

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AZURITY PHARMACEUTICALS, INC.
AZURITY PHARMA INDIA LLP
SLAYBACK PHARMA LLC,
Petitioners

v.

HERON THERAPEUTICS, INC.,
Patent Owner.

Case PGR2025-00036
Patent No. 12,115,255

PATENT OWNER'S PRELIMINARY RESPONSE

Table of Contents

I.	INTRODUCTION	1
II.	BACKGROUND	3
	A. CINV and NK-1 Receptor Antagonists.....	3
	B. Heron Overcame Merck’s Failure.....	4
	C. The USPTO Granted Heron Several Patents, Including the ’255 Patent, Expressly Rejecting the Same Prior Art Arguments that Slayback Proffers in this PGR.....	6
	D. Judge Bryson Also Found Heron’s Inventions Patentable over CN845 and Other Prior Art	7
III.	LEVEL OF ORDINARY SKILL	9
IV.	SLAYBACK FAILS TO DEMONSTRATE A MOTIVATION TO INCREASE EMULSIFIER CONCENTRATION IN CN845 WITH A REASONABLE EXPECTATION OF SUCCESS.....	9
	A. Slayback’s Obviousness Analysis Ignores Judge Bryson’s Dispositive Findings.....	12
	B. Slayback Provides No Persuasive Evidence Showing That A POSA Would Have Increased CN845’s Emulsifier Concentration...	17
V.	SLAYBACK FAILS TO DEMONSTRATE LACK OF WRITTEN DESCRIPTION SUPPORT.....	22
VI.	SLAYBACK FAILS TO DEMONSTRATE LACK OF ENABLEMENT.	30
VII.	CONCLUSION.....	32

LIST OF EXHIBITS

Exhibit No.	Description	Previously Submitted
2001	<i>Heron Therapeutics, Inc. v. Slayback Pharma LLC</i> (DNJ-2-24-cv-00423), D.I. 63 (“Defendants’ Reply Brief in Support of Motion to Transfer Venue to District of Delaware Pursuant to 28 U.S.C. § 1404(a) (Redacted)”)	X
2002	<i>Heron Therapeutics, Inc. v. Azurity Pharmaceuticals, Inc.</i> (DDE-1-24-cv-01363), D.I. 81 (“Stipulation and Order to Amend Schedule”)	X
2003	Prosecution History for U.S. Application Serial No. 18/418,030 which issued as the ’255 patent (“’255 Patent Prosecution History”)	X
2004	<i>Heron Therapeutics, Inc. v. Slayback Pharma LLC</i> (DNJ-2-24-cv-00423), D.I. 1 (“Complaint for Patent Infringement”)	X
2005	<i>Heron Therapeutics, Inc. v. Slayback Pharma LLC</i> (DNJ-2-24-cv-00423), D.I. 59 (“Opinion Granting Motion to Transfer Venue to District of Delaware”)	X
2006	<i>Heron Therapeutics, Inc. v. Azurity Pharmaceuticals, Inc.</i> (DDE-1-24-cv-01363), D.I. 1 (“Complaint for Patent Infringement”)	X
2007	<i>Heron Therapeutics, Inc. v. Azurity Pharmaceuticals, Inc.</i> (DDE-1-24-cv-01363), D.I. 30 (“Scheduling Order”)	X
2008	<i>Heron Therapeutics, Inc. v. Azurity Pharmaceuticals, Inc.</i> (DDE-1-24-cv-01363), 12/30/2025 Hearing Transcript (Redacted)	X
2009	<i>Heron Therapeutics, Inc. v. Azurity Pharmaceuticals, Inc.</i> (DDE-1-24-cv-01363), 01/13/2025 Defendants’ Invalidity Contentions	X
2010	U.S. Patent 11,744,800 (“the ’800 patent”)	X
2011	U.S. Patent 12,290,520 (“the ’520 patent”)	X

2012	<i>Heron Therapeutics, Inc. v. Slayback Pharma LLC</i> (DDE-1-24-cv-00830), D.I. 80 (“Scheduling Order”)	X
2013	<i>Heron Therapeutics, Inc. v. Azurity Pharmaceuticals, Inc.</i> (DDE-1-24-cv-01363), D.I. 46 (“Joint Stipulation and Order Regarding Claim Construction”)	X
2014	04/28/2025 Email from J. Goldstein Regarding Reduction of Asserted Claims	X
2015	RESERVED	
2016	<i>Heron Therapeutics, Inc. v. Fresenius Kabi USA, LLC</i> (DDE-1-22-cv-00985), D.I. 182 (“Fresenius’s Opening Post-Trial Brief (Redacted)”)	X
2017	Zhou Wei <i>et al.</i> , “Preparation of Aprepitant Emulsion for Intravenous Injection,” <i>Chinese Journal of Pharmaceuticals</i> , 2012, 43(12), 1003-1006 (“Zhou Article”)	
2018	Gonglun Chen & Daniel Tao, “An Experimental Study of Stability of Oil-In-Water Emulsion,” <i>Fuel. Proc. Technol.</i> 2005, 86, 499-508	

I. INTRODUCTION

Patent Owner Heron Therapeutics, Inc. (“Heron” or “Patent Owner”) respectfully submits this Preliminary Response responding to the petition for post-grant review (“PGR Petition” or “Petition”) filed by Petitioners Azurity Pharmaceuticals, Inc., Azurity Pharma India LLP, Inc., and Slayback Pharma LLC (“Slayback” or “Petitioner”) challenging claims 1-30 of U.S. Patent No. 12,115,255 (the “’255 patent”). Slayback asserts that the challenged claims are unpatentable under three independent grounds—as allegedly being obvious over a five-reference combination, lacking written description support, and lacking enablement. But, as discussed below, all three grounds are deficient for multiple independently sufficient reasons such that the petition fails to establish that “it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable.” 35 U.S.C. § 324(a).

Slayback’s obviousness attack puts forward the same or similar type of argument that has been rejected numerous times by the USPTO and the district court. For example, as noted in Heron’s brief requesting discretionary denial, Federal Circuit Judge William Bryson, who is presiding over the parallel litigation, found Heron’s related patents valid in a detailed opinion (now on appeal). (Paper 6 (“Discretionary Denial Request”) at 11-12; Ex. 1007 (Fresenius opinion).) In doing so, he rejected the same argument that Slayback puts forth in this PGR. Specifically, Slayback contends here that a person of ordinary skill in the art (“POSA”) would

have been motivated to increase the emulsifier content in CN845 (Ex. 1003), which is an argument that Judge Bryson rejected. After reviewing numerous references, including many of the references that Slayback relies upon, Judge Bryson found no motivation to modify CN845 with a reasonable expectation of success to arrive at emulsifier content higher than 10%, as discussed below in Section IV.A.

Slayback conveniently ignores Judge Bryson's findings regarding the state of the art, which lacked a prior art intravenous emulsion with emulsifier concentration over 10% in the type of emulsions relevant to this case. Given this deficiency, Slayback relies on generalized assertions that a POSA would have been motivated to increase the emulsifier concentration because doing so provides certain advantages. (*See, e.g.*, Petition at 28-30.) But Slayback's generalized assertions are factually unsupported, as discussed below in Section IV.B.

Slayback's assertions regarding lack of written description support are equally deficient. Slayback does not apply the proper standard for the written description requirement. For example, as discussed below in Section V, Slayback fails to even acknowledge the relevant supporting disclosures in the '255 patent specification, let alone explain why a POSA would not have understood Heron to have possession of the claimed invention in light of these disclosures.

Slayback's ground alleging lack of enablement cannot pass muster at least because it is premised on its inadequate analysis alleging lack of written description.

Moreover, Slayback's bare-bones assertions regarding undue experimentation are plainly deficient, as discussed below in Section VI.

Accordingly, Heron respectfully requests denial of institution of Slayback's PGR Petition.

II. BACKGROUND

A. CINV and NK-1 Receptor Antagonists

Chemotherapy-induced nausea and vomiting ("CINV") is a debilitating side effect of chemotherapy experienced by patients already suffering from cancer. (Ex. 1007 at 6.) It can greatly impact the quality of life of patients with cancer, and in some cases can be so severe that patients are unwilling to continue chemotherapy treatment. (*Id.*) The optimal treatment for CINV is preventing it, which involves using antiemetic medications to block certain neurotransmitters (e.g., NK-1 receptors) associated with nausea and vomiting prior to administering chemotherapy. (*Id.* at 6-7.) The medications include a chemical, referred to as an "antagonist," that inhibits the neurotransmitters. (*Id.*)

The first NK-1 receptor antagonist was aprepitant, which was discovered around 1993. (Ex. 1008 at 7.) In 2003, Merck obtained U.S. Food and Drug Administration (FDA) approval for oral tablets of aprepitant for the treatment of CINV under the trade name Emend®. (Ex. 1007 at 7.) "Oral administration of aprepitant, however, presented [several] problems." (*Id.* at 8.)

Merck thus pursued the development of an intravenous (IV) formulation of its Emend® product, but ultimately abandoned its efforts after many failed attempts, viewing the drug's properties as precluding development altogether. (*Id.* at 8-9; Ex. 1008 at 5 (“The sparing water solubility of aprepitant precluded its formulation in a vehicle acceptable for intravenous administration in humans.”).) Merck instead pivoted to developing a derivate of aprepitant called fosaprepitant and received FDA approval in 2008 for an injectable fosaprepitant dimeglumine product for the treatment of CINV, which it marketed as Emend® for Injection (or Emend® IV). (*Id.*) In the more than 20 years following Merck's discovery of aprepitant, no successful injectable **aprepitant** formulation was developed. (Ex. 1007 at 48-49.)

B. Heron Overcame Merck's Failure

The inventors of the '255 patent did what Merck scientists and others failed to do: they overcame the very low solubility of aprepitant (which has been likened to “cement dust” (*e.g.*, Ex. 1007 at 7)) and created a safe and effective IV aprepitant drug product for the treatment of patients suffering from CINV. Specifically, the '255 patent claims aprepitant emulsion formulations of aprepitant suitable for intravenous administration for treatment of emesis. (Ex. 1001 at 1:22-24.) Heron's patents, including the '255 patent, claim an unprecedented amount of a particular excipient, *an emulsifier such as egg yolk lecithin*, in combination with other specific ingredients and concentrations in an emulsion for intravenous use, including

comprising the NK-1 receptor antagonist aprepitant. For example, the '255 patent discloses “13 wt/wt % to 16 wt/wt % . . . 17 wt/wt %, 18 wt/wt %, 19 wt/wt %, or 20 wt/wt %” of an emulsifier, such as egg yolk lecithin. (*E.g.*, Ex. 1001 at 3:49-58; 11:28-60 (disclosing “13 wt/wt % to 20 wt/wt %” of a phospholipid emulsifier such as egg yolk lecithin).) Additionally, the '255 patent discloses a ratio of the emulsifier, such as egg yolk lecithin, to the NK-1 receptor antagonist, such as aprepitant, of “about 20:1” or “20:1 to 25:1.” (*Id.* at 17:38-45.) Heron’s discovery of using these amounts and ratios of emulsifier in an aprepitant emulsion for intravenous use are recited in the '255 patent claims. (*E.g.*, *id.* at claim 1 (“[a]n injectable emulsion, comprising: 0.7-0.8 wt % aprepitant . . . 13 wt/wt % to 20 wt/wt % of an emulsifier”), claim 7 (“wherein the egg lecithin is present in the emulsion at about 18 wt/wt %”), claim 8 (“wherein the ratio of egg lecithin to aprepitant is between about 20:1 to 25:1”).)

Such formulations possess unexpected stability compared to the prior art aprepitant emulsions, and this stability confers significant clinical usefulness and benefit. For instance, Examples 1-3 and 6 of the '255 patent disclose embodiments of aprepitant emulsions that were stable for at least two months at room temperature. (Ex. 1001 at 19:38-20:17 (Example 1), 20:20-67 (Example 2); 21:1-46 (Example 3), 22:60-23:59 (Example 6).) In contrast, Examples 4 and 5 of the '255 patent, which used ingredients and concentrations of those ingredients that were disclosed in the

prior art, including the CN845 reference asserted by Slayback as prior art, formed solid crystals of aprepitant within just four days at room temperature. (*E.g.*, Ex. 1040 at 2-3.) These crystals meant that these formulations were not suitable for administration into the veins of patients. The unexpected physical stability over the prior art is a key feature of Heron's claimed aprepitant emulsions.

**C. The USPTO Granted
Heron Several Patents, Including
the '255 Patent, Expressly Rejecting the Same
Prior Art Arguments that Slayback Proffers in this PGR**

As previously discussed, the Petition presents the same or similar prior art arguments that the USPTO has rejected numerous times. (*See, e.g.*, Discretionary Denial Request at 32-33.) Specifically, the Petition presents CN845 (referred to as "Zhou" by Petitioner) as its primary reference alleging it is "nearly anticipatory." (Petition at 1.) But CN845 was considered by the Office (and Judge Bryson), and each time Heron's inventions were found patentable and non-obvious over CN845 and other prior art. For example, when allowing the claims of the '255 patent, the Office explained that the claims were not obvious based on CN845 given the stability properties imparted by the higher emulsifier concentration:

[CN845]’s ratio of emulsifier to aprepitant (the NK-1 antagonist) is below the ratio required by the claimed invention. It appears that *the amount of emulsifier* is critical in the claimed invention because, according to the instant specification, the aprepitant emulsion possess[es] favorable stability properties[.]”

(Ex. 1021 at 43-44 (emphasis added); *see also id.* (“In order to arrive at the claimed composition, one of ordinary skill in the art would have to modify [CN845]’s aprepitant emulsion to increase the amount of phospholipid to 13-20 wt/wt%” but that CN845 “does not provide sufficient guidance and motivation to” do so.).)

Examiners across several related patents arrived at the same conclusion: there would have been no motivation to increase the amount of emulsifier above CN845, and Heron demonstrated criticality with respect to the amount of emulsifier in the claimed formulations. (*E.g.*, Ex. 1046 at 62 (“The wt. % of the egg yolk lecithin [in CN845] is far too low, as is the ratio of egg yolk lecithin to aprepitant.”).)

D. Judge Bryson Also Found Heron’s Inventions Patentable over CN845 and Other Prior Art

Before Slayback’s PGR (and the companion PGR-00035), others have tried and failed to invalidate Heron’s patents. Fresenius was the first to challenge Heron’s patents. The parties in the Fresenius litigation spent over two years litigating before Judge Bryson, ultimately culminating in a four-day trial in the District of Delaware. At trial, Fresenius advanced arguments *similar to those now raised by Slayback in*

this PGR, primarily relying on the CN845¹ reference (with other background references) to support its obviousness theories. (Ex. 1007 at 26 (“In brief summary, Fresenius’s theory of obviousness is that the Chinese patent application CN845, disclosed an emulsion consisting of essentially the same components and prepared by the same process as the emulsion disclosed in [Heron’s asserted patents].”).) The Court found that “Fresenius has not proved by clear and convincing evidence that the asserted claims are invalid for obviousness under 35 U.S.C. § 103 or for the lack of adequate written description under 35 U.S.C. § 112.” (Ex. 1007 at 57.) After a review of the prior art presented to the Court, including Slayback’s primary reference CN845, Judge Bryson found that “a POSA would not have had a motivation to increase the concentration of [*the emulsifier*] lecithin above 10%” as Heron’s claimed 14% was a “substantial departure from what was taught in the relevant prior art.” (Ex. 1007 at 39-40, 43 (emphasis added).) Judge Bryson also found that “a POSA . . . would not have had a reasonable expectation of success with an emulsifier level that high.” (Ex. 1007 at 40-41, 43.)

¹ Exhibit 1003, which Petitioner references as “Zhou” in the Petition, is referred to as “CN845” in the Fresenius Opinion.

Mylan was the second challenger to Heron's patents. Like Fresenius before it—and Slayback now—Mylan principally relied on CN845 (with the same or similar background references) to support its obviousness arguments. Judge Bryson presided over all stages of the Mylan litigation for more than a year and a half, until the parties entered into a stipulated dismissal less than two weeks before trial was scheduled to begin.

III. LEVEL OF ORDINARY SKILL

Slayback applies the definition of a person of ordinary skill in the art (“POSA”) proposed by Heron in the Fresenius litigation. (Petition at 13-14.) The Petition fails to meet the requirements for institution under this definition.

IV. SLAYBACK FAILS TO DEMONSTRATE A MOTIVATION TO INCREASE EMULSIFIER CONCENTRATION IN CN845 WITH A REASONABLE EXPECTATION OF SUCCESS

The '255 patent includes two independent claims, namely claims 1 and 30. Independent claim 1 of the '255 patent recites “[a]n injectable pharmaceutical emulsion, comprising: . . . **13 wt/wt % to 20 wt/wt % of an emulsifier**” (emphasis added). Independent claim 30 recites “[a]n injectable pharmaceutical emulsion, comprising: about 0.7-0.8 wt % aprepitant; an egg phospholipid emulsifier; . . . wherein **the ratio of the emulsifier to aprepitant is about 20:1 to 25:1 (wt/wt %)**” (emphasis added). Dependent claim 6, like other dependent claims, provides further limitations directed to the wt/wt % concentration of egg lecithin (which is a type of

emulsifier as recited in claim 5). In the case of dependent claim 6, the concentration of egg lecithin is about 17 wt/wt %.

Claim 8, which depends from claim 1 via claim 5, recites that “the ratio of egg lecithin to aprepitant is between about 20:1 to 25:1,” where as noted above, claim 5 recites that “the emulsifier is an egg lecithin.” In addressing claim 8, Slayback relies on its obviousness rationale for claim 1 without providing any additional substantive positions. (Petition at 40). Slayback then references its obviousness rationale for claims 1 and 8 to address the alleged obviousness of claim 30. (Petition at 49-50.) Thus, in responding to Slayback’s arguments, Heron’s below rebuttal is focused on claim 1 and is also applicable to claim 30 for the purposes of this PGR proceeding.²

² Regarding the ratio of the emulsifier to aprepitant in claim 30, Slayback asserts, while referencing its arguments for claim 8, that “the range of emulsifier to aprepitant ratios permitted in claim[] 8[] . . . is narrower than the emulsifier to aprepitant ratios covered by claim 1” (Petition at 40) and “therefore the corresponding emulsifier to aprepitant ratio [] would have also been obvious” (*id.*). (See Petition at 49-50.) Heron’s rebuttals herein are responsive to the arguments that Slayback made and should not be considered as adopting Slayback’s characterization of the claims.

Slayback's obviousness ground relies on the combination of CN845 (Ex. 1003, referred to as "Zhou" in the Petition), Washington (Ex. 1004), Bagwe (Ex. 1005), Weng (Ex. 1006), and Wan (Ex. 1010). (Petition at 12.) Slayback alleges that CN845 is "nearly anticipatory" while the other references (Washington, Bagwe, Weng, and Wan) "simply reflect common knowledge in the art regarding emulsion components/amounts" (Petition at 1-2; *see also id.* at 15 ("[CN845] discloses emulsions meeting nearly every limitation" and "[a]nything not explicitly addressed by [CN845] would have been obvious to a POSA in view of the knowledge in the art.").) CN845 discloses an appetant emulsion that has a "0.5 ~ 10% emulsifier" concentration. (Petition at 16-17 (citing Ex. 1003 at Abstract).) CN845, however, does not disclose, among other things, the claimed 13 wt/wt % to 20 wt/wt % emulsifier concentration that is the subject of Slayback's obviousness allegations. Slayback, however, contends that a POSA would have been motivated to modify CN845's formulations to use these claimed values, including by increasing the emulsifier concentration, and would have reasonably expected that increasing the emulsifier concentration would have resulted in a stable emulsion. (Petition at 27.) As confirmed by Slayback's own prior art, and buttressed by Judge Bryson's findings in the Fresenius litigation, Slayback's assertions are meritless.

**A. Slayback’s Obviousness Analysis
Ignores Judge Bryson’s Dispositive Findings**

In the Fresenius litigation, Judge Bryson considered the question of whether the prior art suggested increasing the emulsifier concentration in CN845 above 10%, including to 14%. (Ex. 1007 at 33-41.) He concluded that the prior art (including the CN845 and Washington references that form the basis of Slayback’s obviousness challenge) does not “justify the conclusion that a POSA would be motivated to increase the level of emulsifier concentration as high as 14% and that the POSA would have a reasonable expectation of success in producing a stable emulsion with an emulsifier concentration that high.” (*Id.* at 40-41.)

In making this finding, Judge Bryson stressed the state of the art, which consistently had emulsifier concentrations well below 10% in the type of emulsions relevant to this case. (*Id.* at 40-41 (“In view of the general consistency of the references in disclosing **emulsifier concentrations well below 10%**, I find that a POSA would not have had a motivation to increase the concentration of lecithin above 10%, including a concentration of at least 14%, and would not have had a reasonable expectation of success with an emulsifier level that high.”) (emphasis added).³) For example, he found that “as of 2014 [the date of the invention], all

³ Egg lecithin is a type of emulsifier.

FDA-approved emulsions based on egg yolk lecithin used concentrations of 1.2% or less.” (*Id.* at 38; *see also id.* (noting Fresenius’ expert Dr. Rabinow also “admitted that he ‘did not identify a single prior art document that disclosed a formulation containing more than 10 percent egg lecithin.’”).) He also found that the prior art “would therefore suggest to a POSA that formulators should focus on emulsifier concentrations well below 10% rather than concentrations in excess of 10%.” (*Id.*)

Slayback does not address this dispositive failure in the prior art; like Fresenius, it has failed to identify a single intravenous emulsion in the prior art that includes, for example, a concentration of emulsifier over 10% in the type of emulsions relevant to this case. (*See generally* Petition at 25-34.⁴) In fact, Slayback outright ignores the later publication of the first-named inventor of CN845 (Ex. 2017,

⁴ As explained later below, the microemulsions documents Slayback cites are not relevant for the same reasons that Judge Bryson explained in the Fresenius decision. (*E.g.*, Ex. 1007 at 36 (finding that both Fresenius’s and Heron’s experts agreed that CN845 disclosed classical emulsions, not microemulsions); *id.* (finding that both Fresenius’s and Heron’s experts agreed that classical emulsions and microemulsions have different properties); *id.* at 36-37 (finding that microemulsions had different formulation considerations than emulsions).)

the “Zhou article”) where he settled on an “optimal” emulsifier concentration much lower than 10%. (Ex. 2017 at 1 (Abstract).)

Specifically, among the prior art references supporting Judge Bryson’s finding was an article published in 2012 listing as lead author Wei Zhou (Ex. 2017), one of the inventors of CN845 (Ex. 1003). The Zhou article came after CN845 and provided follow-on results after what it described as “pre-experimental and single factor investigation.” (Ex. 2017 at 7.) The Zhou article is referenced throughout Judge Bryson’s opinion as “Zhou” or the “Zhou article.” (Ex. 1007 at 10, 12-13, 16-17, 19-21, 27-29, 32-35, 37-41.) Judge Bryson found that “[t]he Zhou article supplemented the disclosures in the CN845 application” and that “Zhou reported the optimal concentration of ingredients in the formulation to be 0.25% aprepitant [and] **2.5% egg yolk phospholipid . . .**” (Ex. 1007 at 12-13 (citing Ex. 2017 at 9, 11) (emphasis added); *see also id.* at 19 (“Dr. Steven Little, Heron’s formulation expert, noted that Zhou regarded an emulsifier concentration of 2.5% as optimal.”), 27, 34-35.)⁵ By identifying a 2.5% emulsifier concentration as part of “[t]he optimal formulation of aprepitant formulation” (Ex. 2017 at 1 (Abstract)), the Zhou article

⁵ Egg yolk phospholipid is another name for the emulsifier egg lecithin. (*See* Ex. 2003 at 33-34 (¶¶[0089]-[0090]); *see also* Ex. 1007 at 12 n.4.)

demonstrates that even the first-named inventor of CN845 did not consider, much less desire, **increased** emulsifier concentration. (Ex. 1007 at 38.) Slayback's outright failure to address the Zhou article despite being clearly aware of it based on Judge Bryson's opinion warrants denial of institution especially because the Zhou article unequivocally negates Slayback's contention regarding a POSA's motivation to increase CN845's emulsifier concentration to arrive at the values recited in the claims. To be clear, the "Zhou" document that Slayback cites is the earlier CN845 patent application publication, and not the later Zhou article that was also discussed by Judge Bryson.

Slayback's failure to address key issues and findings from the Fresenius litigation that are germane to the obviousness ground in its PGR Petition do not end with the Zhou article. Judge Bryson also made findings with respect to Washington (Ex. 1004), Hingorani (Ex. 1009), and Khan (Ex. 1016) which are not addressed in the Petition. Slayback's failure to address Judge Bryson's findings regarding these references is especially glaring as it otherwise discusses these references in its Petition.

Regarding Washington's disclosures, Judge Bryson found that "the example formulations discussed in the Washington reference contain only 1.2% lecithin." (Ex. 1007 at 38; *see also id.* at 17 (introducing Washington).) Indeed, even the example of an emulsion of s-Emopamil, a drug that is "preferentially located at the interface,"

contained only 1.2% egg lecithin. (Ex. 1004 at 2, 11-12.) Similarly, Judge Bryson found that Hingorani “used a concentration of only about 1% egg yolk lecithin.” (Ex. 1007 at 38; *see also id.* at 35 n.8 (introducing Hingorani).) And, about Khan, Judge Bryson found its “disclosure is consistent with the undisputed expert testimony that, above a certain level, increasing the emulsifier level will not further improve stability.” (Ex. 1007 at 35.). All of this evidence, amongst more, led Judge Bryson to find that “the other prior art references taught emulsifier concentrations at the low end of the 0.5% to 10% range disclosed in CN845 and close to or below the 2.5% concentration disclosed in Zhou” (*id.* at 38) and that “[i]n view of the general consistency of the references in disclosing emulsifier concentrations **well below 10%, I find that a POSA would *not* have had a motivation to increase the concentration of lecithin above 10%, including a concentration of at least 14%, and would *not* have had a reasonable expectation of success with an emulsifier level that high**” (*id.* at 40-41 (emphasis added)).

Slayback’s citation to Bagwe (Petition at 30, citing Ex. 1005) for its disclosure that an emulsion can have 1-20% emulsifier does not help Slayback because that disclosure in Bagwe is not specific to intravenous emulsions, oil-in-water emulsions, or even liquid emulsions. (Ex. 1005 at 6.) As Slayback failed to show that the cited disclosures in Bagwe describe intravenous emulsions, it cannot prove that these disclosures are relevant—a topical ointment, for example, is very different than an

intravenous injection. Indeed, Judge Bryson found that prior art cited by Fresenius “not to be probative of the issues . . . because . . . they do not discuss intravenous formulations.” (Ex. 1007 at 38-39 n.9.) Again, Slayback fails to acknowledge, let alone address, Judge Bryson’s considerations directly relevant to Slayback’s obviousness ground.

For at least the reasons given above, Slayback fails to demonstrate that it will prevail in showing that it is more likely than not that at least one of the challenged claims is unpatentable with respect to its obviousness challenge.

**B. Slayback Provides No
Evidence Showing That A POSA Would
Have Increased CN845’s Emulsifier Concentration**

Slayback builds its obviousness challenge on the misplaced assertion that a POSA would have been motivated to increase the emulsifier content because doing so provides certain advantages. (*See, e.g.*, Petition at 29 (“[A] POSA would have had a reasonable expectation of arriving at claim 1 by increasing the relative concentration of the emulsifier to improve solubility and avoid precipitation.”), 30 (“An increase in emulsifier concentration was expected to afford smaller droplet size.”).) Without a prior art document that discloses an emulsifier concentration of 13-20% in a type of emulsion relevant to this case, this kind of general reasoning is unpersuasive. But even if considered, the reasoning cannot withstand scrutiny.

As noted above, Slayback fails to even acknowledge the Zhou article, which builds on CN845 and discloses what it described as the “**optimal** formulation of aprepitant emulsion” which had an emulsifier concentration of 2.5%—much less than CN845’s disclosed 0.5% to 10% range for emulsifier concentration. (Ex. 2017 at 1 (Abstract) (emphasis added); *see supra* Section IV.A.) Slayback fails to explain why a POSA, despite knowing of the lower emulsifier concentration value in the Zhou article being identified as an optimal value, would have been motivated to increase emulsifier concentration in CN845’s formulation to arrive at the claimed invention.

Slayback’s reliance on Khan (Petition at 27-28 (citing Ex. 1016 at 5)) similarly fails because Khan also does not indicate any preference for higher or lower emulsion concentration. Instead, Khan reports that “[a]t high emulsifier concentration emulsion instability occurs because of rapid coalescence” citing a study showing where 0.5% emulsifier was identified as “optimal.” (Ex. 1016 at 5; Ex. 2018 at 4.) Again, Slayback fails to address why a POSA would have been motivated with a reasonable expectation of success to increase the emulsifier concentration in CN845 in view of Khan (and without the benefit of the disclosures of Heron’s patents).

Slayback’s claim that “aprepitant’s solubility was known to be improved by a concentration dependent increase in surfactant” (Petition at 28 (citing Ex. 1009)) is

misleading because the portion of the subject reference (Hingorani) that Slayback cites discusses non-emulsion formulations with, *e.g.*, no oil, and none of the surfactants disclosed in that cited study were egg lecithin. (Ex. 1009 at 6 (¶[0043]) (increasing concentration of surfactants such as cremophor, polysorbate, and poloxamer “for aprepitant using water alone as solvent”).) Slayback provides no explanation as to how this is relevant to CN845 and the claimed emulsions, which include oil among other ingredients.

Citing Hippalgaonkar (Ex. 1018 at 8), Slayback contends that “[a]n increase in emulsifier concentration was expected to afford smaller droplet size.” (Petition at 30.) Not only does Slayback ignore other methods for obtaining smaller droplet size, such as further homogenization, but it also ignores the general proposition in CN845 that the particle size of the emulsions it disclosed is “50nm~150nm.” (Ex. 1003 at 4 (¶[0012]).) Slayback does not explain why a POSA would want to go below the “50nm~150nm” particle size in CN845, particularly when the droplet size quoted by Slayback is 1 micron (or 1000 nanometers). (*See* Petition at 29 (citing Ex. 1019 at 5).) Emulsions with 1.2% emulsifier were widely understood to achieve sufficiently small droplet size. Indeed, all of the FDA-approved intravenous emulsions used 1.2% emulsifier. (*See supra* Section IV.A.)

Slayback also argues that “[t]he only parameter to be determined was the appropriate ‘window’ for emulsifier concentration—a matter of routine

experimentation” (Petition at 32.) Yet, Slayback entirely disregarded the follow-on work by Wei Zhou in which he disclosed what he described as “[t]he optimal formulation of aprepitant emulsion” with 2.5% egg lecithin. (Ex. 2017 at 1 (Abstract).) Additionally, Slayback not only failed to prove that a POSA would have considered higher concentrations of emulsifier, but also failed to prove that a POSA would have increased the emulsifier concentration as a matter of routine experimentation despite “the general consistency of the references in disclosing emulsifier concentrations well below 10%.” (*See* Ex. 1007 at 40-41.) Thus, it simply cannot be said that arriving at the claimed amount of emulsifier, including the ratios of emulsifier to aprepitant, would have been a matter of routine optimization. Moreover, Judge Bryson expressly rejected this “routine experimentation” theory noting that “the analysis in cases dealing with routine optimization within a range disclosed in the prior art is inapplicable here” because the claimed emulsifier concentration (14%) in the related patents “was not within the 0.5% to 10% range discussed in CN845.” (Ex. 1007 at 39 (citing *Pfizer Inc. v. Sanofi Pasteur Inc.*, 94 F.3d 1341, 1347–49 (Fed. Cir. 2024); *E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1005–10 (Fed. Cir. 2018)).) As the emulsifier content that is the subject of Slayback’s Petition (*e.g.*, 13-20%) is outside the 0.5% to 10% range

disclosed in CN845, Slayback's reliance on the routine experimentation theory to support its obviousness rationale is inapplicable for the same reasons.⁶

For at least these additional reasons, denial of institution is warranted.

⁶ Slayback mischaracterizes *Purdue Pharma L.P. v. Accord Healthcare, Inc.*, No. 2023-1953, 2024 WL 5244764 (Fed. Cir. Dec. 30, 2024), asserting that the “Federal Circuit recently clarified that there is no ‘brightline rule’ that would restrict the application of ‘routine experimentation’ here even the absence of overlapping/encompassing emulsifier concentrations in view of the motivations for increasing such amounts that Petitioner has identified.” (Petition at 35 (citing *Purdue Pharma L.P.*, 2024 WL 5244764, at *12).) There was no such finding—the Court was simply addressing an argument that “it was improper for the [district] court to rely on routine experimentation because ‘routine experimentation applies only where the claimed invention merely identifies the “optimum or workable ranges” of previously disclosed conditions.”” *Purdue Pharma L.P.*, 2024 WL 5244764, at *12 (emphasis added). The Court’s response was that it was “unaware of such a brightline rule.” *Id.* The prior art at issue in *Purdue* disclosed overlapping ranges (*id.* at *8-9), and so did not involve a scenario like here where CN845 does not disclose emulsifier concentration ranges that overlap with the claimed ranges.

**V. SLAYBACK FAILS TO DEMONSTRATE
LACK OF WRITTEN DESCRIPTION SUPPORT**

Slayback asserts that the independent claim 1 feature of “**13 wt/wt % to 20 wt/wt % of an emulsifier**” (emphasis added) and the ratio of emulsifier to aprepitant set forth in independent claim 30 (“about 0.7-0.8 wt % aprepitant; an egg phospholipid emulsifier; . . . wherein **the ratio of the emulsifier to aprepitant is about 20:1 to 25:1 (wt/wt %)**”) lack written description support under 35 U.S.C. § 112(a). (Petition at 55-56.) Slayback’s arguments in this regard do not pass muster because it applies the wrong standard for compliance with the written description requirement. Slayback ignores the ’255 patent specification’s disclosure supporting the subject claim features and fails to explain why this disclosure would not have reasonably conveyed to a POSA that Heron had possession of the claimed invention. Slayback’s attempts at mischaracterizing issues from the Fresenius litigation involving related patents do not change the supporting disclosure in the specification, and if anything, further confirm that the challenged claims here have written description support.

To comply with the written description requirement under § 112(a), the specification’s disclosure is considered sufficient when it “reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.” *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351

(Fed. Cir. 2010). “[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art.” *Id.* “[E]xamples are not necessary to support the adequacy of a written description.” *See Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006); *see also Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1308 (Fed. Cir. 2015) (“There is no rigid requirement that the disclosure contain ‘either examples or an actual reduction to practice.’”) (quoting *Ariad*, 598 F.3d at 1352). As discussed below, Slayback fails to show that the challenged claims lack written description support.

As noted in Section IV above, independent claim 1 of the ’255 patent recites “[a]n injectable emulsion, comprising: . . . **13 wt/wt % to 20 wt/wt % of an emulsifier**” (emphasis added). Independent claim 30 recites “[a]n injectable pharmaceutical emulsion, comprising: about 0.7-0.8 wt % aprepitant; an egg phospholipid emulsifier; . . . wherein **the ratio of the emulsifier to aprepitant is about 20:1 to 25:1 (wt/wt %)**” (emphasis added).⁷

The as-filed ’255 patent specification (Ex. 2003 at 20-42) discloses emulsifier concentrations of “about . . . 13 wt/wt % to 20 wt/wt %” as set forth in claim 1.

⁷ See n.2.

(Ex. 2003 at 34 ([0091]), 36-37 ([0102]), 23 ([0023])).⁸ The as-filed '255 patent specification also discloses emulsifier concentrations of, for example, “about . . . 17 wt/wt %.” (*Id.*)

Additionally, the '255 patent specification discloses embodiments where the ratio of emulsifier to the NK-1 receptor antagonist (*e.g.*, aprepitant) tracks the ratio set forth in claim 30:

In some embodiments, **the ratio of emulsifier to NK-1 receptor antagonist (wt %:wt %)** in the composition ranges from **about 10:1 to 30:1, 10:1 to 20:1, 15:1 to 30:1, 20:1 to 25:1, 18:1 to 22:1, 19:1 to 20:1, or 10:1 to 30:1.** In other embodiments, the ratio of emulsifier:NK-1 receptor antagonist (wt %:wt %) in the composition is about 10:1, 11:1, 13:1, 14:1, 15:1, 18:1, 19:1, 20:1, 21:1, 22:1 23:1, 24:1, 25:1, or 30:1.

(Ex. 2003 at 25 ([0030]) (emphasis added).)⁹

The '255 patent specification similarly discloses examples with a 20:1 ratio of egg lecithin (a type of emulsifier) to aprepitant. (*E.g.*, Ex. 2003 at 45-46 ([0134]

⁸ Phospholipids are a type of emulsifier. (Ex. 2003 at 33-34 ([0089]-[0090]).)

⁹ Aprepitant is a type of NK-1 receptor antagonist. (Ex. 2003 at 22 ([0012]).)

and Table 2) (describing Example 2); *see also id* at 23 (¶[0023]) (identifying egg lecithin as an emulsifier).)

As shown above, the '255 patent specification expressly discloses the features of “13 wt/wt % to 20 wt/wt % of an emulsifier” (*e.g.*, claim 1) and the ratio of emulsifier to aprepitant range from “about 20:1 to 25:1 (wt/wt %)” (*e.g.*, claims 8 and 30).

Slayback’s arguments fail to acknowledge, let alone address, the above-noted support for the above claim limitations. (*See generally* Petition at 54-69.) This is fatal to Slayback’s ground asserting lack of written description. By failing to explain why a POSA would not have understood that Heron had possession of the claimed invention in light of this express support, Slayback does not even do the bare minimum to meet the threshold for showing the claims lack written description support. For at least this reason, Slayback’s PGR Petition does not meet the standard for institution.

Slayback’s argument that the claims lack written description support because the “exemplified emulsions” in the '255 patent do not show a ratio of emulsifier to aprepitant of more than 20:1 (Petition at 65-66) is simply wrong. The specification is not required to have examples of a claimed embodiment. *See Falko-Gunter Falkner*, 448 F.3d at 1366 (Fed. Cir. 2006) (“[E]xamples are not necessary to support the adequacy of a written description.”). Indeed, Judge Bryson made this point in

the Fresenius litigation. (Ex. 1007 at 55-56.) Again, despite citing to portions of Judge Bryson’s opinion elsewhere in its Petition, Slayback fails to reconcile its lack of written description support theory with the proper standard for written description support Judge Bryson applied in his opinion. (*See, e.g.*, Petition at 66-68.)

Instead of applying the proper standard for the written description support requirement, Slayback relies heavily on out-of-context statements *from the Fresenius litigation* relating to the prior art at-issue and the asserted claims *in that litigation* (where the asserted recited emulsifier concentration of 14 %)—Slayback alleges that these statements support its lack of written description argument for the challenged claims *in this proceeding*. (*See, e.g.*, Petition at 56-60 (repeatedly citing to Heron’s opening post-trial brief (Ex. 1020), Heron’s responsive post-trial brief (Ex. 1027), Heron’s opening statement (Ex. 1026), the trial transcripts (Exs. 1032-1034), and Judge Bryson’s opinion (Ex. 1007)); *see also id.* at 56 (“Each of these [asserted] claims [in the Fresenius litigation] required 0.7% (wt/wt) aprepitant and 14% (wt/wt) of an emulsifier (i.e., egg yolk lecithin).”).) For example, Slayback argues that “the ’255 patent’s description needed to convey the possession of emulsions that were now beyond the ‘critical’ and ‘unexpected’ values—and do so under the impossible standards that Heron articulated during trial with Fresenius.” (Petition at 64.) Not so.

For example, Heron never asserted during the Fresenius litigation that concentrations of emulsifier higher than 14% were not part of the invention or would not be stable (it is not disputed that at least emulsions with 13-15% emulsifier were stable and part of the invention). Indeed, Slayback fails to point to a single Heron statement from the Fresenius litigation that the amounts of emulsifier claimed in the '255 patent lack written description support. (*See, e.g.*, Petition at 56-60.) In other words, Heron never suggested, much less argued, during litigation that an upper limit of 14% was critical despite Slayback's misleading suggestions to the contrary.

Moreover, just like its deficient obviousness analysis discussed above (*see supra* Section IV), Slayback ignores key findings by Judge Bryson that undermine its analysis. For example, Slayback fails to address Judge Bryson's analogous finding in the Fresenius litigation that limitation reciting a range of pH values in a related patent had written description support because the patent specification recited the same range of pH values. (Ex. 1007 at 55 ("[T]he mere recitation of the range of pH values in the specification and in the claims is sufficient to satisfy the written description requirement of 35 U.S.C. § 112.")) Just like in the Fresenius litigation, the express recitation of the emulsifier concentration (*e.g.*, claim 1) or range of emulsifier to aprepitant ratio (*e.g.*, claims 8 and 30) in the '255 patent specification tracking the language in the challenged claims is sufficient to satisfy the written

description requirement here. There is simply no question that the claim features at issue are expressly supported by the '255 patent specification, and Slayback's failure to explain why that alone is not sufficient for written description support is dispositive of this issue.

Slayback merely cites some cases that allegedly stand for the proposition that express support of claim features in the patent specification is insufficient for written description support. (Petition at 67.) But Slayback neither discusses these cases, nor applies their reasoning to the '255 patent claims. (*Id.*) In other words, Slayback does not explain why a POSA would not have understood Heron to have possession of the claimed invention when, as noted above, the patent specification expressly supports the recited ranges.

For example, Slayback cites to *Biogen Int'l GmbH v. Mylan Pharms.*, 18 F.4th 1333, 1343 (Fed. Cir. 2021). (Petition at 67.) But in *Biogen*, the claims recited "several DMF doses in the 100-1,000 mg/day range as 'effective' without even identifying a target disease." *Biogen Int'l GmbH*, 18 F.4th at 1344. On the other hand, the claimed injectable pharmaceutical emulsion with "13 wt/wt % to 20 wt/wt % of an emulsifier" (*e.g.*, claim 1) and the ratio of emulsifier to aprepitant ranges from "about 20:1 to 25:1 (wt/wt %)" (*e.g.*, claims 8 and 30) is expressly supported by the '255 patent specification. Thus, the bare-bones arguments

Slayback advances are insufficient to demonstrate that the challenged claims lack written descriptions support.

Furthermore, Slayback's characterization of Heron's prosecution strategy (Petition at 60-64) is purely speculative and thus should be dismissed. Slayback boldly suggests, without any evidence, that "by the time Heron prosecuted the '255 patent, the Examiners had been utterly convinced that the range of 11%-15% (wt/wt) emulsifier was crucial to patentability." (Petition at 63.) Slayback fails to explain its basis for asserting that the examiners concluded that concentrations of egg lecithin greater than 15% were not part of the invention or would not be stable, especially when the earlier patent applications simply did not include claims reciting emulsifier at a concentration greater than 15%. (*See generally* Petition at 60-64.)

Directly undercutting Slayback's speculation is the Examiner's stated reasons for allowance in the '255 patent prosecution history, where the Examiner expressly allowed the claims over CN845 and other cited prior art. (Ex. 2003 at 159-160.)

Thus, contrary to Slayback's unfounded suggestions, the Examiner's findings simply confirm the written description support for the claimed invention.¹⁰

For at least the reasons given above, Slayback fails to demonstrate that it will prevail in showing that it is more likely than not that at least one of the challenged claims is unpatentable with respect to its written description challenge.

VI. SLAYBACK FAILS TO DEMONSTRATE LACK OF ENABLEMENT

Slayback related its lack of enablement challenge to its lack of written description support challenge. (Petition at 70 ("Much of the discussion in Section VII, *supra*, concerning Heron's admissions . . . are [*sic*, is] applicable here.")) Thus,

¹⁰ Slayback also ignores file histories of other Heron patents where the Examiner acknowledged the criticality of emulsifier concentration at other higher ranges, when the submitted claims disclosed other ranges, such as 13 wt/wt% to 15 wt/wt% emulsifier. (*See, e.g.*, Ex. 1046 at 61 (Examiner acknowledging that "Applicant has demonstrated criticality of the range in regard to the [13-15] wt. / wt. % of egg yolk lecithin [emulsifier] and the ratio of egg yolk lecithin to aprepitant, thereby overcoming any assertion of obviousness the Examiner could make . . ."); *see also id.* at 1 (claim 1 reciting "13 wt/wt% to 15 wt/wt% egg yolk lecithin [emulsifier].").)

Slayback's arguments regarding lack of enablement should be rejected at least for the same reasons discussed above in Section V. As an example, just like its deficient written description challenge, Slayback fails to confront the express disclosure in the '255 patent specification of the claim features at issue and fails to explain why, when provided with such explicit disclosure, the claims are not enabled. (*See, e.g.*, Petition at 70-72.) Additionally, Slayback broadly ignores the patent's description of the disclosed emulsions (*e.g.*, Ex. 1001 at 2:43-9:14), the methods of making the disclosed emulsions (*e.g.*, *id.* at 12:25-19:4), uses of the disclosed emulsions (*e.g.*, *id.* at 19:6-31), and examples of the disclosed emulsions (*e.g.*, *id.* at 19:33-32:45). Slayback's deficient analysis regarding alleged lack of enablement fails to meet the threshold institution.

Moreover, to demonstrate a lack of enablement, Slayback was required to show that the specification fails to teach a POSA how to make and use the full scope of the claimed invention without "undue experimentation." *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (internal citation omitted). Factors to be considered in determining whether undue experimentation is required include the amount of direction or guidance presented, the presence or absence of working examples, the state of the prior art, and the quantity of experimentation necessary. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Slayback's enablement analysis is deficient in this regard because while it gives lip service to the *Wands*

factors, it does not analyze them in any level of detail with respect to the challenged claims to support its non-enablement theory. (*See generally* Petition at 70-72.)

Accordingly, Slayback fails to demonstrate that it will prevail in showing that it is more likely than not that at least one of the challenged claims is unpatentable with respect to its enablement challenge.

VII. CONCLUSION

For the foregoing reasons, Heron respectfully requests denial of Slayback's PGR petition.

Respectfully submitted,

Dated: July 14, 2025

By: /Naveen Modi/
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CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), the undersigned certifies that the foregoing Patent Owner's Preliminary Response contains, as measured by the word-processing system used to prepare this paper, 6,968 words. This word count does not include the items excluded by 37 C.F.R. § 42.24.

Respectfully submitted,

Dated: July 14, 2025

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CERTIFICATE OF SERVICE

I certify that I caused to be served on the counsel identified below a true and correct copy of the foregoing Patent Owner's Preliminary Response by electronic means on July 14, 2025:

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