IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NIVAGEN PHARMACEUTICALS, INC., Plaintiff, v. AMNEAL PHARMACEUTICALS, INC., AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS PVT LTD., and AMNEAL EU, LTD., Defendants.	C.A. No. 24-846-GBW

DECLARATION OF MANSOOR M. AMIJI, PH.D. IN SUPPORT OF DEFENDANTS' OPPOSITION TO NIVAGEN'S MOTION FOR A TEMPORARY RESTRAINING ORDER AND PRELIMINARY INJUNCTION

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I. INTRODUCTION

1. I, Mansoor M. Amiji, Ph.D., have been retained by Greenberg Traurig, LLP on behalf of Defendants Amneal Pharmaceuticals, Inc., Amneal Pharmaceuticals of New York, LLC, Amneal Pharmaceuticals LLC, Amneal Pharmaceuticals Pvt. Ltd., and Amneal EU, Ltd. (collectively, "Defendants" or "Amneal") as an independent expert consultant.

2. I submit this declaration in support of Defendants' Opposition to Nivagen's Motion for a Temporary Restraining Order and for a Preliminary Injunction, including supporting exhibits and declarations. One of Nivagen's supporting declarations is the Declaration of Barrett Rabinow, Ph.D. ("Rabinow Declaration").

3. I understand that in its Motion for a Temporary Restraining Order and for a Preliminary Injunction Nivagen asserts that Amneal infringes Claim 11 of U.S. Patent No. 11,813,291 ("the '291 Patent") and Claims 3 and 13 of U.S. Patent No. 11,925,661 ("the '661 Patent") (collectively, "Asserted Patents"). I have been asked to address validity and alleged infringement relating to the Asserted Patents and the accused Amneal Product.

4. This declaration contains my opinions responding to certain opinions contained in the Rabinow Declaration. This declaration also contains my opinions regarding the noninfringement and invalidity of Claim 11 of the '291 Patent and Claims 3 and 13 of the '661 Patent (collective for the claims, "Asserted Claims").

5. In accordance with Federal Rule of Civil Procedure 26(a)(2)(B), this declaration also contains the bases for my opinions; the facts and data I considered in forming my opinions; the exhibits I use to support my opinions; my qualifications, including a list of all publications authored by me; a list of cases in which, during the previous five years, I testified as an expert at trial or by deposition; and a statement of the compensation to be paid for my services and testimony in this case.

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6. If called to testify, I expect to testify about my professional background, qualifications, and experience; my opinions regarding noninfringement and invalidity, and my responses to Dr. Rabinow's opinions regarding same.

7. I may also testify in rebuttal to opinions offered by experts testifying on behalf of Nivagen at any hearing on Nivagen's Motion for a Temporary Restraining Order or for a Preliminary Injunction, deposition, or trial. I reserve the right to amend and supplement my opinions in light of evidence presented by Nivagen and additional information made available to me in the future. I also reserve the right to amend and supplement my opinions and this declaration to respond, to the extent necessary to positions taken by Nivagen and any witnesses Nivagen presents.

8. I also reserve the right to convey my opinions through demonstrative exhibits at any temporary restraining order/preliminary injunction hearing or at trial. I have not yet created the exhibits I may use, but they will likely include charts, diagrams, photographs, presentations, and blowups to illustrate or explain my opinions in this declaration. I also reserve the right to provide a technology tutorial. In addition, I may use materials cited in this report to assist me in preparing demonstratives, such as graphics and animations, for my testimony or in the event I am asked to provide a technology tutorial.

II. BACKGROUND AND QUALIFICATIONS

9. I am an expert in the field of pharmaceutical sciences and drug formulation development and characterization including in the field of parenteral treatments and dosage forms. Specifically, I specialize in drug formulation development and targeted delivery of therapeutics and have extensive experience with sterile injectable aqueous and non-aqueous formulations. I have been an expert in this field since prior to 2020 (i.e., the earliest possible priority date based

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on the face of the Asserted Patents). I have relied upon my training, knowledge, and more than 30 years of experience in the relevant art to form my opinions.

10. In 1988, I graduated with high honors from Northeastern University and received a Bachelor of Science degree in Pharmacy and became a Registered Pharmacist in Massachusetts. In 1992, I received a Ph.D. in Pharmaceutical Science/Pharmaceutics from the School of Pharmacy and Pharmaceutical Sciences at Purdue University, under the supervision of Showalter Distinguished Professor Kinam Park. During my graduate studies at Purdue University, I took several pharmaceutics courses and had hands-on training in pharmaceutical formulations during my graduate training.

11. My doctoral dissertation entitled "Surface Modification of Biomaterials with Water-Soluble Polymers: A Steric Repulsion Approach" focused on surface modification with water-soluble polymers for steric repulsion of proteins and cells from biomaterials to improve their compatibility in the body. and water-soluble polymers. During my PhD training, I used buffered aqueous solutions to prepare different compositions.

12. After receiving my Ph.D. in 1992, I worked as a Senior Research Scientist for Columbia Research Laboratories ("CRL") in Madison, Wisconsin. At CRL, I worked on polymeric delivery systems for various types of therapeutic agents.

13. I am currently the University Distinguished Professor and Professor of Pharmaceutical Sciences in the School of Pharmacy, Bouve College of Health Sciences at Northeastern University in Boston, Massachusetts. I am also jointly appointed as a Professor in the Department of Chemical Engineering in the College of Engineering at Northeastern University. I am also currently an Affiliate Faculty Member in the Department of Biomedical Engineering at Northeastern University. I have taught and carried out research in pharmaceutical sciences at

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Northeastern University since 1993, and from 2010 to 2016, I served as the Chairman of the Department of Pharmaceutical Sciences. In 2000, I was a Visiting Research Scholar in the Department of Chemical Engineering at the Massachusetts Institute of Technology ("MIT") in Cambridge, Massachusetts, in the laboratory of Professor Robert Langer.

14. As a tenured faculty member at Northeastern University, I have 31 years of experience in teaching physical pharmacy and drug formulations to both graduate and undergraduate students. In theory and laboratory courses that I have taught and continue to teach, I extensively cover the manufacturing, composition, physico-chemical properties, and pharmacokinetics of pharmaceutical formulations and delivery systems. I also serve as a consultant to several pharmaceutical, biotechnology, and medical device companies regarding product development and drug delivery.

15. I have published extensively over the course of my career and am ranked as a Thompson-Reuters Highly Cited (top 1%) author in Pharmacology and Toxicology. I have edited and coauthored over 10 books, 70 book chapters and more than 400 peer reviewed scientific articles. The topics of these materials include the design and development of pharmaceutical dosage forms, pharmacokinetics, drug metabolism, dose delivery and controlled release systems, and the use/formulation of related excipients and methods. I have been involved in and consulted on multiple projects over the years, both in industry and academia, about the aforementioned topics. To that end, I have taught courses in physical pharmacy, pharmaceutics; drug design, evaluation, and development; dosage forms; and pharmacokinetics.

16. In 2002, I co-edited a teaching textbook "Applied Physical Pharmacy – 1st Edition", published by McGraw-Hill to specifically cover topics such as pH, buffers and isotonic solutions, colligative properties, solubility, and dispersions. This book is now in its 3rd edition and is used

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extensively for teaching these concepts to pharmacy students in the United States and throughout the world.

17. I have served as a grant reviewer for the National Institutes of Health, the Department of Defense, the United States Department of Agriculture, and the American Chemical Society. I am a member of several professional and industrial societies, including the American Association of Pharmaceutical Sciences ("AAPS") and the Controlled Release Society ("CRS"), and have participated as a reviewer for more than 80 scientific journals.

18. I have also received a number of professional awards and honors, including the Nano Science and Technology Institute ("NSTI") Fellowship Award for Outstanding Contributions towards the Advancement in Nanotechnology, Microtechnology, and Biotechnology in 2006; a Fellowship and Meritorious Manuscript Award from the AAPS in 2007; the Tsuneji Nagai Award from the CRS in 2012; the Northeastern University School of Pharmacy Distinguished Alumni Award in 2016; and Purdue University College of Pharmacy Distinguished Alumni Award in 2019. In 2024, I was also elected as a Fellow of the American Institute of Medical and Biological Engineering ("AIMBE"). Over the course of my career, I have advised numerous post-doctoral associates, doctoral students, master's students, visiting scientists, and research fellows.

19. I am also the inventor or co-inventor on a number of issued patents and pending patent applications, including nine issued within the United States.

20. I lecture extensively on various topics on the leading edge of modern pharmaceutical sciences, and I regularly attend numerous worldwide pharmaceutical conferences. I have submitted a large number of abstracts to conferences and journals in the field of

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pharmaceutical sciences. I have been an invited speaker at national and international scientific conferences.

21. I am a founder of and scientific advisor to many pharmaceutical companies, including Nemucore Medical Innovations and Targagenix, Inc., which have licensed my patents on lipid-based drug delivery systems and are in the process of developing a commercial product.

22. In addition to serving as a long-term member of the AAPS and on the Scientific Advisory Board of the CRS, I have also served as a permanent member of the National Institutes of Health's grant review panel and many other public funding agencies in the U.S. and across the world. I am an Editor for the Americas of the journal: Drug Delivery and Translational Research, an official journal of the CRS, and Associate Editor of several peer-reviewed journals and on the editorial board of about a half dozen other scientific journals.

23. Additional details concerning my background, training, and experience are contained in my current *Curriculum Vitae*, attached hereto as **Exhibit A.**

24. Based on my education, training, and experience, including my research expertise in pharmaceutical product development and drug formulation development of over 30 years, I believe that I am qualified to provide useful technical information regarding the subject matter of this case.

III. COMPENSATION AND PRIOR TESTIMONY

25. For my work in this case, I am being compensated at my standard rate of $900 per hour plus reasonable expenses. My compensation is not dependent on the outcome of this litigation, nor does my compensation have any bearing on the opinions set forth in this report, or the opinions I may offer at trial of this litigation.

26. The following is a list of my prior testimony given at trial or by deposition in the past five years:

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- *Lipocine, Inc. v. Clarus Therapeutics, Inc., Patent Interference No. 106,045 (McK)*
- *Cadence Pharmaceuticals Inc., et al. v. InnoPharma Licensing LLC, et al., C.A. No. 1:14-cv-01225-LPS (D. Del.)*
- *Impax Laboratories, Inc. v. Actavis Laboratories FL, Inc. et al., C.A. No. 2:2015-cv-06934 (D.N.J.)*
- *Reckitt Benckiser LLC v. Aurobindo Pharma Limited, C.A. No. 14-cv-1203-LPS (D. Del.)*
- *AMAG Pharmaceuticals, Inc. v. Sandoz, Inc., C.A. No. 16-1508-PGS-LHG (D.N.J.)*
- *Alcon Research, Ltd. v. Watson Laboratories. Inc., C.A. No. 16-129-LPS-SRF (D. Del.)*
- *Onyx Therapeutics, Inc. v. Cipla Limited, et al., C.A. No. 16-988-LPS (D. Del)*
- *Almirall, LLC v. Taro Pharmaceutical Industries Ltd., C.A. No. 17-663-JFB-SRF (D. Del.)*
- *Galderma Labs. LP v. Teva Pharmaceuticals USA, Inc., C.A. No. 17-1783-RGA (D. Del.)*
- *FWK Holdings LLC v. Shire PLC et al., C.A. No. 16-cv-12653-ADB (Lead) and No. 17-cv-10050-ADB (Consol.) (D. Mass.)*
- *Impax Laboratories, Inc., v. Zydus Pharmaceuticals Inc & Cadilla Healthcare, C.A. No. 17-cv-13476 (SRC)(CLW) (D.N.J)*
- *Par Pharmaceutical, Inc. et al v. Eagle Pharmaceuticals, Inc., C.A. No. 18-cv-00823 (CFC) (D. Del.)*
- *Vifor Fresenius Medical Care Renal Pharma Ltd. et al v. Lupin Atlantis Holdings SA et al, C.A. No. 18-cv-00390 (MN) (D. Del.)*
- *Pharmacyclics, et al., v. Cipla, et al., C.A. No. 1:18-cv-00192-CFC (Consol.) (D. Del.)*
- *Lipocene, Inc. v. Clarus Therapeutics, Inc., C.A. No. 1:19-cv-622-WCB (D. Del.)*
- *Thorne Labs v Trustees of Dartmouth, C.A. No. IPR2021-00268 (PTAB).*
- *Trutek Corp. v. BlueWillow Biologics, et al., C.A. No. 2:21-cv-10312-SJM-RSW (E.D. Mich).*
- *Microspherix, LLC v. Merck Sharp & Dohme Corp. and Organon USA, Inc., C.A. No. 17-cv-3984 (RMB/JBC) (D. NJ).*
- *Genzyme Corp. and Aventis v. Novartis Gene Therapy, Inc. and Novartis Pharmaceuticals, Corp., C.A. No. 21-1736-RGA (D, Del).*
- *Exceltis USA, Inc. et al., v. Lupin, LTD and Lupin Pharmaceuticals, Inc., C.A. 1:22-cv-00434-RGA (Deposition) (D, Del).*
- *Exceltis USA, Inc. et al., v. Lupin, LTD and Lupin Pharmaceuticals, Inc., C.A. 1:22-cv-00434-RGA (Trial) (D, Del).*

IV. SUMMARY OF OPINIONS

27. In my opinion, based on the materials I have reviewed as well as my training and experience, with respect to the Amneal Product[1]:

- Amneal did not and does not infringe Claim 11 of the ’291 Patent;
- Amneal did not and does not infringe Claims 3 and 13 of the ’661 Patent;
- Claim 11 of the ’291 Patent is invalid in view of the prior art.
- Claims 3 and 13 of the ’661 Patent are invalid in view of the prior art.

[1] I describe details of the Amneal Product in Section VII -below.

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28. My analysis and opinions are based on my understanding of the ’291 and ’661 Patents, and my understanding of the accused Amneal Product as a person having ordinary skill in the art now and at the time of the alleged invention.

V. APPLICABLE LEGAL PRINCIPLES

29. I am not an attorney and will not offer legal opinions. However, I have been informed by counsel of several principles concerning claim construction, infringement/non-infringement and validity/invalidity of a patent, which I rely upon in arriving at my opinions.

A. Noninfringement

30. I understand that an infringement analysis requires a two-step approach. First, the claims are properly construed by the Court in accordance with claim construction principles. Second, the claims, as construed, are applied to the Accused Product.

31. It is my understanding that each and every limitation is essential in proving infringement, and that the absence of even one limitation in an accused product or process avoids infringement.

32. It is my understanding that the patentee has the burden of proving infringement by a preponderance of the evidence. I understand this standard to require that the patentee present evidence that, as a whole, shows that the fact sought to be proved is more probable than not.

33. To establish direct infringement, a plaintiff must prove that a defendant makes, uses, offers to sell or sells, within the United States, or imports into the United States, an accused product that embodies each and every limitation of the claim.

34. It is my understanding that there are two types of direct infringement: literal infringement and infringement under the doctrine of equivalents.

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a. Literal Infringement

35. It is my understanding that to literally infringe a claim, an accused product or process must literally meet each and every limitation of the claim.

b. Doctrine of Equivalents

36. I understand that if an accused product does not literally infringe a claim, it may infringe a claim under the doctrine of equivalents if there are insubstantial differences between the claim and an accused product.

37. It is also my understanding that the doctrine of equivalents analysis proceeds on an element-by-element basis and that a generalized showing of equivalency between the claim as a whole and the allegedly infringing product is insufficient.

38. It is my understanding that the doctrine of equivalents provides a limited exception to the principle that claim meaning defines the scope of the exclusivity in our patent system. I further understand that the Federal Circuit has referred to the doctrine of equivalents as an "exceptional" basis for liability that must be carefully limited.

39. I understand that an infringement analysis under the doctrine of equivalents considers whether the accused product performs substantially the same function, in substantially the same way, to achieve substantially the same result, as disclosed in the claim.

40. I understand that to prove infringement under the doctrine of equivalents, the patentee must provide particularized testimony and linking argument as to the insubstantiality of the differences between the claimed invention and the accused device.

B. Invalidity

41. I understand that an issued United States patent is presumed valid. I have written this declaration with the understanding that a party challenging the validity of an issued United States patent bears the burden of proving invalidity by "clear and convincing evidence." I

understand that clear and convincing evidence requires more than "a preponderance of the evidence" but less than "beyond a reasonable doubt." I have used the "clear and convincing" evidence standard throughout this Report.

42. Further, I understand that each patent claim is considered separately for purposes of invalidity.

43. I understand that prior art includes any of the following items received into evidence during trial:

- any product or method that was publicly known or used by others in the United States before the date of invention of an asserted claim;
- patents that issued more than one year before the filing date of the patent, or before the date of invention of an asserted claim;
- publications having a date more than one year before the filing date of the patent, or before the date of invention of an asserted claim;
- any product or method that was in public use or on sale in the United States more than one year before the patent was filed; and
- any product or method that was made by anyone before the named inventors created the patented product or method where the product or method was not abandoned, suppressed, or concealed.

44. I understand that a prior art "reference" is any single one of the above, e.g., a patent, publication, or product.

45. I understand that a patent is to be understood from the perspective of a hypothetical "person of ordinary skill in the art," also known as a "POSITA," to which the patent pertains. I understand that, in considering what the claims of a patent require, what was known prior to that patent, and what a prior art reference discloses, one must use the perspective of a POSITA. I have been instructed to consider all the issues addressed in this declaration from the perspective of a POSITA.

1. Anticipation

46. I understand that a patent claim is invalid if the claimed invention is not new. It is my understanding that a patent claim is invalid as "anticipated" by a prior art reference if a person of ordinary skill in the art would have understood that each and every element of the claim is disclosed in a single prior art reference (e.g., a single patent or publication), and that those elements are arranged or combined in the same way as in the claim, so that a person of ordinary skill in the art, looking at that single prior art reference, would be able to make and use at least one embodiment of the claimed invention.

47. I understand that a prior art reference may disclose a claim limitation "inherently," if that limitation is necessarily present in the reference.

2. Obviousness

48. I further understand that a patent claim is invalid as "obvious" if, at the time the claimed invention was made, the differences between the claimed invention and the prior art are such that the subject matter of the claim as a whole would have been obvious to a person having ordinary skill in the art to which the subject matter pertains.

49. I understand that a determination of whether a claim is obvious should be based on the following factors: (1) the level of ordinary skill in the art at the time the claimed invention was made; (2) the scope and content of the prior art; (3) the differences, if any, that existed between the claimed invention and the prior art; and (4) secondary considerations of non-obviousness, if any.

50. I understand that "secondary considerations of non-obviousness" are sometimes referred to as "objective indicia" that may be considered in determining obviousness and include:

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- whether the claimed invention was commercially successful as a result of the merits of the claimed inventions (rather than the result of design needs or market pressure, advertising, or similar activities);
- whether the claimed invention satisfied a long-felt need;
- whether others had tried and failed to make the claimed invention;
- whether the claimed invention achieved unexpected results;
- whether others in the field praised the claimed invention;
- whether others in the field expressed surprise or disbelief regarding the claimed invention;
- whether others copied the claimed invention;
- whether others sought or obtained rights to the patent from the patent-holder;
- whether the inventor proceeded contrary to accepted wisdom in the field; and
- whether others independently invented the claimed invention before or at about the same time as the named inventor thought of it (this factor suggests obviousness, not non-obviousness).

51. I understand that the existence of each and every element of the claimed invention in the prior art does not by itself show obviousness because most, if not all, true inventions rely on building blocks from prior art. I understand that if the prior art as a whole teaches away from combining elements in the manner required by a patent claim, the claim may not be obvious.

52. I also understand that it is important to be careful not to determine obviousness using hindsight because many true inventions can seem obvious after the fact. Obviousness must be considered from the perspective of a person of ordinary skill in the art at the time the claimed invention was made, and it is improper to consider what is known today or what is learned from the teaching of the patent. Thus, it is improper to use the patent as a "road map" for selecting and combining prior art.

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53. I understand that a claim can be found invalid as obvious if it is the result of, for example:

- combining prior art elements according to known methods to yield predictable results;
- simply substituting one known element for another to yield predictable results;
- using a known technique that improves similar devices, methods, or products in the same way;
- applying a known technique to a known device, method, or product ready for improvement to yield predictable results;
- choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success (i.e., "obvious to try"); and
- known work in one field of endeavor that may prompt variations of the invention for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art.

54. I further understand that a claim can be obvious if the elements of the claim that are not found in a reference or combination of references can be supplied by the "common sense" of a person of ordinary skill in the art.

VI. BASES FOR MY OPINIONS

A. Materials Considered

55. **Exhibit B** provides a list of the materials I considered in preparing this declaration. I also relied on my experience, education, and knowledge of the art.

B. Person of Ordinary Skill in the Art

56. I understand that a patent is to be understood from the perspective of a hypothetical "person of ordinary skill in the art," also known as a "POSITA," to which the patent pertains. I understand that, in considering what the claims of a patent require, what was known prior to that patent, and what a prior art reference discloses, one must use the perspective of a POSITA. I have

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been instructed to consider all the issues addressed in this declaration from the perspective of a POSITA.

57. I understand that I am to consider several factors in analyzing the level of ordinary skill in the art for a particular patent:

- the education of the inventor(s);
- the type of problems encountered in the art and the prior art solutions to those problems;
- the rapidity with which innovations are made;
- the sophistication of the technology; and
- the education level of workers in the relevant field.

58. I also understand that a POSITA is not an automaton and possesses an ordinary amount of creativity.

59. The subject matter of the ’291 and ’661 patents falls within the medical/pharmaceutical arts, and specifically the field of parenteral treatments and dosage forms. It is my opinion that the level of skill in the art is relatively high, with practitioners having an advanced degree in chemistry, biology and/or pharmaceutics, and a few years of experience in preparing parenteral formulations. A person of ordinary skill in the art easily would have understood the prior art references referred to herein, and would have the capability to draw inferences from them.

60. I understand Dr. Rabinow testified that “a POSA at the time of the alleged invention would have had at least a Ph.D. degree in chemistry or biochemistry 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, and development, optimization, and manufacture, including experience with

processes and techniques for minimizing impurities in and improving the stability of, pharmaceutical drug products during manufacture and storage."

61. As of 2020 (the earliest potential priority date based on the provisional application cited on the face of the Asserted Patents), I was at least a POSITA under both my definition of a POSITA and Dr. Rabinow's definition of a POSITA.

62. My opinions would not change if Dr. Rabinow's definition of a POSITA were adopted instead of my definition.

VII. AMNEAL'S POTASSIUM PHOSPHATE PRODUCT (THE "AMNEAL PRODUCT")

63. The Amneal Product is described in the FDA-Approved Amneal Package Insert that Amneal publicly disclosed on its website. (**Exhibit C**, https://amnealnaloxone.com/wp-content/uploads/2024/07/PotassiumPhosphatesIVB.pdf- ("Amneal Package Insert")).

64. According to the Amneal Package Insert, the Amneal Product is indicated as follows to treat adults and pediatric patients suffering from hypophosphatemia:

> **----------INDICATIONS AND USAGE----------**
> Potassium Phosphates in Sodium Chloride Injection is a phosphorus replacement product indicated as a source of phosphorus to correct hypophosphatemia in adults and pediatric patients who weigh 40 kg or greater when oral or enteral replacement is not possible, insufficient or contraindicated. (1)

(Ex. C, p. 1).

65. The Amneal Package Insert provides the following Dosage and Usage Instructions:

----------DOSAGE AND ADMINISTRATION----------

Important Preparation Instructions

- Do NOT dilute prior to administration (2.1)
- Use this potassium phosphates in sodium chloride injection product only in patients who require the entire 15 mmoL phosphorus dose (potassium 22 mEq) and not any fraction thereof. Otherwise, consider an alternative formulation of potassium phosphate. (2.1)

Important Administration Instructions

- Potassium Phosphates in Sodium Chloride Injection is only for administration to a patient with a serum potassium concentration less than 4 mEq/dL; otherwise, use an alternative source of phosphorus. (2.2)
- Use of this potassium phosphates in sodium chloride injection product increases the risk of hyperkalemia in patients weighing less than 40 kg, including life threatening cardiac events. (5.3)
- See full prescribing information for important administration instructions. (2.2)

Recommended Dosage

- This product contains phosphorus 15 mmol and potassium 22 mEq (phosphorus 0.06 mmol/mL and potassium 0.088 mEq/mL). (2.3)
- Monitor serum phosphorus, potassium, calcium and magnesium concentrations. (2.3)
- See full prescribing information for recommendations on initial or single dosing, repeated dosing, concentration and infusion rate. (2.1, 2.2, 2.3)

(Ex. C, p. 1).

66. The Amneal Package Insert provides the following Dosage Forms and Strengths:

----------DOSAGE FORMS AND STRENGTHS----------

Injection:

- Phosphorus 15 mmol/250 mL (0.06 mmol/mL) and Potassium 22 mEq/250 mL (0.088 mEq/mL) clear, colorless solution filled in a single-dose intravenous infusion bag. (3)

(Ex. C, p. 1).

67. The Amneal Package Insert includes the following Description of the Amneal Product:

11 DESCRIPTION

Potassium Phosphates in 0.9% Sodium Chloride Injection, for intravenous use, is a phosphorus replacement product containing phosphorus 0.06 mmol/mL and potassium 0.088 mEq/mL. It is a sterile, non-pyrogenic, ready-to-use diluted solution containing a mixture of monobasic potassium phosphate, USP and dibasic potassium phosphate, USP in 0.9% sodium chloride. No dilution is required before administration. It is supplied in 250 mL single-dose intravenous infusion bag.

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Monobasic Potassium Phosphate is chemically designated KH_2PO_4, molecular weight 136.09, white, odorless crystals or granules freely soluble in water.

Dibasic Potassium Phosphate is chemically designated K_2HPO_4, molecular weight 174.18, colorless or white granular salt freely soluble in water.

Each mL contains 4.48 mg of monobasic potassium phosphate, USP and 4.72 mg of dibasic potassium phosphate, USP.

Each mL contains phosphorus, 0.06 mmol (equivalent to 1.86 mg phosphorus); potassium, 0.088 mEq (equivalent to 3.40 mg of potassium); sodium chloride, USP, 9 mg and water for injection, USP (q.s.).

Note: 1 mmol of phosphorus is equal to 1 mmol phosphate.

This product contains no more than 25 mcg/L of aluminum.

The pH is 5.8 to 7.2 and the osmolarity is 0.455 mOsmol/mL (calc).

(Ex. C, p. 10).

VIII. THE ASSERTED PATENTS

A. U.S. Patent No. 11,813,291

68. U.S. Patent No. 11,813,291 **(Exhibit D)** was filed on October 12, 2021. The application that issued as the ’291 Patent was assigned U.S. Patent Application No. 17/499,001 (“the ’291 patent application”). The ’291 patent application claims the benefit of U.S. Provisional Patent Application 63/090,518 **(Exhibit E)** filed on October 12, 2020. The ’291 patent application published as U.S. Patent Application Publication No. 2022/0110969 (“Pandya”) **(Exhibit F)** on April 14, 2022.

69. The ’291 Patent names Brijeshkumar B. Pandya, Govind R. Jagadale, Dasaradhi Lakkaraju, Bala Tripura Sundari Chodavarapu, Anand Shukla, and Jwalant Shukla as the inventors.

70. The ’291 Patent is assigned on its face to Nivagen Pharmaceuticals, Inc.

71. The ’291 Patent is directed to “compositions and methods for potassium phosphates solutions for injection, especially as it relates to solutions with ultra-low concentrations of aluminum where the solutions are packaged in a ready-to-use container at volumes and concentrations suitable for direct administration to a patient.” (Ex. D, ’291 Patent at 1:11-16.)

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72. The ’291 Patent identifies “[t]he inventive subject matter” as “various compositions and methods of ready-to-use (RTU) potassium phosphates solutions for intravenous administration to patients in need thereof.” (Ex. D, ’291 Patent at 3:13-16.)

73. The ’291 Patent states that such allegedly “[i]nventive … solutions “will not require any dilution or other manipulation to adjust the solution to a required phosphate and/or potassium concentrate . . ..” (Ex. D, ’291 Patent at 3:21-26.)

74. In addition, the ’291 Patent alleges that “the inventors have now discovered that potassium phosphates solutions can be prepared that are storage stable, sterile, and ready-to-use (RTU), and as such avoid all of the drawbacks of heretofore concentrated potassium phosphates solutions that require prior manipulation and had no significant shelf life.” (Ex. D, ’291 Patent, 4:66-5:4.)

75. The ’291 Patent discloses that “the term ‘ready-to-use’ or ‘RTU’ when used in conjunction with the solutions presented herein refers to a solution that can be directly administered to a patient without prior need for dilution or other adjustment . . ..” (Ex. D, ’291 Patent, 5:40-51 (“Viewed from a different perspective, a ‘ready-to-use’ or ‘RTU’ solution can be delivered from a storage container via peripheral or central catheter to a patient without additional manipulation of the solution in the container.”).)

1. The Prosecution of the ’291 Patent

76. The prosecution history of the ’291 Patent is enclosed as **Exhibit G**. The ’291 patent application was originally filed with 20 claims, of which claims 1, 11 and 17 were independent claims that read as follows:

> 1. An isotonic sterile ready-to-use (RTU) aqueous potassium phosphates solution, comprising potassium phosphates and sodium chloride, wherein the solution comprises 15 mmol/100 ml phosphorus (0.15 mmol/mL) and equal or less than 50 mcg/L aluminum.

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> 11. A sterile ready-to-use (RTU) premixed pharmaceutical product stored in a flexible polymeric container, wherein the pharmaceutical product comprises a potassium phosphates in an aqueous sodium chloride solution containing (a) less than 50 mcg/L aluminum, (b) about 15 mmol/100 ml phosphorus, and (c) about 22 mEq/100 mL potassium.
>
> 17. A method of administering phosphates to a patient in need of phosphorus replacement therapy, comprising: administering, without prior dilution, an isotonic, sterile, and ready-to-use (RTU) solution comprising potassium phosphates and sodium chloride solution from a flexible container to the patient at a rate of infusion and by a route of administration corresponding to the patient's age and degree of need of phosphorus replacement; wherein the solution comprises about 15 mmol/100 ml phosphorus, about 22 mEq/100 mL potassium, and less than 50 mcg/L aluminum.

(Exhibit G, the ’291 patent application, pp. 13-14, Original Claims).

77. The Applicant submitted an information disclosure statement, which identified a few published patent documents. It did not identify any of the “known concentrated potassium phosphates solutions” (Ex. D, ’291 Patent at 5:1-4), in the information disclosure statement.

78. A terminal disclaimer was filed on September 18, 2023 disclaiming any portion of the ’291 patent application that would extend beyond any patent that may issue from the ’661 patent application.

79. There were no claim rejections during prosecution of the ’291 patent. Instead, a Notice of Allowance issued on September 28, 2023 wherein the Examiner amended the claims to remove the parentheticals and to correct other minor form issues. The Examiner also provided the following statement regarding the reasons for allowance:

> The closest prior art is to Koneru et al. (US Patent 11,141,430) which disclose phosphate compositions with a low aluminum content. The difference being that Koneru et al. disclose total phosphorus concentration which is about 1 mM/mL (see col. 8, lines

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> 57-67). Koneru et al. does not disclose or provide motivation to arrive at 0.15 mM/mL as claimed.

(Ex. G, Notice of Allowance, p. 140).

80. The ’291 patent issued on November 14, 2023.

2. Asserted Claim 11 of the ’291 Patent

81. There are 20 claims in the ’291 Patent. However, I understand that in its Motion for a Temporary Restraining Order and for a Preliminary Injunction, Nivagen only asserts that Amneal infringes claim 11 of the ’291 Patent. Claim 11 is reproduced below:

> 11. A sterile ready-to-use premixed pharmaceutical product stored in a flexible polymeric container, wherein the pharmaceutical product comprises a potassium phosphates in an aqueous sodium chloride solution containing (a) less than 50 mcg/L aluminum, (b) about 15 mmol/100 ml phosphorus, and (c) about 22 mEq/100 mL potassium.

(Ex. D, ’291 Patent, claim 11).

B. U.S. Patent No. 11,925,661

82. U.S. Patent No. 11,925,661 **(Exhibit H)** was filed on September 5, 2023, and assigned U.S. Patent Application No. 18/460,941 (“the 661 patent application”). The ’661 patent application is a continuation-in-part of the ’291 patent application. It identifies the same inventors and the same assignee—Nivagen—as the ’291 Patent.

83. The ’661 Patent’s specification includes the same disclosures of the ’291 Patent and also includes additional disclosures that are not in the ’291 Patent. I refer to this additional disclosure as “new matter” in this declaration.

84. The new matter added to the ’661 patent application includes, but is not limited to, Figures 18 and 19 of the ’661 patent, the term “hyper-isotonic” at 3:23 and 4:19 of the ’661 patent; the molar ratio at 5:38-42; and, most importantly (because it relates to the asserted claims), the lower concentration ranges discussed at 24:64 to 29:17. Attached to this declaration as **Exhibit J**

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is a redline comparison of the ’661 Patent to the ’291 Patent. The text in redline shows the new matter in the ’661 Patent.

85. According to the ’661 Patent, Table 1 shows the “rate according to the maximum recommended concentration and infusion rates of a known commercially available product (Potassium Phosphates injection, USP, Fresenius Kabi)” for administering phosphorous replacement therapy “via peripheral venous catheter or central venous catheter.” (Ex. H, ’661 Patent at 1:37-67.)

1. The Prosecution of the ’661 Patent

86. The prosecution history of the ’661 Patent is enclosed as **Exhibit I**. The ’661 patent application was originally filed with 20 claims, of which claims 1, 11 and 17 were independent claims that read as follows:

> 1. A sterile ready-to-use (RTU) aqueous potassium solution, comprising potassium phosphates and sodium chloride, wherein the solution comprises between 1.5 mmol/100 mL (0.015 mmol/mL) and 15 mmol/100 ml phosphorous (0.15 mmol/mL) and equal or less than 50 mcg/L aluminum, and wherein the solution has a pH of between 6.2 and 6.8.
>
> 11. A sterile ready-to-use (RTU) premixed pharmaceutical product stored in a flexible polymeric container, wherein the pharmaceutical product comprises a potassium phosphates in an aqueous sodium chloride solution containing (a) less than 50 mcg/L aluminum, (b) between about 1.5 mmol/100 ml and 15 mmol/100 ml phosphorus, and (c) no more than about 22 mEq/100 mL potassium.
>
> 17. A method of administering phosphates to a patient in need of phosphorus replacement therapy, comprising: administering, without prior dilution, a sterile, and ready-to-use (RTU) solution comprising potassium phosphates and sodium chloride solution from a flexible container to the patient at a rate of infusion and by a route of administration corresponding to the patient's age and degree of need of phosphorus replacement; wherein the solution comprises between 1.5 mmol/100 mL and 15 mmol/100 ml phosphorus, no more than about 22 mEq/100 mL potassium, and less than 50 mcg/L aluminum.

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(Ex. I, the ’661 patent application, Original Claims).

87. A terminal disclaimer was filed on November 16, 2023 disclaiming any portion of the ’661 patent application that would extend beyond the ’291 patent.

88. A Notice of Allowance issued on December 14, 2023 wherein the Examiner amended the claims to remove the parentheticals and to correct other minor form issues. The Examiner also provided the following statement regarding the reasons for allowance:

> The closest prior art is Koneru et al. (US Patent 11,141,430) which discloses phosphate compositions with a low aluminum content. The difference being that Koneru et al. disclose total phosphorus concentration which is about 1 mM/mL (see col. 8, lines 57-67). Koneru et al. does not disclose or provide motivation to arrive at 0.15 mM/mL as claimed.

(Ex. I, Notice of Allowance at p. 4).

89. A corrected Notice of Allowance issued on December 26, 2023 which was substantially similar to the December 14, 2023 Notice of Allowance.

90. The ’661 patent issued on March 12, 2024 with 20 claims.

2. Asserted Claims of the ’661 Patent

91. I understand that in its Motion for a Temporary Restraining Order and Preliminary Injunction, Nivagen asserts that Amneal infringes claims 3 and 13 of the ’661 Patent. Claim 3 is a dependent claim, which depends from claim 2. Claim 2 is a dependent claim, which depends from independent claim 1. Claim 13 is a dependent claim, which depends from claim 12. Claim 12 is a dependent claim which depends from independent claim 11. Claims 3 and 13, including the claims from which they dependent, are reproduced below:

> 1. A sterile ready-to-use aqueous potassium solution, comprising potassium phosphates and sodium chloride, wherein the solution comprises between 1.5 mmol/100 mL and 15 mmol/100 ml phosphorous and equal or less than 50 mcg/L aluminum, and wherein the solution has a pH of between 6.2 and 6.8.

> 2. The solution of claim 1, wherein the potassium phosphates comprise potassium dihydrogen phosphate and potassium hydrogen phosphate at a molar ratio of about 0.7 to 1.3.
>
> 3. The solution of claim 2, wherein the potassium dihydrogen phosphate is present in the solution an amount of between about 112 mg/100 ml and about 1,120 mg/100 ml and wherein the potassium hydrogen phosphate is present in the solution in an amount of between about 118 mg/100 ml and about 1,180 mg/100 ml.
>
> 11. A sterile ready-to-use premixed pharmaceutical product stored in a flexible polymeric container, wherein the pharmaceutical product comprises a potassium phosphates in an aqueous sodium chloride solution containing (a) less than 50 mcg/L aluminum, (b) between about 1.5 mmol 100 ml and 15 mmol/100 ml phosphorus, and (c) no more than about 22 mEq/100 mL potassium.
>
> 12. The pharmaceutical product of claim 11, wherein the potassium phosphates comprise potassium dihydrogen phosphate and potassium hydrogen phosphate at a molar ratio of about 0.7 to 1.3, and/or wherein the potassium dihydrogen phosphate is present in the solution an amount of between about 112 mg/100 ml and about 1,120 mg/100 ml and wherein the potassium hydrogen phosphate is present in the solution in an amount of between about 118 mg/100 ml and about 1,180 mg/100 ml.
>
> 13. The pharmaceutical product of claim 12, wherein the sodium chloride is present in the aqueous solution in an amount of up to 900 mg/100 ml.

(Ex. H, ’661 Patent, claims 1-3, 11-13).

IX. NONINFRINGEMENT

92. As discussed above, Nivagen has asserted Claim 11 of the ’291 Patent and Claims 3 and 13 of the ’661 Patent. I reserve my right to address additional claims throughout this proceeding, including with respect to Nivagen’s Motion for a Temporary Restraining Order and for a Preliminary Injunction.

A. The Amneal Product Does Not Infringe Claim 11 of the ’291 Patent Literally Or Under the Doctrine of Equivalents

93. I understand that Nivagen has only asserted infringement of Claim 11 of the ’291 Patent.

94. I further understand that Nivagen has only asserted infringement under the doctrine of equivalents ("DOE"). It is therefore my understanding that Nivagen has waived any literal infringement argument at least for purposes of this motion for injunctive relief. I reserve the right to provide opinions with respect to whether Amneal literally infringes the '291 Patent, should Nivagen raise those arguments.[2]

95. Claim 11 of the '291 Patent recites:

> [11pre]A sterile ready-to-use premixed pharmaceutical product stored in a flexible polymeric container, wherein the pharmaceutical product comprises
>
> [11i] a potassium phosphates in an aqueous sodium chloride solution containing
>
> [11ii] (a) less than 50 mcg/L aluminum,
>
> [11iii] (b) about 15 mmol/100 ml phosphorus, and
>
> [11iv] (c) about 22 mEq/100 mL potassium.

96. As an initial matter, concerning claim construction, the phrase "ready-to-use" appears in the preamble of the Asserted Claims.

97. A POSITA would recognize that the specification of the '291 Patent defines the phrase "ready-to-use" as follows:

> In this context it is noted that the term "**ready-to-use**" or "RTU" when used in conjunction with the solutions presented herein refers to a solution that can be directly administered to a patient without prior need for dilution or other adjustment such as addition of saline or other tonicity agent). Viewed from a different perspective, a "**ready-to-use**" or "RTU" solution can be delivered from a storage container via peripheral or central catheter to a patient without additional manipulation of the solution in the storage container. Therefore, the terms "**ready-to-use**" and "RTU" are interchangeably used with the term "ready-to-administer".

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[2] I note that because all twenty (20) of the claims in the '291 patent include the same limitation(s) that are not infringed by Amneal, it is my opinion and conclusion that none of the claims of the '291 patent would be infringed by Amneal's product.

(Ex. D, the ’291 patent at 5:40-51) (emphasis added).

98. Additionally, a POSITA would recognize that the specification of the ’291 Patent states in the “Summary of the Invention” section:

> Such solutions will not require any dilution or other manipulation to adjust the solution to a required phosphate and/or potassium concentration and can be administered as a single unit at a rate of administration that will not require specific calculations.

(Ex. D, the ’291 patent at 3:21-26).

99. In view of the foregoing, I have interpreted the phrase “ready-to-use” in the Asserted Patents to mean that the composition is to be administered to a patient without additional manipulation, which, in my opinion, is how a POSITA would understand the meaning of “ready-to-use” in the Asserted Claims.

100. The Amneal Product has a phosphorous concentration of 15 mmol/250 ml and a potassium concentration of 22 mEq/250 mL. (Ex. C, p. 1). This equates to 6 mm/100 ml phosphorous and 8.8 mEq/100 mL potassium concentration, respectively. I understand that Nivagen asserts that these concentrations in the Amneal Product meet limitation [11iii] and limitation [11iv] under the doctrine of equivalents despite the Amneal Product being 2.5 times less concentrated for both the phosphorous concentration and potassium concentration.

101. As discussed above, I understand that a doctrine of equivalents analysis is done on a limitation-by-limitation basis and considers whether the accused product is insubstantially different from the claimed invention or meets the function-way-result test.

102. Dr. Rabinow generally opines that the Amneal Product is insubstantially different from the claimed product. I disagree.

103. Initially, a POSITA would not understand the Amneal Product to be insubstantially different from the claimed product due to the substantial differences in the ***concentrations*** of phosphorous and potassium as between the Amneal Product and the claimed invention.

104. As to limitation [11iii], the Amneal Product contains a concentration of only 6 mml/100 ml of phosphorous (i.e., a 60% lower phosphorous concentration) while the claimed concentration requires "about 15 mml/100 ml," which is not insubstantially different. Rather, a POSITA would consider this phosphorous concentration in the Amneal Product significantly different than the claimed phosphorous concentration. The claimed product is a pharmaceutical—a POSITA would understand that in such a product, concentrations are purposefully chosen for desired effect of the drug in a patient. 60% less phosphorous concentration is significantly less than the purposeful amount in the claimed pharmaceutical, therefore a POSITA would understand it is not insubstantially different.

105. Similarly, as to limitation [11iv], the Amneal Product has a concentration of only 8.8 mEq/100 mL of potassium (i.e., 60% lower potassium concentration) than the concentration of "about 22 mEq/100 mL" that is required by the claim(s), which is also not insubstantially different. Rather, a POSITA would understand this potassium concentration in the Amneal Product is significantly different than the claimed potassium concentration. For the same reasons as discussed above, the claimed product is a pharmaceutical—a POSITA would understand that in such a product, concentrations are purposefully chosen for desired effectiveness of the drug in a patient. 60% less potassium concentration is significantly less than the purposeful amount in the claimed pharmaceutical, therefore a POSITA would understand it is not insubstantially different.

106. On this I must further note that Dr. Rabinow's opinion that the Amneal Product is insubstantially different from the claimed product contradicts the patent and specifically the

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"ready-to-use" functionality of the claimed product. After acknowledging the patent's disclosure of the alleged invention's administration "without the need for dilution or other adjustment" (*see, e.g.*, D.I. 14 at ¶¶55 and 59), Dr. Rabinow ignores those unambiguous specification disclosures and the language of the claims, by opining that the claimed 100 mL concentrations of both phosphates and potassium could be "diluted to 250 mL" (*id*. at ¶59) and that the "additional" adjusted volume would be insubstantially different. (*Id*. at ¶60.) But Claim 11 is directed to a "ready to use" formulation and requires specific concentrations. As discussed above, a POSITA would understand that "ready-to-use" refers to a composition that is administered to a patient without additional manipulation, e.g., dilution. Indeed, the '291 Patent refers to the "ready-to-use" functionality of the claimed product an "inventive" feature. (Ex. D, '291 Patent at 3:13-16.) Accordingly, a POSITA would understand that the Amneal Product is substantially different from the claims and therefore is not an equivalent under the Doctrine of Equivalents.

107. In view of the concession of no literal infringement and the substantial differences between the Amneal Product and the limitations in Claim 11 of the '291 Patent addressed above, in my opinion there is clearly no infringement of Claim 11 of the '291 Patent either literally and/or under the doctrine of equivalents. Extending the doctrine of equivalents to cover the Amneal Product would render the claimed limitations meaningless (e.g, the required concentrations as claimed and the ready-to-use requirement). Accordingly, in my opinion, Claim 11 is not infringed at least for the reasons set forth above. I reserve my right to address any additional limitations in Claim 11 or any of the other claims of the patent.

108. I also understand that claims that are invalid cannot be infringed. While it is my opinion that Claim 11 of the '291 Patent is not infringed, as explained in Section X.C., if Claim 11 of the '291 Patent is expanded under the doctrine of equivalents to cover the Amneal Product—

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which it should not—Claim 11 would be invalid because under Nivagen's theory the claimed phosphorous and potassium concentrations are disclosed in the prior art (e.g., 2019 Fresenius Kabi Package Insert for Potassium Phosphates Injection).

B. The Amneal Product Cannot Infringe Claims 3 and 13 of the '661 At Least Because They Are Invalid

109. I understand that claims that are invalid cannot be infringed. As explained below, the claims 3 and 13 of the '661 Patent are invalid as anticipated by Pandya (i.e., the published '291 patent application (Exhibit F)) and are invalid as anticipated and/or obvious in view of the prior art (e.g., 2019 Fresenius Kabi Package Insert for Potassium Phosphates Injection (Exhibit K)) and general knowledge of a POSITA. Thus, the Amneal Product cannot infringe Claims 3 and 13 of the '661 Patent.

X. INVALIDITY

110. Claims 3 and 13 of the '661 Patent are invalid based on U.S. Patent Application Publication No. 2022/0110969 ("Pandya") (Exhibit F), which is Nivagen's own published '291 patent application. Pandya published on April 14, 2022, which is more than a year before the filing of the '661 Patent on September 5, 2023. The '661 Patent contained new matter disclosing the range of phosphorous recited in Claims 3 and 13 of the '661 Patent. (*See* Exhibit J, pp. 1, 21-22, Redline Comparison of the '291 and '661 Patent specifications). Therefore, Claims 3 and 13 of the '661 Patent are not entitled to an earlier priority date than September 5, 2023 and Pandya is prior art to the '661 Patent.

A. Claims 3 and 13 of the '661 Patent Are Invalid as Anticipated By Pandya

111. In my opinion, claims 3 and 13 of the '661 patent are invalid as anticipated in view of the published '291 patent application -- U.S. Patent Application Publication No. 2022/0110969 ("Pandya") (Exhibit F).

112. In my opinion, a POSITA would understand that the priority date of claims 3 and 13 of the ’661 Patent is September 5, 2023. This is because claims 3 and 13 each recite that the concentration range of phosphorous is 1.5 mmol/100 mL to 15 mmol/100 mL. I reviewed a comparison of the specification of the ’661 patent to the specification of the ’291 patent, and the ’291 patent does not include any written description that the phosphorous concentration can be as low as 1.5 mmol/100 mL. (**Exhibit J**.) Rather, that written description, which I understand is referred to as new matter, first appeared in the specification of the ’661 patent application filed on September 5, 2023.

113. Pandya published on April 14, 2022, more than a year before the filing of the continuation-in-part application that issued as the ’661 Patent on September 5, 2023. Therefore, I understand that Pandya is prior art to the ’661 Patent. Pandya contains substantially the same disclosure as the ’661 Patent but without the new matter. Claims 3 and 13 of the ’661 Patent are anticipated because Pandya discloses a species that falls clearly within the claim scope.

114. Pandya discloses a 100 mL sterile ready-to-use potassium phosphate solution with 15 mmol/100 mL of phosphorous, 22 mEq/100 mL of potassium, 9 mg/mL of sodium chloride, not more than 50 mcg/L of aluminum and a pH between 6.2 and 6.8 (Exhibit F, Pandya at Tables 3, 4, and 8 and ¶ [0011]). Pandya also teaches the solution can be packed in flexible polyolefin bags that are stored in an aluminum pouch. (*Id.*, Table 2 and ¶¶ [0034]-[0035]). Pandya further teaches the solution can be prepared with 1,120 mg/100 mL (8.2 mmol/100 mL of phosphorus) of potassium dihydrogen phosphate and 1,180 mg/100 mL (6.8 mmol/100 mL of phosphorus) of potassium hydrogen phosphate.[3] (*Id.*, at ¶ [0032]). Pandya reports the stability of numerous

[3] This calculates to a molar ratio of potassium dihydrogen phosphate to potassium hydrogen phosphate of 1.2 (8.2/6.8 = 1.2).

examples that exhibit the aforementioned properties. (*Id.,* at Figures 9, 12, 13, 14 (the autoclaved lots) and 16). Pandya also teaches the solution can be administered at an infusion rate of 6.8 mmol and 15 mmol of phosphorous per hour. (*Id.*, at ¶ [0044]).

115. Pandya therefore teaches a species exhibiting each and every element of Claims 3 and 13 of the '661 Patent. In my opinion, Claims 3 and 13 of the '661 patent are clearly anticipated.

116. As shown in the chart below, Claim 3 is anticipated by Pandya. Claim 3 depends from Claim 2, which depends from Claim 1. Below is a claim chart showing that each limitation in Claim 3 of the '661 Patent is disclosed in Pandya:

Claims of the '661 Patent	**U.S. Patent Application Publication No. 2022/0110969 ("Pandya")**
1. A sterile ready-to-use aqueous potassium solution, comprising potassium phosphates and sodium chloride, wherein the solution comprises between 1.5 mmol/100 mL and 15 mmol/100 ml phosphorous and equal or less than 50 mcg/L aluminum, and wherein the solution has a pH of between 6.2 and 6.8.[4]	[0016] In a still further aspect of the inventive subject matter, the inventors also contemplate a method of administering phosphates to a patient in need of phosphorus replacement therapy, and contemplated methods include **a step of administering, without prior dilution, an isotonic, sterile, and ready-to-use (RTU) solution comprising potassium phosphates and sodium chloride solution from a flexible container to the patient at a rate of infusion** and by a route of administration corresponding to the patient's age and degree of need of phosphorus replacement. **Most typically, the solution comprises about 15 mmol/100 ml phosphorus, about 22 mEq/100 mL potassium, and less than 50 mcg/L aluminum.** [0046] **Formulation of ingredients for potassium phosphates in sodium chloride injection 15 mmol/100 ml solution.** As set forth in Tables 3-4 below, exemplary amounts of potassium phosphate monobasic (potassium dihydrogen phosphate, KH_2PO_4), potassium phosphate dibasic (potassium hydrogen phosphate, K_2HPO_4) are the active pharmaceutical ingredients (API), thereby serving an active function. For a 15 mmol/100 ml concentration of phosphorus, 11.2 mg/mL KH_2PO_4 and 11.8 mg/mL K_2HPO_4 are added to

[4] As corrected by the May 14, 2024 certificate of correction.

	water with mixing as disclosed herein. The deionized water is to volume (quantum satis (Q.S.)), which for the ready-to-use (RTU) formulation disclosed herein, is fixed at 100 ml. Sodium chloride (NaCl) is an admixture carrier and tonicity agent having a IIG limit of 0.9″ weight/volume (w/v). Accordingly, for a 100 ml solution, 900 mg of NaCl is added. [0081] For the stability studies, the inventors investigated stability of a phosphorus solution containing saline that was prepared according to FIG. **3** from water and potassium dihydrogen phosphate (KH_2PO_4), potassium hydrogen phosphate (K_2HPO_4), and sodium chloride (NaCl), wherein the potassium dihydrogen phosphate was present in the solution an amount of about 1,120 mg/100 ml (8.2 mmol/100 ml), wherein the potassium hydrogen phosphate was present in the solution in an amount of about 1,180 mg/100 ml (6.8 mmol/100 ml), and wherein the sodium chloride was present in the solution in an amount of about 900 mg/100 ml. **Thus, the solution contained 15 mmol/100 ml phosphorus (0.15 mmol/mL), 22 mEq/100 mL potassium, and had an aluminum content of about 30 mcg/L.** Table 20 provides an overview of the packaging materials used and filling/autoclaving conditions employed. [0082]… All formulations listed in FIGS. **9-17** had an aluminum content of less than 50 mcg/L, with most formulations having an aluminum concentration of between about 7-27 mcg/L. [0011] In some embodiments, the potassium phosphates comprise potassium dihydrogen phosphate (KH2PO4) and potassium hydrogen phosphate (K2HPO4), wherein the potassium dihydrogen phosphate is present in the solution an amount of about 1,120 mg/100 ml (8.2 mmol/100 ml) phosphorus wherein the potassium hydrogen phosphate is present in the solution in an amount of about 1,180 mg/100 ml (6.8 mmol/100 ml) phosphorus, and/or wherein potassium is present in the solution in an amount of about 22 mEq/100 mL. **Preferably, but not necessarily, sodium chloride is present in the solution in an amount of about 900 mg/100 ml, and/or the solution has a pH of between 6.2 and 6.8.**

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	See also, Tables 3, 4 and 8 and Figures 9, 12, 13, 14 (the autoclaved embodiment) and 16.
2. The solution of claim 1, wherein the potassium phosphates comprise potassium dihydrogen phosphate and potassium hydrogen phosphate at a molar ratio of about 0.7 to 1.3.	*See* discussion for claim 1. [0032] Therefore, in exemplary embodiments, the RTU potassium phosphates in sodium chloride solution includes potassium dihydrogen phosphate (KH_2PO_4) and potassium hydrogen phosphate (K_2HPO_4). Typically, the potassium dihydrogen phosphate is at an amount of about 1120 mg/100 ml (**8.2 mmol/100 ml of phosphorus**) and the potassium hydrogen phosphate is at an amount of about 1180 mg/100 ml (**6.8 mmol/100 ml of phosphorus**). [0081] For the stability studies, the inventors investigated stability of a phosphorus solution containing saline that was prepared according to FIG. **3** from water and potassium dihydrogen phosphate (KH_2PO_4), potassium hydrogen phosphate (K_2HPO_4), and sodium chloride (NaCl), wherein the potassium dihydrogen phosphate was present in the solution an amount of about 1,120 mg/100 ml (**8.2 mmol/100 ml**), wherein the potassium hydrogen phosphate was present in the solution in an amount of about 1,180 mg/100 ml (**6.8 mmol/100 ml**), and wherein the sodium chloride was present in the solution in an amount of about 900 mg/100 ml. Thus, the solution contained 15 mmol/100 ml phosphorus (0.15 mmol/mL), 22 mEq/100 mL potassium, and had an aluminum content of about 30 mcg/L. ***Emphasis added. For molar ratio, 8.2 mmol/6.8 mmol = 1.2***
3. The solution of claim 2, wherein the potassium dihydrogen phosphate is present in the solution an amount of between about 112 mg/100 ml and about 1,120 mg/100 ml and wherein the potassium hydrogen phosphate is present in the solution in an amount of between about 118 mg/100 ml and about 1,180 mg/100 ml.	*See* discussion for claim 2. [0032] Therefore, in exemplary embodiments, the RTU potassium phosphates in sodium chloride solution includes potassium dihydrogen phosphate (KH_2PO_4) and potassium hydrogen phosphate (K_2HPO_4). **Typically, the potassium dihydrogen phosphate is at an amount of about 1120 mg/100 ml (8.2 mmol/100 ml of phosphorus) and the potassium hydrogen phosphate is at an amount of about 1180 mg/100 ml (6.8 mmol/100 ml of phosphorus).** [0081] For the stability studies, the inventors investigated stability of a phosphorus solution

	containing saline that was prepared according to FIG. **3** from water and potassium dihydrogen phosphate (KH_2PO_4), potassium hydrogen phosphate (K_2HPO_4), and sodium chloride (NaCl), **wherein the potassium dihydrogen phosphate was present in the solution an amount of about 1,120 mg/100 ml (8.2 mmol/100 ml), wherein the potassium hydrogen phosphate was present in the solution in an amount of about 1,180 mg/100 ml (6.8 mmol/100 ml), and wherein the sodium chloride was present in the solution in an amount of about 900 mg/100 ml.** Thus, the solution contained 15 mmol/100 ml phosphorus (0.15 mmol/mL), 22 mEq/100 mL potassium, and had an aluminum content of about 30 mcg/L.

117. As shown below, Claim 13 is also anticipated by Pandya. Claim 13 depends from Claim 12, which depends from Claim 11. Below is a claim chart showing that each limitation in Claim 13 of the ’661 Patent is disclosed in Pandya:

11. A sterile ready-to-use premixed pharmaceutical product stored in a flexible polymeric container, wherein the pharmaceutical product comprises a potassium phosphates in an aqueous sodium chloride solution containing (a) less than 50 mcg/L aluminum, (b) between about 1.5 mmol [sic] 100 ml and 15 mmol/100 ml phosphorus, and (c) no more than about 22 mEq/100 mL potassium.	[0016] In a still further aspect of the inventive subject matter, the inventors also contemplate a method of administering phosphates to a patient in need of phosphorus replacement therapy, and contemplated methods include a step of administering, without prior dilution, an isotonic, sterile, and **ready-to-use (RTU) solution comprising potassium phosphates and sodium chloride solution from a flexible container** to the patient at a rate of infusion and by a route of administration corresponding to the patient's age and degree of need of phosphorus replacement. **Most typically, the solution comprises about 15 mmol/100 ml phosphorus, about 22 mEq/100 mL potassium, and less than 50 mcg/L aluminum.** [0046] Formulation of ingredients for potassium phosphates in sodium chloride injection 15 mmol/100 ml solution. As set forth in Tables 3-4 below, exemplary amounts of potassium phosphate monobasic (potassium dihydrogen phosphate, KH_2PO_4), potassium phosphate dibasic (potassium hydrogen phosphate, K_2HPO_4) are the active pharmaceutical ingredients (API), thereby serving an active function. For a 15 mmol/100 ml concentration of phosphorus, 11.2 mg/mL KH_2PO_4 and 11.8 mg/mL K_2HPO_4 are added to

	water with mixing as disclosed herein. The deionized water is to volume (quantum satis (Q.S.)), which for the ready-to-use (RTU) formulation disclosed herein, is fixed at 100 ml. Sodium chloride (NaCl) is an admixture carrier and tonicity agent having a IIG limit of 0.9″ weight/volume (w/v). Accordingly, for a 100 ml solution, 900 mg of NaCl is added. [0081] For the stability studies, the inventors investigated stability of a phosphorus solution containing saline that was prepared according to FIG. **3** from water and potassium dihydrogen phosphate (KH_2PO_4), potassium hydrogen phosphate (K_2HPO_4), and sodium chloride (NaCl), wherein the potassium dihydrogen phosphate was present in the solution an amount of about 1,120 mg/100 ml (8.2 mmol/100 ml), wherein the potassium hydrogen phosphate was present in the solution in an amount of about 1,180 mg/100 ml (6.8 mmol/100 ml), and wherein the sodium chloride was present in the solution in an amount of about 900 mg/100 ml. Thus, the solution contained 15 mmol/100 ml phosphorus (0.15 mmol/mL), 22 mEq/100 mL potassium, and had an aluminum content of about 30 mcg/L. **Table 20 provides an overview of the packaging materials used** and filling/autoclaving conditions employed. [0082]… All formulations listed in FIGS. **9-17** had an aluminum content of less than 50 mcg/L, with most formulations having an aluminum concentration of between about 7-27 mcg/L. [0011] In some embodiments, the potassium phosphates comprise potassium dihydrogen phosphate (KH2PO4) and potassium hydrogen phosphate (K2HPO4), wherein the potassium dihydrogen phosphate is present in the solution an amount of about 1,120 mg/100 ml (8.2 mmol/100 ml) phosphorus wherein the potassium hydrogen phosphate is present in the solution in an amount of about 1,180 mg/100 ml (6.8 mmol/100 ml) phosphorus, and/or wherein potassium is present in the solution in an amount of about 22 mEq/100 mL. Preferably, but not necessarily, sodium chloride is present in the solution in an amount of about 900 mg/100 ml, and/or the solution has a pH of between 6.2 and 6.8.

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	See also, Tables 3, 4 and 8 and Figures 9, 12, 13, 14 (the autoclaved embodiment) and 16.
12. The pharmaceutical product of claim 11, wherein the potassium phosphates comprise potassium dihydrogen phosphate and potassium hydrogen phosphate at a molar ratio of about 0.7 to 1.3, and/or wherein the potassium dihydrogen phosphate is present in the solution an amount of between about 112 mg/100 ml and about 1,120 mg/100 ml and wherein the potassium hydrogen phosphate is present in the solution in an amount of between about 118 mg/100 ml and about 1,180 mg/100 ml.	*See* discussion for claim 11. [0032] Therefore, in exemplary embodiments, the RTU potassium phosphates in sodium chloride solution includes potassium dihydrogen phosphate (KH_2PO_4) and potassium hydrogen phosphate (K_2HPO_4). **Typically, the potassium dihydrogen phosphate is at an amount of about 1120 mg/100 ml (8.2 mmol/100 ml of phosphorus) and the potassium hydrogen phosphate is at an amount of about 1180 mg/100 ml (6.8 mmol/100 ml of phosphorus).** [0081] For the stability studies, the inventors investigated stability of a phosphorus solution containing saline that was prepared according to FIG. **3** from water and potassium dihydrogen phosphate (KH_2PO_4), potassium hydrogen phosphate (K_2HPO_4), and sodium chloride (NaCl), **wherein the potassium dihydrogen phosphate was present in the solution an amount of about 1,120 mg/100 ml (8.2 mmol/100 ml), wherein the potassium hydrogen phosphate was present in the solution in an amount of about 1,180 mg/100 ml (6.8 mmol/100 ml),** and wherein the sodium chloride was present in the solution in an amount of about 900 mg/100 ml. Thus, the solution contained 15 mmol/100 ml phosphorus (0.15 mmol/mL), 22 mEq/100 mL potassium, and had an aluminum content of about 30 mcg/L.
13. The pharmaceutical product of claim 12, wherein the sodium chloride is present in the aqueous solution in an amount of up to 900 mg/100 ml.	*See* discussion for claim 12. [0081] For the stability studies, the inventors investigated stability of a phosphorus solution containing saline that was prepared according to FIG. **3** from water and potassium dihydrogen phosphate (KH_2PO_4), potassium hydrogen phosphate (K_2HPO_4), and sodium chloride (NaCl), wherein the potassium dihydrogen phosphate was present in the solution an amount of about 1,120 mg/100 ml (8.2 mmol/100 ml), wherein the potassium hydrogen phosphate was present in the solution in an amount of about 1,180 mg/100 ml (6.8 mmol/100 ml), **and wherein the sodium chloride was present in the solution in an amount of about 900 mg/100 ml.** Thus, the solution contained 15 mmol/100 ml phosphorus

	(0.15 mmol/mL), 22 mEq/100 mL potassium, and had an aluminum content of about 30 mcg/L.

118. Accordingly, it is my opinion that Pandya discloses each limitation and therefore clearly anticipates Claims 3 and 13 of the '661 Patent.

B. Claims 3 and 13 of the '661 Patent Are Invalid as Anticipated and/or Obvious In View of the 2019 Fresenius Kabi Package Insert for Potassium Phosphates Injection

119. I understand that the Fresenius Kabi Package Insert ("FK PI") (Exhibit K) for potassium phosphates injection was available to the public on or shortly after November 2019.[5] I understand that FK PI is for the potassium phosphates product marketed by Fresenius Kabi since 2019.

120. Prior to any earliest potential priority date of the '291 and '661 patents, a POSITA would have been aware of the FK PI, which describes an intravenous solution for correcting hypophosphatemia comprising 6.80 mmol/100 of phosphorus and 10 mEq/100 ml of potassium. Ex. K, p. 4-6 (2 Dosage and Administration).

121. In my opinion, the FK PI discloses a ready-to-use or ready-to-administer product with the phosphorous and potassium concentrations within the ranges claimed in Claims 3 and 13. The product in the FK PI can be prepared and stored for up to 14 days. Ex. K, p. 4-5 (2.1 Preparation and Administration in Intravenous Fluids to Correct Hypophosphatemia).

122. Portions of the FK PI are shown below:

[5] *See* https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=212832 (showing the Approval date of 11/26/2019 for Fresenius Kabi's NDA 212832).

FK PI

----------DOSAGE FORMS AND STRENGTHS ----------
Injection:
- phosphorus 15 mmol/5 mL (3 mmol/mL) and potassium 22 mEq/5 mL (4.4 mEq/mL) in a single-dose vial. (3)
- phosphorus 45 mmol/15 mL (3 mmol/mL) and potassium 66 mEq/15 mL

(4.4 mEq/mL) in a single-dose vial. (3)

Ex. K, p. 1

2.1 Preparation and Administration in Intravenous Fluids to Correct Hypophosphatemia

Preparation

• Potassium Phosphates Injection is for *intravenous infusion* into a central or peripheral vein *only after dilution*.

• **Using aseptic technique, withdraw the required amount from the vial and add to 0.9% Sodium Chloride Injection, USP (normal saline)** or 5% Dextrose Injection, USP (D5W). **For adults and pediatric patients 12 years of age and older a total volume of 100 mL or 250 mL is recommended.** For pediatric patients less than 12 years of age, use the smallest recommended volume, considering daily fluid requirements and the maximum concentration for peripheral and central administration shown in Table 1.

• The concentration of the diluted solution should take into consideration the age of the patient, the amounts of phosphorus and potassium in the dose, and is dependent upon whether administration will be through a peripheral or central venous catheter. The recommended maximum concentrations are shown in Table 1:

TABLE 1: Maximum Recommended Concentration of Potassium Phosphates Injection by Age and Route of Administration (Peripheral vs. Central)

Patient Population	Peripheral Venous Catheter	Central Venous Catheter
Adults and Pediatric Patients 12 Years of Age and Older	phosphorus 6.8 mmol/100 mL (potassium 10 mEq/100 mL)	phosphorus 18 mmol/100 mL (potassium 26.4 mEq/100 mL)
Pediatric Patients Less than 12 Years of Age	phosphorus 0.27 mmol/10 mL (potassium 0.4 mEq/10 mL)	phosphorus 0.55 mmol/10 mL (potassium 0.8 mEq/10 mL)

- Visually inspect the solution for particulate matter and discoloration before and after dilution and prior to administration. Do not administer unless solution is clear, and seal on the vial is intact.

Id., at p. 2 (emphasis added).

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> Storage and Stability
> …
> • After dilution, the solution is stable for a maximum of 4 hours at room temperature 20°C to 25°C (68°F to 77°F) **or 14 days under refrigeration at 2°C to 8°C (36°F to 46°F)**.

Id., at p. 3 (emphasis added).

> **11 DESCRIPTION**
> Potassium Phosphates Injection, USP, a phosphorus replacement product containing phosphorus 3 mmol/mL and potassium 4.4 mEq/mL. It is a sterile, non-pyrogenic, concentrated solution containing a mixture of monobasic potassium phosphate and dibasic potassium phosphate in water for injection. It is supplied as a 5 mL and 15 mL single-dose vials and a 50 mL Pharmacy Bulk Package vial.
>
> Monobasic Potassium Phosphate is chemically designated KH_2PO_4, molecular weight 136.09, white, odorless crystals or granules freely soluble in water.
>
> Dibasic Potassium Phosphate is chemically designated K_2HPO_4, molecular weight 174.18, colorless or white granular salt freely soluble in water.
>
> Each mL contains 224 mg of monobasic potassium phosphate and 236 mg of dibasic potassium phosphate.
>
> Each mL contains 3 mmol phosphorus (equivalent to 93 mg phosphorus) and 4.4 mEq potassium (equivalent to 170 mg of potassium). Note: 1 mmol of phosphorus is equal to 1 mmol phosphate. The pH is 6.0 to 7.0. **This product contains no more than 2000 mcg/L of aluminum** *[*see *Warnings and Precautions (5.5)]*.
>
> The osmolarity is 7.4 mOsmol/mL (calc).
>
> The solution is administered after dilution or admixing by the intravenous route.

Id., at p. 12 (emphasis added).

123. The FK PI instructs the pharmacist to prepare the potassium phosphate solution in either 100 mL or 250 mL of 0.9% saline. The FK PI states the solution is stable for 14 days once prepared and refrigerated. Ex. K, pp. 2-3.

124. The FK PI informs the POSITA of potential aluminum toxicity and the need to prepare parenteral dosage forms with low aluminum content. Ex. K, p. 8 (5.5 Aluminum Toxicity).

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It is my opinion a POSITA would have been motivated to prepare a parental dosage form with a low aluminum concentration as recited in the claims of the ’291 and ’661 patents to avoid known toxicity issues.

125. In my opinion, a person of ordinary skill in the art would have been motivated to prepare a ready to use/administer parenteral dosage form with a volume of 100 or 250 mL and a range of phosphorus concentrations from 6.80 mm/100 ml to 15 mmol/100 mL based on the teachings of the FK PI. The motivation to prepare these ready to use/administer dosage forms is the knowledge that dosing errors resulting in serious adverse events, including death, have occurred with the improper use of concentrates. In particular, a POSITA would recognize that preparing the solution prior to an emergency situation and storing it in a ready-to-use form would lead to less dosing errors.

126. Based on my review of the FK PI, the FK PI teaches the concentrations, amounts, and molar ratios within the scope of Claims 3 and 13 of the ’661 Patent.

127. The FK PI teaches a ready to administer solution with 6.8 mmol/100 mL of phosphorus and 10 mEq/100 mL potassium prepared from a concentrate with 224 mg/mL of potassium dihydrogen phosphate (a.k.a. monobasic potassium phosphate) and 236 mg/mL of potassium hydrogen phosphate (a.k.a. dibasic potassium phosphate). Ex. K, p. 12 (“Each mL contains 224 mg of monobasic potassium phosphate and 236 mg of dibasic potassium phosphate.”) Using simple arithmetic, 2.27 mL (6.8 / 3 = 2.27) of the concentrate (3 mmol/mL of phosphorus and 4.4 mEq/mL of potassium) would be added to 100 mL of 0.9% saline to obtain the 6.8 mmol/100 mL solution.

128. Section 11 of the FK label teaches each mL of concentrate has 224 mg of potassium dihydrogen phosphate (a.k.a. monobasic potassium phosphate) with a molecular weight of

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136.09. To determine the number of mmols/mL in the concentrate, the calculation is: 224 mg divided by 136.09 mg/mmoles = 1.65 mmoles/mL. Using 2.27 mL of the concentrate to prepare 100 mL, means 1.65 mmols x 2.27 mLs = 3.75 mmols of potassium dihydrogen phosphate is present in the 6.8 mmol/100 mL dilution.

129. Section 11 of the FK PI also teaches each mL of concentrate has 236 mg of potassium hydrogen phosphate (a.k.a. dibasic potassium phosphate) with a molecular weight of 174.18. To determine the number of mmols/mL of concentrate, the calculation is: 236 mg divided by 174.18 mg/mmoles = 1.35 mmoles/mL. Using 2.27 mL of the concentrate to prepare 100 mL, means 1.35 mmols x 2.27 = 3.06 mmols of potassium hydrogen phosphate is present in the 6.8 mmol/100 mL dilution.

130. The potassium dihydrogen phosphate to potassium hydrogen phosphate ratio for the FK PI is 3.75/3.06 = 1.2, which falls within the molar ratio ranges in Claims 3 and 13.

131. Simple arithmetic further confirms the 6.8 mmol/100 mL solution will have about 508.48 mg/100 mL of potassium dihydrogen phosphate[6] and 535.72 mg/100mL of potassium hydrogen phosphate.[7]

132. With respect to the aluminum content, Applicants for the ’661 patent have admitted that the 6.80 mmol/100 mL solution prepared according to the FK PI will have less than 50 mcg/L of aluminum. Specifically, the ’518 provisional application filed in 2020 contained the following figure, which the Applicants later removed:

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[6] 224 mg/mL x 2.27 mL = 508.48 mg
[7] 236 mg/mL x 2.27 mL = 535.72 mg

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Route	Conc.	Aluminum Content in Admixture NDA *As per NDA Approved Product
Peripheral	6.8 mmol/100 mL	45 mcg/L
	6.8 mmol/Hour	
Central	18 mmol/100 mL	120 mcg/L
	15 mmol/Hour	100 mcg/L

(Exhibit E, the ’518 provisional at Figure 2).

133. Section 11 of the FK PI teaches the concentrate has a maximum amount of 2000 mcg/L of aluminum or 2 mcg/mL. Assuming the concentrate has the maximum amount of aluminum, i.e. 2 mcg/mL, adding 2.27 mL of the concentrate to 97.73 mL of saline will result in 4.54 mcg of aluminum in the 100 mL dilution, which converts to 45.4 mcg/L (4.54 mcg/100 mL X 1000 mL/L). This value is consistent with the 45 mcg/L presented in Figure 2 of the provisional application. (Exhibit E, the ’518 provisional at Figure 2). This also assumes that the 97.73 mL of saline contributes 0 or negligible amounts of aluminum, which in my opinion, is a reasonable assumption.

134. The FK PI does not expressly disclose the pH of the 6.80 mmol/100 mL ready to use/administer solution. In my opinion, the pH of the ready to use/administer composition will inherently be between 6.2 and 6.8 when prepared by the pharmacist according to the FK PI. Support for this belief can be found in the ’661 patent, Tables 21-25 wherein a 6 mmol/100 mL solutions prepared exhibited a pH in the range of 6.59 to 6.74.

135. Claim 3 of the ’661 Patent is anticipated by the FK PI. A comparison of the prior art FK PI and Claim 3 is shown below.

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Claims of the '661 Patent	The FK PI
1. A sterile ready-to-use aqueous potassium solution, comprising potassium phosphates and sodium chloride, wherein the solution comprises between 1.5 mmol/100 mL and 15 mmol/100 ml phosphorous and equal or less than 50 mcg/L aluminum, and wherein the solution has a pH of between 6.2 and 6.8.[8]	**2.1 Preparation and Administration in Intravenous Fluids to Correct Hypophosphatemia** <u>Preparation</u> • Potassium Phosphates Injection is for *intravenous infusion* into a central or peripheral vein *only after dilution*. • **Using aseptic technique, withdraw the required amount from the vial and add to 0.9% Sodium Chloride Injection, USP (normal saline)** or 5% Dextrose Injection, USP (D5W). **For adults and pediatric patients 12 years of age and older a total volume of 100 mL or 250 mL is recommended.** For pediatric patients less than 12 years of age, use the smallest recommended volume, considering daily fluid requirements and the maximum concentration for peripheral and central administration shown in Table 1. The FK PI teaches a ready to administer solution with 6.8 mmol/100 mL of phosphorus and 10 mEq/100 mL potassium. *See* Table 1 (phosphorous 6.80mmol/100 mL and potassium 10mEq/100 mL). <u>Storage and Stability</u> … • After dilution, the solution is stable for a maximum of 4 hours at room temperature 20°C to 25°C (68°F to 77°F) **or 14 days under refrigeration at 2°C to 8°C (36°F to 46°F)**. Section 11 of the FK PI teaches the concentrate has a maximum amount of 2000 mcg/L of aluminum. This equates to 45mcg/L, which is less than 50mcg/L recited in the claim. Applicants for the ’661 patent have also admitted that the 6.80 mmol/100 mL solution prepared according to the FK PI will have less than 50 mcg/L of aluminum. *See* Exhibit E, the ’518 provisional at Figure 2. In my opinion, the pH of the ready to use/administer composition will inherently be between 6.2 and 6.8 when prepared by the

[8] As corrected by the May 14, 2024 certificate of correction.

	pharmacist according to the FK PI label. Support for this belief can be found in the '661 patent, Tables 21-25 wherein a 6 mmol/100 mL solution prepared with the same ingredients as present in the FK PI ready to use/administer composition exhibit a pH in the range of 6.59 to 6.74.
2. The solution of claim 1, wherein the potassium phosphates comprise potassium dihydrogen phosphate and potassium hydrogen phosphate at a molar ratio of about 0.7 to 1.3.	*See* discussion for claim 1. As explained above, the FK PI teaches a ready to administer solution with 6.8 mmol/100 mL of phosphorus and 10 mEq/100/mL potassium prepared from a concentrate with 224 mg/mL of potassium dihydrogen phosphate (a.k.a. monobasic potassium phosphate) and 236 mg/mL of potassium hydrogen phosphate (a.k.a. dibasic potassium phosphate). Using simple arithmetic 2.27 mL of the concentrate (3 mmol/mL of phosphorus and 4.4 mEq/mL of potassium) would be added to 100 mL of 0.9% saline to obtain the 6.8 mmol/100 mL solution. Simple arithmetic further confirms the 6.8 mmol/100 solution will have about 508.48 mg/100 mL of potassium dihydrogen phosphate[9] and 535.72 mg/100 mL of potassium hydrogen phosphate.[10] **The values further calculate to about 3.75 mmoles of potassium dihydrogen phosphate and about 3.06 mmoles of potassium hydrogen phosphate which is a ratio of 1.2.**
3. The solution of claim 2, wherein the potassium dihydrogen phosphate is present in the solution an amount of between about 112 mg/100 ml and about 1,120 mg/100 ml and wherein the potassium hydrogen phosphate is present in the solution in an amount of between about 118 mg/100 ml and about 1,180 mg/100 ml.	*See* discussion for claim 2. Simple arithmetic confirms the 6.8 mmol/100 mL solution obtained from the FK PI will have about 508.48 mg/100 mL of potassium dihydrogen phosphate and 535.72 mg/100 mL of potassium hydrogen phosphate.

136. The FK PI does not describe the use of a flexible package or flexible polyolefin package as recited in claim 13 of the '661 patent. It is my opinion that these features were

[9] 224 mg/mL x 2.27 mL = 508.48 mg
[10] 236 mg/mL x 2.27 mL = 535.72 mg

obvious matters of design choice to a POSITA at the time of the ’661 patent, because flexible polyolefin bags for parental dosage forms were well known in the art.

137. A comparison of the FK PI and Claim 13 is shown below. Claim 13 is invalid as obvious in view of the FK PI. Claim 13 depends from Claim 12, which depends from Claim 11. Below is a claim chart showing the analysis:

Claims of the '661 Patent	The FK PI
11. A sterile ready-to-use premixed pharmaceutical product stored in a flexible polymeric container, wherein the pharmaceutical product comprises a potassium phosphates in an aqueous sodium chloride solution containing (a) less than 50 mcg/L aluminum, (b) between about 1.5 mmol [sic] 100 ml and 15 mmol/100 ml phosphorus, and (c) no more than about 22 mEq/100 mL potassium.	**2.1 Preparation and Administration in Intravenous Fluids to Correct Hypophosphatemia** <u>Preparation</u> • Potassium Phosphates Injection is for *intravenous infusion* into a central or peripheral vein *only after dilution*. • **Using aseptic technique, withdraw the required amount from the vial and add to 0.9% Sodium Chloride Injection, USP (normal saline)** or 5% Dextrose Injection, USP (D5W). **For adults and pediatric patients 12 years of age and older a total volume of 100 mL or 250 mL is recommended.** For pediatric patients less than 12 years of age, use the smallest recommended volume, considering daily fluid requirements and the maximum concentration for peripheral and central administration shown in Table 1. The FK PI teaches a ready to administer solution with 6.8 mmol/100 mL of phosphorus and 10 mEq/100/mL potassium. *See* Table 1 (phosphorous 6.80mmol/100 mL and potassium 10mEq/100 mL). <u>Storage and Stability</u> … • After dilution, the solution is stable for a maximum of 4 hours at room temperature 20°C to 25°C (68°F to 77°F) **or 14 days under refrigeration at 2°C to 8°C (36°F to 46°F)**. Section 11 of the FK PI teaches the concentrate has a maximum amount of 2000 mcg/L of aluminum. This equates to 45mcg/L, which is less than 50mcg/L recited in the claim. Applicants for the

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	’661 patent have also admitted that the 6.80 mmol/100 mL solution prepared according to the FK PI will have less than 50 mcg/L of aluminum. *See* Exhibit E, the ’518 provisional at Figure 2. In my opinion, the pH of the ready to use/administer composition will inherently be between 6.2 and 6.8 when prepared by the pharmacist according to the FK PI label. Support for this belief can be found in the ’661 patent, Tables 21-25 wherein a 6 mmol/100 mL solution prepared with the same ingredients as present in the FK PI ready to use/administer composition exhibit a pH in the range of 6.59 to 6.74. A Person of Ordinary Skill in the Art would have been familiar with polymeric plastic bags for storing parenteral solutions for injection. Flexible polyolefin bags for parental dosage forms, for example, were well known in the art.
12. The pharmaceutical product of claim 11, wherein the potassium phosphates comprise potassium dihydrogen phosphate and potassium hydrogen phosphate at a molar ratio of about 0.7 to 1.3, and/or wherein the potassium dihydrogen phosphate is present in the solution an amount of between about 112 mg/100 ml and about 1,120 mg/100 ml and wherein the potassium hydrogen phosphate is present in the solution in an amount of between about 118 mg/100 ml and about 1,180 mg/100 ml.	*See* discussion for claim 11. As explained above, the FK PI teaches a ready to administer solution with 6.8 mmol/100 mL of phosphorus and 10 mEq/100/mL potassium prepared from a concentrate with 224 mg/mL of potassium dihydrogen phosphate (a.k.a. monobasic potassium phosphate) and 236 mg/mL of potassium hydrogen phosphate (a.k.a. dibasic potassium phosphate). Using simple arithmetic 2.27 mL of the concentrate (3 mmol/mL of phosphorus and 4.4 mEq/mL of potassium) would be added to 100 mL of 0.9% saline to obtain the 6.8 mmol/100 mL solution. Simple arithmetic further confirms the 6.8 mmol/100 solution will have about 508.48 mg/100 mL of potassium dihydrogen phosphate[11] and 535.72 mg/100 mL of potassium hydrogen phosphate.[12] The values further calculate to about 3.75 mmoles of potassium dihydrogen phosphate and about 3.06 mmoles of potassium hydrogen phosphate which is a ratio of 1.2.
13. The pharmaceutical product of claim 12, wherein the sodium chloride is present in the aqueous solution in an amount of up to 900 mg/100 ml.	*See* discussion for claim 12. **Using aseptic technique, withdraw the required amount from the vial and add to**

[11] 224 mg/mL x 2.27 mL = 508.48 mg
[12] 236 mg/mL x 2.27 mL = 535.72 mg

	0.9% Sodium Chloride Injection, USP (normal saline) or 5% Dextrose Injection, USP (D5W). FK PI, p. 3. The 6.8 mmol/100 mL solution will contain 900 mg of sodium chloride.

138. Accordingly, in my opinion, the FK PI insert anticipates at least Claim 3 and anticipates or renders obvious claim 13 in view of the general knowledge of a POSITA. In my opinion, these claims are invalid.

139. I understand that Nivagen bears the burden of proving any secondary considerations relating to an obvious inquiry. Presently, I am unaware of any evidence of commercial success, unexpected results, long felt need, failure of others, evidence of copying, licenses showing industry respect for the claimed subject matter, or skepticism of skilled artisans prior to the alleged invention of the claimed compositions. However, if Nivagen presents any alleged evidence of secondary considerations, I reserve my right to respond.

C. If Claim 11 of the ’291 Patent Is Found to Be Infringed Under the Doctrine of Equivalents, It Must Be Invalid as Obvious in View of the FK PI

140. As explained in Section IX.A. above, it is my opinion that Claim 11 of the ’291 Patent is clearly not infringed literally or under the doctrine of equivalents. I note that Nivagen’s argument is that the concentrations of phosphorous and potassium—despite each concentration being 60%—are “insubstantially different” than recited in Claim 11. As explained above, I disagree with Nivagen’s position. However, if Nivagen’s position were accepted, Claim 11 would necessarily be invalid in view of the FK PI which discloses concentrations of phosphorous concentration (6.8 mmol/100 mL) and potassium concentration (10 mEq/ 100 mL) . Notably, Applicants admit that the concentrations in the FK PI are in the prior art. (*See* ’661 Patent at 1:37-67.)

141. The FK PI does not describe the use of a flexible package or flexible polyolefin package as recited in claim 11 of the ’291 patent. It is my opinion that these features are obvious matters of design choice because flexible polyolefin bags for parental dosage forms were well known in the art.

142. A comparison of the prior art and the claimed subject matter is shown below. Claim 11 would be invalid as obvious in view of the FK PI if a Court were to find that limitations (b) and (c) can be expanded to 6mmol/100 mL and 8.8mEq/100 mL as in the Amneal Product:

Claims of the ’291 Patent	The FK PI
11. A sterile ready-to-use premixed pharmaceutical product stored in a flexible polymeric container, wherein the pharmaceutical product comprises a potassium phosphates in an aqueous sodium chloride solution containing (a) less than 50 mcg/L aluminum, (b) about 15 mmol/100 ml phosphorus, and (c) about 22 mEq/100 mL potassium.	**2.1 Preparation and Administration in Intravenous Fluids to Correct Hypophosphatemia** <u>Preparation</u> • Potassium Phosphates Injection is for *intravenous infusion* into a central or peripheral vein *only after dilution*. • **Using aseptic technique, withdraw the required amount from the vial and add to 0.9% Sodium Chloride Injection, USP (normal saline)** or 5% Dextrose Injection, USP (D5W). **For adults and pediatric patients 12 years of age and older a total volume of 100 mL or 250 mL is recommended.** For pediatric patients less than 12 years of age, use the smallest recommended volume, considering daily fluid requirements and the maximum concentration for peripheral and central administration shown in Table 1. The FK PI teaches a ready to administer solution with 6.8 mmol/100 ml phosphorus and 10 mEq/100 mL potassium. *See* Table 1 (phosphorous 6.80mmol/100 mL and potassium 10mEq/100 mL). <u>Storage and Stability</u> … • After dilution, the solution is stable for a maximum of 4 hours at room temperature 20°C to 25°C (68°F to 77°F) **or 14 days under refrigeration at 2°C to 8°C (36°F to 46°F)**.

	Section 11 of the FK PI teaches the concentrate has a maximum amount of 2000 mcg/L of aluminum. This equates to 45mcg/L, which is less than 50mcg/L recited in the claim. Applicants for the '661 patent have also admitted that the 6.80 mmol/100 mL solution prepared according to the FK PI will have less than 50 mcg/L of aluminum. *See* Exhibit E, the '518 provisional at Figure 2. A Person of Ordinary Skill in the Art would have been familiar with polymeric plastic bags for storing parenteral solutions for injection. Flexible polyolefin bags for parental dosage forms, for example, were well known in the art.

143. Accordingly, as discussed in Section X.B. and in this paragraph, Claim 11 of the '291 Patent would be invalid under Nivagen's strained, and in my view unreasonable, position that 6.0 mmol/100 mL and 8.8 mEq/ 100 mL is insubstantially different than 15.0 mmol/100 ML and 22 mEq/100 mL. Again, in my opinion, these differences are substantial and there cannot possibly be infringement literally or by equivalence.

144. I understand that Nivagen bears the burden of proving any secondary considerations relating to an obvious inquiry. Presently, I am unaware of any evidence of commercial success, unexpected results, long felt need, failure of others, evidence of copying, licenses showing industry respect for the claimed subject matter, or skepticism of skilled artisans prior to the alleged invention of the claimed compositions. However, if Nivagen presents any alleged evidence of secondary considerations, I reserve my right to respond.

XI. CONCLUSION

145. Based upon my knowledge, education, skills, experience, and my assessment of the materials listed in Exhibit B, it is my opinion that Claim 11 of the '291 Patent is clearly not infringed under the doctrine of equivalents due to the significant differences in the Amneal Product compared to asserted Claim 11. If Claim 11 of the '291 Patent is, however, impermissibly expanded as argued by Nivagen, it is my opinion that it is invalid in view of the FK PI. It is also

my opinion that Claims 3 and 13 of the ’661 Patent are clearly invalid as anticipated by Pandya (which is the published ’291 Application). Claims 3 and 13 are also invalid as anticipated and/or obvious in view of the FK PI and therefore, they cannot be infringed.

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I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct to the best of my knowledge, information, and belief.

Executed on August 25th, 2024

Mansoor M. Amiji, Ph.D.

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that on August 27, 2024, a copy of the foregoing document was served on the counsel listed below in the manner indicated:

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