for degradation of phenobarbital, Parker teaches that the method to avoid impurities is “the removal of water from the formulation”—which refers to the water component in a liquid formulation. (*Id.* at [0005]; Ex. 2029 at ¶ 47). Parker identifies PEAU and phenyl butyric acid (“PBA”)—not 2EPMM or PBG—as hydrolysis degradation products for phenobarbital. (*Id.* at [0006], [0030]). Though Parker recognizes other impurities as phenobarbital degradation products, including 2EPMM and PBG, Parker attributes them to results of oxidation, pH change, or heat. (*See id.* at [0007], Table 1; Ex. 2029 at ¶ 50). Parker does not suggest that 2EPMM and PBG require further control, or that they could be controlled by reducing the water content in a liquid formulation, or disclose any other way to reduce the level of these impurities. (Ex. 2029 at ¶¶ 53-55, 66-67).

Claiming there existed a “need for formulations that contain or generate relatively low amounts of [hydrolysis-related] impurities” (*i.e.*, PEAU and PBA), Parker states that its disclosed invention “addresses the need for stable, essentially

impurity-free formulations.” (*Id.* at [0016]; *see also id.* at [0030] (defining “hydrolysis impurities” as PEAU and PBA, and noting the “current” limit for PEAU at 10%)). Parker discloses purportedly inventive “phenobarbital solutions for injection that are extremely stable and that do not generate any significant amounts of impurities during extended storage.” (*Id.* at [0017]). However, “the stable formulations” disclosed in Parker “have been found to exhibit 1% or less, preferably 0.8% or less of hydrolysis impurities.” (*Id.* at [0029]; Ex. 2029 at ¶ 53). The inventors characterized the reduction of PEAU to 0.8% as “excellent,” “substantial” and a “low level.” (Ex. 1012 at [0035], [0066]). Both the specification and the claims repeatedly highlight the 0.8% threshold and tout it as a successful reduction in PEAU impurity. (*See, e.g., id.* at [0036], [0065], [0067], claim 1).

Notably, Parker says nothing about lyophilization. Parker was discussed in the specification of the ’076 patent, and thus considered by the examiner when allowing the patent to issue.

3. West-Ward (Ex. 1013)

West-Ward appears to be a February 4, 2025 printout of a website that was “Updated 08/11.” (Ex. 1013, West-Ward, at 1). West-Ward discloses a phenobarbital sodium liquid solution product for intramuscular or slow IV injection. (*Id.*). The contents of the liquid formulation are 65 mg or 130 mg of active ingredient, 0.678 mL of propylene glycol, 0.1 mL alcohol, and benzyl alcohol 0.015

mL in Water for Injection, as well as optionally hydrochloric acid for pH balancing. (*Id.*). Therefore, West-Ward discloses a liquid solution formulation similar to the “stable” formulation disclosed in Parker. Parker discloses PEAU level of “1% or less, preferably 0.8% or less of hydrolysis impurities,” with no mention of the level of 2EPMM or PBG, which are not characterized as hydrolysis impurities in Parker. (Ex. 2029 at ¶ 53). However, West-Ward is prior art to Parker. Parker describes previous “commercially marketed pharmaceutical products” as containing “up to 10% of PEAU” after two years of storage. (Ex. 1012 at [0006], [0030]).

4. U.S. Pat. App. Pub. No. 2021/0085608 (“the ’608 Publication”) (Ex. 1005)⁴

The ’608 Publication is the published version of the ’881 Application, which originated from Nivagen and which the ’076 patent claims priority to.

III. DEFINITION OF PERSON OF ORDINARY SKILL IN THE ART

A POSA at the time of the claimed inventions (whether 2019 or 2022) would have had a Ph.D. degree in chemistry, biochemistry, or pharmaceuticals, and at least 2 years of experience (or less education but more years of experience, i.e., an M.S. with at least 3–5 years of experience, or a B.S. with a minimum of 6 years of experience) with pharmaceutical drug product formulation, analysis, development,

⁴ Patent Owner Nivagen refers to the ’511 Application, the ’881 Application, the ’608 Publication together as the Pre-CIP Applications.

optimization, and manufacture, including experience with processes and techniques for minimizing impurities in, and improving the stability of, pharmaceutical drug products during their manufacture and storage. (Ex. 2029, Klibanov Decl. at ¶ 20). At least part of the POSA's experience would include designing and/or manufacturing lyophilized pharmaceutical compositions. (*Id.* at ¶ 21).

Although Sun and Dr. Suryanarayanan offer a slightly different definition of a POSA, none of the arguments or expert opinions appear to be impacted by the distinction. (*See id.* at ¶ 22).

IV. CLAIM CONSTRUCTION

In supposedly acquiescing to Nivagen's claim construction, Sun lays bare the results-oriented nature of its approach. In the district court, Sun argues that the '076 patent specification contains a disclaimer so clear that it restricts the term "composition" to formulations that do not include an organic solvent or preservative. (Ex. 2004 at 3). Yet here, Sun asks the Court to invalidate the '076 patent based on a different claim construction (plain and ordinary meaning with no disclaimer)—a position markedly at odds with its district court approach. Petition at 13 n.2.

Sun's two-forum, irreconcilable-argument strategy is precisely what the adoption of the *Phillips* standard for Board proceedings was intended to curb—"patent infringers ... aggressively argu[ing] inconsistent positions on claim scope in different forums with impunity—a broad scope before the PTAB, and a narrow

scope before the district court.” *See* Cmt. 8, 83 Fed. Reg. 51340–59 at 51350 (Oct. 11, 2018). As explained in further detail below, Sun’s Grounds 2 and 3 depend entirely on the proposition that its district court-proffered construction is wrong. This hit to Sun’s credibility itself provides a reason for denying institution.

Nonetheless, both in the district court and for the purposes of this proceeding, Nivagen does not believe any claim terms require construction.

V. THE PETITION SHOULD BE DENIED BECAUSE IT PRESENTS NO GROUND ON WHICH PETITIONER IS REASONABLY LIKELY TO PREVAIL.⁵

A. Ground 1 Fails Because Petitioner’s Cited Art Does Not Render the Claims of the ’076 Patent Obvious.

As an IPR petitioner, Sun bears the ultimate burden “to prove unpatentability by a preponderance of the evidence.” *Sanofi-Aventis Deutschland GmbH v. Mylan Pharms. Inc.*, 66 F.4th 1373, 1379 (Fed. Cir. 2023) (internal quotation marks omitted). A patent is invalid as obvious “if 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.” 35 U.S.C. § 103(a)

⁵ If the Board institutes this IPR, Nivagen reserves the right to raise other arguments in response to the Petition, including that objective indicia of nonobviousness favor validity of the ’076 patent.

(2012). “If all elements of a claim are found in the prior art, ... the factfinder must further consider the factual questions of whether a person of ordinary skill in the art would be motivated to combine those references, and whether in making that combination, a person of ordinary skill would have had a reasonable expectation of success.” *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1368 (Fed. Cir. 2016) (quoting *Dome Patent L.P. v. Lee*, 799 F.3d 1372, 1380 (Fed. Cir. 2015)). “To satisfy its burden of proving obviousness, a petitioner cannot employ mere conclusory statements. The petition must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness.” *Corephotonics, Ltd. v. Apple Inc.*, 84 F.4th 990, 1004 (Fed. Cir. 2023). “This burden of persuasion remains with the petitioner at all times.” *Id.* at 1003.

The Petition fails to present an obviousness case reasonably likely to meet these standards.

1. A POSA would not be motivated to combine PIF, Parker, and West-Ward with a reasonable expectation of success in achieving the inventions of claim 1.

The Petition does not set forth a case of obviousness. First, Sun fails to demonstrate that each of the limitations of claim 1 is in the prior art. Specifically, none of Sun’s references disclose a lyophilized pharmaceutical product with the recited doses and at least 98% phenobarbital sodium, or a “storage stable” lyophilized phenobarbital product. Indeed, according to Sun’s reference Parker,

which was also before the examiner during the prosecution of the '076 patent, commercial products that were previously sold and used could nevertheless contain very high level of impurities, such as up to 10% PEAU. (Ex. 1012 at [0006], [0030]). None of Sun's references disclose the very low impurity levels (less than 0.1% or 0.05% for PEAU, less than 0.05% for 2EPMM and PBG, or undetectable levels, upon storage) described in the '076 patent. None of Sun's references disclose a method to reduce impurities to such low levels and achieve storage stability. In the case of 2EPMM and PBG that are not disclosed as hydrolysis prone (*e.g.* Parker, Ex. 1012 at [0007], [0030]), Sun's references neither disclose nor suggest any reduction in their levels upon storage whatsoever.

Sun also fails to show that a POSA would have been motivated to select and combine these specific references to achieve the claimed inventions. The Petition does not address why, after Parker reported its "extremely stable" liquid formulation, (Ex. 1012 at [0017]), a POSA would abandon the liquid formulation approach and go back to modifying the older Japanese lyophilized product which had not been shown to meet even *Parker's* "up to 0.8% PEAU after two years of storage" standard. And finally, even if a POSA were to have tried, the art would not have given a POSA a reasonable expectation of succeeding.

a. PIF, Parker, and West-Ward do not disclose all of the limitations of claim 1.

i. The references do not disclose a pharmaceutical product comprising $\geq 98\%$ (assay percentage) phenobarbital sodium lyophilized composition.

Sun's and Dr. Suryanarayanan's claim that PIF discloses $\geq 98\%$ phenobarbital sodium lyophilized composition is based on stretching PIF beyond what the reference actually teaches (or would make obvious) to a POSA. Read properly, PIF does not disclose a pharmaceutical product with at least 98% assay percentage of the phenobarbital sodium API.

PIF does not disclose the assay % of the API in the Nobelbar product it purportedly describes. There is no disclosure in PIF that the API equals or exceeds 98% of the labeled dose amount (i.e. 274 mg of phenobarbital sodium). (Ex. 2029 at ¶ 59 at element [1d]). There is no disclosure that the % API can be carefully controlled in manufacturing to achieve $\geq 98\%$.

PIF's disclosure in fact suggests otherwise—that the assay % of the API in the Nobelbar product had not been carefully controlled during or after manufacturing. PIF describes a lyophilized phenobarbital composition that purports to have “no additives,” but it is not clear what that means. (Ex. 2029 at ¶¶34-37). “No additives” does not necessarily mean “API only.” (*Id.*) There is no disclosure on whether other substances that can get into contact with the API during manufacturing (such as water moisture) or afterwards (such as leachables like lubricant from the rubber stopper) can change the API contents in the product. (*See*

id. at ¶¶35-37).

Furthermore, PIF discloses that there were significant amounts of impurities in the API, such as PEAU and other related substances, and the total level of these impurities was not carefully controlled. For example, PIF discloses a minimum of 0.09% of “related substances” during a dissolution stability testing. (Ex. 1009 at 8; Ex. 2029 at ¶¶38-39). This “related substances” level rapidly increased to 0.49% in the presence of water. (Ex. 1009 at 8; Ex. 2029 at ¶ 73.). Other impurities could have existed in significant amounts in these samples, but their levels were not tested for or controlled. (Ex. 2029 at ¶38 (the “0.09%” level “at the start” does not include all impurities in the API in the samples tested)).

In a storage stability testing, PIF reports “no change” to “related substance” even when the moisture contents in the vials did increase—which would alert a POSA that hydrolysis of the API had likely occurred in the vials during the up-to-36-month stability testing. (*Id.* at ¶42). Since PEAU is a hydrolysis-generated manufacturing process impurity of the API, this “no change” disclosure in the presence of increasing moisture level over a long period of time would not make sense to a POSA unless it just meant “did not cross a threshold.” (*Id.* at ¶43). However, there is no disclosure what that threshold might be, or what “related substances” were tested for in this storage testing. PIF does not report the total level of impurities within the API during the testing—its reporting of any levels of

“related substances” is not specific, nor is it comprehensive. (*See* Ex. 2029 at ¶39 (“a POSA would be unable to tell what substances were detected or quantified in any of the testing PIF describes”); ¶40 (2EPMM and PBG, for example, were not disclosed in PIF)).

These unclear and conflicting reporting regarding what “related substances” were controlled and how any conclusions from the testing were reached does not give a POSA any clarity on what the Nobelbar product was and how it was manufactured. There is no disclosure that the impurities levels and the ensuing assay % of the product were carefully controlled during the manufacturing of this commercial product. (*Id.* at ¶¶41, 43).

In conclusion, there is no disclosure in PIF that the Nobelbar product comprises $\geq 98\%$ assay percentage of the API. (*Id.* at ¶59, chart at element [1d]).

There is also no disclosure of the assay % of the disclosed formulation in Parker or the commercial product relating to the West-Ward reference. (*See id.* (chart at [1d] regarding Parker and West-Ward)). In addition, there is no disclosure of how impurities present in the API were controlled or could be controlled during manufacturing of a liquid solution commercial product to ensure the $\geq 98\%$ assay percentage required by claim 1 of the '076 patent.

To the contrary, Parker discloses that previous liquid solution phenobarbital sodium commercial products, which includes the West-Ward product, contained “up

to 10% of PEAU and up to 1.0% of PBA.” (Ex. 2012 at [0006]). These numbers reflect “the rather lax standards for the purity of phenobarbital commercial products in general at the time.” (Ex. 2029 at ¶49).

ii. The references do not disclose a “storage stable” lyophilized pharmaceutical product—i.e., a product with a vastly improved impurity profile upon storage.

Sun glosses over claim 1’s requirement of a “storage stable” pharmaceutical product as if it were unimportant. Yet that storage stability is a key feature of claim 1, and one that Sun fails to demonstrate that the prior art would guide a POSA to.

As an initial matter, the claim 1 preamble is limiting. “A preamble or a portion of it is limiting when other parts of the patent’s claims rely on predicates in the preamble, or when the preamble is otherwise necessary to give ‘life, meaning, and vitality’ to the claim language.” *In re Xencor, Inc.*, 130 F.4th 1350, 1357–58 (Fed. Cir. 2025). A preamble “should not be read as limiting, on the other hand, when it merely gives a statement of purpose or intended result.” *Id.* A preamble need not formally constitute an antecedent in order to be read as a claim limitation. *Id.* at 1358.

The preamble here defines the claimed invention; it is a “pharmaceutical product” (specifically, a storage stable one) that has two elements, a single use dose vial and a composition with certain characteristics. Without the “product” of the preamble, the invention of claim 1 has no singular unifying term that renders it

“structurally complete.” *See id.* at 1357. Accordingly, the Board should treat the “storage stable pharmaceutical product” preamble language as limiting.

Sun does not rely on West-Ward or Parker to satisfy the “storage stable” product requirement (nor could it). *See* Pet. at 19–20. The PEAU threshold after storage disclosed in Parker is 0.8%, which is very high compared to the <0.1%, <0.05%, or undetectable levels described in the ’076 patent. There is also no disclosure that the PEAU level in the Parker formulation was held steady during storage, or of any levels for 2EPMM and PBG. (Ex. 1012 at [0035]; Ex. 2029 at ¶53). The West-Ward reference is prior art to Parker, and should be describing a liquid formulation product with up to “10%” of PEAU. (Ex. 1012 at [0006]).

The ’076 patent addressed Parker in the Background of the Invention, pointing out that, “while the amount of impurities in Parker’s liquid formulation may have decreased compared to prior formulations, impurities such as PEAU are still present in undesirable amounts, *particularly after extended storage.*” (Ex. 1001 at 2:20-24 (emphasis added)). As discussed above, the commercial product described in West-Ward preceded Parker, and is described categorically by Parker as not sufficiently stable upon storage. (Ex. 1012 at [0006]).

Sun’s two-sentence argument about why PIF discloses storage stability does not meet the moment. Sun relies on only two facts: (1) Nobelbar was approved in Japan, and (2) the PIF reference reports “no change” of “related substances” in a

long-term storage test. Pet. at 19. Neither of these disclosures support Sun’s argument that the PIF reference showed “storage stability.” That Nobelbar is commercially approved says nothing about its specific storage stability as a POSA would understand that term in the context of the ’076 patent—*i.e.*, a lyophilized phenobarbital product where the impurities levels are very low and do not substantially increase over time. As discussed above, a POSA would not have understood PIF’s report of “no change” as a disclosure of storage stability within the meaning of the ’076 patent claims. (Ex. 2029 at ¶41 (stability testing in PIF might not have been done on the commercial product); ¶42 (the meaning of “no change” in PIF is not clear to a POSA due to the increase of moisture content in the vials that was reported for the same testing, and the term could just mean “did not cross a threshold” and allow an increase in the impurity levels), ¶43 (drug approval in Japan in response to a lack of any intravenous phenobarbital products in Japan at the time does not indicate storage stability within the meaning of the ’076 patent)).

b. A POSA would not be motivated to combine the teachings of PIF, Parker, and West-Ward to arrive at claim 1.

i. Sun’s improper framing of the question facing a POSA reveals impermissible hindsight in the obviousness analysis.

Sun’s motivation-to-combine analysis is riddled with hindsight. The problems start at the outset, where Sun declares that a “POSA would have been motivated in

2019 to develop a stable, lyophilized, highly pure phenobarbital sodium composition given that it was known that phenobarbital sodium was an effective drug to treat seizures, and degraded via hydrolysis into harmful impurities.” Pet. at 15. Yet “[d]efining the problem in terms of its solution reveals improper hindsight in the selection of the prior art relevant to obviousness.” *Insite Vision Inc. v. Sandoz, Inc.*, 783 F.3d 853, 859 (Fed. Cir. 2015) (quoting *Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 881 (Fed. Cir. 1998)). The Petition does not even attempt to explain why a POSA would be experimenting with phenobarbital in 2019—first marketed in liquid form at least 40 years prior. (*See, e.g.* Ex. 1040 at 1 (describing how, once an intravenous phenobarbital liquid formulation product was discontinued in Japan in the 1980’s, intramuscular preparations were used intravenously in Japan, or “imported intravenous phenobarbital products” were used); Ex. 1015, Suryanarayanan Decl. at ¶ 59 (phenobarbital products were available for more than 50 years)).

Instead of Sun’s invention-driven “straight to phenobarbital” definition of the problem, a POSA would be seeking to develop a better anti-seizure medication than what existed before (or perhaps a little more narrowly, to improve an existing anti-seizure medication). Yet to solve that problem, a POSA has a huge universe of active ingredients, dosage forms, and potential drawbacks to choose from. Sun provides no explanation on why a POSA would have focused on phenobarbital to begin with.

The question here is whether “a person of ordinary skill in the art would narrow the research focus to lead to the invention,” and in doing so have “selected and combined these prior art elements”—*i.e.*, the specific references the Petition relies on—“in the normal course of research and development to yield the claimed invention.” *Insite Vision Inc.*, 783 F.3d at 860; *Unigene Lab’ys, Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1360 (Fed. Cir. 2011).

According to Sun, a POSA would have (1) selected phenobarbital from amongst all of the active pharmaceutical ingredients, (2) chosen to create a very highly pure phenobarbital composition, (3) selected lyophilization from among the many means that could potentially increase formulation stability, (4) decided to control the specific impurities of PEAU, 2EPMM, and PBG in the reconstituted composition, (5) controlled them at the claimed thresholds, and (6) picked the highly specific dosages in the claims. To find obviousness, “*Unigene* requires a roadmap” that answers these questions. *Bausch Health Ireland Ltd. v. Padagis Israel Pharms. Ltd.*, 2022 WL 17352334, at *33 n.20 (D.N.J. Dec. 1, 2022). Yet, as explored in more detail, Sun never explains why a POSA draws any of these conclusions and makes any of these choices.

Ultimately, Sun’s obviousness analysis mirrors the very flaw that the Federal Circuit identified in *WBIP, LLC v. Kohler Co.*, where it explained that “[t]oo often the obviousness analysis is framed as an inquiry into whether a person of skill, with

two (and only two) references sitting on the table in front of him, would have been motivated to combine (or ... could have combined) the references in a way that renders the claimed invention obvious.” 829 F.3d 1317, 1337 (Fed. Cir. 2016). Yet, as *WBIP* explained, “[t]he real question is whether that skilled artisan would have plucked one reference out of the sea of prior art ... and combined it with [other] conventional ... elements to address some need present in the field,” or put another way, “[w]hether a skilled artisan would be motivated to make a combination includes whether he would select particular references in order to combine their elements.” *Id.*

Thus, Sun has not sustained its burden to demonstrate a POSA’s motivation to (1) focus on phenobarbital only; (2) focus on the three references Sun relies on among all phenobarbital art; and (3) combine the references involving two different technologies (liquid solution formulations which were longstanding and numerous, and the one-off lyophilization product of phenobarbital sodium) to address impurities that were not addressed before and achieve vastly improved levels of specific impurities that were never reported before from using either technology.

ii. A POSA would not be motivated to develop a storage stable lyophilized product that reduces impurities beyond that in the prior art.

First, there was no motivation for a POSA to improve upon phenobarbital sodium products in 2019. According to Sun, the reason a POSA would lyophilize a

phenobarbital composition is to create a stable and reduced-impurity pharmaceutical product. Yet, Parker had already reduced PEAU and another hydrolysis-caused degradation product, PBA, in a liquid formulation to a level that was much improved over the previous commercial products, and that appeared to be acceptable to the FDA. (Ex. 1012 at [0006], [0017], [0029]-[0030], [0036]; *see* Ex. 2029 at ¶¶ 90-92). Sun cites to no reference *post-Parker* to show any motivation for furthermore improvement upon the PEAU level disclosed in the “extremely stable” Parker formulation. Sun cites to no reference to show that the “up to 0.8% PEAU upon two years of storage” level disclosed in Parker needed further improvement.

PIF, on the other hand, discloses initial impurity level of at least 0.09% in a dissolution stability testing, which then increased to 0.49% after 24 hours in water. (Ex. 1019 at 8 section IV-6; Ex. 2029 at ¶ 94). There is no teaching in PIF to reduce the impurity level further, certainly not to the level of storage stability (e.g. <0.05% or “undetectable” levels obtained after months of storage) in the ’076 patent claims.

Second, Sun identifies no concerns for the 2EPMM and PBG impurities in any references. (*See* Ex. 2029 at ¶¶ 87, 93). Beyond some unspecified general desire to reduce impurities, Sun identifies no reason why a POSA would further seek to improve the impurity profile of phenobarbital products. In Parker, 2EPMM and PBG are disclosed, but they are *not* characterized as hydrolysis degradation products. (Ex. 1012 at [0006]-[0007], [0030]). Parker left these two impurities

alone while addressing reducing hydrolytic degradation of the API, and does not make any suggestions on reducing 2EPMM and PBG levels as a goal or how to achieve it. (See Ex. 2029 at ¶¶ 66-67).

In conclusion, the very references that Sun relies on would discourage a POSA from seeking an improved impurity profile by any means, let alone by lyophilization. (Ex. 2029 at ¶¶ 95-96).

iii. A POSA would not be motivated to achieve a composition of at least 98% assay percentage of phenobarbital sodium.

Sun identifies no reason why a POSA would target a lyophilized composition including at least 98% phenobarbital. The Petition adduces no evidence that the “98%” level confers a particularly advantageous property that a POSA would desire, nor that the art recognized 98% as a target.

iv. A POSA would not be motivated to combine teachings from references about liquid phenobarbital solutions to design a lyophilized phenobarbital product.

Even if a POSA were to seek to improve on the storage stability and impurity profile of phenobarbital products, Sun draws the wrong conclusion—that the POSA would seek to make a lyophilized product. Its own references suggest otherwise.

First, it would be necessary for Petitioner to show, but it fails to do so, that there was some reason for a POSA to change the approach Parker took, which was to make a better *liquid formulation*, and to reach back to an effort in Japan almost a

decade prior, to make a *lyophilized* phenobarbital product, and then somehow to decide to improve upon it in terms of storage stability and specific levels of disclosed and undisclosed specific impurities. The Parker liquid formulation is not designed for lyophilization, (Ex. 2029 at ¶ 89), so a POSA could not simply lyophilize it—a POSA would have to start anew and design a lyophilization formulation and process. Yet, there is no indication to a POSA that the impurity profile or storage stability of a lyophilized product like Nobelbar would be better than what Parker could achieve. (*Id.* at ¶¶ 85-88).

Second, employing a lyophilization process to make a product for treating neonatal seizures introduced an additional, unwanted step in the administration process—reconstitution (dissolution of the lyophilized cake in a suitable carrier liquid). Phenobarbital is often administered to stop a seizure episode while it is occurring. (*See, e.g.*, Ex. 1013 at 2–3 (reflecting indicated use for “emergency control of certain acute convulsive episodes”)). Adding a reconstitution step which necessarily takes extra time to do conflicts with the goals of treating seizures as quickly as possible. (Ex. 1032 at 8 (“Reconstitution ... has direct implications on patient safety”; “A short and reproducible reconstitution time will also save the precious time and labor of caregivers while dealing in emergency situations”)). This drawback would also have discouraged a POSA from pursuing a lyophilized product.

Third, another known issue with a hydrolysis-prone lyophilized product is moisture content that can originate from the rubber stopper of the vial. This is demonstrated by the disclosure of increasing moisture in the vial during the storage stability testing. (Ex. 1009 at 7; Ex. 2029 at ¶ 74). This will cause concern to a POSA. (Ex. 2029 at ¶ 102).

Accordingly, a POSA with these references in hand would seek to improve upon Parker and make a liquid solution formulation, and thus, would not arrive at the claimed inventions.

v. In the real world, those in the field did not look to lyophilization to reduce impurities, despite the publication of PIF.

Sun's argument boils down to a POSA in 2019 seeking to further improve upon Parker would (1) abandon the Parker "liquid formulation" approach, and (2) develop a lyophilization formulation and process based on a brief description of a product in PIF, which does not teach better storage stability and impurity profile compared to Parker. The real-world story refutes Sun's view. *Minnesota Min. & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1575 (Fed. Cir. 1992) ("[R]eal world considerations provide a colorful picture of the state of the art, what was known by those in the art, and a solid evidentiary foundation on which to rest a nonobviousness determination.").

Nobelbar was approved in Japan in 2008, and the related PIF appears to have

been available from at least 2011. (Ex 2029 at ¶ 88). Nonetheless, years later, when Parker and colleagues were seeking to improve on the stability and impurity profile of phenobarbital products in the United States, and even knowing that PEAU was a hydrolysis-caused degradation product, they took a decidedly different route than lyophilization. (*Id.*). That history speaks volumes here.

c. A POSA would not reasonably expect success in achieving the invention of claim 1.

None of the references that Sun relies upon give a POSA a reasonable expectation of success in achieving an improved impurity profile in a stable lyophilization product, even if a POSA were motivated to create such a product.

As a general matter, the chemical arts are unpredictable. *See In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) (referring to chemistry as a “less predictable field” because “minor changes in a product or process may yield substantially different results”). Parker discloses various degradation pathways but addresses only hydrolysis (Ex. 1012 at [0006]-[0007]), which would suggest to a POSA that there is no one-size-fits-all solution to improve storage stability by reducing all the different categories of impurities in a phenobarbital product. (Ex. 2029 at ¶ 98).

Sun’s cited references do little to reduce the trial-and-error uncertainty. Parker teaches a POSA that it was unexpected to achieve the improved impurity profile described therein. (Ex. 1012 at [0068]). West-Ward does not disclose “any either qualitative or quantitative aspects of phenobarbital sodium degradation upon long-

term storage.” (Ex. 2029 at ¶ 99). Neither gives any reason for a POSA to expect that an even better impurity profile would be achievable through formulation development.

PIF, on the other hand, does not disclose the levels of PEAU, 2EPMM, or PBG in the product, but does disclose at least 0.09% “related substances” that are hydrolysis-prone, plus probably more impurities that were not tested for, which again would not give a POSA reason to expect that even lower impurities levels *upon long-term storage* would be achievable. (*Id.* at ¶¶ 100-102).

Accordingly, a POSA would not reasonably expect to achieve the storage stable, lyophilized composition with an improved impurity profile that the Nivagen inventors achieved.

- 2. PIF, Parker, and West-Ward do not render claims 2–20 obvious for the same reasons as claim 1, as well as others.**
 - a. The references do not disclose, and a POSA would not be motivated to obtain, a reconstituted composition with the specifically claimed impurity thresholds with a reasonable expectation of success.**

Numerous of the claims require that the claimed compositions have either one or more of impurities PEAU, 2EPMM, and PBG controlled to a specific threshold under certain stability conditions. Sun has not established that these limitations are disclosed in, or would be obvious from, the prior art. Nor, even were they disclosed, would a POSA be motivated to combine them and expect to do so. (Ex. 2029 at ¶¶

60, 63-68, 70-77, 80-82, 84).

PEAU. Neither Parker nor West-Ward describe reducing the amount of PEAU in a lyophilized product. (*See, e.g., id.* at ¶ 60 (pertaining to claims 2-4, 6, but equally applicable to the remaining challenged claims), ¶¶ 75, 84). And as explained above, PIF is silent about the amount of PEAU in its formulation, initially or over time (other than the ambiguous “no change” notation). (*See, e.g., id.* at ¶¶ 60, 72-74, 84).

Sun relies on so-called “documented success of stable formulations like Nobelbar described in PIF” in “minimiz[ing] PEAU to very low levels” “certainly no more than 0.1%” to explain that a POSA would use PIF to achieve the claimed impurity levels. Pet. at 25. But the only support it offers is Dr. Suryanarayan’s declaration, which merely repeats the Petition verbatim. (*Compare* Pet. at 25 with Ex. 1015, Suryanarayanan Decl. at ¶ 142). As explained above, PIF does not disclose the amount of PEAU to a POSA.

Parker, which had as its goal minimizing the amount of PEAU, declared victory in 2015 when achieving a level of up to 0.8% PEAU—8 or 16 times the claimed impurity threshold in the ’076 patent. (Ex. 2012 at [0017]). This creates two issues for Sun. First, as discussed above, it is unclear why a POSA would be motivated to develop a formulation to further reduce the amount of PEAU in light of Parker’s success. And second, given that Parker expressly sought to reduce the level of PEAU impurities in the phenobarbital compositions and did so only to a

0.8% threshold, a POSA would not reasonably expect success in achieving a level that is an order of magnitude lower.

PBG. Here, the prior art Sun relies on gives even less information than with PEAU. PIF and West-Ward do not discuss PBG at all. (*See* Ex. 2029 at ¶¶ 66-67, 76-77, 84). And while Parker described PBG as a degradation product that can be caused by oxidation or reaction with a base, it says nothing about PBG's connection to hydrolysis. (*See id.* (citing Ex. 1012 at [0006]-[0007], [0030])). As discussed above, Parker provides no rationale that would motivate a POSA to reduce the amount of PBG, no methodology for doing so, and no particular threshold that a POSA might want to reach. Nor would Parker cause a POSA to reasonably expect that lyophilization would reduce the amount of PBG, given its lack of disclosure of the creation of PBG as a result of hydrolysis.

2EPMM. Sun's argument regarding 2EPMM is the weakest of all. West-Ward and PIF do not mention it. (*See id.*). Parker discloses 2EPMM as a degradation product of phenobarbital that results from reactions other than the hydrolysis that lyophilization or use of alternative solvents is supposed to solve. (*Id.* (citing Ex. 1012 at [0006]-[0007], [0030])). Parker does not, however, quantitate, much less teach how to lower, 2EPMM. Nor does Parker give a reason *why* a POSA would want to lower the amount of 2EPMM. It also provides no guidance regarding setting a specific threshold to achieve, or any reason to believe that a POSA could reduce the

amount of 2EPMM—a degradant Parker identified as caused by oxidation, heat, and pH reactions—through lyophilization, let alone to a specific threshold. (Ex. 2029 at ¶¶ 93-94).

b. The references do not disclose, and a POSA would not be motivated to obtain, an amorphous formulation with the recited stability and impurity levels with a reasonable expectation of success.

Sun has not demonstrated that any of the references teach an amorphous lyophilized composition, let alone motivate a POSA to create one. To the contrary, as the '076 specification teaches, a POSA would have been motivated to avoid amorphous compositions when seeking a more stable, lyophilized phenobarbital composition.

Sun's attempt at proof is scant: it posits that a POSA would have known that lyophilization converts materials to amorphous forms, and thus, would have understood PIF to disclose an amorphous phenobarbital sodium composition. *See* Pet. at 27. That lyophilization *can* produce an amorphous composition—a general chemistry fact—does not mean a POSA would know whether Nobelbar is amorphous, crystalline, or a combination of the two. Indeed, the only disclosure about the crystalline nature of Nobelbar relates to the active ingredient *before* lyophilization. (*See* Ex. 2029 at ¶ 44). Nothing actually teaches the result that Sun and Dr. Suryanarayanan just assume: an amorphous lyophilized composition. (*See id.* at ¶¶ 61, 69, 78, 83-84).

Even if PIF did disclose amorphous lyophilized compositions, a POSA would have no reason to have combined that teaching in making a new, improved-purity lyophilized composition. PIF certainly does not teach any benefits of amorphous compositions. And, as the specification of the '076 patent explains, “conventional wisdom teaches that crystalline material is more stable than amorphous material,” which would lead a POSA away from using amorphous material to create a formulation with improved stability and a superior impurity profile. (*See* Ex. 1001 at 2:59–65 (citing prior art in support)).

B. Grounds 2 & 3 Fail At Least Because They Rely on the '608 Publication, Which Is Not Prior Art to the '076 Patent.

Sun's Grounds 2 and 3 seek to invalidate the '076 patent under the theory that the '076 patent's priority for its claims dates back only to the '914 Application—a continuation-in-part application filed more than one year after the publication of the prior familial application, the '881 Application, as the '608 Publication. Sun's position is both legally wrong and unsupported by the relevant patent documents.

First, to try to break the chain of priority, Sun invents a limitation on the claims that, according to its own claim construction here, does not exist—specifically, a requirement that there be no organic solvent present for all claims. And for those claims that say nothing about crystallinity at all, Sun seeks to require Nivagen to have disclosed in the specification every type of potential crystalline percentage. In so doing, Sun ignores the law of written description, which requires

that Nivagen adequately describe its invention, not every conceivable embodiment. *Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 127 F.4th 896, 916 (Fed. Cir. 2025).

Even if Sun were correct, however, the pre-CIP specifications, in both the narrative portion and original claims, adequately convey that the Nivagen inventors conceived of inventive embodiments of varying crystalline-to-amorphous ratios and did not limit their invention to organic-solvent-free compositions. Accordingly, the '608 Publication is not prior art, dooming Sun's Grounds 2 and 3.⁶

1. Sun's imposition of a heightened written description requirement is legally erroneous.

Let's be clear about what Sun is arguing—claims that are *silent* about the type of solvent employed are invalid for failing to describe in the specification a certain category of solvents. And claims that are *silent* about whether the compositions are wholly, partially, or not amorphous are invalid for purportedly not describing non-amorphous embodiments. This makes little sense, and it's legally wrong.

Under the plain and ordinary meaning (the construction that Sun accedes to here, Pet. at 13 n.2), the claims permit organic and non-organic solvents to be present or absent in the claimed lyophilized composition—Sun presents no argument otherwise. And the plain and ordinary meaning of “composition” permits any

⁶ Nivagen does not, and need not now, address whether Sun has shown that, if the '608 Publication were prior art, the claims are obvious or anticipated.

percentage of crystalline structure, from 0–100%. No disagreement from Sun here either. Thus, Sun’s arguments amount to claims that Nivagen was required to include in the written specification features of embodiments that may be present by virtue of the “comprising” transitional phrase, and not because they are enumerated claim features. *See generally* *Teva Branded Pharm. Prods. R&D, Inc. v. Amneal Pharms. of New York, LLC*, 124 F.4th 898, 913 (Fed. Cir. 2024) (quoting *CIAS Inc. v. Alliance Gaming Corp.*, 504 F.3d 1356, 1360 (Fed. Cir. 2007)) (“[T]he potential presence of additional features is the bedrock understanding of a ‘comprising’ claim, which ‘[i]n the patent claim context’ means ‘including but not limited to.’); *see also* Ex. 1003, ’511 Appl. Pros. History, at 29 [00105] (describing inventors’ understanding of “comprising” as open-ended).⁷ Yet “[w]ritten description asks whether **that which is claimed** is adequately described.” *In re Entresto*, 125 F.4th 1090, 1098 (Fed. Cir. 2025) (emphasis added); *Allergan USA v. MSN Labs. Private Ltd.*, 111 F.4th 1358, 1373 (Fed. Cir. 2024). Or put another way, Section 112(a)’s written description requirement “applies to what the patent discloses and claims as ‘the invention.’” *Teva Branded Pharm. Prods.*, 124 F.4th at 914 (quoting 35 U.S.C. § 112(a), (b)). Under Sun’s claim construction position here, neither the crystalline/amorphous

⁷ Page numbers cited in Exhibit 1003 refer to the page number of the exhibit, not in the underlying provisional patent application.

structure nor presence/absence of organic solvents are features that are claimed as an invention in the '076 patent claims. End of story.

Taken to its logical conclusion, Sun's version of written description would be the death knell to "comprising claims," as it would require inventors to describe anything that could be encompassed within the scope of the claim, regardless of its impact on the claim itself. For good reason, the Federal Circuit has already rejected Sun's reasoning. *Regeneron Pharms*, 127 F.4th at 916 (quoting *Cordis Corp. v. Medtronic AVE, Inc.*, 339 F.3d 1352, 1365 (Fed. Cir. 2003) (internal quotation marks omitted)) ("The specification does not need to describe 'every conceivable and possible future embodiment of [the] invention.'").

Imagine if Sun contended that the full scope of the claim was not adequately described because the relevant specifications do not describe compositions that include chocolate frosting. To be sure, the claims read on embodiments that would have chocolate frosting in them so long as they remain pharmaceutical products. Yet no one would argue that the claims fail to adequately describe the full scope of the invention merely because the specification does not identify every conceivable addition to the claimed ingredients.

Also imagine bicycles were just invented. The inventors described the new device made of steel in their patent application. Only one bicycle was actually made, and it was made of steel. The inventors might even state that steel is suitable for

making bicycles, and they prefer using steel to make bicycles. Yet, no one would argue that the inventors cannot claim “bicycles” per se—because they did not adequately describe bicycles made of copper or aluminum.

The same reasoning applies here. That Sun can conjure many types of ingredients that can be added (or not) to the claimed pharmaceutical compositions does not render claims invalid because their specification does not identify every such hypothetical.

Because Nivagen did not need to describe the presence or absence of unclaimed, organic solvents or crystalline formulations as part of the claimed compositions, Sun’s priority attack on these bases fail.

2. The specification of the pre-CIP Applications adequately describes inventive compositions that have crystalline structures.

Even if Sun had the law correct, to prevail, the Board must be convinced that, as of 2019 or 2020, the inventors did not conceive of inventive compositions that had some portion in a crystalline structure. The specifications and claims of the pre-CIP Applications dictate otherwise.⁸

First, the pre-CIP specification is replete with references to embodiments that

⁸ For ease, Nivagen refers specifically to the version of the specification found in the ’608 Publication. The same subject matter is found in subsequent applications.

are not fully amorphous. The clearest is one that Sun recognizes: percentages of the amount of amorphous lyophilized composition *preferably* (*i.e.*, not to the exclusion of other amounts) from “at least 20%” to “95%.” Pet. at 47; Ex. 1005 at [0012]. From this “preferred mixtures” disclosure, a POSA would understand that “the ’608 Publication also specifically discloses a crystalline form of the lyophilized phenobarbital sodium composition in addition to an amorphous lyophilized phenobarbital sodium composition.” (Ex. 2029, Klibanov Decl. at ¶ 137). A POSA reading this disclosure would understand that the two forms can co-exist in a mixture, and the inventors stated a preference for certain mixtures. (*Id.* at ¶ 138).

Therefore, Sun’s cited case about obviousness not sufficing is inapposite; rather, here, there is express disclosure of crystalline embodiments. At the very least, disclosing the amount of amorphous formulation inherently discloses the companion amount of crystalline formulation, which must necessarily be present. *See Yeda Rsch. & Dev. Co. v. Abbott GMBH & Co. KG*, 837 F.3d 1341, 1345 (Fed. Cir. 2016) (“Under the doctrine of inherent disclosure, when a specification describes an invention that has certain undisclosed yet inherent properties, that specification serves as adequate written description to support a subsequent patent application that explicitly recites the invention’s inherent properties.”).

Second, when the ’608 Publication contrasts an amorphous lyophilized phenobarbital sodium composition with prior art disclosures of a crystalline

material, as Dr. Klibanov explains, *none of the comparator crystalline material was lyophilized*. (Ex. 2029 at ¶ 141). It is also true one of the inventors, Dr. Lakkaraju, discussed the stability of amorphous and crystalline materials *in general* during the prosecution of the '881 Application. (*Id.* at ¶ 142). Nothing would dissuade a POSA from understanding the clear disclosures in the original application's specification as they were written: that both a crystalline form and an amorphous form of the *lyophilized* phenobarbital sodium composition are disclosed, and they can form mixtures, and the inventors stated their preference for mixtures of certain proportions.

Third, parts of the specification give attention to the amorphous nature of certain inventive compositions. That alone cannot limit the disclosure or the inventions. *Cf. ScriptPro LLC v. Innovation Assocs.*, 833 F.3d 1336, 1341 (Fed. Cir. 2016) (“[A] specification’s focus on one particular embodiment or purpose cannot limit the described invention where that specification expressly contemplates other embodiments or purposes.”). Embodiments do not import limitations into claims—even if they consistently have a particular feature. *See Cadence Pharms. Inc. v. Exela PharmSci Inc.*, 780 F.3d 1364, 1369 (Fed. Cir. 2015) (“[E]ven if ‘all of the embodiments discussed in the patent’ included a specific limitation, it would not be ‘proper to import from the patent’s written description limitations that are not found in the claims themselves.’” (quoting *Flo Healthcare Solutions, LLC v. Kappos*, 697

F.3d 1367, 1375 (Fed. Cir. 2012)).

A perfect example of Sun's attempt to limit the inventions to the disclosed method is its invocation of paragraphs 70 and 78 of the '511 Provisional Application as support that the claimed compositions must be amorphous. Pet. at 63, 65. Paragraph 78 specifically explains a method for producing a storage-stable lyophilized composition, and in the case of the data "reference[d] [in] Fig. 5B–5C," the lyophilized Phenobarbital Sodium is amorphous." (Ex. 1003, at 19 [0078]). Similarly, paragraph 70 identifies "a lyophilized Phenobarbital Sodium formed by the methods disclosed herein [that] results in a storage-stable lyophilized Phenobarbital Sodium powder," but explains that the powder had an "amorphous structure" "with reference to the polarized light photomicrographs of Figs. 1A–1F and the XRPD analysis shown in Fig 5A–5D." From these reference-specific conclusions, it does not follow that every inventive composition is amorphous.

3. The originally filed claims of the pre-CIP applications already disclose inventive compositions that have crystalline structures.

Beyond the narrative specifications, the claims of the pre-CIP Applications also demonstrate the inventors' possession of both crystalline and amorphous lyophilized compositions. "Originally filed claims have long been held to be part of the specification to be considered in any § 112 analysis." *Allergan USA, Inc.*, 111 F.4th at 1374. And for the purposes of the analysis here, any claims in the '511

Application *or* the '881 Application would rebut Sun's argument by demonstrating priority in an application predating the '608 Publication (thus rendering the '608 Publication not prior art).

Claims in both the '511 Application and the '881 Application demonstrate that the inventors conceived of inventive compositions that were mixtures of amorphous and crystalline materials. As the following chart demonstrates, the inventors included claims that included specific requirements that the compositions be amorphous in some claims, but not all:

Whether Composition Can Only Be Amorphous	'511 Provisional Application	'881 Application
Expressly Required	Claim 1: "A composition consisting essentially of lyophilized <i>amorphous</i> Phenobarbital Sodium"	Claim 1: "A pharmaceutical composition comprising lyophilized <i>amorphous</i> Phenobarbital Sodium." Claim 16: "A method of treating an individual in need of Phenobarbital Sodium, the method comprising: adding saline or dextrose to a composition comprising lyophilized <i>amorphous</i> Phenobarbital Sodium immediately prior to administration to form a Phenobarbital Sodium Solution..."

<p>Silent</p>	<p>Claim 17: “A method of reducing formation of degradation products of Phenobarbital Sodium reconstituted in all aqueous solution</p> <p>... comprising ...</p> <p>Lyophilizing the Phenobarbital Sodium solution to form <i>stable lyophilized Phenobarbital Sodium.</i>”</p>	<p>Claim 2: “A method of producing a storage-stable form of lyophilized Phenobarbital sodium that forms no more than 0.2% phenylethylacetylurea (PEAU) when reconstituted in an aqueous solution,</p> <p>the method comprising:</p> <p>adding Phenobarbital Sodium to water to form a Phenobarbital Sodium solution ... and</p> <p>lyophilizing the Phenobarbital Sodium solution.”</p>
----------------------	--	---

(Ex. 1003, '511 Appl. Pros. History, at 30–32 cls. 1 & 17; Ex. 1004, '881 Appl. Pros. History, at 230–32, cls. 1, 2, & 16; *see also* Ex. 2029 at ¶¶ 139-140). Because claim interpretation “must give meaning to all the words in [the] claims” and should avoid “mak[ing] expressly recited features redundant,” that the inventors described the inventive compositions in some but not all places as amorphous is strong evidence that the inventors did not limit their invention to amorphous formulations only. *See Apple, Inc. v. Ameranth, Inc.*, 842 F.3d 1229, 1237 (Fed. Cir. 2016); *Funai Elec. Co. v. Daewoo Elecs. Corp.*, 616 F.3d 1357, 1372 (Fed. Cir. 2010) (quoting *Exxon Chemical Patents, Inc. v. Lubrizol Corp.*, 64 F.3d 1553, 1557 (Fed. Cir. 1995)).

4. Sun’s legally irrelevant arguments including a disclaimer-type argument regarding crystallinity of the claimed compositions are erroneous and must be disregarded.

In seeking to undermine the specification’s description of crystalline lyophilized phenobarbital sodium compositions, Sun relies on legally irrelevant facts. For example, the law is well settled that a specification can have adequate written description even if the “Examples, Tables, or Figures” do not make a particular disclosure. *Compare Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1352 (Fed. Cir. 2010) (en banc) (“[T]he written description requirement does not demand either examples or an actual reduction to practice [T]he description requirement does not demand any particular form of disclosure.”) *with* Pet. at 44–45. Sun walks through each of the specification’s uses of “crystalline,” concluding that “[t]here is not a single instance where Patent Owner uses the term ‘crystalline’ to refer to any alleged inventive composition of the Original Applications.” Pet. at 47. Nivagen did not have to; Section 112 does not require verbatim disclosure where the subject matter is otherwise disclosed. *Compare* Pet. at 45–47 *with Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997) (noting that “the exact terms need not be used *in haec verba*, so long as the specification ‘contain[s] an equivalent

description of the claimed subject matter”) (quoted in *Ariad*, 598 F.3d at 1352).⁹ As discussed above, the specification discloses both crystalline and amorphous lyophilized compositions, which can exist in mixtures.

Along the same lines, Petitioner argues that “[a]ll claims that issued from the Original Applications were expressly limited to ‘amorphous’ compositions.” Pet. at 46. This argument is completely irrelevant, because the initial claims of the Original Applications that the inventors submitted reflect their possession of non-amorphous embodiments, as discussed above.

The prosecution history does not save, or even help, Sun’s argument. First, whether a specification (here, of an earlier familial application) adequately describes an invention has nothing to do with an applicant’s prosecution history statements where claim scope is not at issue. *Cf. Trading Techs. Int’l, Inc. v. Open E Cry, LLC*, 728 F.3d 1309, 1319 (Fed. Cir. 2013) (explaining how claim construction analysis, which examines prosecution history, differs from written description analysis, which looks to the “bounds of the specification”). Sun wanted the claims to be given their full scope here, and stated as such. Pet at 13 n.2. Nevertheless, Sun makes a disclaimer-type argument. In any event, at most, if such a disclaimer existed, it

⁹ Dr. Klivanov also explains why Dr. Suryanarayanan’s analysis of the use of “crystalline” in the specification is flawed. (*See* Ex. 2029 at ¶ 141).

would limit the claims to only amorphous compositions—formulations that Sun agrees that the operative specifications support. *See id.* at 49. In other words, a “disclaimer” read into the ’076 claims would align the original specification and the “disclaimer”-containing ’076 patent claims perfectly, eliminating the very basis for Sun’s argument of a lack of sufficient written support. It’s not clear why Sun looks to the prosecution history statements it highlights, since they do not support its written description argument and conflict with Sun’s claim construction position here.¹⁰

¹⁰ To be clear, Nivagen does not concede that all of the ’076 patent claims are limited by prosecution disclaimer to amorphous compositions; rather, it is irrelevant to the dispute that Sun presents. Of course, claims 5, 12, 15, and 20 expressly limit the claims to amorphous compositions. Sun does not dispute that these are adequately described with respect to their crystalline properties. Pet. at 49 (“[T]here is no written description in the Original Applications for any claims that are not limited to amorphous phenobarbital sodium.”). If Sun’s theory that all of the claims are limited solely to amorphous compositions were to be accepted, these claims are redundant and do no additional work—a result to be avoided. That is an issue for claim construction not raised here.

5. The specifications of the pre-CIP Applications adequately describe inventive compositions with organic solvents.

As discussed above, under the correct reading of the law on written description, the plain and ordinary meaning of the claims do not require written description specifically directed to compositions with organic solvents or without organic solvents. However, even if Nivagen were required to describe compositions with organic solvents in them, it did so. A POSA would understand that a solid composition resulting from the lyophilization process will have residual solvents in it, regardless of whether these particular solvents were added to the bulk solution as intended ingredients for the lyophilization process. (Ex. 2029 at ¶¶ 118-122). The residual organic solvents can originate from the manufacturing of the active ingredient, which then carry over into the lyophilized cake. (*Id.* at 121). Thus, regardless of the disclosure or lack thereof in the specification of *adding organic solvent* as an *intended ingredient* in the bulk solution for lyophilization, a POSA would understand that the inventors conceived of stable, highly pure lyophilized phenobarbital compositions that may contain residual organic solvents. (*Id.* at 122).

As Dr. Klivanov explains, “the lyophilizing process involves freezing the bulk solution and then drying it under vacuum to cause solvent sublimation, resulting in a so-called solid “cake.” (*Id.* at ¶¶ 30, 120). Water can be used as a solvent for the bulk solution, but organic solvents or “co-solvents” can also be “intentionally added ... to a bulk solution for the lyophilization process.” (*Id.* at ¶ 118). When organic

solvents were added to the bulk solution, some of it will be present in the lyophilized cake as residual organic solvents. (*Id.* at ¶ 120). However, residual organic solvents in the lyophilized cake can come from another source, which is *the organic solvent used for the manufacture of the active ingredient phenobarbital sodium itself*. (*Id.* at ¶¶ 29, 121). This portion of the residual organic solvents, which are brought into the lyophilized solid “cake” through the API itself, is ignored by Petitioner and Dr. Suryanarayanan, but it exists, and is understood by a POSA. (*Id.* at ¶ 122). Accordingly, a POSA would not assume that a product of a manufacturing process is free of residual solvents, absent a specific statement to that effect. (*Id.*).

Sun’s cited portions of the specification do not undermine Dr. Klibanov’s reasoning. To orient, here are the relevant quotes (emphasis added):

- **Paragraph 7.** “In addition to the degradation impurities, the current marketed liquid formulation of Phenobarbital Sodium (e.g., Phenobarbital Sodium for Injection USP, 65 mg/mL or 130 mg/ml), *includes organic solvents such as alcohol, which are not desirable in general and indeed not suitable for administration to newborns* as described in the art.”
- **Paragraph 78.** “Surprisingly, *the inventors have determined that the presently disclosed method produces a storage-stable lyophilized Phenobarbital Sodium that maintains its stability up to at least 6 months under accelerated stability conditions which is equivalent to 24 months at RT. With reference to FIGS. 5B-5C*, the lyophilized Phenobarbital Sodium is amorphous. In particular, the lyophilized Phenobarbital Sodium is non-

crystalline unlike the USP grade P API shown comparatively in FIG. 5D. The lyophilized Phenobarbital Sodium is stable and ready for reconstitution in either water for injection, 0.9% Saline or 5% Dextrose for intravenous (IV) or intramuscular (IM) administration. ***The presently disclosed formulation does not contain any organic solvents or preservatives which is specifically advantageous for administration to newborns and neonates.*** Moreover, the resulting lyophilized Phenobarbital Sodium forms below the quantitation limit of 0.05% phenylethylacetylurea (PEAU), and no detectable amount of 2-ethyl-2-phenylmalonamide (2EPMM) or alpha-phenylbutyrylguanidine (PBG) when reconstituted in water after storage of the lyophilized Phenobarbital Sodium for up to 6 months under accelerated stability conditions which is equivalent to 24 months at RT.

Neither of these paragraphs require the inventive compositions—especially if made by a process other than the inventive one—to be free of any residual organic solvents. In paragraph 7, the inventors identified the presence of organic solvents as an undesirable feature in the prior art marketed *liquid formulations* (similar to the Parker formulation), especially for babies. But the inventors did not *distinguish* their invention over that deficiency; that is, the inventors did not say in the surrounding context that their invention did not include organic solvents. Instead, the invention is a lyophilized product that does reduce the amount of organic solvents compared to the prior art liquid formulation, by virtue of the lyophilization process. Merely identifying the undesirability of a prior art feature is insufficient to disclaim that feature without clear and unmistakable disavowal. *See Epistar Corp. v. Int’l Trade*

Comm’n, 566 F.3d 1321, 1336 (Fed. Cir. 2009) (“[D]isparaging comments alone do not necessarily show a manifest or express disavowal of the criticized subject matter.”); *e.g.*, *Ventana Med. Sys., Inc. v. Biogenex Lab’ys, Inc.*, 473 F.3d 1173, 1181 (Fed. Cir. 2006) (concluding that “general statements by the inventors indicating that the invention is intended to improve upon prior art” “will not be interpreted to disclaim every feature of every prior art device discussed in the “BACKGROUND ART” section of the patent.”);¹¹ *cf.* *Computer Docking Station Corp. v. Dell, Inc.*, 519 F.3d 1366, 1375 (Fed. Cir. 2008) (“Prosecution disclaimer does not apply, for example, if the applicant simply describes features of the prior art and does not distinguish the claimed invention based on those features.”).

Nor does it follow from a statement that organic solvents are “undesirable” that they must be completely absent from an improved composition even at a residual

¹¹ The statement at issue in *Ventana* is arguably closer to the line than Paragraph 7, as it at least included an objective of the invention tied to the disparagement. It read: “The previously known devices are limited in their performance and unable to satisfy the needs for automated, high precision immunohistology. It is an object of this invention to provide a device which provides more rapid, reliable and more reproducible results than standard methods”

amount; the same rationale supports *minimizing* the presence of organic solvents even if not totally eliminated. Sun has not shown that paragraph 7 disavows inventions containing organic solvent under the “exacting” standard—“words of manifest exclusion or restriction” “both so clear as to show reasonable clarity and deliberateness, and so unmistakable as to be unambiguous evidence of disclaimer.” *Thorner v. Sony Comput. Entm’t Am. LLC*, 669 F.3d 1362, 1366 (Fed. Cir. 2012); *Dealertrack, Inc. v. Huber*, 674 F.3d 1315, 1322 (Fed. Cir. 2012).¹²

For paragraph 78, as with the dispute about disclosure of crystalline formulations, a POSA would understand that the inventors are discussing a specific product they achieved from performing the inventive method, and not the contours of any conceivable inventive composition. Paragraph 78 explains that the inventors are describing a product of the disclosed, inventive methods—that is, the tangible lab result described in Figs 5B–5C. That the particular formulation resulting from a particular run of the inventive method did not have any organic solvents does not preclude another compound within the scope of the claims from doing so, or more precisely, does not mean the inventors did not conceive of such possibilities. To the

¹² There is no basis to find a disavowal here, but if there were, it would operate only to disavow levels of organic solvents comparable to what was found in the prior art, not the presence of *any* organic solvent.

contrary, the written description shows that the inventors knew that using “comprising” left open the possibility “that the referenced elements, components, or steps may be present, or utilized, or combined with other elements, components, or steps that are not expressly referenced.” (Ex. 1003, at 29 [00105]). One such combined component could be a residual organic solvent.

As with the dispute about the description of non-amorphous compositions, Sun advances arguments foreclosed by black letter written description law. Disclosures in “Examples, Tables, or Figures” are not necessary to satisfy Section 112, though Sun implies otherwise. *Ariad*, 598 F.3d at 1352; Pet. at 42. That claims from a parent application issued expressly excluding intended added organic solvents in bulk solutions says nothing about whether the inventors *also* possessed inventive compositions that did not exclude organic solvents. *Compare In re Float’N’Grill LLC*, 72 F.4th 1347, 1350 (Fed. Cir. 2023) (quoting *Antares Pharma, Inc. v. Medac Pharma Inc.*, 771 F.3d 1354, 1358 (Fed. Cir. 2014) (“An applicant is free to seek an expanded scope of coverage beyond that originally sought by filing a continuation or divisional application during the pendency of a parent application and may therein include claims extending to the full scope of the subject matter described in the original specification under 35 U.S.C. § 112(a).”) *with* Pet. at 43 (Sun’s argument). Finally, Sun invites error in asking the Board to assume the insufficiency of the pre-CIP specification from the fact that the inventors elaborated

in a subsequent disclosure with additional matter. *Compare* Pet. at 44 with *PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1305 n.4 (Fed. Cir. 2008) (“Determining the effective filing date each claim in a CIP application is entitled to can be quite complex. Since CIPs generally add new matter, the claims may be fully supported by the parent application or they may rely on the new matter for support.”).¹³

Accordingly, though not legally required, the pre-CIP specifications provide written description support for embodiments of the '076 patent claims with organic solvents.¹⁴

¹³ Sun weaves an interesting narrative about the inventors deliberately withholding certain information in their prior disclosures, learning of Sun’s interest in phenobarbital products, and “resurrecting its” [supposedly] “disregarded data.” Pet. at 44. Sun does not support these accusations with factual support, nor does it explain how they are relevant.

¹⁴ If the specification disavows formulations with organic solvents in them in a clear and unmistakable way (as Sun says), then such a disavowal would equally limit the claim scope as well (which is what Sun argues in the district court). Such a scenario creates parity, not incongruity, between the written description and the claims. Hence, Sun’s acquiescence to a scope of claim construction here broader than in the

6. The originally filed claim 1 of the pre-CIP '881 Application discloses inventive compositions that can contain any amount of residual organic solvent.

Similar to the discussion regarding crystallinity above, at least one claim of a pre-CIP Application demonstrates the inventors' possession of both organic solvent-containing (including residual solvents originating as a bulk solution ingredient, as part of the API preparation, or both), and organic solvent-free, compositions.

Claim 1 in the '881 Application, filed in 2020 and later published as the '608 Publication, Ex. 1005, reads:

A pharmaceutical composition comprising lyophilized amorphous Phenobarbital Sodium.

In terms of the presence or absence of organic solvents in the claimed composition, this originally-filed claim is silent, which matches in form all of the challenged '076 patent claims. Because “[o]riginally filed claims have long been held to be part of the specification to be considered in any § 112 analysis,” Sun has not set forth a “lack of written description” theory here to challenge the claim of priority of the '076 patent claims. *Allergan*, 111 F.4th at 1374.

district court is an attempt to manufacture invalidity where none exists, and in a manner that Sun does not press in the district court. *See supra* at Part IV.

7. Because the '076 patent properly claims priority to the '511 Application, Petitioner's anticipation and obviousness arguments necessarily fail.

As demonstrated above, the pre-CIP Applications “reasonably convey[] to those skilled in the art that the inventor[s] had possession of the claimed subject matter as of the[ir] [respective] filing date[s.]” *Ariad*, 598 F.3d at 1351. Accordingly, the claims of the '076 patent properly claim priority to the pre-CIP Applications, each of which predates the '608 Publication. As a result, the '608 Publication is not prior art under Section 102(a)(1) because it did not publish “before the effective filing date of the claimed invention[s].” Grounds 2 and 3 fail.

VI. CONCLUSION

For the reasons already identified in Nivagen's motion for a discretionary denial, the Director and Board should decline to institute for prudential reasons. *See* Paper No. 7, Patent Owner's Br. in Supp. of Req. for Discretionary Denial (July 18, 2025). But if the Board decides to examine the merits, it should find Sun's positions lacking. Because the Petition fails to show that the challenged claims are reasonably likely to be found unpatentable, the Board should decline to institute *inter partes* review.

Respectfully Submitted,

Dated: August 18, 2025

/s/ Shashank Upadhye
Shashank Upadhye (Reg. No. 48,209)

Yixin H. Tang (*pro hac vice*)
Brent Batzer (Reg. No. 66,160)
Christopher M. Bruno (*pro hac vice* to
be filed)
Upadhye Tang LLP
109 Symonds Drive, #174
Hinsdale, IL 60522-0174
(312) 598-2610

*Attorneys for Patent Owner Nivagen
Pharmaceuticals, Inc.*

CERTIFICATE OF WORD COUNT

Under 37 C.F.R. § 42.24(d), Patent Owner certifies that Patent Owner's Preliminary Response has a word count of 13,102, excluding the portions exempted by 37 C.F.R. § 42.24(a), as calculated by the built-in word-count function in the Microsoft Word software used to prepare this document.

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. §§ 42.6(e), the undersigned certifies that on August 18, 2025, I caused a complete copy of the foregoing Patent Owner's Preliminary Response, and all supporting exhibits to be served via FedEx on Petitioner's counsel of record at:

J. Derek Vandenburg
Alexandra J Olsen
Samuel T. Lockner
Peter M. Kohlhepp
Carlson Caspers Vandenburg & Lindquist
225 South Sixth Street, Suite 4200
Minneapolis, MN 55402
(612) 436-9618

A courtesy copy was also sent electronically to counsel of record for Petitioner at the following email addresses:

- dvandenburg@carlsoncaspers.com
- aolsen@carlsoncaspers.com
- slockner@carlsoncaspers.com
- pkohlhepp@carlsoncaspers.com



Shashank Upadhye (Reg. No. 48,209)