UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Par Health, Inc.
Petitioner,
v.

InfoRLife, S.A.
Patent Owner,

Case IPR2026-00036
Patent No. 12,370,153

PETITION FOR *POST-GRANT* REVIEW
UNDER 35 U.S.C. §§ 321-329 AND 37 C.F.R. § 42.200 *et seq.*

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LISTING OF CHALLENGED CLAIMS

Independent Claim 1	
1-pre	A ketamine product comprising
1a	an aqueous ketamine solution comprising about 0.5 to about 2.5 mg/mL ketamine, a tonicity adjusting agent, and water for injection,
1b	wherein the ketamine solution is preservative-free and anti-microbial free,
1c	wherein the ketamine product is sterile and ready-to-use (RTU),
1d	wherein the pH of the aqueous ketamine solution is about 3.5 to about 5.5, and
1e	wherein the ketamine product has a shelf-life of more than six months when stored at a controlled room temperature between 15-30ºC.

Dependent Claim 2	
2	The ketamine product of claim 1, wherein the ketamine product has been terminally sterilized.

Dependent Claim 3	
3	The ketamine product of claim 1, wherein the ketamine is at a concentration of about 1 mg/mL to about 2 mg/mL.

Dependent Claim 4	
4	The ketamine product of claim 1, wherein the aqueous ketamine solution is contained in an infusion bag comprising at least one port sealed with a closure.

Dependent Claim 5	
5	The ketamine product of claim 1, wherein the aqueous ketamine solution has an osmolality of about 270-330 mOsmol/kg.

Dependent Claim 6	
6	The ketamine product of claim 4, wherein the at least one port comprises a multilayer polyolefin and styrene block copolymer tube material.

Dependent Claim 7	
7	The ketamine product of claim 4, wherein the closure comprises a plastic material.

Dependent Claim 8	
8	The ketamine product of claim 4, wherein the closure is a twist-off closure and comprises a membrane that creates a barrier, splitting the twist-off closure in two parts, wherein a first of the two parts is an inferior part of the membrane that is in direct contact with the ketamine solution, and the second of the two parts is a superior part of the membrane that is in contact with a zone that forms an air chamber into the closure.

Dependent Claim 9	
9	The ketamine product of claim 7, wherein the closure is a twist-off closure that comprises polypropylene (PP), low density polyethylene (LDPE), polyolefin block copolymer, or any combination thereof.

Dependent Claim 10	
10	The ketamine product of claim 4, wherein the infusion bag comprises a flexible multilayer film comprising a polymer selected from the group consisting of polyethylene, polypropylene, modified polyolefin-polyethylene polymers, styrene-polyolefin based polymers, block copolymers, and a combination thereof.

Dependent Claim 11	
11	The ketamine product of claim 4, wherein the infusion bag comprises a flexible multilayer film comprising 2 to 5 layers wherein at least one layer comprises polypropylene styrene-block copolymer.

Dependent Claim 12	
12	The ketamine product of claim 4, wherein the infusion bag comprises a 3-layer film wherein at least one layer comprises polypropylene styrene-block copolymer.

Dependent Claim 13	
13	The ketamine product of claim 4, wherein the infusion bag is contained within an overwrap.

Dependent Claim 14	
14	The ketamine product of claim 13, wherein the overwrap comprises four layers comprising polyester, aluminum, polypropylene, and polyester.

Dependent Claim 15	
15	The ketamine product of claim 1, wherein the ketamine product has been autoclaved.

Independent Claim 16	
16-pre	A ketamine product comprising
16a	an aqueous ketamine solution comprising about 0.5 to about 2.5 mg/mL ketamine, a tonicity adjusting agent, and water for injection,
16b	wherein the ketamine solution is preservative-free and anti-microbial free,
16c	wherein the pH of the aqueous ketamine solution is about 3.5 to about 5.5,

Independent Claim 16	
16d	and wherein the ketamine solution is contained in a terminally sterilized, ready-to-use infusion container, and
16e	wherein the ketamine product has a shelf-life of more than six months when stored at a controlled room temperature between 15-30°C.

Dependent Claim 17	
17	The ketamine product of claim 16, wherein the tonicity adjustment agent comprises sodium chloride, dextrose, glycerin, mannitol, potassium chloride, or any combination thereof.

Dependent Claim 18	
18	The ketamine product of claim 1, wherein the ketamine or a pharmaceutically acceptable salt thereof is chemically stable following 24 months of storage at 25°C ± 2°C with relative humidity (RH) at 40% ± 5%.

Dependent Claim 19	
19	The ketamine product of claim 1, wherein the ketamine content of the aqueous ketamine solution after accelerated storage at 40°C ± 2°C / <25% RH for 6 months is greater than 97%; and/or wherein the ketamine content of the aqueous ketamine solution after long-term storage for 12 months at 25°C ± 2°C/40% RH ± 5% RH is 97% or greater compared to the ketamine content before storage.

Dependent Claim 20	
20	A method of treating a subject in need of analgesia, comprising administering the ketamine product of claim 1 to the subject as a continuous infusion.

Independent Claim 21	
21-pre	A ketamine product comprising

Independent Claim 21	
21a	an aqueous ketamine solution comprising about 0.5 to about 2.5 mg/mL ketamine, a tonicity adjusting agent, and water for injection,
21b	wherein the ketamine solution is preservative-free and anti-microbial free,
21c	wherein the pH of the aqueous ketamine solution is about 3.5 to about 5.5,
21d	wherein the ketamine solution is contained in an infusion bag,
21e	wherein the ketamine product has been aseptically filled,
21f	and wherein the ketamine product is sterile and ready-to-use (RTU),
21g	and wherein the ketamine product has a shelf-life of more than six months when stored at a controlled room temperature between 15-30°C.

Dependent Claim 22	
22	The ketamine product of claim 16, wherein the ketamine or a pharmaceutically acceptable salt thereof is chemically stable following 24 months of storage at 25°C ± 2°C with relative humidity (RH) at 40% ± 5%.

Dependent Claim 23	
23	The ketamine product of claim 21, wherein the ketamine or a pharmaceutically acceptable salt thereof is chemically stable following 24 months of storage at 25°C ± 2°C with relative humidity (RH) at 40% ± 5%.

Petitioner Par Health, Inc. ("Par" or "Petitioner") respectfully requests post-grant review ("PGR") of claims 1–23 (the "Challenged Claims") of U.S. Patent No. 12,370,153 (Ex. 1001, "'153 patent") purportedly owned by InfoRLife, S.A. ("InfoRLife" or "Patent Owner").

I. INTRODUCTION

The '153 patent is directed to ready-to-use ketamine premix formulations for direct intravenous infusion for use in a subject in need of anesthesia for a diagnostic or a surgical procedure. In particular, the premixed ketamine solution of the '153 patent is shelf-stable and does not have antimicrobials (such as benzethonium chloride). Ketamine was sold in concentrated vial form at least in the United States, which when administered intravenously required adding the ketamine solution to a diluted IV solution, such as sterile water for injection, sodium chloride solution, saline, or dextrose. The concentrated products available also included preservatives, such as benzethonium chloride. The '153 patent suggests that there was need for a sterile ready to use infusion container of ketamine which could be administered directly to the patient without manipulation to preserve the sterility of the product, that also did not contain a preservative. The patent purports to satisfy this need by filling a suitable infusion bag (i.e. one which will not interact with the drug product)

with a premixed solution, that may be administered directly to the patient and is stable, without a preservative or antimicrobial, for 24 months at room temperature.

Ground 1: Anticipation

This Petition challenges the patentability of the ’153 patent because a New Zealand datasheet for a Ketamine (Biomed) product (“Biomed”) discloses each limitation of Challenged Claims 1, 3–5, 13 and 18–20. Biomed discloses a “ready-to-use” ketamine solution, which does not include a preservative, which is packaged in an infusion bag, and which is stable at room temperature for 24 months.

Ground 2: Obviousness

This Petition further challenges the patentability of the ’153 patent because Biomed, in view of REMINGTON: THE SCIENCE AND PRACTICE OF PHARMACY (Adeboye Adejare ed., 23rd edition 2021) (“Remington 2021”), commercially available infusion bags in the prior art, and the knowledge of the person of ordinary skill in the art, renders obvious each limitation of Challenged Claims 1, 2, 4, 6–17 and 21–23. In combination with the disclosures of Biomed, Remington 2021 further teaches that there are two pathways for manufacturing sterile drug products: aseptic filling and terminal sterilization, as well as the methods for each. The POSA would understand that the sterile Biomed product would undergo one of these two methods to confirm sterility, and that a suitable infusion bag to maintain sterility, avoid

interactions with the drug product, and allow for infusion directly to the patient, would be considered given that the product was intended to be administered intravenously to the patient in need thereof.

Because this Petition establishes, by a preponderance of the evidence, that the Challenged Claims are anticipated and/or obvious in view of the prior art, there is a reasonable likelihood "that at least one of the claims challenged in the petition is unpatentable." 37 C.F.R.§ 42.208(c). This Petition should therefore be instituted.

II. MANDATORY NOTICES PURSUANT TO 37 C.F.R. § 42.8(A)(1)

A. Real Party-in-Interest under 37 C.F.R. § 42.8(b)(1) and 35 U.S.C. § 322(a)(2)

Pursuant to 37 C.F.R. § 42.8(b)(1), Petitioner certifies that the real parties-in-interest are:

Par Health, Inc.

Petitioner Par Health, Inc. has the sole authority to direct all activities relating to the Petitioner and this Petition or any further proceedings related to this Petition.

B. Related Matters under 37 C.F.R. § 42(b)(2)

Pursuant to 37 C.F.R. § 42.8(b)(2), Petitioner is unaware of any related matters.

C. Lead and Backup Counsel under 37 C.F.R. § 42.8(b)(3)-(4)

Petitioner hereby identifies its lead and backup counsel as follows:

Lead Counsel	Backup Counsel
Richard J. Berman, Reg. No. 39,107 richard.berman@afslaw.com ARENTFOX SCHIFF LLP 1717 K Street, NW Washington, DC 20006-5344 Tel.: 202.857.6000	Janine A. Carlan, Reg. No. 42,387 janine.carlan@afslaw.com ARENTFOX SCHIFF LLP 1717 K Street, NW Washington, DC 20006-5344 Tel.: 202.857.6000 Julie A. Vernon (*phv* forthcoming) julie.vernon@afslaw.com ARENTFOX SCHIFF LLP 233 S Wacker Dr, #7100 Chicago, IL 60606 Tel: 312.258.5500

D. Service Information under 37 C.F.R. § 42.8(b)(4)

This Petition is being served by Federal Express Next Business Day Delivery to the correspondence address of record for the '153 Patent:

Rothwell, Figg, Ernst & Manbeck, P.C.
901 New York Avenue, N.W.
Suite 900 East
Washington, DC 20001

Please direct all correspondence to lead and back-up counsel at the contact information above. Petitioner also consents to service by email at: Par_Health-153PGR@afslaw.com.

E. Power of Attorney under 37 C.F.R. § 42.10(b)

A Power of Attorney is being filed concurrently herewith with designation of the counsel above.

III. REQUIREMENTS FOR PGR UNDER 37 C.F.R. § 42.204

A. Grounds for Standing under 37 C.F.R. § 42.204(a)

Petitioner certifies that the '153 patent is available for PGR and that Petitioner is not barred or estopped from requesting PGR on the Challenged Claims on the identified grounds. This Petition is timely because it was filed within 9 months of the date on which the '153 patent was granted, July 29, 2025.

B. Identification of Challenge and Precise Relief Requested, 37 C.F.R. § 42.204(b)

Petitioner requests cancellation of the Challenged Claims. The Petition is supported by the Declaration of Dr. Michael Maurin (Ex. 1003), a technical expert with decades of experience in developing and manufacturing pharmaceutical formulations. *Id.* at ¶¶ 5–7; Ex. 1004 ("Maurin CV").

Ground	Claims	Basis	Publication
1	1, 3–5, 13 and 18–20	§ 102	Biomed
2	1, 2, 4, 6–17, and 21–23	§ 103	Biomed and a POSA's knowledge in view of Remington 2021 and Commercially-Available Infusion Bags

C. Prior Art Publication

Petitioner relies upon the following publications:

Ketamine (Biomed) ("Biomed") (Ex. 1005) is a data sheet for a ketamine product manufactured by Biomed Limited and approved in New Zealand, which is dated June 15, 2021. *Id.* at 11. Biomed is prior art to the '153 patent under 35 U.S.C. § 102(a)(1).

REMINGTON: THE SCIENCE AND PRACTICE OF PHARMACY (Adeboye Adejare ed., 23rd edition 2021) ("Remington 2021") (Ex. 1006) was published in 2021. Remington 2021 is prior art to the '153 patent under 35 U.S.C. § 102(a)(1).

The patent-admitted commercially available infusion bags ("Commercially-Available Infusion Bags") include M312 and M315 films of SealedAir Nexcel products, and Technoflex Inerta® bags. SealedAir Nexcel Product Data Sheet (M312 Film) ("M312 Film Data Sheet") (Ex. 1007) published in October 2021. *Id.* M312 Film Data Sheet is prior art to the '159 patent under 35 U.S.C. § 102(a)(1). SealedAir Nexcel Product Data Sheet (M315 Film) ("M315 Film Data Sheet") (Ex. 1008) published in October 2021. *Id.* M315 Film Data Sheet is prior art to the '159 patent under 35 U.S.C. § 102(a)(1). Sylvie Ponlot, *Sensitive Molecules Get Their Own Bags*, 7 FLEXMAG 1 (2014) ("Technoflex Inerta") (Ex. 1009) published in April 2014. *Id.* at Cover. Technoflex Inerta is prior art to the '153 patent under 35 U.S.C. § 102(a)(1).

IV. OVERVIEW OF THE '153 PATENT

The '153 patent, titled "Ready-to-Use Ketamine Premix Formulation" was filed with the USPTO on July 11, 2024, and issued as a patent on July 29, 2025. Ex. 1001. It claims priority to U.S. Provisional Application No. 63/153,225 filed on July 12, 2023. *Id.*

A. Specification

The '153 patent describes the alleged invention as a sterile, ready-to-use, stable aqueous solution of ketamine or a pharmaceutically acceptable salt thereof suitable for direct intravenous infusion to a patient in need of anesthesia for a diagnostic or surgical procedure. Ex. 1001 at Abstract, 1:15-20, 18:60-64; Ex. 1003, ¶ 87.

The background of the '153 patent describes previously existing commercially available ketamine formulations approved by the FDA. In the United States, the most common ketamine products for injection were concentrated vials which required dilution prior to administration to the patient. *Id.* at 1:58-67. These contained benzethonium chloride as a preservative. *Id.* at 1:34-36. A few limitations of these vials included that they needed to be used immediately after dilution, and that the vials were single-use and required disposal after opening even if the entire contents of the vial were not required. *Id.* at 1:63-2:2; Ex. 1003, ¶ 88. Other

limitations and shortcomings of the prior single-use concentrated ketamine solution vials included additional costs and inconvenience, the risk of potential contamination due to inadvertent medical error, and limited stability prohibiting long-term storage. Ex. 1001 at 2:24-29. The patent alleges a ready to use dosage of a stable, preservative-free ketamine solution would overcome the issues in the existing products. *Id.* at 2:40-44; Ex. 1003, ¶ 89.

The background of the ’153 patent discusses that the container closure for a product for parenteral use should take into consideration drug product formulation properties, dosage, type of application, stability, including stability when subjected to extreme conditions (such as terminal sterilization), sterility, container closure integrity, storage conditions and duration, and end-user friendliness, Ex. 1001 at 1:48-54, to ensure compliance with storage and handling specifications for maintaining functionality and drug delivery accuracy. *Id.* at 1:44-48; Ex. 1003, ¶ 90.

The ’153 patent is directed to a premixed formulation of ketamine, or a pharmaceutically acceptable salt thereof, also containing a tonicity adjusting agent, a pH adjusting agent, and water for injection, in an intravenous bag or infusion container, which does not require dilution prior to administration to the patient. Ex. 1001 at 2:49-63, 7:28-34. The solution is free from any antimicrobial or preservative,

such as benzethonium chloride. *Id.* at 7:28-34, 19:9-14. In certain aspects, the pH of the aqueous ketamine solution is about 3 to about 6. *Id.* at 3:11-16; Ex. 1003, ¶ 91.

The ’153 patent acknowledges that the packaging of the product can affect the condition of formulations. Ex. 1001 at 2:31-40 (mentioning for the primary plastic packaging for the infusion container: compatibility with the contents, minimizing extractables and leachables, solvent-resistance and durability). The patent states that “[t]he packaging of a pharmaceutical product should desirably be stable and mutually compatible under terminal sterilization conditions, as packaging materials and terminal sterilization can affect the condition of different formulations.” *Id*. at 2:36-40. The ’153 patent describes the types of intravenous bags for use in the invention, including those commercially available as Polyelite EHC® film bags manufactured by Hosokawa, Inerta 103 manufactured by Technoflex, Nexcel brand M312 and M312A® films by SealedAir Corporation, and M312 films from other manufacturers. *Id.* at 8:17-41; Ex. 1003, ¶ 92.

The specification states that the polyolefin film of the infusion bag may be a M312 film, such as Nexcel brand M312A film manufactured by SealedAir Corporation, an M315 film manufactured by SealedAir Corporation, an APP-series film manufactured by Polycine, such as APP-114S film, a polypropylene film, like those manufactured by Technoflex, such as an Inerta® film, e.g. Inerta 103, or a

cycloolefin polymer with a middle layer made up of linear low density polyethylene polymer and an outer layer made up of low density polyethylene polymer, such as those manufactured by Hosokawa. Ex. 1001 at 9:42-10:19; Ex. 1003, ¶ 93. The foregoing commercially available films for use in the invention are stable, with low leachables, and without physical deformation during terminal sterilization. *See, e.g.*, Ex. 1001 at 8:37-40,10:39-65; Ex. 1003, ¶ 94.

The '153 patent discusses the processes of sterilization disclosed in U.S. Patent Nos. 5,439,643 and 8,617,467 as "a sterilizing agent or process is used to kill microbes and other pathogens to create a sterile final product" by methods such as steam sterilization, heat sterilization (e.g., autoclave), radiation treatment (e.g., Gamma, E-beam, ultraviolet), or by chemical sterilization (e.g., ethylene oxide). Ex. 1001 at 10:41-49; Ex. 1003, ¶ 95. The patent also contains five examples, regarding exemplary formulations, stability studies, manufacturing process development, and stress studies. Ex. 1003, ¶¶ 96-98.

B. Prosecution History

The examiner repeatedly denied the claims as anticipated by Ketalar or rendered obvious by Ketalar in view of "Conrad," a reference regarding sterile bags of the drug fentanyl. The examiner described the identical disclosure in Ketalar of the claimed formulation (ketamine, sodium chloride, and water for injection), and

on that basis found that the claimed stability limitations (chemical stability, number of particles of certain sizes, ketamine content after accelerated storage, and shelf life) and osmolality would be inherent to the formulation itself, and therefore disclosed in Ketalar though not set forth explicitly. Final Rejection, dated Dec. 19, 2024, at 3-4, Ex. 1002 at 260-261. The examiner explained that Ketalar was described as a "sterile" and "USP Grade" product, such that it would have followed aseptic filling and/or terminal sterilization processes as also set forth in certain claim limitations. Ex. 1002 at 261 ("sterility of a product is a known function of autoclaving to one of skill in the art, and FDA approved injections/infusions for *in vivo* administration in humans are for sterile/aseptic products."); Ex. 1003, ¶ 100.

The examiner noted that with respect to the numerous limitations directed to the bag containing the ketamine formulation, "what is disclosed as subject matter in these claims, even per Applicant's own specification is in fact commercially available infusion bags." Non-Final Rejection, dated Oct. 23, 2024, at 5-7, Ex. 1002 at 218-220; Final Rejection, dated Dec. 19, 2024, at 6-8, Ex. 1002 at 263-265; Ex. 1003, ¶ 101.

The applicant disputed the examiner's rejection(s) on the basis that Ketalar was not "ready-to-use," but required dilution prior to administration. Reply to Non-Final Rejection, dated Nov. 25, 2024, at 7-8, Ex. 1002 at 240-241; Amendment With

a Request for Continued Examination, Mar. 14, 2025, at 10-11, Ex. 1002 at 290-291. Once diluted, Ketalar required short-term disposal, allegedly not meeting the stability proposed by the claims of at least six months at 15-30°C. The applicant argued this showed lack of reasonable expectation of success for a stable pre-diluted ready-to-use formulation of ketamine. The applicant also distinguished Ketalar on the basis that it contained a preservative, unlike the claimed formulation. Amendment With a Request for Continued Examination, Mar. 14, 2025, at 15-16, Ex. 1002 at 295-296; Ex. 1003, ¶ 102.

The applicant also argued that the limitations were supported by the secondary consideration of unexpected results by comparison to the concentrated ketamine vial products which were available, and alleged that the prior art taught away from storing pre-diluted ketamine solution for prolonged periods. Reply to Non-Final Rejection, dated Nov. 25, 2024, at 10, Ex. 1002 at 243-244; Ex. 1003, ¶ 103.

Following an interview between the examiner and the applicant on March 19, 2025, an agreement was reached indicating the claims were in condition for allowance if applicant agreed to amendments to the claims including removing certain stability limitations, and adding the "no anti-microbial" and pH range limitations to the independent claims. Applicant indicated its agreement in a call on March 20, and a Notice of Allowance was issued. Ex. 1002 at 357; Ex. 1003, ¶ 104.

V. CLAIM CONSTRUCTION

Claims are given their "ordinary and customary meaning," as understood by a skilled artisan and the prosecution history pertaining to the patent. 37 C.F.R. § 42.200(b). The Board need only construe claim terms to the extent necessary to resolve a controversy. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Ltd.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017). The ordinary and customary meaning may be displaced if a patentee chose to be their own lexicographer. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996); *Hill-Rom Servs. v. Stryker Corp.*, 755 F.3d 1367, 1371 (Fed. Cir. 2014). When "the specification [] reveal[s] a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess, the inventor's lexicography governs." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005) (*en banc*). "If a patentee chooses to become his or her lexicographer, he or she 'must be bound by the express definition.'" *Sinorgchem Co. v. ITC*, 511 F.3d 1132, 1136 (Fed. Cir. 2007). The specification "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Phillips*, 415 at 1313 (citation omitted). A court should consider the patent's prosecution history as well, as "the prosecution history provides evidence

of how the PTO and the inventor understood the patent." *Id.* at 1317 (citation omitted).

A. "ready-to-use (RTU)" (claims 1, 16, 21)

The claims contain the terms "ready-to-use (RTU)" (*see* claims 1, 16, and 21) to describe the ketamine product (claims 1 and 21) and the infusion container (claim 16). The patentee has acted as its "own lexicographer" by explicitly defining this term in the specification: "premixed compositions that are suitable for administration to a patient without further manipulation (e.g., a pharmaceutical formulation that is in the container from which the product is administered to the patient (such as an infusion bag or prefilled syringe) and does not require dilution or admixing before administration)." Ex. 1001 at 15:66-16:5.

The definition set forth in the specification is consistent with the use of the term "ready-to-use" as it is applied throughout the specification. *See, e.g.*, *id.* at 2:52-57 ("The ready-to-use premixed pharmaceutical compositions of ketamine of the present invention are formulated for administration to a patient, without the need to reconstitute or dilute the composition prior to administration, e.g., in a ready-to-use infusion bag (also referred to as a "ready-to-use bag"); 15:61-64 ("For example, in contrast to non-premixed formulations of ketamine, the premixed compositions

provided herein are suitable for administration to a patient without dilution"); Ex. 1003, ¶ 107.

Multiple times throughout the prosecution history, the applicant defined its alleged invention consistent with the definition above, in distinguishing the claims from the prior art concentrated vials of ketamine (Ex. 1003, ¶ 109):

- "The specification defines the term 'ready-to-use' or 'ready to use' as referring to 'premixed compositions that are suitable for administration to a patient without further manipulation (e.g., a pharmaceutical formulation that is in the container from which the product is administered to the patient (such as an infusion bag or prefilled syringe) and does not require dilution or admixing before administration.' (Paragraph [0075])." Reply to Non-Final Office Action, dated Nov. 25, 2024, at 7 (Ex. 1002 at 240); *see also* Amendment With a Request For Continued Examination, dated Mar. 14, 2025, at 11 (Ex. 1002 at 330).

- "A 'ready-to-use drug product' is a term of art meaning 'a drug product . . . from which the entire drug content of the container(s) is administered to the patient,' which 'may simplify the preparation and administration of a drug compared to preparing and administering an exact weight- or BSA-based dose to the patient.'" Citing FDA Guidance for Industry. Distinguishing over Ketalar because it is not sterile, ready-to-use, because it is a "concentrated product that must be manipulated to transfer it to an infusion container and diluted to an appropriate concentration—those steps compromise sterility and mean that the product Ketalar product is not 'ready-to-use.'" Reply to Non-Final Office Action, dated Nov. 25, 2024, at 7-8 (Ex. 1002 at 240-241).

- Refuting the examiner's broader interpretation of "ready-to-use" by indicating that the specification expressly defined the term (as set forth above) and citing to MPEP 2111.01(IV)(A) for the proposition that "'[w]here an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim'" to argue "[t]hus, the Office Action's various different interpretations are unnecessary and irrelevant where the only definition that controls is the one that is expressly provided in

the specification." Amendment With a Request For Continued Examination, dated Mar. 14, 2025, at 10 (Ex. 1002 at 290).

- Distinguishing the alleged invention by concluding "the Office's reliance on a dilution step means that the proposed modification to [Ketalar] results in something that does not meet the definition of ready-to-use required by the claims." Amendment With a Request For Continued Examination, dated Mar. 14, 2025, at 14 (Ex. 1002 at 333).

On this basis, "ready-to-use (RTU)" should be construed as "premixed compositions that are suitable for administration to a patient without further manipulation (e.g., a pharmaceutical formulation that is in the container from which the product is administered to the patient (such as an infusion bag or prefilled syringe) and does not require dilution or admixing before administration)." While the patentee acted as its own lexicographer and its definition should govern, that definition is consistent with the plain and ordinary meaning of the term "ready-to-use" to a POSA. Ex. 1003, ¶ 106. Preparing a solution for administration may include multiple steps, such as transferring the solution to a different container (vial to syringe, for example), or diluting a concentrated solution (syringe contents to infusion bag). *Id.* A solution which is "ready" for "use" means it can be administered to the patient, and requires no further steps prior to that administration. *Id.* For a drug product typically requiring a dilution step, such as a concentrated drug product, that would necessarily require the solution to be premixed to the correct concentration. *Id.*

B. "chemically stable" (claims 18, 22, 23)

The claims contain the term "chemically stable" (*see* claims 18, 22, 23) to describe the ketamine product (claims 1, 16, and 21). The patentee has acted as its "own lexicographer" for this term as well by also explicitly defining this term in the specification: "a chemical compound which retains its chemical structure and useful properties on a timescale of its expected usefulness. Specifically, the usefulness of the compound is maintained in the environment in which it is stored." Ex. 1001 at 15:43-47. In the context of pharmaceutical formulations, the POSA would understand this definition to generally equate to "having an acceptable shelf life" of the product. Ex. 1003, ¶ 110.

VI. LEVEL OF ORDINARY SKILL IN THE ART

A person of ordinary skill in the art ("POSA") at the relevant time (*e.g.*, the July 12, 2023, filing date of the '225 provisional application), would have been an individual or team of individuals working together to make pharmaceutical products, such as who possess a doctoral degree in pharmaceutics, chemistry, such as pharmacology or pharmacy, or chemical engineering who has several years of practical experience with formulation of injectable drug delivery products, or someone possessing a Bachelors or Master's degree in one or more of the preceding

disciplines but with a correspondingly greater level of experience with formulating injectable drug delivery products. Ex. 1003, ¶ 34.

VII. BACKGROUND AND ASSERTED PRIOR ART

A. Ketamine Was Available in Vial and Infusion Forms

(RS)-2-(2-chlorophenyl)-2-(methylamino)cyclohexanone hydrochloride ("ketamine hydrochloride," a salt of ketamine) is an anesthetic agent which has been used since at least 1970. Ex. 1001 at 1:37-43; Ex. 1010 at 314; Ex. 1003, ¶ 36. Ketamine can be administered to a patient intravenously, intramuscularly, orally, rectally, or subcutaneously, because it is both water and lipid soluble. Ex. 1003, ¶ 38; Ex. 1011 at 49. A comparison of oral to intravenous administration demonstrated that peak effect was delayed in the oral route (15-30 minutes compared to 1-5 minutes), and that oral route compared to intravenous administration had lower peak serum concentrations ($1/5^{th}$) and lower bioavailability (16% compared to 90%). Ex. 1003, ¶ 38; Ex. 1011 at 49. Intravenous administration of ketamine includes continuous intravenous infusion ("CIVI"). CIVI can take place over a period of hours or days. Ex. 1003, ¶ 39; Ex. 1012 at 642.

Ketamine was available in mixtures of the isomers (racemic, meaning equal amounts of the (R) and (S) isomers) in concentrations of 10, 50, and 100 mg/mL in formulations which included a preservative, benzethonium hydrochloride. Ex. 1003,

¶ 40; Ex. 1013 at 61. Parenteral formulations of ketamine hydrochloride have been available in injectable and infusion forms in the United States for many years, under the brand name Ketalar® Injection. Ex. 1003, ¶ 43; Ex. 1001 at 1:57-67 (confirmed in the '153 patent). Ketalar is a ketamine hydrochloride injection available as of 2012 which is a sterile solution in a vial for intravenous or intramuscular (i.m.) injection in concentrations containing the equivalent of either 10, 50, or 100 mg ketamine per milliliter and not more than 0.1 mg/mL Phemerol® (benzethonium chloride) as a preservative. Ex. 1014 at 1. The 100 mg/mL concentration of Ketalar has to be diluted with water, sodium chloride, saline, or dextrose in water solution prior to administration to patients. *Id.* at 4-5; Ex. 1003, ¶ 42.

B. Intravenous Drugs Administered by Infusion

When drugs are administered intravenously using an infusion bag, the prescribed medication is diluted with a sterile solution and typically hooked near the patient from a pole. The bag itself is connected through a tube to a catheter and then into a patient's vein to administer its contents, for example, medication, nutrition, or electrolytes. Ketamine administration can occur through infusion methods as well as through direct intravenous injection. Ex. 1014 at 4-5; Ex. 1003, ¶ 46. The body of an infusion bag can be made of multiple layers of medical grade plastics, and have various numbers and types of ports. Plastic films are used to make IV-bags. For

example, the Technoflex Inerta® contains two ports, one of which has a twist off closure. Other types of bags and films may contain ports which have a rubber closure, or are sealed (such as that pictured on the left port of the Technoflex Inerta). They also have ports which allow for infusion of the drug, and often, sealing of the bag to prevent contamination. Ex. 1003, ¶¶ 47-48.

Formulators are aware that a drug intended for intravenous administration must be isotonic with body fluids, meaning that, in the case of ketamine administered by intravenous infusion, the solution has the same, or nearly the same, osmotic pressure as blood serum, and would also be aware of the methods for adjusting tonicity, including common excipients to adjust tonicity such as sodium chloride, dextrose, and glycerin. *Id.*, ¶¶ 50-52; Ex. 1015 at 208; Ex. 1006 at 581.

Parenteral drug products, which include intravenous and infusion formulations, must be sterile. Ex. 1003, ¶ 53; Ex. 1006 at 579. There are two routes for manufacturing a sterile product: aseptic processing and terminal sterilization. Ex. 1003, ¶ 54; Ex. 1016 at 2-3; Ex. 1006 at 597. The European Commission standards follow the same requirement for sterility and methods for achieving it for parenteral products. Ex. 1003, ¶¶ 58-59; Ex. 1017; Ex. 1018 at 4.

When using terminal sterilization, of which there are different methods, consideration must be given to the container and the drug product itself to ensure

that the active pharmaceutical ingredient does not degrade at those conditions, and that the container can withstand the intensity of the cycle without itself degrading and contaminating the product. Ex. 1003, ¶ 55.

For formulations which cannot be terminally sterilized, they are required to follow aseptic processing techniques to obtain and maintain sterility. *Id.*, ¶ 56. Aseptic processing is the preparation and filling of drugs under very specific cleanliness conditions to ensure the sterility of the drug is maintained throughout its manufacture and filling. *Id.* A primary step for a drug too unstable for terminal sterilization is to undergo sterile filtration to remove particulate matter and/or microbial contamination from the formulation. *Id.* Unlike terminal sterilization, which kills existing contaminants, filtration physically removes them as the microorganisms are adsorbed, retained on, or near, the matrix of the filter. *Id.* In order to avoid reintroduction of microorganisms (i.e. to maintain the sterility of the formulation), all subsequent steps must be performed by aseptic processing. *Id.* This includes donning a litany of personal protective equipment (PPE), using sterile equipment, and rigorous environmental controls, among other requirements, all intended to reduce the possibility of contamination during manufacturing. Ex. 1003, ¶ 56.

C. Asserted Grounds References

1. Ketamine (Biomed) ("Biomed", Ex. 1005)

Biomed, dated June 15, 2021, is the data sheet for a New Zealand product that was first approved on May 5, 2011. Ex. 1005 at 11. Biomed discloses a "clear, colourless isotonic solution for injection or infusion" which "contains no preservative" and contains sodium chloride, water for injection, and ketamine hydrochloride, at a pH of 3.5 to 5.5 *Id.* at 1, 10. Biomed discloses that "[e]ach 100 mL of Ketamine 100 mg per 100 mL contains ketamine hydrochloride equivalent to 100 mg ketamine base." *Id.* at 1. Biomed discloses that it requires storage at or below 25° C, and that it is for single use only. *Id.* at 10-11. Biomed is available in a flexible 100 mL IV bag with overwrap, and in IV infusion bags has a shelf life of 24 months from the date of manufacture. *Id.* at 10. Thus, Biomed discloses a ketamine product with 100 mg per 100 mL of ketamine in an infusion bag. *Id.* at 1, 10.

Biomed is indicated "as the sole anaesthetic agent for diagnostic and surgical procedures that do not require skeletal muscle relaxation. . . [F]or the induction of anaesthesia prior to the administration of other general anaesthetic agents . . . [or T]o supplement low-potency agents such as nitrous oxide." *Id.* at 1. Biomed discloses that it could be administered by intravenous infusion or intravenous injection, and

that increments of the full induction dose "may be repeated, as needed, for maintenance of anaesthesia." *Id.* at 2.

2. REMINGTON: THE SCIENCE AND PRACTICE OF PHARMACY (Adeboye Adejare ed., 23rd edition 2021) ("Remington 2021", Ex. 1006)

Remington 2021 discloses that the general considerations for development of parenteral products includes sterilization, listing terminal sterilization and aseptic processing or filtration. Ex. 1006 at 579 (Table 29.3). Remington 2021 further discloses that "[d]epending on the product, either terminal sterilization in its final container or aseptic filling may be adopted" when a parenteral product is manufactured, referring to Figure 29.4. *Id.* at 587.

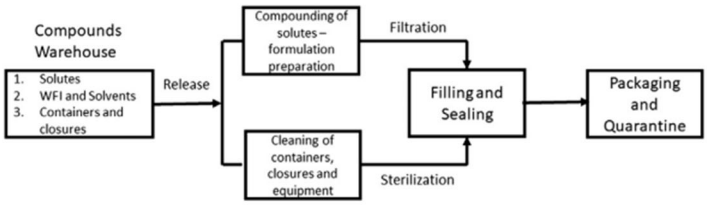

FIGURE 29.4 General flow of operations in parenteral manufacturing.

Id. at 588 (Figure 29.4).

Remington 2021 teaches that a parenteral product sterilized by filtration must follow "stringent requirements" to prevent contamination during the subsequent filling step, a process termed "aseptic fill." *Id.* at 595.

Remington 2021 further provides that:

> Whenever possible, the parenteral product should be sterilized within as short a time as possible after being sealed in its final container (terminal sterilization). Since this usually involves a thermal process, due consideration must be given to the effect of the elevated temperature on the stability of the product. Many products, both pharmaceutical and biological, are affected adversely by temperatures required for thermal sterilization. Therefore heat-labile products should be sterilized by a nonthermal method, usually by filtration through bacteria-retaining filters. Subsequently, all operations must be carried out in an aseptic manner, so that contamination is not introduced into the filtrate.

Id. at 597.

3. **Patent-Admitted Commercially Available Infusion Bags ("Commercially-Available Infusion Bags")**

i. SealedAir Nexcel Product Data Sheet (M312 Film) ("M312 Film Data Sheet", Ex. 1007)

M312 Film Data Sheet discloses a clear, 5-layer, polyolefin-based extrusion for a film for medical and pharmaceutical applications. Ex. 1007 at 1-2. M312 Film Data Sheet discloses that it was "specifically developed to be a superior performing primary packaging film for terminally sterilized medical and pharmaceutical solutions." *Id.* at 2. M312 Film Data Sheet further discloses that it was "designed to be chemically inert and have extremely low levels of extractables with a wide range of solutions – even under the demanding conditions of 121° C autoclave sterilization," and that it was "designed for demanding packaging applications, such as saline, dextrose," including "parenteral drugs." *Id.* at 2. It discloses numerous benefits of the film, which include low extractables, and being sterilizable. *See id.*

ii. SealedAir Nexcel Product Data Sheet (M315 Film) ("M315 Film Data Sheet", Ex. 1008)

M315 Film Data Sheet discloses a clear, 4-layer, polyolefin-based extrusion for a film for medical and pharmaceutical applications. Ex. 1008 at 1-2. M315 Film Data Sheet discloses that it was "specifically developed to be a superior performing primary packaging film for terminally sterilized medical and pharmaceutical solutions." *Id.* at 2. M315 Film Data Sheet further discloses that it was "designed to be chemically inert and have extremely low levels of extractables with a wide range of solutions – even under the demanding conditions of 121° C autoclave sterilization," and that it was "designed for demanding packaging applications, such as saline, dextrose" including "parenteral drugs." *Id.* at 2. It discloses numerous benefits of the film, which include being multilayered for superior abuse resistance, tubular extrusion which minimizes particulates, having extremely low extractables, and being sterilizable. *See id.*

iii. Sylvie Ponlot, *Sensitive Molecules Get Their Own Bags*, 7 FLEXMag 1 (2014) ("Technoflex Inerta", Ex. 1009)

Technoflex Inerta discloses the line of Inerta® IV drug delivery bags manufactured by Technoflex. Inerta bags are polypropylene sterile bags which are aseptically filled. Ex. 1009 at 6. They can be fitted with either one or two tubes, with "boat ports" welded directly onto the bag body (annotated pictured below). *Id.*

A twist-off is welded to the tubular part of the first boat port, and the second is welded shut. *Id.* Inerta bags are sterilized then placed in double packaging. *Id.*

VIII. GROUND 1: ANTICIPATION OF CLAIMS 1, 3–5, 13 AND 18-20 BY BIOMED

A claim is invalid as anticipated if a single, prior art reference describes every element of the claimed invention, either expressly or inherently, based on the knowledge of a POSA, such that a POSA could practice the invention without undue experimentation. *See Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999); *Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003). "Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates." *Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999); *see also Schering*, 339 F.3d at 1377, 1379; *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1376

(Fed. Cir. 2005) (quoting *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1349 (Fed. Cir. 2002)). For a prior art pharmaceutical product, properties or results which "naturally flow" from any intended use of the product are inherently disclosed. *Perricone*, 432 F.3d at 1378 (claims found inherently anticipated which described certain benefits with topical skin formulation, because "the particular benefits" associated with topical skin application "naturally flow form those methods even if not recognized as benefits"); *King Pharm., Inc. v. Eon Labs, Inc.*, 616 F.3d 1267, 1274-77 (Fed. Cir. 2010) (prior art formulation with increased drug bioavailability inherently anticipated later claims to formulation). Information which is not explicitly contained in a prior art reference may still be considered in the anticipation analysis if known to a POSA and/or expressly incorporated by reference into the reference. *See, e.g.*, *Ultradent Prods., Inc. v. Life-Like Cosmetics, Inc.*, 127 F.3d 1065, 1069 (Fed. Cir. 1997). The disclosure of a single value within a claimed range will anticipate the entire claimed range. *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 782 (Fed. Cir. 1985) ("When, as by a recitation of ranges or otherwise, a claim covers several compositions, the claim is 'anticipated' if *one* of them is in the prior art.").

A. Independent Claims

1. Independent Claim 1

i. Preamble: "A ketamine product comprising"

Biomed describes a ketamine product available in New Zealand. Ex. 1003, ¶ 11; Ex. 1005 at 1.

ii. "an aqueous ketamine solution comprising about 0.5 to about 2.5 mg/mL ketamine, a tonicity adjusting agent, and water for injection,"

Biomed describes a ketamine product available in New Zealand before the effective filing date which contains 100 mg/100 mL (i.e. 1 mg/mL) ketamine. Ex. 1005 at 1. The concentration is within the claimed range, and thus anticipates the claimed range. Ex. 1003, ¶ 111.

Biomed contains sodium chloride and water for injection, and is an isotonic solution for infusion. Ex. 1005 at 1, 10; Ex. 1003, ¶ 112. The '153 patent discloses that sodium chloride is a tonicity adjusting agent (see, e.g., Ex. 1001 at 3:8-10), consistent with the disclosure of Remington 1995 ("[t]he first two of these methods [of adjusting tonicity] can be used with a three step problem solving process based on sodium chloride."). Ex. 1015 at 620-21. Thus, Biomed anticipates the claimed limitations. Ex. 1003, ¶ 112.

iii. "wherein the ketamine solution is preservative-free and anti-microbial free,"

Biomed does not contain a preservative or an anti-microbial. Ex. 1005 at 1. The only excipients Biomed contains are sodium chloride and water for injection, and the label explicitly states that "[the formulation] contains no preservative." *Id.*; Ex. 1003, ¶ 113. The only excipients listed in Biomed are sodium chloride and water for injection. The POSA would understand that these are not preservatives or anti-microbials. *Id*. Indeed, the '153 patent discloses that sodium chloride is a tonicity adjusting agent (see, e.g., Ex. 1001 at 3:8-10), consistent with the disclosure of Remington 1995 ("[t]he first two of these methods [of adjusting tonicity] can be used with a three step problem solving process based on sodium chloride."). Ex. 1015 at 620-21. Therefore, a POSA would understand that Biomed does not contain a preservative or an anti-microbial. Ex. 1003, ¶ 113.

iv. "wherein the ketamine product is sterile and ready-to-use (RTU),"

Biomed is available in a flexible 100 mL IV bag with overwrap. Ex. 1005 at 10. Biomed is administered by intravenous infusion. *Id.* at 2. The POSA would recognize that as an approved product in New Zealand for intravenous administration, Biomed would have needed to be sterile. Ex. 1003, ¶ 114. Remington 2021 provides that sterilization is a consideration for the development of parenteral

products, generally, and Chapter 2.6.1 of the relevant regulatory guidance for New Zealand products, the European Pharmacopoeia, confirms that parenteral preparations "should be tested for sterility" to assess compliance with the European Pharmacopoeia. *See*, *e.g.*, Ex. 1006 at 579; Ex. 1018 at 158. There are no instructions for dilution prior to administration, thus a POSA would understand that Biomed is ready-to-use (RTU). Ex. 1005 at 2; Ex. 1003, ¶ 114.

v. "wherein the pH of the aqueous ketamine solution is about 3.5 to about 5.5,"

Biomed is formulated as an acid (pH 3.5 to 5.5) solution. Ex. 1005 at 1. The range of pH for Biomed overlaps with, and thus anticipates, the claimed range of a pH of the aqueous ketamine solution of about 3.5 to about 5.5. Ex. 1003, ¶ 115.

vi. "and wherein the ketamine product has a shelf-life of more than six months when stored at a controlled room temperature between 15-30°C."

Biomed instructs that it should be stored at or below 25°C and not refrigerated or frozen, which a POSA would understand as overlapping with, and thus anticipating, the claimed range of 15-30°C. Ex. 1005 at 10; Ex. 1003, ¶ 116. Biomed discloses that it has a shelf life of 24 months for the 100 mg per 100 mL (*i.e.* 1 mg/mL) IV Infusion bags, which encompasses the claimed range of "a shelf-life of more than six months," thus anticipating the claimed range. Ex. 1005 at 10; Ex. 1003, ¶ 116.

vii. Conclusion

Based on the foregoing, claim 1 of the ’153 patent is anticipated by Biomed. Ex. 1003, ¶ 117.

B. Dependent Claims

1. Claim 3

> 3. The ketamine product of claim 1, wherein the ketamine is at a concentration of about 1 mg/mL to about 2 mg/mL.

The concentration of the Biomed 100 mg/100 mL ketamine product (1 mg/mL) is within, and thus anticipates, the claimed range. Ex. 1005 at 1. Therefore, claim 3 of the ’153 patent is anticipated. Ex. 1003, ¶ 119.

2. Claim 4

> 4. The ketamine product of claim 1, wherein the aqueous ketamine solution is contained in an infusion bag comprising at least one port sealed with a closure.

Biomed is available in a flexible 100 mL IV infusion bag with overwrap. Ex. 1005 at 10; Ex. 1003, ¶ 121. Biomed is administered as an intravenous infusion, and there are no instructions that would indicate to a POSA that the product is not administered directly to the patient. Ex. 1005 at 2. Thus, Biomed is intended to be directly administered to the patient. A POSA would immediately understand that any IV infusion bag containing an infusion solution administered directly to a patient would have to have at least one port sealed with a closure to facilitate the

administration. Ex. 1003, ¶ 121. Therefore, claim 4 of the '153 patent is anticipated. *Id*.

3. **Claim 5**

> 5. The ketamine product of claim 1, wherein the aqueous ketamine solution has an osmolality of about 270-330 mOsmol/kg.

Biomed discloses that the infusion solution is isotonic, and therefore discloses this limitation. Ex. 1005 at 1. Isotonicity refers to the osmotic pressure of a solution: if in solution, human erythrocyte cells "maintain their 'tone,'" i.e., are not hypertonic or hypotonic, the solution is said to be "isotonic." Ex. 1015 at 207; Ex. 1003, ¶ 123. Thus, the POSA would immediately understand that the Biomed product would need to have equal osmotic pressure to serum to reduce the risk of hemolysis. Ex. 1003, ¶ 123.

Remington 1995 discloses that normal serum osmolality is 285 mOsmol/kg and acknowledges that the literature recognizes a range around 275-305 mOsmol/L as serum osmolality (i.e., isotonic) (recording 280-295 mOsmol/L, 275 to 300 mOsmol/L, 290 mOsmol/L, 306 mOsmol/L, and 275-295 mOsmol/kg). Ex. 1015 at 615. Therefore, a POSA would know that Biomed's disclosure of an isotonic infusion solution is within, and thus anticipates, the claimed range of an osmolality of about 270-330 mOsmol/kg. Ex. 1003, ¶ 124. Therefore, claim 5 of the '153 patent is anticipated. *Id.*

4. **Claim 13**

> 13. The ketamine product of claim 4, wherein the infusion bag is contained within an overwrap.

Biomed is available as a 100 mg per 100 mL IV infusion in a flexible 100 mL IV bag with overwrap. Ex. 1005 at 10. Therefore, claim 13 of the '153 patent is anticipated. Ex. 1003, ¶ 126.

5. **Claim 18**

> 18. The ketamine product of claim 1, wherein the ketamine or a pharmaceutically acceptable salt thereof is chemically stable following 24 months of storage at 25°C ± 2°C with relative humidity (RH) at 40% ± 5%.

As set forth above in Section V.B, the POSA would understand that "chemically stable" for the purposes of the '153 patent generally equates to having an acceptable shelf life of the product, *i.e.* where there is resistance to degradation in its environment "on a timescale of its expected usefulness." Ex. 1003, ¶ 128. Biomed teaches to "[s]tore at or below 25 °C" and discloses that the 100 mg per 100 mL IV infusion bag product has a 24-month shelf life. Ex. 1005 at 10. Regarding the relative humidity limitation, a POSA would know that "[w]here no specific directions or limitations are provided in the article's labeling, articles must be protected from moisture" in "[a] place that does not exceed 40% average relative humidity at 20° (68° F) or the equivalent water vapor pressure at other

temperatures." *See* Ex. 1019 at 1-2, 6; Ex. 1003, ¶ 128. Therefore, claim 18 of the '153 patent is anticipated because this limitation is present in Biomed. Ex. 1003, ¶ 128.

6. **Claim 19**

> 19. The ketamine product of claim 1, wherein the content of the aqueous ketamine solution after accelerated storage at 40°C ± 2°C / <25% RH for 6 months is greater than 97%; and/or wherein the ketamine content of the aqueous ketamine solution after long-term storage for 12 months at 25°C ± 2° C/40% RH ± 5% RH is 97% or greater compared to the ketamine content before storage.

Biomed inherently discloses a ketamine product wherein the content of the aqueous ketamine solution after accelerated storage at 40°C ± 2°C / <25% RH for 6 months is greater than 97%; and/or wherein the ketamine content of the aqueous ketamine solution after long-term storage for 12 months at 25°C ± 2° C/40% RH ± 5% RH is 97% or greater compared to the ketamine content before storage. The ketamine content after this length of time of storage at these conditions is an inherent characteristic that will naturally result from storing the formulation at these conditions. Ex. 1003, ¶ 130. The patent itself confirms this conclusion. Table 6 of the '153 patent found that at the claimed conditions for accelerated storage, the same formulation as the 100 mg per 100 mL Biomed formulation (ketamine hydrochloride, sodium chloride (isotonic) and water for injection, pH between 3.5-5.5 (*compare* Ex. 1001, Tables 1 and 5 *with* Ex. 1005 at 1, 10) had assay amounts of

100.5%, 101.7% and 100.6%. Ex. 1001, Table 6. Therefore, claim 19 of the '153 patent is anticipated because this limitation is inherently present in Biomed. Ex. 1003, ¶ 130.

7. Claim 20

> 20. A method of treating a subject in need of analgesia, comprising administering the ketamine product of claim 1 to the subject as a continuous infusion.

Biomed is indicated for the "induction of anesthesia" or as the "sole anaesthetic agent." Ex. 1005 at 1; *see also id.* at 7 ("Ketamine is a rapid-acting, general anaesthetic producing an anaesthetic state characterized by profound analgesia."). Biomed is administered as a continuous infusion. *Id.* at 2 ("It is recommended that ketamine infusion be administered slowly (over a period of 60 seconds)."). Therefore claim 20 of the '153 patent is anticipated because this limitation is present in Biomed. Ex. 1003, ¶ 132.

IX. GROUND 2: OBVIOUSNESS OF CLAIMS 1, 2, 4, 6–17, AND 21–23 OVER BIOMED AND A POSA'S KNOWLEDGE, IN VIEW OF REMINGTON 2021 AND COMMERCIALLY-AVAILABLE INFUSION BAGS

Claims 1, 2, 4, 6–17, and 21–23 would have been obvious in view of the prior art: Biomed, Remington 2021, and Commercially-Available Infusion Bags (exemplified in M312 Film Data Sheet; M315 Film Data Sheet and Technoflex Inerta), and the knowledge of the POSA. Ex. 1003, ¶ 133.

The ketamine (Biomed) product, described above at Section VIII, which description is incorporated herein by reference, is available in an infusion bag which contains 100 mg/100 mL (1 mg/mL) ketamine with a shelf life of 24 months from the date of manufacture. It contains only ketamine, sodium chloride, and water for injection, at a pH of 3.5 to 5.5, and it is an isotonic solution for infusion. It is indicated for anesthesia, and administered directly to the patient without prior manipulation required. The POSA would recognize that Biomed was sterile, because, as described, *e.g.*, in Remington 2021, industry practice required injectable products to be sterile. *Id.* In addition to being industry practice, national guidelines would require Biomed to be sterile. Biomed is a product approved for sale in New Zealand, meaning that it would follow the European Pharmacopoeia for applicable guidance and monographs. Ex. 1003, ¶ 135. Ph. Eur. 2.6.1 specifies that parenteral products would need to be tested for sterility to confirm that the product complies with the European Pharmacopoeia. Ex. 1018 at 158.

The POSA would have been motivated to combine the teachings of a pre-mixed, not requiring dilution for administration, *i.e.* "ready-to-use," formulation of ketamine, such as ketamine (Biomed), with bags in the prior art that could withstand terminal sterilization, for the product to be injected directly to the patient. Ex. 1003, ¶ 133. Biomed is indicated as the sole anaesthetic agent, and/or for the induction of

anaesthesia prior to the administration of other general anaesthetic agents, which is administered directly to the patient without prior manipulation required. Ex. 1005 at 2, 10. The POSA would recognize that for treating a patient it would be advantageous to have a direct-to-patient formulation, such as Biomed (*see* Ex. 1005 at 10, 6.5 Nature and contents of container, "Ketamine 100 mg per 100 mL IV Infusion is available in flexible 100 mL IV bag with overwrap"), that would avoid the potential for contamination and dosing and administration errors. Ex. 1003, ¶ 137.

As intravenous products must be sterile, the POSA would be motivated to combine the ketamine (Biomed) product with commercially available bags that could be terminally sterilized. To the extent the bags could not be terminally sterilized, the POSA would have been motivated to undertake aseptic procedures to ensure the sterility of the final product such that it could be administered directly to the patent. *Id.*

Remington 2021, a well-known treatise to pharmaceutical formulators, would disclose to the POSA that a sterile product could be manufactured through two mechanisms, filtration and sterilization. Ex. 1006 at 587-88 (Table 29.4); Ex. 1003, ¶ 136. The POSA would know, as confirmed by Remington 2021, that products adversely affected by the heat of thermal sterilization should be filtered through

bacteria-retaining filters, followed by aseptic operations to prevent reintroduction of contaminants. Ex. 1006 at 587-88; Ex. 1003, ¶ 136. Consequently, Remington 2021 teaches, and the POSA would understand, that should the product require filtration, "aseptic filling" must follow. Ex. 1006 at 595; Ex. 1003, ¶ 136. In New Zealand, the governing 2019 Sterilization Guideline which would have been relevant to ketamine (Biomed) is consistent with the disclosure of Remington 2021. Ex. 1020 at 4 (the relationship of aseptic processing and sterile filtration is "closely related and difficult to consider separately, since sterile filtration in most cases is followed by at least one aseptic processing step such as filling."). Accordingly, the two methods for sterilization that the POSA would immediately envision are terminal sterilization and aseptic filling. Ex. 1003, ¶ 133.

The POSA would be motivated to combine Biomed with the patent-admitted commercially available infusion bags, which were disclosed as suitable for the invention, and which marketing materials confirm were aseptically filled and/or resistant to terminal sterilization. Ex. 1003, ¶¶ 137, 142. While Biomed does not specify the 100 mL IV bag with overwrap used, the POSA would be aware that ketamine was used as an analgesic for infusion treatments and would consider having a suitable infusion bag that would be sufficient to serve that same purpose of

administering directly to the patient, meaning it enables the manufacture and subsequent administration of a sterile drug product. *Id.*

A POSA would understand that a suitable infusion bag[1] would require that the ketamine formulation is not contaminated or negatively impacted by the composition of components of the bag. Ex. 1003, ¶ 138. The POSA also would understand that the infusion bag would need to be terminally sterilized or aseptically filled to ensure a sterile drug product for the patient, and that commercially available infusion bags were available for this purpose. *Id.*; Ex. 1018 at 158; Ex. 1020 at 4-5, 19; Ex. 1006 at 587-88, 595, 597; *see generally* Ex. 1009; Ex. 1008 at 1-2; Ex. 1007 at 1-2.

The specification admits that there were many commercially available infusion bags and films available in the prior art, including numerous options from Hosokawa, SealedAir Corporation (Nexcel brand), etc. Indeed, a POSA reading the specification would understand that the inventors did not invent a novel infusion bag, but rather merely listed suitable commercially available bags. Ex. 1003, ¶ 139; Ex. 1003 at 8:17-41, 9:42-10:19. As the patent admits, the commercially available bags in the prior art had the properties of the claims, including the material and layers. The ports and material of the ports would have been readily ascertainable to

[1] Reference to infusion or intravenous "bags" include the "films" that are used to comprise them.

the POSA from viewing and assessing these commercially available bags. Ex. 1003, ¶ 140.

Commercial literature describes the numerous films and bag products listed in the patent. Ex. 1003, ¶ 141. For example, SealedAir Nexcel's M312 and M315 films are described in datasheets, describing the multi-layered, polyolefin-based extrusion film, and its use for medical and pharmaceutical application. *See* Ex. 1007 at 1-2; Ex. 1008 at 1-2. Technoflex Inerta describes Inerta® bags as single or multi-tubular, aseptically filled polypropylene bags, with a twist off on one port, which are placed in double packaging. Ex. 1009 at 6. Technoflex Inerta includes an image of the Inerta® IV drug delivery bag which clearly depicts two ports, one with a twist-off, and one welded shut. *Id.* at 6. The twist-off closure forms two chambers, one in contact with the formulation, and one forming an air chamber.

The patent-admitted commercially available infusion bags satisfy the limitations of claims 6–12 and 14 as the applicant confirmed they were suitable for use in the invention. *See* Ex. 1001 patent at 8:17-41, 9:42-10:19; Ex. 1003, ¶ 142. All of the commercially available products listed would be expected to have at least one port, and as disclosed in the patent and confirmed in the M312 Film Data Sheet, M315 Film Data Sheet, and Technoflex Inerta, the film or bag is multilayer (including up to 5 layers) and polyolefin-based, including the closure. *See* Ex. 1007

at 2 (describing a 5-layer polyolefin-based extrusion film); Ex. 1008 at 2 (describing a 4-layer, polyolefin-based extrusion film); Ex. 1009 at 6 (stating that Inerta bags are polypropylene sterile bags).

For the foregoing reasons and those set forth below, a POSA would regard the combination of the claimed bags and films with the Biomed pre-mixed formulation as obvious to have a sterile ketamine solution administrable directly to patients. Ex. 1003, ¶ 144. The POSA would have had a reasonable expectation of success in developing a ready-to-use ketamine product without a preservative, with the claimed shelf life and meeting the claimed stability parameters, as Biomed infusion bags have a shelf life of 24 months, the chemical composition would be stable under long term storage at 25°C ± 2°C / 40% ± 5% RH for twelve months, including as to the ketamine content, and the POSA would expect commercially available bags to withstand sterilization and that the shelf life would not decrease once the bags were either aseptically filled or terminally sterilized. *Id.*, ¶ 133.

A. Independent Claim 1

> 1. A ketamine product comprising an aqueous ketamine solution comprising about 0.5 to about 2.5 mg/mL ketamine, a tonicity adjusting agent, and water for injection, wherein the ketamine solution is preservative-free and anti-microbial free, wherein the ketamine product is sterile and ready-to-use (RTU), wherein the pH of the aqueous ketamine solution is about 3.5 to about 5.5, and wherein the ketamine product has a shelf-life of more than six months when stored at a controlled room temperature between 15-30°C.

Independent claim 1 is further invalid as obvious for the same reasons as set forth above that this claim would be anticipated as fully disclosed by Biomed, and the analysis regarding the anticipation of claim 1 at Section VIII.A is incorporated herein by reference. Based on an analysis of the scope and content of the prior art and a comparison of the prior art to the patent claim in light of the level of ordinary skill in the art, a POSA would find any differences between the prior art and the claim insubstantial and any necessary modification of the prior art to achieve the limitations of claim 1 would be well within the ordinary skill, and a POSA would have more than a reasonable expectation of success in achieving the limitations of claim 1. Ex. 1003, ¶ 145.

B. Dependent Claim 2

> 2. The ketamine product of claim 1, wherein the ketamine product has been terminally sterilized.

The POSA would recognize that as an approved product for intravenous administration, Biomed would have needed to be sterile. Ex. 1003, ¶ 147. A POSA also would recognize that sterilization could be accomplished either by terminal sterilization or through the use of aseptic filling methods, as disclosed in Remington 2021 and confirmed by relevant guidelines. Ex. 1018 at 158; Ex. 1020 at 4-5, 19; Ex. 1006 at 587-88, 595, 597. Therefore, claim 2 of the ’153 patent is invalid as obvious. Ex. 1003, ¶ 147.

C. Dependent Claim 4

> 4. The ketamine product of claim 1, wherein the aqueous ketamine solution is contained in an infusion bag comprising at least one port sealed with a closure.

Dependent claim 4 is further invalid as obvious for the same reasons as set forth above that this claim would be anticipated as fully disclosed by Biomed, and the anticipation analysis undertaken at Section VIII.B.2 is incorporated herein by reference. Based on an analysis of the scope and content of the prior art and a comparison of the prior art to the patent claim in light of the level of ordinary skill in the art, a POSA would find any differences between the prior art and the claim insubstantial and any necessary modification of the prior art to achieve the limitations of claim 4 would be well within the ordinary skill, and a POSA would have more than a reasonable expectation of success in achieving the limitation of claim 4. Ex. 1003, ¶ 148.

D. Dependent Claim 13

> 13. The ketamine product of claim 4, wherein the infusion bag is contained within an overwrap.

Dependent claim 13 is further invalid as obvious for the same reasons as set forth above that this claim would be anticipated as fully disclosed by Biomed, and the anticipation analysis undertaken at Section VIII.B.2 is incorporated herein by reference. Based on an analysis of the scope and content of the prior art and a

comparison of the prior art to the patent claim in light of the level of ordinary skill in the art, a POSA would find any differences between the prior art and the claim insubstantial and any necessary modification of the prior art to achieve the limitations of claim 13 would be well within the ordinary skill, and a POSA would have more than a reasonable expectation of success in achieving the limitation of claim 13. Ex. 1003, ¶ 149.

E. Dependent Claims 6–12, and 14

> 6. The ketamine product of claim 4, wherein the at least one port comprises a multilayer polyolefin and styrene block copolymer tube material.
>
> 7. The ketamine product of claim 4, wherein the closure comprises a plastic material.
>
> 8. The ketamine product of claim 4, wherein the closure is a twist-off closure and comprises a membrane that creates a barrier, splitting the twist-off closure in two parts, wherein a first of the two parts is an inferior part of the membrane that is in direct contact with the ketamine solution, and the second of the two parts is a superior part of the membrane that is in contact with a zone that forms an air chamber into the closure.
>
> 9. The ketamine product of claim 7, wherein the closure is a twist-off closure that comprises polypropylene (PP), low density polyethylene (LDPE), polyolefin block copolymer, or any combination thereof.
>
> 10. The ketamine product of claim 4, wherein the infusion bag comprises a flexible multilayer film comprising a polymer selected from the group consisting of polyethylene, polypropylene, modified polyolefin-polyethylene polymers, styrene-polyolefin based polymers, block copolymers, and a combination thereof.

> 11. The ketamine product of claim 4, wherein the infusion bag comprises a flexible multilayer film comprising 2 to 5 layers, wherein at least one layer comprises polypropylene styrene-block copolymer.
>
> 12. The ketamine product of claim 4, wherein the infusion bag comprises a 3-layer film wherein at least one layer comprises polypropylene styrene-block copolymer.
>
> 14. The ketamine product of claim 13, wherein the overwrap comprises four layers comprising polyester, aluminum, polypropylene, and polyester.

Claims 6–12 and 14 would have been obvious over Biomed in view of the admitted prior art, *i.e.*, the commercially available bags, films, and overwraps described above. Ex. 1003, ¶ 151. The POSA would understand from reading the specification that the inventors did not invent a novel infusion bag and that multiple commercially available bags had the materials and configurations that are set forth in the claims. *Id.* The POSA would have been motivated to use commercially available infusion bags for the purpose of administering a sterile infusion product to a patient. *Id.* Therefore, claims 6–12 and 14 of the '153 patent are invalid as obvious. *Id.*

The commercial literature, including M312 Film, M315 Film, and Technoflex Inerta confirm the availability of the bags disclosed in the patent prior to the effective filing date, and the relevant properties: constructed of polypropylene, and encompassing multi-film designs. Ex. 1007; Ex. 1008; Ex. 1009; Ex. 1003, ¶ 152.

F. Dependent Claim 15

15. The ketamine product of claim 1, wherein the ketamine product has been autoclaved.

Dependent claim 15 would have been obvious over Biomed and Remington 2021. Ex. 1003, ¶ 154. Remington 2021 describes acceptable methods of manufacturing for injectable products, including by aseptic filtration and terminal sterilization. The POSA would understand that terminal sterilization takes many forms, which include the use of heat or steam sterilization in order to sterilize a drug product. Ex. 1018 at 158; Ex. 1020 at 4-5, 19; Ex. 1006 at 587-88, 595, 597; Ex. 1003, ¶ 154. The POSA would further know that this would take place in an autoclave, and would be motivated to use this technique in order to ensure a sterile drug product with a suitable shelf life, and with the knowledge that the infusion bags available could be subjected to terminal sterilization without affecting the drug product. Ex. 1003, ¶ 154. Therefore claim 15 of the '153 patent is invalid as obvious. *Id.*

G. Independent Claim 16

1. Preamble: "A ketamine product comprising"

This limitation is disclosed in Biomed for the same reasons as set forth for these limitations of claim 1, above at Section VIII.A.1, which is incorporated herein by reference. *Id.*, ¶ 155.

2. **"an aqueous ketamine solution comprising about 0.5 to about 2.5 mg/mL ketamine, a tonicity adjusting agent, and water for injection,"**

This limitation is disclosed in Biomed for the same reasons as set forth for these limitations of claim 1, above at Section VIII.A.1, which is incorporated herein by reference. *Id.*, ¶ 155.

3. **"wherein the ketamine solution is preservative-free and anti-microbial free,"**

This limitation is disclosed in Biomed for the same reasons as set forth for these limitations of claim 1, above at Section VIII.A.1, which is incorporated herein by reference. *Id.*, ¶ 156.

4. **"wherein the pH of the aqueous ketamine solution is about 3.5 to about 5.5,"**

This limitation is disclosed in Biomed for the same reasons as set forth for these limitations of claim 1, above at Section VIII.A.1, which is incorporated herein by reference. *Id.*, ¶ 157.

5. **"and wherein the ketamine solution is contained in a terminally sterilized, ready-to-use infusion container,"**

The "terminally sterilized" limitation is obvious for the same reasons as set forth for the corresponding limitation of claim 2. As stated above, the POSA would recognize that as an approved product for intravenous administration, Biomed would have needed to be sterile, and this could be accomplished either by terminal

sterilization or through the use of aseptic filling methods. Ex. 1003, ¶ 158; Ex. 1018 at 158; Ex. 1020 at 4-5, 19; Ex. 1006 at 587-88, 595, 597. The "ready-to-use" limitation is disclosed in Biomed for the same reasons set forth for this limitation of claim 1, above at Section VIII.A.1, and incorporated herein by reference. Ex. 1003, ¶ 158.

6. **"and wherein the ketamine product has a shelf-life of more than six months when stored at a controlled room temperature between 15-30°C."**

This limitation is disclosed in Biomed for the same reasons as set forth for these limitations of claim 1, above at Section VIII.A.1, which is incorporated herein by reference. Ex. 1003, ¶ 159.

7. **Conclusion**

Therefore, claim 16 of the '153 patent is obvious.

H. Dependent Claim 17

17. The ketamine product of claim 16, wherein the tonicity adjustment agent comprises sodium chloride, dextrose, glycerin, mannitol, potassium chloride, or any combination thereof.

Biomed contains sodium chloride and is an isotonic solution for infusion. Ex. 1005 at 1, 10. The '153 patent discloses that sodium chloride is a tonicity adjusting agent. The '153 patent discloses that sodium chloride is a tonicity adjusting agent (see, e.g., Ex. 1001 at 3:8-10), consistent with the disclosure of Remington 1995 ("[t]he first two of these methods [of adjusting tonicity] can be used with a three step

problem solving process based on sodium chloride."). Ex. 1015 at 620-21. Therefore claim 17 of the '153 patent is obvious. Ex. 1003, ¶ 162.

I. Independent Claim 21

1. Preamble: "A ketamine product comprising"

This limitation is disclosed in Biomed for the same reasons as set forth for these limitations of claim 1, above at Section VIII.A.1, which is incorporated herein by reference. *Id.*, ¶ 163.

2. "an aqueous ketamine solution comprising about 0.5 to about 2.5 mg/mL ketamine, a tonicity adjusting agent, and water for injection,"

This limitation is disclosed in Biomed for the same reasons as set forth for these limitations of claim 1, above at Section VIII.A.1, which is incorporated herein by reference. *Id.*, ¶ 163.

3. "wherein the ketamine solution is preservative-free and anti-microbial free,"

This limitation is disclosed in Biomed for the same reasons as set forth for these limitations of claim 1, above at Section VIII.A.1, which is incorporated herein by reference. *Id.*, ¶ 164.

4. **"wherein the pH of the aqueous ketamine solution is about 3.5 to about 5.5,"**

This limitation is disclosed in Biomed for the same reasons as set forth for these limitations of claim 1, above at Section VIII.A.1, which is incorporated herein by reference. *Id.*, ¶ 165.

5. **"wherein the ketamine solution is contained in an infusion bag,"**

This limitation is disclosed in Biomed for the same reasons as set forth for these limitations of claim 1, above at Section VIII.A.1, which is incorporated herein by reference. *Id.*, ¶ 166.

6. **"wherein the ketamine product has been aseptically filled,"**

This limitation would have been obvious over Biomed and Remington 2021. As stated above, the POSA would recognize that as an approved product for intravenous administration, Biomed would have needed to be sterile. *Id.*, ¶ 167. A POSA also would recognize that sterilization could be accomplished either by terminal sterilization or through the use of aseptic filling methods. *Id.*; Ex. 1019 at 158; Ex. 1020 at 4-5, 19; Ex. 1006 at 587-88, 595, 597. Therefore the POSA would have regarded these standard procedures as an obvious choice for manufacturing a sterile product. Ex. 1003, ¶ 167.

7. **"and wherein the ketamine product is sterile and ready-to-use (RTU),"**

This limitation is disclosed in Biomed for the same reasons as set forth for these limitations of claim 1, above at Section VIII.A.1, which is incorporated herein by reference. *Id.*, ¶ 168.

8. **"and wherein the ketamine product has a shelf-life of more than six months when stored at a controlled room temperature between 15-30°C."**

This limitations is disclosed in Biomed for the same reasons as set forth for these limitations of claim 1, above at Section VIII.A.1, which is incorporated herein by reference. *Id.*, ¶ 169.

9. **Conclusion**

Therefore, claim 21 of the '153 patent is obvious.

J. Dependent Claim 22

22. The ketamine product of claim 16, wherein the ketamine or a pharmaceutically acceptable salt thereof is chemically stable following 24 months of storage at 25°C ± 2°C with relative humidity (RH) at 40% ± 5%.

This limitation is disclosed in Biomed for the same reasons as set forth for this limitation of claim 18, in Section VIII.B.5, which is incorporated herein by reference. Ex. 1003, ¶ 172.

K. Dependent Claim 23

23. The ketamine product of claim 21, wherein the ketamine or a pharmaceutically acceptable salt thereof is chemically stable

following 24 months of storage at 25°C ± 2°C with relative humidity (RH) at 40% ± 5%.

This limitation is disclosed in Biomed for the same reasons as set forth for this limitation of claim 18, in Section VIII.B.5, which is incorporated herein by reference. Therefore the POSA would have known and expected that the ketamine product would be chemically stable following 24 months of storage at 25°C ± 2°C with relative humidity (RH) at 40% ± 5%. Ex. 1003, ¶ 174.

X. SECONDARY CONSIDERATIONS

Applicant asserted during prosecution of the ’153 patent that the secondary considerations of teaching away and unexpected results supported the nonobviousness of the alleged invention. Ex. 1002 at 243-244. This is incorrect for the following reasons. Petitioner reserves the right to respond more fully to any secondary considerations raised by Patent Owner in response to this Petition.

There is no evidence of teaching away in the prior art. Ex. 1003, ¶ 177. The applicant’s basis for this claim was that “the prior art specifically teaches away from storing a diluted ketamine solution in room temperature for prolonged periods (e.g., at least six months as required by all pending claims or twenty-four months as recited in dependent claims 23, 31, and 32)” because the concentrated ketamine, once diluted, required immediate use and disposal. Reply to Non-Final Office Action, dated Nov. 25, 2024, at 11, Ex. 1002 at 244. But this argument does not take into

account the Biomed product available in New Zealand, which teaches a ketamine solution within the scope of the claims that is stored at room temperature for 24 months. Ex. 1005 at 10. Particularly for this reason, applicant's argument fails. Ex. 1003, ¶ 176.

Applicant further argued that the extended stability in a ketamine formulation without a preservative was unexpected over the concentrated products available in the prior art. Ex. 1002 at 243-244. This also does not take into account the Biomed product available in New Zealand, which teaches a ketamine solution within the scope of the claims that has extended stability. To show unexpected results, the applicant must make the comparison between the claimed invention and the closest prior art, an analysis not undertaken by the applicant because the closest prior art would be the other ready-to-use ketamine product available, not concentrated products. *UCB, Inc. v. Actavis Lab'ys UT, Inc.*, 65 F.4th 679, 693 (Fed. Cir. 2023) (*quoting Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 977 (Fed. Cir. 2014)); Ex. 1003, ¶ 177. This is at least because (1) concentrated products required manipulation, unlike Biomed in a ready-to-use similar presentation to the claims, and (2) following manipulation, use in a short time period before requiring disposal, unlike Biomed, which was aligned with the longer room temperature stability of the claims. *Id.*

Even if the proper analysis had been undertaken, unexpected results were not shown. Ex. 1003, ¶ 178. "[U]nexpected results that are probative of nonobviousness are those that are 'different in kind and not merely in degree from the results of the prior art.'" *Sun Pharms. Indus., Inc. v. Incyte Corp.*, No. 2019-2011, 2023 WL 5370639, at *5 (Fed. Cir. 2023). To be probative, the alleged unexpected result must confer a superior benefit over the closest prior art. *In re Geisler*, 116 F.3d 1465, 1469 (Fed. Cir. 1997); *Bristol-Myers*, 752 F.3d at 977.

The applicant alleged that the unexpected results were "extended stability" achieved "without a preservative." The "extended stability" could refer to the claimed "shelf-life of more than six months when stored at a controlled room temperature between 15-30°C" (claims 1, 16, 21), "the ketamine or a pharmaceutically acceptable salt thereof is chemically stable following 24 months of storage at 25°C ± 2°C with relative humidity (RH) at 40%±5%" (claims 18, 22-23), and/or "the ketamine content of the aqueous ketamine solution after accelerated storage at 40°C ±2°C/<25% RH for 6 months is greater than 97%; and/or wherein the ketamine content of the aqueous ketamine solution after long-term storage for 12 months at 25°C ±2°C/40% RH ±5% RH is 97% or greater compared to the ketamine content before storage" (claim 19). This is not a superior benefit over Biomed, and at most, should Patent Owner contest the disclosure of Biomed that it

had a shelf-life of 24 months, would be a mere difference in degree, not in kind. *Id.* The ketamine 100 mg per 100 mL IV infusion bag presentation of Biomed had a shelf life of 24 months (Ex. 1005 at 10) without any preservative in the formulation (*id.* at 2). Ex. 1003, ¶ 178. Therefore, there are no unexpected results which would justify nonobviousness of the claims of the '153 patent. *Id.*

XI. DISCRETION UNDER § 325(D) AND § 314

Consistent with the guidance provided by "Interim Director Discretionary Process," Petitioner does not present affirmative arguments in anticipation of what Patent Owner may argue by way of briefing seeking discretionary denial. Petitioner will present arguments in an Opposition Brief, should Patent Owner elect to file a Discretionary Denial Brief.

XII. PAYMENT OF FEES UNDER 37 C.F.R. §§ 42.15(B) AND 42.203

The requisite filing fee is submitted herewith. Challenged Claims 1–23 are requested for review as part of this Petition. If any additional fees are due during this proceeding, the Office is authorized to charge such fees to Deposit Account No. D506990. Any overpayment or refund of fees may also be deposited in this Deposit Account.

XIII. CONCLUSION

For the foregoing reasons, Petitioner has established a reasonable likelihood that claims 1–23 are unpatentable. Petitioner therefore respectfully requests that post grant review of the '153 Patent be granted.

Respectfully submitted,

Dated: March 25, 2026

By: */s/ Richard J. Berman*

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CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. §42.24(a) and (d), the undersigned hereby certify that the foregoing Petition for *Post Grant* Review of U.S. Patent No. 12,230,153 complies with the type-volume limitation of 37 C.F.R. §42.24(a)(1)(ii) and (b)(1)(i) permitting a petition of up to 18,700 words because, exclusive of the exempted portions, it contains 11,832 words as counted by the word processing program used to prepare the paper.

Date: March 25, 2026 Respectfully submitted,

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CERTIFICATE OF SERVICE

Pursuant to 37 CFR §§42.6(e)(4)(i) *et seq.* and 42.105(b), the undersigned certifies that on March 25, 2026, a complete and entire copy of this Petition for *Post Grant* Review of U.S. Patent No. 12,370,153, all supporting exhibits and Power of Attorney, were provided to the Patent Owner at the correspondence address of record as follows:

By Federal Express Next Business Day Delivery to:
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/s/ Nicole S. Lynch
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