

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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INTAS PHARMACEUTICALS LTD.,  
Petitioner

v.

ATOSSA THERAPEUTICS, INC.,  
Patent Owner

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Case PGR2025-00043  
Patent 12,071,391

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**PATENT OWNER'S PRELIMINARY RESPONSE UNDER 37  
C.F.R. §42.107**

**LIST OF EXHIBITS**

<b>Exhibit</b>	<b>Description</b>
EX2001	ATOSSA THERAPEUTICS, INC. QUARTERLY REPORT FORM 10-Q (March 31, 2025)
EX2002	Atossa Therapeutics Proposes Potentially Groundbreaking Study Aimed at Reducing Interval Breast Cancer in High-Risk Women at AACR 2025 (April 29, 2025)
EX2003	Atossa Therapeutics Announces Plans to Pursue Metastatic Breast Cancer Indication for (Z)-Endoxifen and Continued Engagement with FDA on Additional Indications (March 11, 2025)
EX2004	Financials – Intas Pharmaceuticals Ltd., <a href="http://www.intaspharma.com/financials/">http://www.intaspharma.com/financials/</a>
EX2005	Atossa Therapeutics Announces Issuance of Key U.S. Patent Covering Endoxifen (March 08, 2022)
EX2006	Efficacy and Safety of Endoxifen in Bipolar I Disorder Patients, NCT06608641 (Last Updated March 17, 2025), <a href="https://clinicaltrials.gov/study/NCT06608641">https://clinicaltrials.gov/study/NCT06608641</a>
EX2007	Declaration of Sayem Osman
EX2008	Atossa Covenant Not to Sue
EX2009	Atossa Therapeutics Announces Full Results from Phase 2 KARISMA-Endoxifen Study Demonstrating Statistically Significant Reductions in Mammographic Breast Density (Dec. 11, 2024)
EX2010	Atossa Therapeutics Announces First Quarter 2025 Financial Results and Provides a Corporate Update (May 13, 2025)
EX2011	INTENTIONALLY OMITTED
EX2012	Breast Center Year in Review, An Unmet Need in HR-Positive Endocrine-Resistant Breast Cancer, <i>available at</i> <a href="https://jons-online.com/special-issues-and-supplements/2021/2021-year-in-review-breast-cancer/an-unmet-need-in-hr-positive-endocrine-resistant-breast-cancer">https://jons-online.com/special-issues-and-supplements/2021/2021-year-in-review-breast-cancer/an-unmet-need-in-hr-positive-endocrine-resistant-breast-cancer</a>
EX2013	ATOSSA THERAPEUTICS, INC. ANNUAL REPORT FORM 10-K for the Fiscal Year Ended December 31, 2024
EX2014	U.S. Patent No. 11,572,334
EX2015	Intas Requirements For Resolving Disputes With Atossa (FILED UNDER SEAL)

<b>Exhibit</b>	<b>Description</b>
EX2016	Default Protective Order
EX2017	<i>Intas Pharmaceuticals, Limited v. Atossa Therapeutics, Inc.</i> , IPR2025-00799, Pap.1 (Apr. 3, 2025)
EX2018	<i>Intas Pharmaceuticals, Limited v. Atossa Therapeutics, Inc.</i> , PGR2023-00043, Pap.1 (Aug. 18, 2023)
EX2019	Rishab Gupta & Swarndeeep Singh, <i>Endoxifen Approval for Bipolar in India, A Premature or a Pragmatic Decision?</i> , 43(1) J. CLINICAL PSYCHOPHARMACOLOGY 3 (2023)
EX2020	Zonalta, Why Zonalta?, <a href="https://zonalta.in/">https://zonalta.in/</a>
EX2021	Atossa Therapeutics Granted Additional Patent Protection for Endoxifen (August 28, 2024)
EX2022	Declaration of Megan Raymond

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## **I. Introduction**

As with Patent Owner Atossa Therapeutics Inc.'s ("PO" or "Atossa") July 7 brief concerning Discretionary Denial (Pap.7), this §42.107 Preliminary Response confirms the Board should deny the above-captioned Petition ("Petition"/"Pet."). The Petition fails to show claims 1-44 (the "Challenged Claims") of U.S. Patent No. 12,071,391 (the "'391 Patent"/"'391", EX1001) are unpatentable.<sup>1</sup>

The Challenged Claims here are directed to pharmaceutical compositions comprising (Z)-endoxifen and an enteric material, as well as methods for making and administering such compositions, including to treat hormone-dependent breast cancer. All of Petitioner's prior art Grounds (Grounds 1-7) fundamentally misinterpret the Challenged Claims of the '391 Patent and misapply the prior art upon which Petitioner relies.

The Petitioner's argument for invalidity rests on the flawed premise that the "enteric" requirements of U.S. Patent No. 11,572,334 ("the '334 Patent", EX2014) and the '391 Patent are the same. But unlike the claims of the previously adjudicated '334 Patent, which required an endoxifen composition to be "encapsulated in an enteric capsule" (EX2014, cl.1), both independent claims (claims 1 and 32) of the

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<sup>1</sup> Unless stated, statutory and regulatory citations are to 35 U.S.C. or 37 C.F.R., as context indicates, internal citations omitted, and emphases/annotations are added.

'391 Patent's instead require that ***the composition itself comprise both an endoxifen and an enteric material***. EX1001, cl.1. For this reason, Petitioner's arguments regarding collateral estoppel based on the earlier '334 PGR (PGR2023-00043) fail.

Petitioner's anticipation arguments (Ground 1), which rely on Ahmad for the "enteric material" requirement of the Challenged Claims, also fail. Petitioner never argues that Ahmad discloses, or even suggests, the claimed invention of an integrated ***composition comprising both endoxifen and an enteric material***. Petitioner instead directs its analysis to arguing that Ahmad ***encapsulates*** endoxifen in an enteric capsule. Pet.20. This does not meet the claim requirements, and Petitioner fails to meet its burden for Ground 1.

Petitioner's obviousness arguments also fail. Petitioner's only obviousness ground addressing the independent claims is Ground 2, which asserts only single-reference obviousness based on Ahmad and does not seek to fix Ground 1's failing regarding the requirement that the claimed composition include ***both*** endoxifen and enteric material. Ground 2 additionally fails because Petitioner fails to prove the basic requirements for obviousness: it offers only conclusory assertions and a throwaway paragraph that neither identify any specific missing limitations in Ahmad nor explain how or why a POSITA would modify Ahmad to arrive at the claimed composition. Instead, Petitioner improperly reads the enteric material out of the claims and relies on incomplete or irrelevant combinations that do not cure Ahmad's

deficiencies. Grounds 3-7 are limited to challenges to certain dependent claims with no attempt to correct this underlying failure, and thus they, too, fail because the Grounds for the independent claims fail. At least Grounds 3, 5, 6, and 7 additionally fail for reasons related to lacking sufficient particularity.

Petitioner's Ground 8 written description and enablement challenge is likewise deficient, offering only a cursory argument devoid of any expert support and ignoring the express teachings of the specification that describe and enable the claimed compositions.

For these reasons, detailed below, the Petition fails, and the Board should decline to institute review.

## **II. The '391 Patent**

Breast cancer continues to present a formidable public health challenge, remaining the most common form of cancer in women and the second leading cause of cancer death in humans. *See, e.g.*, EX1001, 1:25-28. Hormone-dependent breast cancer represents the most prevalent subtype. EX2001, 18 (“ER+ breast cancer which comprises approximately...78% of all breast cancers.”). Tamoxifen has been a first-line treatment for hormone-dependent breast cancer, but many patients, due to genetic factors or drug interactions, cannot adequately metabolize tamoxifen into its active metabolite, endoxifen, rendering such treatment ineffective for those individuals. *See* EX1001, 2:1-2:27. Tamoxifen is also known to have severe side

effects. *See id.* (Z)-endoxifen, the subject of the '391 Patent, is the “main active metabolite responsible for the clinical efficacy of tamoxifen,” and provides more consistent efficacy, regardless of patient genotype. *See id.* at 2:41-43.

Obtaining relatively pure and stable forms of (Z)-endoxifen proved a challenge until the inventions claimed in the '391 Patent family. *See id.* at 27:40-55. The inventors of the '391 Patent developed a novel synthesis process that avoids the inefficiencies and instabilities of prior methods, yielding a crystallized form of (Z)-endoxifen (at least 90% by weight) with superior stability and commercial-scale feasibility. *See id.*

The stable, highly-pure form of (Z)-endoxifen claimed in the '391 Patent aims to address the urgent need for a safer and more effective treatment and is suitable for direct delivery, bypassing metabolic limitations and providing consistent therapeutic benefit across diverse patient populations. *Id.* at 2:1-58, 2:60-11:15, 96:20-98:66. Moreover, unlike existing synthetic/purification methods, the process disclosed in the '391 Patent achieves higher yield, greater purity, and improved stability, and it is safer, simpler, more economical, and scalable for commercial production. *Id.* at 27:40-55.

### **III. The '391 Claims Require Endoxifen-Enteric Composition**

The Challenged Claims are directed to a composition comprising endoxifen and an enteric material. EX.1001, cl.1. The '391 Patent recognizes that endoxifen

can be degraded by stomach acid, necessitating a formulation that can bypass the stomach and release the drug in the intestines. *See* EX.1001, 39:27-28 (“[T]arget[s] upper small intestines and colon”); cl.38 (“releasing no more than 10% of the (Z)-endoxifen in a stomach of the subject within 2 hours following the administering of the composition”).<sup>2</sup> There are different ways to ensure that the endoxifen is not degraded in the stomach. For example, the (Z)-endoxifen composition can be “*encapsulated* in an enteric capsule,” as in the related ’334 Patent. EX2014, cl.1. Alternatively, as in the claims of the ’391 Patent challenged here, an enteric material can be *part of the composition with (Z)-endoxifen*. EX1001, cl.1.

Both independent claims of the ’391 Patent recite “[a] composition comprising an *endoxifen and an enteric material*.” *See* EX1001, cl.1, cl.32. The claims thus plainly require that the two named components—endoxifen and enteric material—be part of the same composition itself (a composition which, in turn, can further be, *e.g.*, formed into a tablet (claim 5), or formulated as, *e.g.*, part of a suspension (as in claim 30)).

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<sup>2</sup> Petitioner recognizes that endoxifen is subject to degradation in the acidic conditions of the stomach and that enteric materials may be used to prevent release of the endoxifen in the stomach and, instead, release the active substance in the intestines. Pet.6.

In addition to the plain language of the claims, the doctrine of claim differentiation also supports this interpretation of the claim. *See Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1326 (Fed. Cir. 2003) (“Our court has made clear that when a patent claim ‘does not contain a certain limitation and another claim does, that limitation cannot be read into the former claim in determining either validity or infringement.’”). The related ’334 describes a composition where the enteric requirement is *not* part of the composition, reciting “[a]n oral formulation comprising an *endoxifen composition encapsulated in an enteric capsule.*” EX2014, cl.1. In other words, the enteric aspect of the ’334 claims is not part of the composition itself. In contrast, the ’391 requires “[a] *composition comprising an endoxifen and an enteric material.*” This distinction is shown below in Petitioner’s own comparison (excerpted here from the Petition):

391 Patent	334 Patent (Unpatentable)
<p>1. A composition comprising an endoxifen and an enteric material, wherein:                      the endoxifen comprises a compound of Formula (III):</p> <div data-bbox="342 506 712 695" style="border: 1px solid black; padding: 5px; margin: 10px auto; width: fit-content;"> <p style="text-align: right; font-size: small;">Formula (III)</p> </div> <p>or a pharmaceutically acceptable salt thereof, and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.</p>	<p>1. An oral formulation comprising an endoxifen composition encapsulated in an enteric capsule, wherein the endoxifen composition comprises a compound of Formula (III):</p> <div data-bbox="951 506 1321 695" style="border: 1px solid black; padding: 5px; margin: 10px auto; width: fit-content;"> <p style="text-align: right; font-size: small;">Formula (III)</p> </div> <p>wherein at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.</p>

Pet.20. Thus, while the composition need not be homogenous, the '391's claims cannot be satisfied, for example, by a composition of endoxifen *without* an enteric material (e.g., internal enteric content), even if the entirety of the endoxifen composition itself is encapsulated by an outermost enteric coating.

The dependent claims of the '391 Patent are consistent with this understanding of the claim. For example, claim 9 recites “*the composition*” of claim 1 (not just the Formula (III) endoxifen compound) “formulated as a suspension.” Petitioner appears to acknowledge the requirement that the composition include *both* enteric material and the claimed endoxifen Formula (III) in discussing claim 9 in Ground 8 (regarding §112). Petitioner there argues that the “391 Patent specification fails to describe a formulation in which the enteric material is suspended in a fluid with the

endoxifen.” Pet.74. But, Petitioner’s arguments in Ground 8 are inconsistent with the interpretation of the claims on which it bases its obviousness argument for Ground 1, where in analyzing claim 9 Petitioner *ignores the requirement that the composition be a suspension that includes enteric material* in addition to endoxifen. See Pet.28.

Moreover, the specification describes a composition of endoxifen *with* an enteric material. For example, the specification explains “the enteric tablets, enteric caplets...*may be uncoated.*” EX1001, 40:1-2; *see id.* at 54:37-42; *contrast* Pet.73-75 (Ground 8); *see also* supra §VII; EX1001, 36:9-16 (“Compositions intended for oral use may be prepared in solid or fluid unit dosage forms.”), 36:65-37:2 (“excipients that can be *used in the compositions*... can include...control release agents”), 39:1-21, 38:56-67; 39:22-51; 39:56-68; 39:22-51 (“compositions may comprise one or more of pH-dependent [*i.e.*, enteric] polymers such as acid insoluble polymers.”). In contrast, consistent with the composition claimed in the ’334 Patent, the specification describes an endoxifen “composition” that is itself formulated as, *e.g.*, a tablet or caplet or capsule then “coated” with enteric material: “Compositions formulated for oral delivery as disclosed herein, for example, tablets, caplets, and capsules, *may be coated* with one or more enteric coating agent, control release agent or film forming agent to control or delay disintegration and absorption *of the*

*compositions comprising endoxifen or salts thereof* in the gastrointestinal tract and thereby provide a sustained action over a longer period of time.” *Id.* at 38:56-67.

#### IV. Collateral Estoppel Does Not Apply Because the '391 Claims Are Materially Different

Petitioner incorrectly argues that the Board’s Final Written Decision in the '334 PGR (“the '334 FWD”), which reviewed the different claims of grandparent '334 Patent, should have a collateral estoppel effect here. Pet.14. But no collateral estoppel applies, including because of the material differences between the claims of the '391, which recite “[a] *composition comprising an endoxifen and an enteric material,*” and the '334, which recite “[a]n oral formulation comprising an *endoxifen composition encapsulated in an enteric capsule,*” again as shown below in Petitioner’s own comparison (excerpted here from the Petition):

391 Patent	334 Patent (Unpatentable)
<p>1. A composition comprising an endoxifen and an enteric material, wherein: the endoxifen comprises a compound of Formula (III):</p> <div data-bbox="344 1461 699 1642" style="text-align: center;"> <p>Formula (III)</p> </div> <p>or a pharmaceutically acceptable salt thereof, and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.</p>	<p>1. An oral formulation comprising an endoxifen composition encapsulated in an enteric capsule, wherein the endoxifen composition comprises a compound of Formula (III):</p> <div data-bbox="927 1461 1282 1642" style="text-align: center;"> <p>Formula (III)</p> </div> <p>wherein at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.</p>

Pet.20; *see also Intas Pharms. Ltd. v. Atossa Therapeutics, Inc.*, PGR2023-00043, Pap.37, 5 (Jan. 29, 2025).

The difference is dispositive. *No collateral estoppel applies to the '391 claims because the issues here were neither "identical" nor "actually litigated" in the '334 PGR.*<sup>3</sup> *See VirnetX Inc. v. Apple, Inc.*, 909 F.3d 1375, 1377 (Fed. Cir. 2018) (requiring "a prior action present[ing] an identical issue" and that "the prior action actually [was] litigated" for collateral estoppel to apply); *Sacramento Mun. Util. Dist. v. United States*, 566 F. App'x 985, 994 (Fed. Cir. 2014) (requiring "identity of the issues in a prior proceeding" and "actual litigation of those issues" for collateral estoppel to apply).

A "composition comprising an endoxifen and an enteric material," as in claim 1 of the '391, is clearly distinct from a composition that *is not required to include an enteric material*, as in claim 1 of the '334. The requirement regarding something "enteric" in the '334 relates to the complete composition itself being "encapsulated in an enteric capsule." EX2014 cl.1; *see also* cl.3 ("the enteric capsule is uncoated"),

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<sup>3</sup> The Ground 5 prior art combination here (Ahmad in view of de Villiers (EX1007) and Ghandi (EX1022)) also differs from any prior art combination asserted in the '334 PGR. Further, Ground 8 here, which is directed towards written description and enablement, is unrelated to any ground raised in the '334 PGR.

cl.4 (“the enteric capsule further comprises an enteric coating”), cl.8 (“the enteric capsule comprises hydroxypropylmethyl cellulose”), cl.14 (“the endoxifen composition comprises from 0.01 mg to 200 mg (Z)-endoxifen per enteric capsule”), cl.15 (“encapsulated in an enteric capsule”).

Unlike the claims of the '391 Patent, the '334 claims have no requirement that the composition itself contain an enteric material or even that there be an enteric material somewhere *within* the enteric capsule. *See VirnetX Inc.*, 909 F.3d at 1377; *Sacramento Mun. Util. Dist.*, 566 F. App'x at 994; *Palo Alto Networks, Inc. v. Centripetal Networks, Inc.*, IPR2021-01153, Pap.10, 18 (Jan. 24, 2022) (“Collateral estoppel does not apply because there are differences between the claim limitation at issue here and the adjudicated claim limitations at issue in the prior IPRs.”); *Dr. Reddy's Lab'ys., Ltd. v. Monosol RX, LLC*, IPR2016-01111, Pap.14, 17 (Dec. 5, 2016) (finding collateral estoppel inapplicable where prior decision did not resolve the issue of whether the same prior art disclosed a different limitation in the challenged patents). The '334 Patent claimed a dosage form where an enteric function had to be provided by the capsule coating. *See EX2014*, cl.1. The '391 Patent claims the underlying composition itself, where the enteric material is an ingredient of the composition combined with the endoxifen. *See supra*, §III. Petitioner's conflating the two is a central flaw in its Petition and, *inter alia*, negates its assertion of collateral estoppel.

**V. Ahmad Fails to Anticipate Claims 1-6, 8, 9, 11-15, 20, 23, 26-37, 40-44 (Ground 1)<sup>4</sup>**

Petitioner's Ground 1 asserts anticipation based on Ahmad for the vast majority of Challenged Claims. But, as discussed below, Ahmad fails to disclose a key limitation required by every independent claim: a *composition comprising an endoxifen and an enteric material*.

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<sup>4</sup> Petitioner's summary table in "Identification of Grounds" purports to include claims 3 and 30 in its anticipation ground (Ground 1) (Pet.3), but Petitioner provides *no argument or evidence* mapping the limitations of claim 3 or 30 to the Ahmad reference under its anticipation theory (Pet.19-34). The substantive heading and sections for Ground 1 in the body of the Petition also omit claim 3 entirely. *See* Pet.19 ("Ground 1: Claims **1, 2, 4-6, 8, 9, 11-15, 20, 23, 26-37, and 40-44** Are Anticipated by Ahmad"). And while the sub-heading for Section X.F of the Petition includes claim 30 (Pet.28-30), the subsequent textual analysis completely ignores it. By failing to offer *any* analysis or evidence, Petitioner has failed to meet its burden for any anticipation challenge to claims 3 and 30. And in fact, Petitioner itself seems to recognize that Ahmad does *not* teach claim 3 in view of its obviousness arguments in Ground 2. *See* Pet.40-42.

**1. Ahmad’s Teachings of Enteric *Coating* Fail to Disclose The Claimed Endoxifen-Enteric *Composition***

In order to anticipate under § 102, a reference “must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements ‘*arranged as in the claim.*’” *Net MoneyIN Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008) (further noting that “‘arranged as in the claim’ is readily understood in relation to claims drawn to things such as ingredients mixed in some claimed order”). Here, both independent claim 1 and 32 of the ’391 Patent recites “[a] *composition comprising an endoxifen and an enteric material.*” See EX1001, cl.1, cl.32. As discussed above (*see supra*, §III), the plain language of the claim requires that the composition comprises both an endoxifen and an enteric material in the composition itself. But Petitioner argues only that Ahmad discloses a *composition of endoxifen* that can subsequently be *encapsulated in an enteric coating*. See, e.g., Pet.9, 20, 27. Petitioner never attempts to show (nor could it) that Ahmad teaches the *claimed* composition, which itself must include both endoxifen and an enteric material.

Petitioner’s argument relying on Ahmad’s disclosure is (based on Petitioner’s own assertions) confined to *a composition that includes only endoxifen (and not also an enteric material)*, and that is subsequently encapsulated by an enteric *coating*. See Pet.20. As reproduced below, the *entirety* of Petition’s anticipation

argument for the claimed composition in Claim 1 (and Claim 32) is limited to these disclosures:

***A composition comprising an endoxifen and an enteric material,***

Ahmad is titled “Endoxifen compositions and methods” and “provides compositions containing endoxifen.” Ex. 1003, Title, Abstract. Ahmad teaches that “[w]hen desired, [the] composition containing endoxifen or endoxifen-lipid complex can be encapsulated in enteric-coated capsules to protect it from acids in the stomach.” *Id.*, 18:19-21. Ahmad explains that the “enteric coatings prevent release of medication before it reaches the small intestine.” *Id.*, 18:22-24. It further teaches that “[e]nteric coating of capsules filled with compositions containing endoxifen can be done as methods known in the art.” *Id.*, 18:27-29. Thus, Ahmad teaches compositions comprising endoxifen and an enteric material. McConville, ¶54.

Pet.20 (bold italic original, underline added); *see also* Pet.24-25 (“Claim 32 recites a ‘method comprising administering to a subject’ a composition that is identical to the composition of claim 1.”).

Likewise, Petitioner’s own expert, Dr. McConville, repeatedly characterizes Ahmad’s disclosure in these same terms. *See, e.g.*, EX1033, ¶¶29, 54. For example, Dr. McConville explains that “Ahmad is titled ‘Endoxifen compositions and methods’ and ‘provides ***compositions containing endoxifen.***” *Id.* at ¶54 (citing EX.1003, Title, Abstract). He explains that this composition can ***then*** (“[w]hen desired”) be “***encapsulated in enteric-coated capsules.***” *Id.* at ¶54 (“Ahmad further

teaches that “[w]hen desired, [the] *composition containing endoxifen* or endoxifen-lipid complex *can be encapsulated in enteric-coated* capsules to protect it from acids in the stomach.”) (citing EX1003, 18:19-21). Indeed, throughout his declaration, Dr. McConville repeatedly describes Ahmad as disclosing an “enteric coating” distinct from the composition itself. *See, e.g., id.* at ¶66 (“Ahmad discloses an enteric *coated* capsule. Ahmad explains that the described enteric capsule is designed to prevent release of the drug throughout its time in the stomach until it reaches the intestine.”); ¶67 (“Ahmad discloses an enteric coated capsule such that the capsule does not release drug throughout its time in the stomach. Thus, Ahmad to [sic] teaches the use of an *enteric coating*.”).

Thus, every portion of Ahmad relied upon by Petitioner describes a “composition containing endoxifen” that can then be coated with a separate external “enteric coating.” *See* EX.1003, 18:19-21 (“When desired, [the] *composition containing endoxifen...can be encapsulated in enteric-coated capsules* to protect it from acids in the stomach”). Critically, these disclosures *fail to disclose an enteric material that is a component (with endoxifen) of the composition itself*. At most, these disclosures purport to describe (1) a pharmaceutical composition of endoxifen (2) encapsulating the finished composition in a separate external enteric coating. *See* EX1003, 18:27-29 (“Enteric coating of capsules filled with composition containing endoxifen...can be done as methods known in the art.”).

Petitioner's reliance on Cole (Ex. 1010) to demonstrate the purported *enablement* of Ahmad further proves that Petitioner's reliance on Ahmad's disclosures is limited to enteric coating, and not enteric material in the drug composition. *See* Pet.20. For example, the Petition relies on Cole to teach "that 'enteric coated' products are designed to remain intact in the stomach and then to release the active substance in the upper intestine' and that 'the reasons for using *enteric coated preparations* are well documented.'" Pet.21. Like Ahmad, and according to Petitioner's own assertions, these disclosures from Cole merely describe the same enteric coating, rather than enteric material in the drug composition. Indeed, Cole provides no teaching, and Petitioner cites to none, on how to formulate a composition where endoxifen and an enteric material are both combined into a single, integrated composition. By using a reference limited to enteric coating to purportedly enable Ahmad's disclosure, Petitioner underscores that it relies on Ahmad for its alleged teaching of a drug composition that is merely encapsulated in an external enteric coating.

Thus, Petitioner identifies no teaching in Ahmad that the enteric material is a component *of the endoxifen composition*, as claimed. This alone is fatal to Petitioner's anticipation Ground 1.

**2. Collateral Estoppel Does Not Apply And Does Not Fix the Petitioner’s Flaw**

Petitioner’s argument that the Board may find various Ground 1 claims anticipated by Ahmad based on the Board’s earlier findings from the ’334 PGR is inapposite. *See* Pet.19. As discussed above in §IIV, the ’334 claims *expressly* recited “endoxifen composition *encapsulated in* an enteric capsule,” and the Board’s analysis hinged on that language. *See, e.g.*, EX2018, 5. In contrast, the ’391 claims deliberately dispense with the capsule limitation and instead require a distinct composition, *i.e.*, combination of both endoxifen and enteric material, which ***Petitioner never asserts is disclosed by Ahmad.***<sup>5</sup> *See VirnetX Inc.*, 909 F.3d at 1377 (requiring “a prior action present[ing] an identical issue” and that “the prior action actually [was] litigated” for collateral estoppel to apply); *Sacramento Mun. Util. Dist.*, 566 F. App’x at 994; *Palo Alto Networks, Inc.*, IPR2021-01153, Pap.10, 18

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<sup>5</sup> In the event this PGR is instituted, PO may also address other differences in the claims. For example, the Board in the ’334 relied on its determination that those claims were narrow because they claimed only free base forms of Formula (III) of endoxifen and not the salt forms. *See Intas Pharms. Ltd.*, PGR2023-00043, Pap.37, 10-13. The claims here, in contrast, explicitly cover both free base and salt forms. EX1001, cl.1 (“the endoxifen comprises a compound of Formula (III)...or a pharmaceutically acceptable salt thereof”).

(“Collateral estoppel does not apply because there are differences between the claim limitation at issue here and the adjudicated claim limitations at issue in the prior IPRs.”). Petitioner’s attempt to invoke “collateral estoppel” fails under the very authority it cites. *See Google LLC v. Hammond Develop. Int’l, Inc.*, 54 F.4th 1377, 1381 (Fed. Cir. 2022) (holding that for collateral estoppel to apply, a party must show, *inter alia*, “resolution of the issue was essential to a final judgment in the first action”).

### 3. The Dependent Claims Are Not Anticipated

Because Ahmad fails to disclose a necessary element of independent claims 1 and 32, Ahmad also fails to anticipate any of the Challenged Claims that depend from them.

Petitioner’s incorrect interpretation of the Challenged Claims is underscored by its analysis of various of the dependent claims, where Petitioner addresses a composition comprising endoxifen but *not* a composition comprising both endoxifen *and* an enteric material. For example, claim 9 requires “the composition is formulated as a suspension.” The plain language of this claim therefore requires that the endoxifen and the enteric material be part of the suspension. Claims 11-15 and 31 depend from claim 9 and include additional requirements regarding that claimed suspension. In Ground 8, Petitioner acknowledges “the composition” in claim 9 includes both the enteric material and the endoxifen and that *both* must be part of

the suspension. Pet.74 (arguing the claim requires the “enteric material is suspended *in a fluid with the endoxifen*”). However, in Ground 1, for claims 9 and those that depend from it, Petitioner does not even mention “enteric material” or attempt to show that the enteric material is part of the claimed suspension. Pet.28-30. Petitioner attempts to show only that the endoxifen meets the requirements of the suspension. See Pet.28 (for claim 9, arguing only that Ahmad teaches “[p]harmaceutical preparations...include...suspensions”; for claim 11, arguing “Ahmad teaches that (Z)-endoxifen can be administered as a suspension” and saying nothing about the enteric material), Pet.29 (for claims 12 and 14, arguing “Ahmad teaches that its composition of (Z)-endoxifen can include an alcoholic vehicle...Ahmad would have been used as a fluid with Ahmad’s suspension containing (Z)-endoxifen”), 29-30 (for claims 13, 15, and 31, arguing “Ahmad teaches that its composition of (Z)-endoxifen can include an alcoholic vehicle such as ethanol... POSA would have understood that the ‘alcoholic vehicle’ of ethanol described by Ahmad would have been used as a fluid”); see also EX1033, ¶¶70-75. Similarly, claims 4-6, which recite a tablet, capsule, or delayed-release formulation, are not anticipated because Petitioner points to no teaching in Ahmad showing that it teaches that these dosage forms are made from the specific integrated endoxifen-enteric material composition required by claim 1. See Pet.26-28; see also, e.g., Pet.30-31 (regarding claim 23 (requiring a disintegrant in the composition), and

arguing Ahmad teaches composition of the active ingredient and a disintegrant); 33-34 (arguing pharmacokinetics properties of “Ahmad’s composition”). The same is true for every other challenged dependent claim.

Additionally, Petitioner’s anticipation by inherency argument for claims 36, 37, 40, and 41 (Pet.33-34), which recite pharmacokinetic (PK) properties, fails for the same reasons the Board rejected Petitioner’s inherency arguments in the ’334 PGR. To prove anticipation by inherency, Petitioner must show that the claimed pharmacokinetic (PK) properties are *necessarily* present in the Ahmad reference, not merely probable or possible. *See Intas Pharms. Ltd.*, PGR2023-00043, Pap.37 at 47-48 (citing *Endo Pharms. Sols., Inc. v. Custopharm Inc.*, 894 F.3d 1374, 1381 (Fed. Cir. 2018)). In the ’334 PGR, the Board explicitly found that Petitioner failed to make this showing, stating it was “not persuaded by Petitioner’s inherent...argument” because Petitioner merely assumed, without evidence, that the claimed PK properties “would necessarily be the natural result of administering the 90% (Z)-endoxifen formulation of Ahmad.” *Id.* at 47. The Board reasoned that because the “synthetic pathways of Ahmad and the ’334 Patent are different, [] the resulting products would have different impurity profiles, which would impact the pharmacokinetics of the formulation,” and Petitioner failed to prove otherwise. *Id.* Petitioner presents the same flawed inherency argument here, and has not shown that Ahmad’s composition would necessarily and inevitably result in the specific

pharmacokinetic properties recited in the claims. Its anticipation argument therefore also fails as a matter of law. *See Endo Pharms.*, 894 F.3d at 1381.

Thus, Petitioner has failed to show by a preponderance of the evidence that Ahmad discloses each and every limitation of the Challenged Claims. Accordingly, Ground 1 fails.

## **VI. Petitioner's Obviousness Grounds Fail**

### **A. Ground 2: Ground 2 Does Not Cure (Or Even Address) Ahmad's Failure to Disclose a Composition Comprising an Enteric Material<sup>6</sup>**

Petitioner asserts single-reference obviousness based on Ahmad for Ground 2. Pet.38-46. Other than Ground 1, Ground 2 is the only Ground that challenges the independent claims. However, Petitioner's Ground 2 arguments for the independent claims does not fix (or even try to fix) Ground 1's failing regarding the requirement that the composition include *both* endoxifen and enteric material and asserts only single-reference obviousness based on Ahmad. Pet.38-46. Because Petitioner *does*

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<sup>6</sup> The Petition's obviousness Ground 2 relies on its anticipation arguments in Ground 1 and fails to provide any independent analysis or evidence for, *e.g.*, claim 30. *See* Pet.38-39. As noted above, Ground 1 also failed to provide *any* analysis of, *e.g.*, claim 30. *See* n.4. Therefore, by failing to offer *any* analysis or evidence, Petitioner has failed to meet its burden for any obviousness challenge under Ground 2 to claim 30.

*not offer even an allegation* (let alone particularized arguments, or citation to a relevant disclosure) that a POSITA would have included the enteric material within the endoxifen composition itself, as claimed, this perfunctory sentence cannot cure Ahmad's fatal omission. Thus, just as Ahmad fails to anticipate the Challenged Claims, it fails to render them obvious.

**B. Grounds 3-7: Petitioner's Arguments Regarding Dependent Claims Fail Because Petitioner Failed to Establish the Independent Claims Are Anticipated or Obvious**

Petitioner's obviousness arguments in Grounds 3 through 7 would modify Ahmad by adding specific additional features recited in the dependent claims, such as a particular salt, excipient, dosage form, or pharmacokinetic property. However, as established in detail above, Ground 1 and Ground 2 fail for both independent claims because Ahmad does not teach (and Petitioner has not argued that Ahmad alone renders obvious) the "composition comprising an endoxifen and an enteric material." Thus, Petitioner's arguments for how a POSITA would modify Ahmad to render obvious added limitations in the *dependent claims* are legally deficient, and Grounds 3-7 also fail. One cannot render a dependent claim obvious by adding requirements to a base reference that fails to teach or obviate the independent claim in the first place. See *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992) ("[D]ependent claims are nonobvious if the independent claims from which they

depend are nonobvious.”). Further, Grounds 3-7 fail to specify whether they rely on the independent claim analysis from Ground 1, Ground 2, or both.

Petitioner’s obviousness Grounds 3-7 also reinforce Petitioner’s flawed interpretation that improperly *reads out the enteric material from the claimed composition* required by the independent claims. Indeed, they incorrectly treat the requirements of the dependent claims that are directed to certain requirements of “the composition” as directed only to the claimed endoxifen. *See, e.g.,* Pet.56 (arguing, with respect to claim 10 (Ground 5), “[t]herefore, it would have been routine and within the skill of a POSA to have formulated *a suspension of highly-pure (Z)-endoxifen* as taught by Ahmad with a syrup or elixir vehicle as taught by de Villiers” and never addressing the requirement that the enteric material be part of the suspension), 59-60 (conceding that “Ahmad *does not explicitly disclose the use of an enteric material in a suspension*” and arguing, with respect to claims 12-15 and 31 (Ground 5), “[i]t would have been routine and within the skill of a POSA to have formulated *a suspension of highly-pure (Z)-endoxifen* as taught by Ahmad with an alcohol, ethanol, of sorbitol, mineral oil, plant oils, and/or vegetable oils, as taught by de Villiers” but not addressing the enteric requirement); 69 (arguing, with respect to claim 17-19, 38, and 39, that “[I]ike Ahmad, Cole teaches enteric coated capsules” and that “the active ingredient is...entirely contained in the capsule until

the capsule breaks open” and not addressing the requirement that the enteric material be part of the composition)).

Because Ahmad fails to disclose or render obvious a necessary element of independent claims 1 and 32, Ahmad also fails to render obvious any of the Challenged Claims that depend from them. Accordingly, Grounds 3-7, which address only dependent claims, entirely fail as well, and the Petition should be denied. *See Azurity Pharms., Inc. v. Exelixis Inc.*, IPR2025-00210, Pap.11, 29 (June 4, 2025) (denying institution based on the merits, finding that “on the current record Petitioner has not shown that the combination of [the asserted art] would inherently result in [the claimed limitation] and Petitioner has not shown that it has a reasonable likelihood that it would prevail on the obviousness ground.”).

**C. Ground 2: Petitioner’s Throwaway Obviousness Arguments Are Insufficient to Meet its Burden**

The petition must include “a detailed explanation of the significance of the evidence,” including “where each element of the claim is found in the prior art patents or printed publications relied upon.” 37 C.F.R. §§42.22(a)(2), 42.104(b)(4). This requirement is “of the utmost importance.” *Intelligent Bio-Systems, Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1369 (Fed. Cir. 2016). Petitioner’s obviousness analysis for nearly all claims in Ground 2 (claims 1, 2, 4-6, 8, 9, 11-15,

20, 23, 26-37, and 40-44), on the other hand, rest on a single throwaway paragraph.<sup>7</sup> *See* Pet.38-39. In this paragraph, Petitioner fails to even identify any specific claim element that it contends may be missing from Ahmad and thus necessarily fails to provide the required obviousness analysis, including an explanation and support for how and why a POSITA would have been motivated to modify Ahmad to include any such missing element. *See In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364,

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<sup>7</sup> Instead of relying on Ahmad for each limitation, Petitioner asserts “each of the elements of these claims were also separately known and obvious in view of the knowledge of a POSA.” Pet.38. And while Petitioner identifies certain *other* references that it argues disclose discrete limitations of the claim, those references are not part of the Ground. Instead, Petitioner relies on extensive conclusory assertions from its experts to suggest that those non-asserted prior art disclosures represent the “view of the knowledge of a POSA.” *Id.* For example, Dr. McConville’s “opinions” are largely verbatim or near-verbatim assertions merely parroted from the Petition without any independent analysis or supporting evidence. *Compare* Ex. 1033 ¶¶ 53-145 with Pet.19-72. Such conclusory testimony that merely echoes the Petition should be accorded little to no weight. *See cxLoyalty, Inc. v. Maritz Holdings Inc.*, 986 F.3d 1367, 1378 (Fed. Cir. 2021); *see also* 37 C.F.R. §42.65(a).

1380 (Fed. Cir. 2016) (“To satisfy its burden of proving obviousness, a petitioner cannot employ mere conclusory statements. The petitioner must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness.”); *In re Lee*, 277 F.3d 1338, 1345 (Fed. Cir. 2002) (“The board cannot rely on conclusory statements when dealing with particular combinations of prior art and specific claims, but must set forth the rationale on which it relies.”); *Apple Inc. v. Identity Security LLC*, IPR2022-00170, Pap.9, 28 (July 5, 2022) (denying institution when Petitioner failed to “sufficiently articulate[]” why a person of ordinary skill in the art would have combined the asserted references.); *Sensus USA, Inc. v. Certified Measurement, LLC*, IPR2015-01454, Pap.15, 17 (Dec. 14, 2015) (denying institution where Petitioner “relies on a blanket assertion” of obviousness and “provides no meaningful analysis of its obviousness challenge... independent of its anticipation challenge”). Accordingly, at least 32 of the 34 claims challenged in Ground 2 (claims 1, 2, 4-6, 8, 9, 11-15, 20, 23, 26-37, and 40-44) fail for this independent reason.

**D. Ground 2: Petitioner’s Obviousness Argument for Claim 16 Additionally Fails Because It Relies on Heavily Modified Experiments Performed on a *Different* Reference**

Petitioner fails to identify “with particularity” its challenge to claim 16. 35 U.S.C. §322(a)(3). While the Petition identifies this ground as obviousness over “Ahmand in view of the knowledge of a POSA” (Pet. 46), the substance of its

argument and its expert's declaration diverges significantly from this stated ground. The Petition itself relies on Dr. Bihovsky's stability testing of (Z)-endoxifen synthesized according to another reference, *Liu* (not Ahmad) to support its alleged "expectation of success." See Pet.43-44 (arguing "expectation of success" based on "stability testing of Liu"). Dr. Bihovsky's declaration, however, offers two entirely different theories. First, he argues that the claimed stability is *inherently* disclosed by Ahmad in view of Liu's experiments. EX.1034, ¶¶75-76, 78. Second, he argues that claim 16 is obvious over a *combination* of "Ahmad and Liu." *Id.* at ¶¶81-85. Critically, neither theory is actually asserted in the Petition, and should be rejected. See Pet.46; 37 C.F.R. §42.6(a)(3) ("***Arguments must not be incorporated by reference*** from one document into another document."); *3M Co. v. Evergreen Adhesives, Inc.*, 860 Fed.Appx. 724, 725-727 (Fed. Cir. 2021) (affirming the Board's rejection of Petitioner's "attempt to introduce argument by citation to its expert's declaration in violation of 37 C.F.R. §42.6(a)(3)"); *Medtronic, Inc. v. Teleflex Life Scis. Ltd.*, 86 F.4th 902, 906-7 (Fed. Cir. 2023) (rejecting incorporation by reference); see also *Dongguan Juxing Power Co. v. Noco Co.*, IPR2018-00503, Pap.9, 17 (July 11, 2018) (denying institution, noting that "[t]he only discussion in either the Petition or Dr. Schalkwijk's Declaration that is apparently directed to the issue is ¶84 of the Declaration. The Petition itself, however, does not cite or otherwise reference that paragraph of the Declaration."); *Palo Alto Networks, Inc. v.*

*Centripetal Networks, Inc.*, IPR2021-01154, Pap.11, 18-19 (Jan. 24, 2022) (denying institution, explaining that “the Declaration was not cited in the Petition but rather is referred to indirectly in a portion of the Declaration which is cited in the Petition” and “the Petition improperly incorporates this section of the Declaration by reference because the basis of the... argument is not explained sufficiently in the Petition”).

Building on this improperly articulated and ambiguous ground, Petitioner then attempts to import disclosures from Liu *into* Ahmad through unreliable, modified experiments that differ extensively from the actual teachings of Liu. *See, e.g.*, Pet.42-46; EX1034, ¶¶42-72 (modified experiments of Liu). But Dr. Bihovsky’s own declaration reveals that Liu’s process would *not* actually yield his desired result until he rewrote it *in at least nine separate ways*. EX1034, ¶¶45-61. For example, Dr. Bihovsky (1) changed the experiment’s scale from commercial to laboratory (*id.* at ¶¶45, 56n.6); (2) significantly increased reaction temperature because the reaction was incomplete as written (*id.* at ¶48); (3) added an undocumented pre-drying step for a reagent (*id.* at ¶48n.1); (4) used Celite filtration where not specified (*id.* at ¶49n.3); (5) inserted an extra column chromatography purification step (*id.* at ¶49n.4); (6) substituted nitrogen for Liu’s specified argon atmosphere (*id.* at ¶51n.5); (7) replaced filtration with centrifugation (*id.* at ¶56n.6); (8) obtained a different isomer ratio than Liu (*id.* at ¶57n.7); and (9) physically scratched the flask to induce crystallization when it failed to occur as expected (*id.* at ¶58). These represent

significant substantive departures from Liu’s process. Therefore, the resulting composition cannot be considered a product of Liu’s method (which *was not followed*), let alone be used to infer any expectations of success or inherent properties of a composition *from an entirely different reference* like Ahmad. Petitioner’s obviousness argument for Claim 16 is thus built on a foundation of irrelevant and unreliable experimental data, rather than on actual prior art disclosures, and should be afforded no weight.

**E. Grounds 3, 5, and 6: Petitioner’s Improper “And/Or” Grounds Are Not Sufficiently Particular**

Although labeled as single grounds, Petitioner’s Grounds 3, 5, and 6 in fact rely on multiple references and vague, alternative obviousness theories (*e.g.*, using formulations like “/” or “and/or”), thereby significantly inflating the number of asserted grounds beyond the three identified in the Petition. *See e.g.*, Pet.3 (identifying “Ground 3... Obvious over Ahmad in view of Ahmad 2010/Ahmad 2012”; “Ground 5... Obvious over Ahmad in view of de Villiers/Gandhi”; and “Ground 6... Obvious over Ahmad in view of Stegemann/HPE”); *see also id.* at 64 (asserting that “claims 21 and 22 would have been obvious over Ahmad in view of Stegemann *and/or* the HPE”). By presenting such ambiguous grounds, Petitioner fails to identify “*with particularity*... the grounds on which the challenge to each claim is based,” instead improperly shifting the burden to the Patent Owner and the Board to attempt to parse and reconstruct its theories. *See* 35 U.S.C. §322(a)(3);

*Netflix, Inc. v. DivX, LLC*, 84 F.4th 1371, 1377 (Fed. Cir. 2023) (“[I]t is the petitioner’s burden to present a clear argument.”); *Adaptics Ltd. v. Perfect Co.*, IPR2018-01596, Pap.20, 18, 24 (Mar. 6, 2019) (denying Petition for failing to meet the particularity requirement where Petitioner’s reliance on multiple references “connected by the conjunction ‘*and/or*’ results in a multiplicity of grounds, none of which is presented with sufficient particularity”). The Petition should be denied for this additional reason. See *Elk Eng’g Sdn. Bhd. v. Wilco Marsh Buggies & Draglines, Inc.*, IPR2020-00344, Pap.12, 17-22 (Mar. 4, 2021) (denying rehearing of institution denial where petitioner’s four grounds (of 20) lacked particularity and “infected the entire” petition); *Jiangsu Sainty Sumex Tools Corp. v. Milwaukee Elec. Tool Corp.*, IPR2021-00373, Pap.19, 23-24 (July 6, 2021) (denying institution under §314(a) where petitioner’s asserted combinations included “one or more of” five references “in combination with one or more of common knowledge [or] common sense,” explaining this “approach [] raises a formidable number of possible prior art combinations” and finding “no good reason to subject Patent Owner to the burden and expense of a trial based on so many possible prior art combinations”); *ADT LLC v. Vivint, Inc.*, IPR2022-00634, Pap.7, 13-15 (Oct. 4, 2022) (denying institution where one of petitioner’s grounds lacked particularity and petitioner failed to explain the interplay between its two references relied on for the same limitations noting, if IPR were instituted, lack of particularity would prejudice owner).

**F. Ground 7: Petitioner’s Obviousness Combination is Vague**

Petitioner’s Ground 7 obviousness argument additionally fails because it is not clear what Petitioner is modifying, with what teaching, and what modifications would be made as a result. Pet.67-72. On the one hand, Petitioner does not argue that Ahmad alone anticipates or even renders obvious the claims challenged in Ground 7. But on the other hand, Petitioner does not explain how Ahmad would be modified in the context of Ground 7. *See, e.g., Samsung Elecs. Co. v. Imperium (IP) Holdings*, IPR2015-01233, Pap.14, 17 (Dec. 1, 2015) (denying institution of obviousness ground where Petitioner failed to “identify with sufficient specificity what limitations are missing from [the prior art] that a person of ordinary skill in the art would have modified those references to supply”); *Google Inc. v. EveryMD.com LLC*, IPR2014-00347, Pap.9, 26 (May 22, 2014) (denying institution where Petitioner failed to provide “a meaningful explanation of the elements of Belanger’s system that are to be combined with the elements of Shah’s system”). To the extent Petitioner intended to rely on Cole’s enteric coating instead of Ahmad’s, Petitioner provides no explanation for why POSITA would be motivated to change the coating from that Petitioner contends is already disclosed in Ahmad. *See Virtek Vision Int’l ULC v. Assembly Guidance Sys., Inc.*, 97 F.4th 882, 888 (Fed. Cir. 2024) (holding that “an assertion that because two coordinate systems were disclosed in a prior art reference and were therefore “known,” that satisfies the motivation to combine

analysis... is an error as a matter of law. It does not suffice to simply be known. A reason for combining must exist.”); *Life Spine, Inc. v. Globus Med., Inc.*, IPR2022-01603, Pap.8, 40 (June 12, 2023) (denying institution where petitioner “has not articulated sufficient reasoning to explain why a POSITA would modify [its base reference] to address a concern [it] already addresses via a different mechanism”); *Google LLC v. Jawbone Innovations, LLC*, IPR2022-00889, Pap.12, 20 (Nov. 14, 2022) (denying institution where petitioner failed to explain “motivat[ion] to solve a problem [the reference] already solves”).

## **VII. Ground 8: Claims 10, 12-15 and 30 Are Described and Enabled**

Petitioner’s two-paragraph throw-away Ground 8 arguments assert unpatentability based on lack of written description and enablement for claims 10, 12-15, and 30. Pet.73-74. Petitioner provides no expert support for this Ground, and does not provide *any* analysis in the Petition directed to enablement. But the burden is on Petitioner to show, “in writing and with particularity, each claim challenged, the grounds on which the challenge to each claim is based, and the evidence that supports the grounds for the challenge to each claim.” 35 U.S.C. §322(a)(3); *see also Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016); *Microbiotica, Ltd. v. Board of Regents, The Univ. of Texas Sys.*, PGR2023-00026, Pap.12, 26-28 (Nov. 21, 2023) (denying institution where “Petitioner’s enablement challenge repeats the written description arguments in one

sentence, and provides no more analysis, much less under the Wands factors.’’). Here, Petitioner has failed its burden.

For enablement, the standard is whether ‘‘a patent’s specification describe[s] the invention ‘in such full, clear, concise, and exact terms as to enable any person skilled in the art’ to ‘make and use’ the invention.’’ *Amgen Inc. v. Sanofi*, 598 U.S. 594, 612 (2023) (citing §112(a)). ‘‘[A] specification may call for a reasonable amount of experimentation to make and use a patented invention.’’ *Id.* ‘‘Nor is a specification necessarily inadequate just because it leaves the skilled artist to engage in some measure of adaptation or testing.’’ *Id.* at 611. ‘‘Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations.’’ *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

Here, Petitioner’s mere allegation of ‘‘enablement,’’ without providing *any* factual analysis, expert evidence, or application of the governing legal framework (including the *Wands* factors), fails to satisfy Petitioner’s burden to demonstrate lack of enablement with the required particularity and should be rejected accordingly. *See, e.g., Microbiotica, Ltd.*, PGR2023-00026, Pap.12, 26-28 (denying institution where ‘‘Petitioner’s enablement challenge repeats the written description arguments in one sentence, and provides no more analysis, much less under the Wands factors’’); *One World Techs., Inc. v. Chervon (HK) Ltd.*, PGR2020-

00060, Pap.16, 50 (Dec. 7, 2020) (denying institution where “neither Petitioner nor [the expert] analyzes any of the Wands factors to support the contention that undue experimentation would be required to make and use the inventions of the challenged claims”).

Petitioner’s cursory written description argument also fails and is inconsistent with its arguments for claim 9 in Ground 1. Each of the claims Petitioner challenges in Ground 8 depends from claim 9. Petitioner argues in Ground 8 that “the 391 patent specification fails to describe a formulation in which *the enteric material is suspended in a fluid with the endoxifen.*” Pet.74. But, in Ground 1, Petitioner *does not acknowledge the requirement of that the composition be a suspension that includes enteric material* in addition to endoxifen. *See* Pet.28; *see supra* §V.1. Further, as shown in the table below, each of claims 10, 12-15, and 30 is sufficiently described in the ’391 Patent:

Claim	Examples of Disclosure in ’391 Patent
<p>[10] The composition of claim 9, wherein the suspension comprises a syrup or an elixir.</p>	<p><i>See, e.g.,</i> EX1001, 36:12-16 (“In at least some embodiments, the compositions are formulated for oral delivery as tablets, caplets, capsules, pills, powders, troches, <i>elixirs</i>, suspensions, <i>syrups</i>, wafers, chewing gums, dragees, lozenges, and the like.”); 54:33-36 (“wherein the composition formulated for oral delivery is a tablet, a caplet, a capsule, a pill, a powder, a troche, <i>an elixir</i>, a suspension, <i>a syrup</i>, a wafer, a chewing gum, a dragee, and a lozenge.”).</p>

<p>[12] The composition of claim 11, wherein the fluid comprises an alcohol.</p>	<p><i>See e.g.</i>, EX1001, 29:46-59 (“Suitable solvents for making endoxifen gluconate or chemical equivalents thereof include...organic solvents such as <b>alcohols</b>,...<b>fatty alcohols</b>,...and water-miscible solvents such as <b>water miscible alcohols</b>”); 29:67-30:1 (“In some embodiments, the <b>solvent is a dehydrated alcohol</b>, such as absolute alcohol.”); 39:1-16 (“Pharmaceutical preparations disclosed herein may comprise a control release agent. Examples of control release agent suitable for use include...<b>long chain alcohols</b>, such as stearyl alcohol, cetyl alcohol, and polyethylene glycol.”); 54:10-24 (“wherein the composition comprises one or more control release agents selected from the group consisting of...<b>long chain alcohols</b>, such as stearyl alcohol, cetyl alcohol”); 82:40-44 (“Results show the (Z)-endoxifen free base is surprisingly stable in <b>alcoholic</b> (for example ethanol and isopropanol (data not shown)) <b>solutions</b> even at elevated temperatures (40° C.) at higher concentrations over 10 days.”).</p>
<p>[13] The composition of claim 12, wherein the alcohol comprises an ethanol.</p>	<p><i>See, e.g.</i>, EX1001, 29:60-63 (“Water-miscible solvents useful for the preparation of endoxifen gluconate are glycerin, <b>ethanol</b>...”); 82:40-44 (“Results show the (Z)-endoxifen free base is surprisingly stable in alcoholic (for example <b>ethanol</b> and isopropanol (data not shown)) solutions even at elevated temperatures (40° C.) at higher concentrations over 10 days.”).</p>
<p>[14] The composition of claim 9, wherein the suspension comprises an</p>	<p><i>See, e.g.</i>, EX1001, 38:3-11 (“Lubricants that can be used in the pharmaceutical</p>

<p>alcohol, a plant oil, a mineral oil, a glycol, an agar, or a mixture thereof.</p>	<p>compositions provided herein include, but are not limited to, calcium stearate, magnesium stearate, <i>mineral oil, light mineral oil</i>, glycerin, sorbitol, mannitol, <i>polyethylene glycol, other glycols</i>, stearic acid, sodium lauryl sulfate, talc, <i>hydrogenated vegetable oil (e.g., peanut oil, cottonseed oil, sunflower oil, sesame oil, olive oil, corn oil, and soybean oil)</i>, zinc stearate, magnesium stearate or potassium stearate, ethyl oleate, ethyl laureate, <i>agar</i>, and <i>mixtures thereof</i>.”).</p>
<p>[15] The composition of claim 9, wherein the suspension comprises ethanol, mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, vegetable oil, stearic acid, sodium lauryl sulfate, or a mixture thereof.</p>	<p><i>See, e.g.,</i> EX1001, 29:60-63 (“Water-miscible solvents useful for the preparation of endoxifen gluconate are glycerin, <i>ethanol</i>...”); 38:3-11 (“Lubricants that can be used in the pharmaceutical compositions provided herein include, but are not limited to, calcium stearate, magnesium stearate, <i>mineral oil, light mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, other glycols, stearic acid, sodium lauryl sulfate</i>, talc, <i>hydrogenated vegetable oil (e.g., peanut oil, cottonseed oil, sunflower oil, sesame oil, olive oil, corn oil, and soybean oil)</i>, zinc stearate, magnesium stearate or potassium stearate, ethyl oleate, ethyl laureate, agar, and <i>mixtures thereof</i>.”).</p>

### VIII. Institution Should be Denied Under §314(a)

“Even when a petitioner demonstrates a reasonable likelihood of prevailing with respect to one or more claims, ...institution of review remains discretionary.”

*Chevron Oronite Co. v. Infineum USA L.P.*, IPR2018-00923, Pap.9, 10 (Nov. 7,

2018) (informative). Indeed, “the Board may consider the number of claims and grounds that meet the reasonable likelihood standard when deciding whether to institute inter partes review under” §314(a). *Id.* at 10-11 (denying institution where “Petitioner demonstrate[d] at most, a reasonable likelihood of prevailing with respect to two dependent claims out of a total of twenty challenged claims”). The same is true here, particularly in light of Petitioner’s flawed interpretation of the claimed composition required by every claim, as well as the additional fundamental failures of each Ground, which make the analysis of those claims and grounds plainly insufficient to meet the threshold for institution. *See* FAQs for Interim Processes, FAQ 9 (“the Board panel will not address discretionary considerations, except where the petition presents an insufficient number of challenges that meet the reasonable likelihood standard indicating that institution is an inefficient use of resources”); *Deeper, UAB v. Vexilar, Inc.*, IPR2018-01310, Pap.7, 42-43 (Jan. 24, 2019) (informative) (denying institution where “Petitioner demonstrate[d] a reasonable likelihood of prevailing with respect to only two claims on one asserted ground” explaining that “instituting a trial with respect to all twenty-three claims and on all four grounds... would not be an efficient use of the Board’s time and its resources.”); *Nanya Tech. Corp. v. Monterey Rsch., LLC*, IPR2021-00171, Pap.8, 21-22 (May 26, 2021) (denying institution where petitioner could “at best

demonstrate a reasonable likelihood of success” on “8 of 20 challenged claims”);  
*Elk Eng’g Sdn. Bhd.*, IPR2020-00344, Pap.12, 17-22.

Thus, even if, *arguendo*, the Board concludes Petitioner has met its burden for portions of certain Grounds, the Board should nevertheless deny institution under §314(a).

## **IX. Conclusion**

For the reasons stated above, Petitioner has failed to show a reasonable likelihood that it will prevail. Both independent claims, and thus all Challenged Claims of the ’391 Patent, require a composition including both (Z)-endoxifen and an enteric material, but the Petition’s entire case, including its anticipation ground (Ground 1) and every obviousness ground (Grounds 2–7), relies on Ahmad for the claimed composition without ever showing *or even arguing* that Ahmad discloses or obviates it. This fundamental failure of Ahmad to disclose or obviate the claimed composition extends to all of these prior art grounds. Petitioner’s perfunctory argument regarding written description and enablement fares no better, as it is presented without substantive analysis and rebutted by clear disclosure in the ’391. The Petition should be denied.

Respectfully submitted,

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Dated: August 5, 2025

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**CERTIFICATE OF WORD COUNT**

The undersigned certifies that the foregoing Patent Owner’s Brief In Support Of Discretionary Denial Under 35 U.S.C. §314(a) complies with the type-volume limitation in 37 C.F.R. §42.24(c)(1) and the “Interim Processes for PTAB Workload Management” (Mar. 26, 2025). According to the word-processing system’s word count, the brief contains 8,358 words, excluding the parts of the brief exempted by 37 C.F.R. §42.24(a)(1).

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**CERTIFICATE OF SERVICE**

The undersigned hereby certifies that a copy of Patent Owner’s Brief In Support Of Discretionary Denial Under 35 U.S.C. §314(a) and the accompanying exhibits have been served in their entirety on August 5, 2025, by causing the aforementioned documents to be electronically mailed to the following attorneys of record for the Petitioner listed below.

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