

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ENCUBE ETHICALS PVT. LTD.,
Petitioner

v.

DERMAVANT SCIENCES GMBH,
Patent Owner

Case IPR2024-00834
U.S. Patent No. 11,590,088

**PATENT OWNER PRELIMINARY RESPONSE
UNDER 37 C.F.R. § 42.107(a)**

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I. INTRODUCTION

The Board should deny institution of *inter partes* review of the '088 patent because the Petition fails on multiple fronts to establish a reasonable likelihood of prevailing with respect to any challenged claim.

First, the Board should exercise its discretion to deny institution under 35 U.S.C. § 325(d). The Petition advances the same or substantially the same art presented to the Office during prosecution without any showing of Examiner error.

The relevant inquiry for the first step in *Advanced Bionics* is whether the Petition presents the same or substantially the same prior art or arguments that were previously presented to the Office. *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 7-8 (P.T.A.B. Feb. 13, 2020) (precedential). That first step is met here: all three references forming the Petition's Grounds—Bissonnette, Sonti, and Chen—were squarely before the Office during prosecution.

First, Petitioner Encube wrongly states that Bissonnette was never before the Office, when in fact the Examiner clearly considered and acknowledged Bissonnette in an IDS. Next, the *patent that issued* from Sonti was also previously presented to the Office in an IDS, and Sonti itself was cited in the '088 patent specification. Finally, not only was Chen cited in an IDS, it is also cumulative to three other Chen references that the Examiner asserted in three novelty rejections

during prosecution.

Given that *Advanced Bionics* step one is clearly met, Encube must show that the Examiner materially erred (*Advanced Bionics* step two) to avoid discretionary denial. But Encube has fallen far short of its burden because its allegation of Examiner error amounts to simple disagreement with the Examiner for not raising the same rejections set forth in the Petition, and not actual error. It is well-established that a mere absence of a rejection based on certain references does not evidence material error. *See Ivantis, Inc. v. Sight Sciences, Inc.*, IPR2022-01533, Paper 14 at 19 (P.T.A.B. Mar. 27, 2023). Moreover, “[i]f reasonable minds can disagree regarding the purported treatment of the art or arguments, it cannot be said that the Office erred in a manner material to patentability.” *Advanced Bionics*, Paper 6 at 9. The Petition is a textbook example of a recycled and rehashed argument that *Advanced Bionics* and 35 U.S.C. § 325(d) ward against.

Second, the Board should also exercise its discretion to deny institution under 35 U.S.C. § 314(a) because the Petition fails to explain its arguments with particularity, as required by 35 U.S.C. § 312 and 37 C.F.R. §§ 42.22(a)(2) and 42.104(b). Throughout all four of its Grounds, Encube repeatedly presents undeveloped and unsupported arguments, which are muddled by frequent internal cross-referencing and improper incorporation by reference. The Petition begins by relying on an inherency theory to meet an express claim limitation in claim 1, yet

never makes a showing to meet the stringent legal standard for inherency. The Petition repeats this deficient argument in each of its obviousness Grounds. And, despite Board decisions and guidance against it, the Petition adopts the oft-criticized tactic of using the phrase “and/or” in half of its Grounds, creating further ambiguities throughout the Petition’s arguments.

What’s more, these deficiencies—which standing alone warrant denial of institution—are further amplified by the Petition’s failure to abide by the Board’s rules on word limits (the Petition is nearly 1,000 words over the limit), and its repeated use of improper incorporation by reference tactics. 37 C.F.R. §§ 42.6, 42.24. Encube has ignored clear statutory requirements for an IPR Petition and brushed aside the Board’s rules and precedential Decisions concerning the same. These failures, both alone and collectively, justify the Board to exercise its discretion to deny institution. Taken together with the Petition’s failure to satisfy § 325(d), the cumulative weight towards denying institution becomes unavoidable.

Third, although the Board need not reach the merits of the Petition in view of the defects discussed above, should the Board nevertheless decide to do so, each Ground fails to establish a reasonable likelihood of prevailing on any challenged claim. The Petition’s anticipation ground (based on Sonti) picks and chooses various claim elements out of nearly one million different options disclosed in Sonti, without providing any explanation or rationale. Such picking and choosing

approach “has no place in the making of a 102, anticipation rejection.” *In re Arkley*, 455 F.2d 586, 587-588 (C.C.P.A. 1972).

The Petition’s obviousness Grounds fare no better, as all three Grounds rely on gross mischaracterizations of the disclosures in Sonti, a misreading of the disclosures in Chen, and self-serving disregard for the disclosures in Bissonnette. Contrary to Encube’s portrayal, Chen does *not* disclose using tapinarof to treat plaque psoriasis. This is a major oversight in the Petition and is relevant to all three obviousness Grounds. Additionally, disclosures in Sonti *confirm* that Chen does not disclose using tapinarof, stating Chen applied “an active ingredient” to its Volunteers. Meanwhile, Bissonnette directly contradicts the Petition regarding a POSA’s motivation and reasonable expectation of success. The Petition relies upon the presence of serious adverse events or patient compliance to argue motivation, but Bissonnette discloses applying tapinarof *twice daily* to successfully treat plaque psoriasis with no serious adverse events or patient compliance issues. Unlike the Petition, a POSA would not ignore these disclosures in Bissonnette.

Lastly, the Petition also fails because it does not address *known* objective indicia of non-obviousness that Encube possessed at the time of the Petition—evidence disclosed in the ’088 patent itself. Thus, the Petition presents a deficient obviousness case, and does not—indeed, cannot—establish a reasonable likelihood of prevailing on any of its Grounds.

The Board should deny institution.

II. OVERVIEW OF THE '088 PATENT

The '088 patent relates to a novel method for treating mild to severe plaque psoriasis comprising topically administering a composition containing about 1.0% tapinarof to a subject once a day. Patent Owner “surprisingly and unexpectedly found” that 1% tapinarof cream formulation applied topically once daily was just as effective as applying 1% tapinarof twice daily. EX1001, 6:52-60. The innovation behind the '088 patent catalyzed the development and launch of the FDA-approved product, VTAMA®, which has helped thousands of plaque psoriasis patients find relief.

The '088 patent claims a method for treating mild to severe plaque psoriasis in a subject comprising topically administering 1% tapinarof to affected areas once a day wherein after topical administration, the subject obtains an improvement to the Physician Global Assessment (PGA) score of 2 grades or achieves a PGA score of 0 or 1. EX1001, 101:42-48. Certain dependent claims recite methods comprising oil-in-water emulsion compositions comprising specific excipients. *Id.*, 101:49-59.

III. PERSON OF ORDINARY SKILL IN THE ART

For the purposes of this Preliminary Response, Patent Owner applies Encube’s POSA definition, but reserves the right to submit its own definition should the Board decide to institute trial.

IV. THE BOARD SHOULD DENY INSTITUTION UNDER 35 U.S.C. § 325(d)

Encube's Petition (1) advances the same or substantially the same art and arguments that were previously presented to the Office and (2) has not demonstrated that the Examiner erred in a manner material to patentability when allowing the challenged claims to issue. Section 325(d) allows the Board to deny institution when these two conditions are met. *See Advanced Bionics*, Paper 6 at 8.

The Petition fails both prongs of *Advanced Bionics*. First, each of Sonti, Chen and Bissonette were indisputably presented to the Office during prosecution.

Second, the Petition identifies no cognizable material error by the Examiner, which is Encube's burden to show. At best, all the Petition shows is mere disagreement with the Examiner for not raising the same rejections set forth in the Petition; not legal error. The absence of a particular rejection does not evidence an error, nor does it provide a basis for institution. *See, e.g., Ivantis*, IPR2022-01533, Paper 14 at 19.

The Board should deny trial and preclude Petitioner from retreading art that the Office has already properly considered.

A. *Advanced Bionics* step one is met: the same prior art previously was presented to the Office

Every reference relied upon in Grounds 1-4 was previously presented to the Office, meeting step one of the *Advanced Bionics* framework.

1. Bissonnette previously was presented

Remarkable, the Petition asserts that: “Bissonnette ... was not before the Office during prosecution and has never been considered.” Pet., 71. This is untrue. Bissonnette, listed on the ’088 patent face page, was cited as Non-Patent Literature Document 4 in an IDS submitted July 22, 2022, and the Examiner acknowledged considering Bissonnette on October 17, 2022. EX1002, 177, 247. Contrary to Encube’s misrepresentation, Bissonnette was presented¹ to the Office, satisfying *Advanced Bionics* step one. See also *Biocon Pharma Ltd. v. Novartis Pharmaceuticals Corp.*, IPR2020-01263, Paper 12 at 9 (P.T.A.B. Feb. 16, 2021) (denying institution because the same or substantially the same reference was listed in an IDS and the Examiner considered it).

2. Sonti previously was presented

Encube admits, “[t]he patent that issued from the Sonti publication—U.S. 10,195,160—is also cited on the face of the ’088 patent ...” Pet., 72 fn. 10. This is

¹ “Previously presented art includes art made of record by the Examiner, and art provided to the Office by an applicant, such as on an Information Disclosure Statement (IDS), in the prosecution history of the challenged patent.” *Advanced Bionics*, Paper 6 at 7–8.

dispositive of *Advanced Bionics* step one. The Sonti '160 patent, listed on the '088 patent face page, was cited as U.S. Patent Document 9 in an IDS submitted July 22, 2022, and the Examiner acknowledged considering the Sonti '160 patent on October 17, 2022. EX1002, 175, 245.

Encube also admits that the '088 patent specification cites and discusses Sonti, but argues it does not meet *Advanced Bionics* step one because Sonti was cited in a section discussing formulations, and “was never discussed by the examiner,” which, according to the Petition, means that “[t]here is no indication Sonti’s teachings regarding methods of treating were ever presented to the Office” Pet., 72. Petitioner’s assertion is wrong as a matter of law. But importantly, whether a reference was “discussed” is not the standard. The relevant inquiry is “whether proffered art or arguments are ‘the same or substantially the same’ as art or arguments previously presented to the Office.” *Advanced Bionics*, Paper 6 at 7. Encube made no attempt to satisfy that inquiry here.

The Petition relies on *Samsung Bioepis Co., Ltd. v. Alexion Pharms., Inc.*, IPR2023-00998, Paper 9 (P.T.A.B. Dec. 8, 2023) to incorrectly assert that “[t]here is no indication Sonti’s teachings regarding *methods of treating* were ever presented to the Office.” Pet., 72 (emphasis in original). Encube is wrong. *Samsung* says nothing about a need to refer to specific teachings in a reference cited in an IDS. Rather, *Samsung* found that references that were cited in an IDS,

or cumulative to those cited, that the Examiner acknowledged satisfied *Advanced Bionics* step one. *Id.*, 62-63. That principle applies with the same force here for Sonti.

3. Chen previously was presented

Chen, too, previously was presented. Petitioner ignores that Chen, listed on the '088 patent face page, was cited as U.S. Patent Document 6 in an IDS filed July 22, 2022, and the Examiner acknowledged considering Chen on October 17, 2022. EX1002, 174, 244. Chen satisfies *Advanced Bionics* step one.

Further, the Petition admits that “Chen (Ex-1013) does contain disclosures similar to the Chen references that were before the examiner (Ex-1027–Ex-1029).” Pet., 72. This is an understatement. The relied-upon disclosures are identical. For example:

Chen (EX1013)	Chen 1, (EX1027), Chen 2 (EX1028), Chen 3 (EX1029)
“A 1% cream of 3,5-dihydroxy-4-isopropylstilbene was prepared for tests on volunteers.” EX1013, 32:25-26; Pet., 31.	“A 1% cream of 3,5-dihydroxy-4-isopropylstilbene was prepared for tests on volunteers.” EX1027, ¶[0096], EX1028, ¶[0171], EX1029, ¶[0190].
“The Volunteers were treated once per day by applying the creams once per day on top of the affected area with the	“The Volunteers were treated once per day by applying the creams once per day on top of the affected area with the

Chen (EX1013)	Chen 1, (EX1027), Chen 2 (EX1028), Chen 3 (EX1029)
basic cream as the control.” EX1013, 32:41-43; Pet., 31.	basic cream as the control.” EX1027, ¶[0099], EX1028, ¶[0175], EX1029, ¶[0194].
“Volunteer 2, Female, 24 years old with plaques on her back.” EX1013, 32:35; Pet., 58.	“Volunteer 2, Female, 24 years old with plaques on her back.” EX1027, ¶[0098], EX1028, ¶[0173], EX1029, ¶[0192].
“Results: the inventive compound showed great efficacy on the Volunteers treated in comparison with the untreated areas and before and after treatment.” EX1013, 32:51-53; Pet., 31.	“Results: the inventive compound showed great efficacy on the Volunteers treated in comparison with the untreated areas and before and after treatment.” EX1027, ¶[0100], EX1028, ¶[0176], EX1029, ¶[0195].

Chen EX1013 is undoubtably cumulative to the EX1027, EX1028, and EX1029 Chen references that each formed the basis of a rejection during prosecution. EX1022. The Petition makes no attempt to show otherwise. For this second reason, Chen satisfies *Advanced Bionics* step one. *See Bio-Rad Lab’s, Inc. v. 10x Genomics*, IPR2019-00566, Paper 21 at 7-11 (P.T.A.B. July 22, 2019) (denying institution because “Petitioner has not indicated, in the context of 35 U.S.C. § 325(d), any material differences” from art presented in an IDS).

The Petition then asserts that “Chen is a secondary reference” and “the Bissonnette/Chen combination was not previously before the Office.” Pet., 72. As already explained, the Petition is wrong because Bissonnette *was* previously before the Office, and its combination with Chen does not change the fact that Chen, too, previously was presented and is indisputably cumulative to art raised in rejections during prosecution.

B. *Advanced Bionics* step 2 is met: Encube provides no evidence of Examiner error

Not only was each of the relied-upon references previously provided to the Office, Encube failed to provide any evidence that the Office erred in a manner material to patentability. *Advanced Bionics*, Paper 6 at 7.

1. The Petition is silent about Examiner error for Bissonnette

For Bissonnette, the Petition asserts solely that “[t]he first condition [of *Advanced Bionics*] is not satisfied,” without any explanation of Examiner error. Pet., 71. This is fatal to Encube’s ability to meet its burden: “[i]f a condition in the first part of the framework is satisfied and *the petitioner fails to make a showing of material error*, the Director generally will exercise discretion not to institute inter partes review.” *Advanced Bionics*, Paper 6 at 8-9 (emphasis added);. Encube has waived any step-two arguments for Bissonnette.

2. The Petition fails to show Examiner error for Sonti

The Petition admits that Sonti previously was presented to the Office but

then speculates that, “to the extent the examiner considered Sonti, the examiner evidently overlooked that Sonti is not just about formulations,” and “[t]here is no indication Sonti’s teachings regarding methods of treating were ever presented to the Office; if they were, then the examiner materially erred by overlooking them.” Pet., 72. But an Examiner’s silence does not evince material error.

First, the full disclosure of Sonti was squarely before the Examiner. This belies Encube’s assertion that “[t]here is no indication Sonti’s teachings regarding methods of treating were ever presented to the Office.” Encube’s argument of material error for Sonti distills to a complaint that the Examiner did not reject the issued claims using Encube’s preferred theories of patentability. But the mere absence of a rejection based on certain references does not evidence material error. *See Ivantis, Inc.*, IPR2022-01533, Paper 14 at 19 (“To the extent Petitioner equates Examiner’s silence in discussing relevant prior art to a material error ..., we are not persuaded.”).

Second, Encube’s assertion that “the examiner materially erred by overlooking [Sonti’s teachings]” is conclusory speculation. Examiners must receive some deference as they are presumed to perform their duties and responsibilities as examiners, understand the cited references, and issue only valid patents. *PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1304 (Fed. Cir. 2008). That is the purpose of the *Advanced Bionics* test. *Advanced Bionics*, Paper 6

at 9 (“At bottom, this framework reflects a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown.”).

The fact that Encube is dissatisfied with the result of prosecution does not show the “material error” required to avoid discretionary denial under § 325(d). After all, “[i]f reasonable minds can disagree regarding the purported treatment of the art or arguments, it cannot be said that the Office erred in a manner material to patentability.” *Advanced Bionics*, Paper 6 at 9.

3. The Petition fails to show Examiner error for Chen

Encube asserts that the Examiner purportedly erred when considering Chen for: (1) being unaware that Chen disclosed treating “plaque psoriasis” and (2) not appreciating that “a POSA would have understood that while Chen did not specifically refer to PGA scores, it did disclose improvements that a POSA would have understood to be the PGA score improvements claimed.” Pet., 73. Neither assertion is supported by the prosecution history. Moreover, a careful review of the prosecution history—which Encube failed to do—evidences the Examiner’s rational reasoning about patentability despite the disclosures in Chen.

a. Encube’s argument around “plaque psoriasis” cherry-picks quotes from the prosecution history

First, the prosecution history refutes Encube’s assertion that the Examiner did not appreciate that Chen disclosed plaque psoriasis.

During prosecution, the Examiner raised three rejections over “Chen 1”

(EX1027), “Chen 2” (EX1028), and “Chen 3” (EX1029) (EX1002, 234-37). For each reference, the Examiner stated: “Since this reference teaches the exact methods, Applicant’s claims are anticipated, and thus, rejected under 35 U.S.C. 102.” EX1002, 236-237. Applicant presented arguments distinguishing the claims from Chen 1, 2, and 3. EX1002, 284-286.

Encube’s Petition chose to ignore the Examiner’s statements that Chen 1, 2, and 3 each “teaches the exact methods” in the claims—methods directed to treating plaque psoriasis. Given the Examiner’s unambiguous statement that Chen 1, 2, and 3 each “[taught] the *exact* methods” in the claims, and presuming—as we must—that the Examiner properly performed his duties, the Examiner’s statement indicates that he was aware of the full disclosure of Chen 1, 2, and 3, including any teachings related to plaque psoriasis. Hoping to show material error, the Petition instead says simply “contrary to what the applicant argued, Chen did disclose treating specifically ‘plaque’ psoriasis” (Pet, 72), implying that applicant’s argument overcoming the Chen 1, 2, and 3 rejections was simply, and solely, that Chen did not disclose treating plaque psoriasis. This is wrong.

Applicant argued that the pending claims were novel because, e.g.: “Chen 1 does not mention treating plaque psoriasis specifically with the compounds described therein;” “Even if Chen 1 disclosed treatment of plaque psoriasis, Chen 1 does not disclose: (i) how to demonstrate that effective treatment of said plaque

psoriasis can be done via numerous measurements, or (ii) what is a measure of effective treatment of said plaque psoriasis.” EX1002, 284. Applicant further asserted that “Chen 1 makes no mention of how to demonstrate that treatment of said plaque psoriasis is effective” and “Chen 1 makes no mention of what is a measure of effective treatment of said plaque psoriasis.” *Id.*² In other words, Applicant repeatedly discussed plaque psoriasis in the context of the Chen references and, rather than simply deny the existence of plaque psoriasis in Chen—as Petitioner wrongly posits—Applicant actually demonstrated to the Examiner’s apparent satisfaction³ that Chen 1, 2, and 3, each “does not teach each and every element of the pending claims,” as required to show a lack of novelty. *Id.*, 284-286.

b. Encube’s argument of material error around “PGA scores” identifies no actual error

Encube acknowledges that Chen does not refer to PGA scores (as applicant

² Applicant made similar arguments for Chen 2 and Chen 3. EX1002, 285-286.

³ In the next Office Action, the Examiner considered Applicant’s arguments “moot because the new ground of rejection does not rely on any reference applied in the prior rejection of record for any teaching or matter specifically challenged in the argument.” EX1002, 292.

noted in prosecution) but nevertheless asserts that the Examiner overlooked that Chen “did disclose improvements that a POSA would have understood to be the PGA score improvements claimed.” Pet., 73. Once again, Encube’s mere dissatisfaction with the result of prosecution does not show the “material error” required to avoid discretionary denial under § 325(d). To show material error, the Petition must demonstrate *how* the Examiner erred—e.g., explaining why the Examiner misapprehended or overlooked the specific, material teachings of the relevant art. The Petition never did this for Chen. *See Bio-Rad Lab’ys, Inc.*, Paper 21 at 11 (finding § 325(d) denial appropriate when “Petitioner has not explained *how* the Examiner erred in its evaluation of the asserted prior art ... [i]nstead, Petitioner has only alleged that the Examiner failed to fully appreciate th[e] references alone and/or in combination.”) (emphasis added).

Encube never identifies *how* the Examiner erred in its evaluation of the asserted art, instead simply speculating that the Examiner “evidently erred or overlooked material disclosures in Chen.” Pet., 72-73. “Discretion to deny institution is appropriate when Petitioner’s argument collapses to an argument that the Petition demonstrates that the claims are unpatentable over this combination, so the Examiner must have materially erred in allowing the claims.” *Medtronic Corevalve LLC v. Speyside Medical, LLC*, IPR2021-00240, Paper 9 at 31 (P.T.A.B. July 23, 2021). Encube’s grounds are premised on exactly this sort of

impermissible reasoning.

c. The Examiner understood that Chen did not disclose applying tapinarof to Volunteers in its Example; Encube does not address this point

Encube also ignored key portions of the prosecution history, including statements in the Notice of Allowability that evidence why the Examiner found the claims patentable over Chen. Encube's failure to fully consider the Examiner's reasons for allowance is yet another fatal omission in its superficial 325(d) analysis.

In the Notice of Allowability, the Examiner stated: "the methods were not found to be obvious or anticipated by the prior art of record. The prior art does not teach or suggest the methods encompassing *compounds substituted in the manner claimed* by the Applicant." EX1002, 312 (emphasis added). This important statement was entirely overlooked in the Petition. The Examiner's conclusion that the "prior art of record," i.e., Chen 1, 2, and 3, does not teach or suggest "methods encompassing compounds substituted in the manner claimed" demonstrates that the Examiner understood that the compound disclosed in Chen's Examples cited in the rejection (and relied upon here in this Petition) was *not* tapinarof.

The Chen references disclose that the subjects in the Examples "were treated once per day by applying the creams once per day on top of the affected area with the basic cream as the control" and "[t]he cream of the invention contained 1%.

3,5-dihydroxy-4-isopropylstilbene, and the other components in the cream described in Example 2(d)⁴.” EX1027, ¶[0099]; EX1028, ¶[0175]; EX1029, ¶[0194]. The Examiner is correct that Chen (1, 2, and 3) “does not teach or suggest the methods encompassing *compounds substituted in the manner* claimed by the Applicant.” EX1002, 312. In other words, it does not teach or suggest applying *tapinarof* according to the ’088 patent claims.

Tapinarof is 3,5-dihydroxy-4-isopropyl-*trans*-stilbene. EX1001, 7:4-20; EX1025, page 3 (“tapinarof is 3, 5-dihydroxy-4-isopropyl-trans-stilbene”). Encube and its declarants acknowledge this. Pet., 8 FN4 and 14 (“‘3,5-dihydroxy-4-isopropyl-trans-stilbene’ which is tapinarof.”); EX1032, ¶¶56, 63, 64; EX1003, ¶77 FN4 and ¶89. But the compositions in each of Chen 1, 2, and 3 “encompass both the trans and cis stereochemical forms of the compounds, and mixtures of the trans and cis forms.” EX1027, ¶[0042]; EX1028, ¶[066]; EX1029, ¶[0083]. Indeed, the Chen 1, 2, and 3 references each expressly lists 3, 5-dihydroxy-4-isopropyl-*trans*-stilbene when relevant. *See, e.g.*, EX1027, ¶¶[0048], [0057], [0107]; EX1028, ¶¶[0102], [0114], [0179]; EX1029, ¶¶[0112], [0119], [0198]. But the Chen references also recite 3, 5-dihydroxy-4-isopropylstilbene (without a *cis* or *trans*

⁴ The other components in the cream described in Example 2(d) are ethanol and “Glaxal base cream.” EX1027, ¶[0088].

designation) numerous times, too. *See, e.g.*, EX1027, ¶¶[0024], [0091], [0099]; EX1028, ¶¶[0057], [0169], [0175]; EX1029, ¶¶[0112], [0188], [0194]. Thus, Chen clearly knew when to designate the compounds as a *cis* form, a *trans* form, or a form that is a mixture of the two. That matters.

In the example applying the 1% cream to Volunteers, Chen applied 1% “3,5-dihydroxy-4-isopropylstilbene.” EX1027, ¶[0099]; EX1028, ¶[0175]; EX1029, ¶[0194]. Since Chen confirms that the compound can be in *cis*, *trans*, or a mixture of the two, Chen’s disclosures of applying “3,5-dihydroxy-4-isopropylstilbene” is a disclosure of using the mixture of *cis* and *trans* forms. Chen did not apply a composition containing 1% tapinarof (3,5-dihydroxy-4-isopropyl-*trans*-stilbene). The Petition glosses over this fact and instead incorrectly tells the Board that 3,5-dihydroxy-4-isopropylstilbene is tapinarof, despite acknowledging elsewhere that tapinarof is specifically, 3,5-dihydroxy-4-isopropyl-*trans*-stilbene. Encube fails to credit the Examiner with recognizing as much when the Examiner concluded that the Chen references “do[] not teach or suggest *the methods encompassing compounds substituted in the manner* claimed by the Applicant.” EX1002, 312 (emphasis added). Petitioner has not demonstrated Examiner error regarding Chen.

V. THE BOARD SHOULD EXERCISE ITS DISCRETION TO DENY INSTITUTION UNDER 35 U.S.C. § 314

The Board should also deny institution because the Petition fails to present

its arguments with particularity as required by both statute and the Board’s rules.

See 35 U.S.C. § 312(a)(3); 37 C.F.R. §§ 42.22(a)(2), 42.104(b). While this deficiency alone provides the Board with grounds for discretionary denial, Encube’s attempts to circumvent the rules on word limits and incorporation by reference provide further reasons to deny institution. *See* 37 C.F.R. §§ 42.6(a)(3), 42.24(a)(1)(i). As shown below, the Petition far exceeds 14,000 words, and Encube’s repeated attempts to incorporate arguments by reference, compound its violations.

A. The Petition fails to explain its arguments with particularity

The Petition fails to explain its arguments with particularity, in contravention of both statutory requirements (35 U.S.C. § 312) and the Board’s rules (37 C.F.R. §§ 42.22(a)(2) and 42.104(b)). “In an IPR, the petitioner has the burden from the onset to *show with particularity* why the patent it challenges is unpatentable.” *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (citing 35 U.S.C. § 312(a)(3)) (emphasis added). Encube failed to meet that burden on several fronts.

1. The Petition presents an undeveloped inherency theory

The Petition relies on an unexplained, undeveloped inherency theory when arguing that “Sonti’s disclosure of treating moderate to severe psoriasis is *inherently* also a method of treating mild psoriasis.” Pet., 14 (emphasis added).

Nowhere does Petition demonstrate—with particularity or otherwise—why this is *necessarily* so. Encube’s own exhibits state that “mild” and “moderate” plaque psoriasis are two clinically different phenotypes of the disease, with different criteria for diagnosis. *See, e.g.*, EX1006, Abstract (“psoriasis may be classified as mild psoriasis, moderate psoriasis, and severe psoriasis.”); EX1015, 3 (Table 1) (listing “mild,” “moderate,” and “severe” separately under “clinical phenotypes.”). Encube’s EX1006 discloses that diagnosis of a particular clinical phenotype for plaque psoriasis is important because a specific treatment for one phenotype (e.g., moderate to severe plaque psoriasis) may not be suitable for treating another phenotype (e.g., mild plaque psoriasis). EX1006, 3 (Table 2) (disclosing that treatments for “mild psoriasis” have “no known serious risks,” while treatments for “moderate psoriasis” have “minimal risks” and treatments for “severe psoriasis” may have “life-altering side[-]effects.”).

The Petition fails to consider that a physician might treat a case of severe plaque psoriasis with a drug known for significant, “life-altering” side effects because the patient is “willing to accept” those side effects “to achieve less disease or no disease.” EX1006, 3 (Table 2). However, according to EX1006, a physician would *not* use the same drug to treat a case of mild psoriasis because the clinical benefit would not outweigh the detrimental side effects. *Id.* Thus, Encube fails to demonstrate that a disclosure of treatment of “moderate to severe” plaque psoriasis

is *necessarily* a disclosure of treatment of mild psoriasis. *Id.*

The law is clear: “[i]nherency ... may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269 (Fed. Cir. 1991) (citations omitted). The Petition’s bare, conclusory statement that treating moderate to severe plaque psoriasis is necessarily the same as treating mild psoriasis cannot meet this burden. *Platinum Optics Tech. Inc. v. Viavi Solutions Inc.*, IPR2021-00424, Paper 11 at 9 (P.T.A.B. Dec. 6, 2021) (“it was *Petitioner’s burden* to show in the Petition that the missing claim limitation ... was inherent in the prior art.” (emphasis added)); *GlaxoSmithKline LLC v. Fibrogen, Inc.*, IPR2016-01318, Paper 13 at 21 (P.T.A.B. Jan. 11, 2017) (rejecting petitioner’s inherency theory because “Petitioner makes too many tenuous and unsupported connections that are *not necessarily so*.” (emphasis added)).

2. The Petition replaces particularity with vagueness by relying repeatedly on “and/or”

The Petition further fails to explain its arguments with particularity because it relies on multiple references and Grounds “connected by the conjunction ‘and/or,’” which “results in a multiplicity of grounds, none of which is presented with sufficient particularity.” *Adaptics Ltd. v. Perfect Co.*, IPR2018-01596, Paper 20 at 18 (P.T.A.B. Mar. 6, 2019) (informative); Pet., 46, 52, 53, 55, 58, 61, 62. For

example, in Ground 3, Encube argues that “claims 7, 21 and 9-10 are obvious for the reasons explained in Ground 1 *and/or* Ground 2, further in view of Bissonnette.” Pet., 46 (emphasis added). This argument presents at least three combinations of art and arguments: (i) Ground 1 and Bissonnette; (ii) Ground 2 and Bissonnette; and (iii) Ground 1, Ground 2, and Bissonnette. *Id.*

The Petition, however, fails to articulate its arguments for these combinations with any particularity. For example, the Petition’s Ground 3A discusses claims 7 and 21, but neither of these claims is challenged in Ground 1 (one of the alleged combinations of art and arguments in Ground 3). Similarly, in Ground 4, Encube argues that “claims 1-4, 6-10, 16, 18, and 21-22 are obvious over Bissonnette further in view of the teachings of Sonti *and/or* Chen.” Pet., 52 (emphasis added). This argument, too, presents at least three different combinations of art and arguments: (i) Bissonnette and Sonti; (ii) Bissonnette and Chen; and (iii) Bissonnette, Sonti, and Chen. *Id.* Rather than explain the combinations of art with any particularity, the Petition repeatedly uses “and/or” phraseology, leaving Patent Owner and the Board to guess at which reference combination is in play for any particular argument. *See, e.g.*, Pet., 52, 53, 55, 58, 61, 62.

The *Adaptics* decision is on point here, where the Board noted that the phrase “and/or” “has been criticized as a device, or shortcut, that damages a

sentence and often leads to confusion or ambiguity.” *Adaptics Ltd.*, IPR2018-01596, Paper 20 at 18, n.13 (citing William Strunk, Jr. and E. B. White, *Elements of Style* (Macmillan 2d ed. 1972), 35). The Board also recognized “Office guidance regarding *inter partes* reexaminations that warned requestors, ‘Do not lump together multiple rejections by using ‘and/or.’” *Id.*, n.14 (citing Best Practices and FAQs for Filing Requests for Reexamination Compliant with 37 CFR 1.510 and 1.915). But this is precisely what the Petition does. Moreover, Encube’s “and/or” approach attempts to shoehorn six unpatentability grounds into the space of two grounds, which further highlights the Petition’s violation of the rule on word limits (discussed below in Section V.B).

3. The arguments for claims 3 and 4 are not fully supported

The Petition also fails to explain with particularity its arguments about dependent claims 3 and 4, at least because the Petition’s arguments lack adequate expert testimony support. When asserting anticipation and obviousness of claims 3 and 4, Encube’s expert, Dr. Liem, relies exclusively on the testimony of Encube’s other expert, Mr. Sudhakar. *See* EX1003, ¶149 (“I understand from Mr. Sudhakar that Sonti discloses [claim 3].”), ¶150 (same for claim 4), ¶223 (“I understand from Mr. Sudhakar that [claim 3] would have been obvious in view of Sonti and the knowledge of a POSA.”), ¶224 (same for claim 4), ¶369 (“As I explained above in Grounds 1 and 2, I understand from Mr. Sudhakar that these claims are disclosed

by Sonti and also would have been obvious in view of the teachings of Sonti.”).

Mr. Sudhakar provides opinions that Sonti allegedly anticipates claims 3 and 4, (EX1032, ¶¶95, 107), but *never analyzes the patentability of claim 1* as part of his analysis. *See id.*, ¶¶88-133. Mr. Sudhakar does not discuss claim 1 at all. *Id.*

Each of claims 3 and 4 depends ultimately from claim 1. EX1001, 101:42-62. Dependent claims 3 and 4 therefore require *all of the limitations of claim 1* (and any intervening claim). With no analysis or even acknowledgement of claim 1’s requirements, Mr. Sudhakar cannot provide credible testimony that either of claims 3 or 4 is anticipated or obvious over the asserted art. Indeed, while Dr. Liem refers to and relies upon the testimony of Mr. Sudhakar to support her opinions on claims 3 and 4, the same cannot be said for Mr. Sudhakar and his opinions on claim 1. Mr. Sudhakar never addresses claim 1 at all, nor does he rely on Dr. Liem’s testimony or analysis for claim 1. *See, generally*, EX1032. In fact, Mr. Sudhakar’s Declaration neither cites nor even acknowledges the Liem Declaration. *Id.*

Accordingly, Mr. Sudhakar’s opinions at least on claims 3 and 4 should be given no weight because he fails to disclose the underlying facts or data on which his opinions are based. 37 C.F.R. § 42.65(a) (“Expert testimony that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight.”); *see also Upjohn Co. v. Mova Pharm. Corp.*, 225 F.3d 1306,

1311 (Fed. Cir. 2000) (“Lack of factual support for expert opinion going to factual determinations, however, may render the testimony of little probative value in a validity determination.” (citation omitted)); and *Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 9 at 15 (P.T.A.B. Aug. 24, 2022) (informative). Likewise, Dr. Liem’s testimony on claims 3 and 4 deserves no weight because she relies on the unsupported and incomplete analysis of Mr. Sudhakar for these claims. EX1003, ¶¶49-50, 223-224, 369; 37 C.F.R. § 42.65(a).

In sum, the Petition suffers from numerous flaws that coalesce in a failure to present arguments with particularity and ultimately results in Encube’s failure to meet its burden as petitioner. As the Board explained in *Adaptics*, “[t]he statutory requirement for particularity in a petition for IPR takes on heightened importance when considered in conjunction with *SAS*’s ‘all-or-nothing’ approach. Because the Board’s practice, in light of *SAS*, is to institute on all grounds asserted in a petition, the Board may consider whether a lack of particularity as to one or more of the asserted grounds *justifies denial of an entire petition*.” IPR2018-01596, Paper 20 at 17 (emphasis added). Encube’s omission of particularity here infects all four of its Grounds and justifies denial of the entire Petition.

B. The Petition contains well over 14,000 words, violating 37 C.F.R. § 42.24(a)(1)(i)

Encube certified that its Petition contains 13,996 words (Pet., 78)—just four

words shy of the 14,000 limit—but a closer look reveals this to be a nearly 1,000-word undercount. The word count is actually approximately 14,832 words, far exceeding the allowed limit. 37 C.F.R. § 42.24(a)(1)(i).

At the outset, it is unclear how Encube arrived at 13,996 words. Patent Owner counts at least 14,066 words in the Petition when converting it to MS Word format and excluding portions provided in 37 C.F.R. § 42.24(a)(1). But Encube’s circumvention of rule 42.24 does not end there. The Petition repeatedly includes *images of text* from exhibits throughout, and relies on the *text in the images* (including highlights and emphasis) for its arguments. *See, e.g.*, Pet., 10, 23, 55, 58, 59, 69. These images of text are not counted by standard word-processing systems and thus provide Encube with a loophole to skirt the Board’s word-limit rule. The table below shows examples:

Petition page	Image of text in petition	Approximate number of words in image <i>not counted</i> by word-processing system
10	EX1005, ¶¶[0287]-[0288]	187 words
23	EX1005, Table 4	140 words
55	EX1013, 32:41-50	95 words
58	EX1013, 32:41-62	212 words
59	EX1008, Table 2	66 words
69	EX1008, Table 2	66 words

Counting the words in the Petition *and* those in the numerous incorporated images of words, equals approximately 14,832 words, well past the 14,000 limit.

The Board consistently upholds rule 42.24 when petitioners exceed the word

limit. *See, e.g., Facebook, Inc. v. Sound View Innovation Holdings, LLC*, IPR2017-01003, Paper 14 at 7 (P.T.A.B. Sept. 1, 2017); *Tesla, Inc. v. Unicorn Energy GmbH*, IPR2022-00110, Paper 5 at 3 (P.T.A.B. Nov. 26, 2021); *St. Jude Medical, LLC v. Snyders Heart Valve LLC*, IPR2018-00105, Paper 12 at 4 (P.T.A.B. Apr. 3, 2018); *EMC Corp. v. Intellectual Ventures I LLC*, IPR2017-00429, Paper 11 at 28 (P.T.A.B. July 5, 2017); *Panduit Corp. v. Corning Optical Comms. LLC*, IPR2017-00528, Paper 7 at 20 (P.T.A.B. May 30, 2017).

In *Facebook*, the Board found that the petition violated rule 42.24 in part by “reproduc[ing] numerous and lengthy passages of text from other documents as images.” IPR2017-01003, Paper 14 at 7. The Board explained that “[t]hese passages of text, because they are in image form, may not have been counted by the word-processing system....” *Id.* The Board also noted the severity of the rule violation, explaining that using “[e]xcessive words in figures, drawings or images, ... to circumvent the rules on word count, may lead to dismissal of a party’s brief....” *Id.* (citing *Pi-Net Int’l, Inc. v. JPMorgan Chase & Co.*, 600 Fed. App’x 774 (Fed. Cir. 2015) (per curiam) (emphasis added)). The same is true for Encube’s Petition, which contains at least 6 images of text amounting to over 750 words not counted by the word-processing system. Pet., 10, 23, 55, 58, 59, 69.

Here, Encube’s Petition, if written and counted properly, exceeds the permitted word count. Encube has not filed a motion for waiver of the word limit

nor provided any other explanation for its violation of rule 42.24. Moreover, as discussed next, the Petition's word-count violation is magnified by the Petition's repeated improper incorporation by reference.

C. The Petition violates 37 C.F.R. § 42.6(a)(3) by improperly incorporating arguments by reference

Encube's Petition improperly incorporates arguments by reference by citing to paragraphs from its expert declaration to supplement its conclusory statements in the Petition, in contravention of 37 C.F.R. § 42.6(a)(3). Rule 42.6 states that "[a]rguments must not be incorporated by reference from one document into another document." *Id.* The Board, in *Cisco Sys., Inc. v. C-Cation Techs., LLC*, explained that incorporating arguments from a declaration into the petition is an improper incorporation by reference:

[T]he Petition includes citations to the Declaration to support conclusory statements for which the Petition does not otherwise provide an argument or explanation ... This practice of citing the Declaration to support conclusory statements that are not otherwise supported in the Petition also amounts to incorporation by reference. IPR2014-00454, Paper 12 at 9 (P.T.A.B. Aug. 29, 2014) (informative).

Encube's Petition repeatedly makes conclusory statements, followed by citations to its expert declarations for support. For example, the Petition thinly states that a "POSA would have been motivated, with a reasonable expectation of success, to administer a topical composition containing 1% tapinarof (as taught by

Sonti) once a day (as also taught by Sonti).” Pet., 30 (citing EX1003, ¶¶187-188).

But the Petition offers no explanation *why* the POSA would have been motivated, nor *why* the POSA would have had a reasonable expectation of success. Instead, the Petition relies on two paragraphs from EX1003 (the Liem Declaration) to support its conclusory statement.

As another example, the Petition states that “[a] POSA would have been motivated, with a reasonable expectation of success, to use the method of treatment of claim 1 on body part(s) that are commonly affected by plaque psoriasis.” Pet., 37 (citing EX1003, ¶¶227-228). Again, there is no explanation *in the Petition* as to *why* a POSA would have been so motivated, or *why* a POSA would have reasonably expected success. The Petition uses the Liem Declaration to bridge that gap. *Id.* And these are not isolated occurrences—Encube’s incorporation by reference tactics pervade the entire Petition. *See, e.g.*, Pet., 16 (conclusory statement of what “a POSA would understand” from Sonti, relying on EX1003, ¶¶129-131); 36 (conclusory statement about what Sonti would have “indicated to a POSA,” relying on EX1032, ¶123); 36 (conclusory statement about nothing “unusual or unexpected” to a POSA, relying on EX1032, ¶125); 48 (conclusory statement that “[c]ombining Sonti’s teaching” with “Bissonnette’s teachings” would have been “the predictable application of a known method,” relying on EX1003, ¶303); 49 (conclusory statement about a “predictable and common-sense

extension” of Sonti, relying on EX1003, ¶306); 57 (conclusory statements about motivation to “improve patient compliance” and “lower treatment cost,” relying on EX1003, ¶¶337-338 and EX1032, ¶¶86-87); 61-62 (conclusory statements regarding “reasons to combine Bissonnette with the teachings of Sonti and/or Chen,” relying on EX1003, ¶¶333, 350-358, 359-363).

The rules forbid such incorporation by reference, and the Board should not consider arguments or evidence not presented squarely in the Petition. Indeed, the Board has a long and consistent history of rejecting petitioners’ arguments for these same faults. *See, e.g., Cisco Sys., IPR2014-00454*, Paper 12 at 10 (informative) (“we will not consider arguments that are not made in the Petition, but are instead incorporated by reference to the cited paragraphs and claims charts of [the expert] Declaration.”); *see also, EiKO Global, LLC v. Blackbird Tech LLC, IPR2017-00980*, Paper 16 at 23 (P.T.A.B. Sept. 1, 2017) (“[a]rguments that are not presented and developed in the Petition, and instead are incorporated by reference to [the expert’s] declaration, are not entitled to consideration.”).

The Board should do the same here.

VI. THE PETITION FAILS TO ESTABLISH A REASONABLE LIKELIHOOD OF PREVAILING ON ANY CHALLENGED CLAIM

Given the multiple Petition’s deficiencies and violations discussed above, the Board can and should deny institution without reaching the merits. But if the Board were to consider the merits, Encube’s Petition still fails because it does not

establish a reasonable likelihood that any challenged claim is unpatentable. Ground 1 (anticipation) fails to show every claim element arranged as claimed, instead picking and choosing disclosures from numerous different lists and embodiments in Sonti. Grounds 2–4 (obviousness) are likewise defective, e.g., for mischaracterizing the teachings in the asserted art and failing to demonstrate that a POSA would have had a reasonable expectation of success.

A. Ground 1: The Petition fails to establish a reasonable likelihood that Sonti anticipates claims 1-4, 6, 8-9, 18, or 22

The Petition alleges that Sonti anticipates claims 1–4, 6, 8–9, 16, 18, and 22, (Pet., 13–28) but fails to demonstrate a reasonable likelihood of prevailing. For anticipation, the prior art 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) (emphasis added) (internal quotation and citation omitted). Rather than make the required showing, Encube instead cherry-picks different claim elements out of multiple lists and different embodiments. Indeed, some of Encube’s arguments rely on combining elements from “physically stable” oil-in-water emulsions with other emulsions that Sonti negatively characterizes as “non-uniform.” Encube’s picking and choosing claim elements out of the disclosure in this manner is contrary to controlling authority and fails to show anticipation. *Id.* at 1369; *see also SFC CO., Ltd. v. LG Chem, Ltd.*, IPR2020-

00178, Paper 16 at 23 (P.T.A.B. May 29, 2020) (“Petitioner’s ‘picking and choosing’ of certain variables and substituents to the exclusion of others ‘has no place’ in the § 102 analysis.” (quoting *Arkley*, 455 F.2d at 587-588)).

1. The Petition improperly picks and chooses from multiple lists and embodiments to arrive at the method of claim 1

Claim 1 recites a method for treating a specified indication (mild to severe plaque psoriasis), with a specified concentration of tapinarof (1%), using a specified administration frequency (once a day), measured with a specified clinical criteria (PGA score) and achieving a specified outcome (PGA score improved by 2 grades or PGA score of 0 or 1). EX1001, 101:42–48. To manufacture an anticipation argument—where none exists—Encube improperly combines disclosures from different lists and embodiments in Sonti. Pet., 13–18. Relying on *Kennametal, Inc. v. Ingersoll Cutting Tool Co.*, 780 F.3d 1376, 1381 (Fed. Cir. 2015), Encube characterizes Sonti’s disclosures as providing a “limited number” of choices, from which a POSA would have “at once envisaged” the claimed method. *See, e.g.*, Pet., 15 (“a *limited number* of diseases ... using a *limited number* of potential amounts of tapinarof”), 16 (“a *limited number* of diseases ... tapinarof strengths ... and application frequencies.”), 18 (“a *limited number* of metrics for plaque psoriasis treatment response.”) (emphasis added).

Contrary to the Petition’s myopic reading, Sonti actually discloses nearly *one million* different treatment options. Encube asserts that “[a] POSA would read

Sonti for all that it discloses” (Pet., 19) when it suits Encube, yet conveniently fails to follow this legal principle when it doesn’t. Rather than acknowledge the myriad disclosures in Sonti, as a POSA would have done, the Petition instead cherry-picks particular variables from Sonti to the exclusion of others, a practice that “has no place in the making of a 102, anticipation rejection.” *Arkley*, 455 F.2d at 588.

a. Sonti discloses nearly a *million* different treatment options

Encube’s improper picking and choosing begins with implying there are but two indications disclosed in Sonti. Pet., 15 (“a limited number of diseases (atopic dermatitis and plaque psoriasis”)). This is flatly wrong. The Petition cites Sonti’s paragraphs [0288], [0285]-[0294], and [0298]-[0300] for this claim element. Pet., 13. Paragraphs [0298]-[0299] alone describe at least *67 different dermatological conditions*; many more than Encube’s implied two.

Encube also grossly underplays Sonti’s disclosures about tapinarof concentrations, asserting that Sonti “us[es] a limited number of potential amounts of tapinarof (including 1%...)” Pet., 15. The Petition cites Sonti’s paragraphs [0196], [0055], [0323], [0327], [0355], [0367], and [0370] here. Pet., 14–15. Paragraph [0055] describes tapinarof “in an amount from about 0.01% to about 5% by weight.” This disclosure provides a range of tapinarof amounts in 0.01% increments—i.e., *500 different amounts of tapinarof*— and a POSA would view these 500 options in combination with the 67 options for dermatological conditions

discussed above.

Encube further misrepresents the number of options for application frequency first by arguing that Sonti discloses a “limited number” of application frequencies and then by selectively quoting only “once daily” out of the many options in Sonti. Pet., 16. The Petition cites Sonti’s paragraph [0387] here. Pet., 16. Paragraph [0387] describes at least *14 application frequencies*. For example, Sonti discloses two dosing options: single-phase and two-phase. For single-phase dosing, Sonti discloses *six options*: “twice daily, once daily, once every other day; twice weekly; three times weekly, or once weekly, with the dose represented by any of the embodiments herein.” EX1005, ¶[0387]. For two-phase dosing, Sonti discloses another *eight options*: “an initial dosage frequency such as once or twice daily, followed by a maintenance phase, such as every other day; twice weekly; three times weekly, or once weekly.”⁵ *Id.* Thus Sonti provides the POSA with at least 14 different options for application frequency.

Given the number of options disclosed in Sonti, a POSA reading “Sonti for all that it discloses” (Pet., 19) would have understood that Sonti discloses

⁵ Two options for initial dosing × 4 options for maintenance phase dosing = 8 total options for two-phase dosing.

approximately 938,000 different treatment options.⁶ Encube’s conclusory statements that a POSA would “at once envisage” the precise combination of elements as recited in the challenged claims are entirely at odds with the myriad possibilities taught in Sonti. Tellingly, the Petition never identifies a single embodiment in Sonti meeting all the elements of claim 1. *See, e.g., NJoy, LLC v. Juul Labs, Inc.*, IPR2024-00231, Paper 15 at 18 (P.T.A.B. June 12, 2024) (rejecting the petitioner’s anticipation argument for picking and choosing from different embodiments in the reference, while noting that “Petitioner does not argue that a single embodiment ... discloses all limitations of challenged claim 14.”).

In *In re Petering*, the Court held that a POSA may “*at once envisage* each member of [a] *limited class*, even though this skilled person might not at once define in his mind the formal boundaries of the class.” 301 F.2d 676, 681 (C.C.P.A. 1962) (emphasis added). But that is a far cry from Sonti’s disclosure—938,000 treatment options is not a “limited class” of choices. The Federal Circuit cautioned in *Mylan v. Merck* (60 years after *Petering*) that “[t]he key term here is

⁶ 67 different disease indications × 500 different tapinarof amounts × 14 different application frequencies × two different clinical criteria (PASI score or PGA score) = 938,000 total options.

‘limited.’” *Mylan Pharms. Inc. v. Merck Sharp & Dohme Corp.*, 50 F.4th 147, 153 (Fed. Cir. 2022) (emphasis added). In *Mylan*, the prior art reference at issue disclosed 33 *different compounds* and 8 *preferred acids*, which could produce a class of 957 *predicted salts*. *Id.* at 153-154. As *Mylan* explained, 957 different options for predicted salts “is a far cry from the 20 compounds ‘envisaged’ by the narrow genus in *Petering*” and thus was ultimately “insufficient to meet the ‘at once envisage’ standard set forth in *Petering*.” *Id.* at 154. The same is true here, as Sonti’s 938,000 different treatment options are a far cry from *Petering*’s 20 compounds.

Moreover, neither the Petition nor Encube’s experts makes any attempt to explain the enormous number of treatment options disclosed in Sonti. Instead what they have done is artificially try to narrow Sonti’s disclosure to only portions that which suits Petitioner’s needs. The Petition thus fails to meet the “at once envisage” standard it relies upon. *See, e.g., Apple Inc. v. Alivecon, Inc.*, IPR2022-00873, Paper 7 at 20-23 (P.T.A.B. Nov. 14, 2022) (finding that petitioner’s expert “does not discuss whether there are other possibilities beyond [the elements arranged as claimed], leaving the Board to “only speculate as to whether the conditions here are sufficient to invoke *Kennametal*’s ‘at once envisage’ standard.”).

b. *Kennametal* does not support Encube’s “at once envisage” argument

Encube’s reliance on *Kennametal* (Pet., 15, 16, 18) is misplaced. In *Kennametal*, there was no dispute that claim 5 of the prior art reference (“Grab”) recited and encapsulated every element of the challenged claim except for “combining ruthenium binders with PVD coatings.” *Kennametal*, 780 F.3d at 1382. The Grab prior art’s claim 5 recited five metal choices (one being ruthenium) together with a coating, and the Grab specification further disclosed three coating options (PVD, CVD, MTCVD)—i.e., 5 metal choices × 3 coating choices = 15 options. *Id.* As *Kennametal* explained, “the question for the purposes of anticipation is whether the number of categories and components disclosed in Grab is so large that the combination of ruthenium and PVD coatings would not be immediately apparent to one of ordinary skill in the art.” *Id.* (internal quotation and citation omitted). The Court found that “substantial evidence supports the Board’s conclusion that *Grab effectively teaches 15 combinations*, of which one anticipates pending claim 1.” *Id.* at 1383 (emphasis added). Thus, in *Kennametal*, the Court viewed Grab’s “15 combinations” as a limited number sufficient to meets the “at once envisage” standard. *Id.*; *see also, Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co., Ltd.*, 851 F.3d. 1270, 1274 (Fed. Cir. 2017) (“*Kennametal* addresses whether the disclosure of a *limited number of combination possibilities* discloses one of the possible combinations.”) (emphasis added)).

Here, Sonti's nearly one million different options are far from the 20 compounds envisaged in *Petering* and from the 15 combinations envisaged in *Kennametal. Mylan*, 50 F.4th at 154. Encube provides no evidence or reasoning to establish that a POSA would have at once envisaged the claimed combination of elements in claim 1, and the Petition's Ground 1 thus fails to establish a reasonable likelihood of prevailing on any of its anticipation arguments. *See, e.g., Advanced Lighting Concepts, LLC v. Mate LLC*, IPR2023-01259, Paper 9 at 17 (P.T.A.B. Feb. 13, 2024) ("Petitioner has provided no evidence or reasoning to persuade us that one of ordinary skill in the art would 'at once envisage' the arrangement or combination."); and *Argentum Pharms. LLC. V. Cipla Ltd.*, IPR2017-00807, Paper 11 at 11-14 (P.T.A.B. Aug 21, 2017).

2. The Petition further mixes and matches embodiments and disclosures in Sonti to arrive at the formulations of claim 3

Encube's failure to establish a reasonable likelihood of prevailing on its anticipation argument for claim 1 is fatal to all of Ground 1, as every challenged claim depends directly or indirectly from claim 1. Pet., 18–28. Patent Owner nevertheless provides the following salient points regarding Encube's anticipation argument for claim 3, which further exemplify the Petition's faulty approach to anticipation.

Claim 3 recites a specific formulation for the claimed method, comprising nine specific ingredients in the oil phase of the emulsion. EX1001, 101:51–56. To

argue anticipation, the Petition selects individual ingredients from at least 13 different formulations embodied in Sonti, some of which Sonti characterizes as “non-uniform.” Pet., 19–22. For example, when discussing “medium chain triglycerides,” “propylene glycol,” and “polysorbate 80,” the Petition relies on Sonti’s *Formulations 21 and 30–33*. Pet., 19–21. When discussing non-emulsifying wax, however, the Petition abandons those formulations, instead relying on Sonti’s *Formulations 1a and 13*. Pet., 20. Encube’s reliance on Sonti’s Formulations 1a and 13 is important. First, Sonti expressly teaches that “chemical degradation of the active ingredient [was] observed” in Formulation 1a. EX1005, ¶¶[0323]-[0324]. Sonti also identifies Formulations 2–14 as “non-uniform” emulsions with solubility and stability issues. EX1001, ¶¶[0013], [0349], FIGs. 1–2. Sonti explains that “the appearance of a non-uniform emulsion ... was characteristic of Formulations 2-14 compared with the physically stable formulation characterized by Formulation[s] 15-40.” EX1005, ¶[0013]. According to Sonti, “it was observed from microscopic analysis that the emulsion structure of these formulations was non-uniform” and that “the active ingredient was not solubilized in either the water phase or the oil phase of the emulsion.” *Id.*, ¶¶[0348], [0350]. The Petition completely ignores these teachings regarding “chemical degradation” of the active in Formula 1a and the “non-uniform” concerns for Formula 13. Pet., 19–22. Nowhere does it address how these

teachings would affect its “picking and choosing” argument for claim 3.

For the next ingredient in claim 3, “diethylene glycol monoethyl ether,” the Petition looks to Sonti’s *Formulations 15–20 and 21*. Pet., 20. For “polyoxyl stearyl ether-2” and “polyoxyl stearyl ether-20,” the Petition relies on a mixture of Sonti’s *Formulations 1a and 13* (Sonti’s “chemical degradation” and “non-uniform” emulsions), and *Formulations 21 and 30–33*. Pet., 21. And for “benzoic acid” and “butylated hydroxytoluene,” the Petition combines disclosures from Sonti’s *Formulation 13* (a “non-uniform” emulsion), *21*, and *30–33*. Pet., 21–22.

In total, the Petition picks and chooses individual ingredients from at least *13 different formulations* disclosed in Sonti and then combines them in an attempt to assert anticipation. Pet., 19–22. The prior art, however, “must clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without *any* need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference.” *Net MoneyIN*, 545 F.3d at 1371 (emphasis in original). In *NJoy v. Juul*, *supra*, the Board concluded that the “Petitioner fails to show that the cited material in [the prior art reference] discloses the limitations of claim 14 arranged in the same way as claimed *without resorting to the need to pick and choose* from disparate disclosures.” *NJoy*, IPR2024-00231, Paper 15 at 19 (citing *Net MoneyIN* at 1371) (emphasis added). The Board should conclude the same here.

3. The Petition’s argument that claims 3 and 4 are anticipated by Sonti lacks supporting expert testimony

The Petition’s arguments for claims 3 and 4 are lack evidentiary support in the form of expert testimony. As already discussed in Section V.A.3, Dr. Liem relies exclusively on Mr. Sudhakar’s testimony to support her opinion that claims 3 and 4 are anticipated and obvious. *See* EX1003, ¶¶149-150, 223-224, 369. Mr. Sudhakar provides opinions that claims 3 and 4 are allegedly anticipated and obvious, but *never analyzes or even considers the patentability of claim 1*. *See* EX1032, ¶¶95, 107, and 88-133. Nor does Mr. Sudhakar refer to Dr. Liem’s analysis of claim 1 or rely on Dr. Liem’s testimony in any way. *Id.* Indeed, Mr. Sudhakar does not cite Dr. Liem’s declaration (EX1003) at all. *See, generally*, EX1032. Thus, neither of Encube’s experts provides a complete opinion or analysis for claims 3 and 4, and the Petition’s arguments lack the required support under 37 C.F.R. § 42.65(a).

B. Grounds 2-4: The Petition fails to establish a reasonable likelihood of prevailing

Encube has not met its burden for obviousness for Grounds 2, 3, and 4. The Petition (i) does not demonstrate a reasonable expectation of success, (ii) overlooks that the purported “need” in its obvious-to-try analysis was already met; and (iii) fails to address objective indicia of non-obviousness that Encube was aware of when it filed the Petition.

1. Encube has not met its burden to establish a reasonable expectation of success

Encube's reasonable expectation of success arguments rely on Chen's applying a compound that is *not* tapinarof to its volunteers and otherwise provided vague cross-referencing, without support, to assert what "was known" from Sonti. Both theories fail.

a. Encube's arguments rely upon Chen's use of a compound that is not tapinarof

Encube asserts that Chen taught "that a topical cream of '1% 3,5-dihydroxy-4-isopropylstilbene' (which is tapinarof...) applied 'once per day' 'showed great efficacy' in treating plaque psoriasis." Pet., 31; *see also id.*, 48-51, 57-59 (arguing that "it was also already known that once daily application was highly effective to treat mild to severe plaque psoriasis, *as both Sonti and the Chen references teach.*" (emphasis added)). Close scrutiny guts Encube's assertion, which collapses because it: (i) presumes—incorrectly—that Chen discloses applying tapinarof to its Volunteers; and (ii) mischaracterizes of Sonti's discussion of Chen.

As discussed in Section IV.B.3.c, Tapinarof is 3,5-dihydroxy-4-isopropyl-*trans*-stilbene. EX1001, 7:4-20. Encube and its declarants acknowledge this. Pet., 8 FN4 and 14; EX1032, ¶¶56, 63, 64; EX1003, ¶77 FN4 and ¶89. Whereas Chen discloses applying "3,5-dihydroxy-4-isopropylstilbene" (i.e., a mixture of *cis* and *trans* forms), to its Volunteers. *See* EX1013, 32:25-26 ("[a] 1% cream of 3,5-

dihydroxy-4-isopropylstilbene was prepared....”), 32:46-47 (“[t]he cream of the invention contained 1% 3,5-dihydroxy-4-isopropylstilbene.”). WO 2001/042231 does the same. EX1012, 20:28-21:24. Neither Encube nor its Declarants explains how a compound that is not tapinarof is informative about efficacy of tapinarof.

Encube also mischaracterizes Sonti’s disclosures when arguing that Sonti “cites two Chen references as showing that tapinarof was ‘suitable for the treatment of... psoriasis.’” Pet., 31 (citing EX1005, ¶[0010], in turn citing, EX1012, EX1013). The Petition conveniently provides partial quotes and an ellipsis for Sonti’s discussion of the Chen references. The complete discussion in Sonti states:

The compound is further described in WO 2001/042231 [EX1012] (Welichem Biotech Inc.) and in U.S. Pat. No. 7,868,047 [EX1013] and as being *suitable for the treatment of* various key dermatological conditions including *psoriasis* and inflammation. Example 3 of the U.S. Pat. No. 7,868,047 patent describes a cream formulation with an active ingredient being made in Galax Base. Applicants have been unable to ascertain any compendial notations or availability of a commercial cream base called “Galax” and therefore its composition remains unknown.

EX1005, ¶[0010] (emphasis shows the fragments of text that Encube cited).

In the full passage, Sonti first notes that “the compound” (tapinarof) is described in WO 2001/042231 (EX1012) and in U.S. Pat. No. 7,868,047 (Chen,

EX1013). EX1005, ¶[0010]. And, while Chen (EX1013) and WO 2001/042231 (EX1012) may *disclose* the compound 3,5-dihydroxy-4-isopropyl-**trans**-stilbene (tapinarof), neither reference discloses *using a composition containing 1% tapinarof* to treat plaque psoriasis, as the Petition posits. Instead as already noted, each discloses applying “3, 5-dihydroxy-4-isopropylstilbene” (i.e., a mixture of *cis* and *trans* forms), to the Volunteers in the Example; and not applying tapinarof. *See* EX1013, 32:25-26 and 46-47; and EX1012, 20:28-21:24.

Chen’s disclosure of applying 3,5-dihydroxy-4-isopropylstilbene (and *not* tapinarof) to its Volunteers is consistent with Sonti’s discussion of the same. Sonti states that Chen “describes a cream formulation with *an active ingredient* being made in Galax Base.” EX1005, ¶[0010]. Here, Sonti says “an active ingredient,” and not tapinarof or even “the compound,” as it did in the previous sentence. *Id.* The Petition failed to recognize and address this critical point in Sonti. Instead cherry-picking convenient sentence fragments to paste together for a purported “teaching” that does not exist.

The Petition’s oversights here are dispositive and foreclose any credible argument for a reasonable expectation of success based on Chen. Indeed, this failed reliance on Chen pervades every obviousness ground, as the Petition repeatedly touts Chen’s supposed “successes” as informing a POSA’s reasonable expectations of success in Grounds 2, 3, and 4. *See, e.g.,* Pet., 31 (referring to the

“impressive efficacy in treating psoriasis” and citing EX1013, 2:56-3:4, 32:35-63).

b. The Petition relies on vague cross-referencing when arguing what was “known” from Sonti

Encube asserts that it was “known” that “1% tapinarof, administered topically once daily, effectively treated plaque psoriasis” because “Sonti teaches this, as explained in Ground 1.” Pet., 31 (citing Petition § VIII.A). Likewise, in Grounds 3-4, Encube simply refers back to arguments made in Grounds 1 and 2 allegedly establishing that Sonti already taught that “a 1% tapinarof topical composition was highly effective to treat plaque psoriasis when applied once daily.” Pet., 48-51, 57-59. However, the Petition offers no further explanation beyond pointing to “§VIII.A.” *Id.* Section “VIII.A” in the Petition however, spans six pages of argument and cities nearly 50 paragraphs from Encube’s two expert declarations. Pet., 13-18 (citing EX1003, ¶¶109-146 and EX1032, ¶¶49-50, 58-63, and 56-57). As the Board explained in *Apple Inc. v. ContentGuard Holdings, Inc.*, IPR2015-00450, Paper 9 at 8 (P.T.A.B. June 29, 2015), this type of “internal cross-references within the Petition and the supporting [expert] Declaration[s] obfuscates the evidentiary support for the Petition’s assertions.” Indeed, such “practice results in multiple levels of abstraction, obscuring Petitioner’s position regarding which reference, and which portion of which reference, teaches or suggests the claim

limitations.”⁷ *Id.* at 7. Nowhere in “§VIII.A” of the Petition does the Petition argue that Sonti teaches that it was “known” that “1% tapinarof, administered topically once daily, effectively treated plaque psoriasis;” the words “effectively treated” never appear in Section VIII.A. Pet., 13-18. And to the extent the Petition is referring to its argument in Ground 1 that “[a] POSA would have known that Sonti’s disclosure of treating moderate to severe psoriasis is inherently also a method of treating mild psoriasis” (Pet., 14), that argument is squarely refuted in Section V.A.1.

Encube then alleges that there were “known reasons to use a lower strength and/or lower application frequency of topical pharmaceutical,” including “(i) reducing risk of side effects by minimizing the body’s systemic exposure to the

⁷ The Petition also relies on this cross-referencing tactic at, e.g., pages 48 (“*See supra* §IX.F”), 51 (“*See supra* §IX.G”), 60 (“*see also supra* §VIII.A.5, §IX.A.3”), and 62 (“*supra* §IX.A.3”). This tactic “improperly shifts the burden of deciphering Petitioner’s arguments onto Patent Owner and the Board, which ... is contrary to the statutory and regulatory provisions governing *inter partes* review proceedings, as well as the best practices outlined in the Office Patent Trial Practice Guide.” *Whole Space Indus Ltd. v. Zipshade Indus. (B.V.I.) Corp.*, IPR2015-00488, Paper 14 at 18 (P.T.A.B. July 24, 2015).

active ingredient, (ii) improving patient compliance with treatment recommendations, and (iii) reducing treatment cost.” Pet., 31-32. These arguments are unexplained and unsupported. Encube again simply incorporates by reference its two expert declarations, providing no explanation or underlying evidence to support its conclusory statements. 37 C.F.R. § 42.6; *Cisco*, IPR2014-00454, Paper 12 at 9 (informative); *see also* Section V.C, *supra*. And, this backup argument fails to consider or explain the disclosures in Bissonnette (EX1008, 2), which directly contradict the Petition’s proffered motivations, as explained below in Section VI.C.3.c.

c. Grounds 2 and 3 fail to establish a reasonable likelihood of prevailing on its challenges to claims 7, 10, and 21

For dependent claims 7, 10, and 21 (unchallenged in Ground 1) the Petition fails to establish a reasonable likelihood of prevailing because the arguments are (i) based on the Petition’s same flawed logic from claim 1, and (ii) an attempt to equate two entirely different clinical indications (atopic dermatitis and plaque psoriasis) with no explanation.

First, for claims 7 and 10, the Petition argues that Sonti “discloses, and also makes obvious, treating a subject ‘diagnosed’ with ‘mild to severe’ (claim 7) and ‘mild to moderate’ (claim 21) plaque psoriasis as claimed for *the same reasons explained with respect to claims 8, 22, and [1.pre] in this Ground 2.*” Pet., 40

(emphasis added). The Petition’s argument for claims 8 and 22 rely on the same flawed inherency logic discussed above for claim 1. The Petition states, again with no supporting evidence, that “[a] subject diagnosed with *moderate to severe* plaque psoriasis *is also one* with a diagnosis falling within the ‘*mild to severe*’ (claim 8) and ‘*mild to moderate*’ (claim 22)” Pet., 38 (emphasis added). Just as in Ground 1, the Petition provides no explanation or analysis beyond this conclusory statement and reliance on a single paragraph of the Liem declaration (EX1003, ¶232). This argument should be rejected as it is an improper incorporation by reference. 37 C.F.R. § 42.6.

Second, the Petition asserts in conclusory fashion that a POSA would have reasonably expected a topical treatment that is effective for *atopic dermatitis* to be effective as a topical treatment for *plaque psoriasis*. For claims 7 and 21, the Petition argues that Sonti “teaches treating a subject having a BSA affected with *atopic dermatitis* that is in the claimed range.” Pet., 42. And for claim 10, after admitting that that Sonti is missing an express claim element (“Sonti does not disclose the decrease in ‘BSA affected recited in Claim 10 with respect to treating plaque psoriasis specifically.’” Pet., 43), Encube nevertheless argues that a POSA would have a reasonable expectation of success because “anti-inflammatory topical treatments for *atopic dermatitis* were commonly used with and expected to work for *plaque psoriasis*.” Pet., 44, 51 (citing EX1003, ¶274) (emphasis added). Once

again, the Petition provides a bare, conclusory statement and incorporates Dr. Liem's declaration by reference. 37 C.F.R. § 42.6(a)(3).

The Petition's only stated rationale for why a POSA would have considered outcomes when treating atopic dermatitis applicable to plaque psoriasis is that "both diseases were known to be inflammatory skin diseases." Pet., 42 (citing EX1005, ¶¶[0272]-[0295] and EX1013, 2:56-3:17 and "32:8-3:4"). The Petition fails to explain why or how this is sufficient knowledge for a POSA to inform the artisan's supposed expectation of success. For example, the relied-upon disclosures in Sonti demonstrate that atopic dermatitis is a completely different indication than psoriasis, with different diagnostic criteria and "at least 28 different scales" for classification. EX1005, ¶[0273]. Meanwhile, psoriasis is scaled on entirely different systems, such as PASI or PGA scoring. *Id.*, ¶¶[0285]-[0287]. The relied-upon disclosures in Chen further demonstrate the differences in these indications, explaining that psoriasis is a "disease characterized not only by inflammation, but also by *proliferation of cells*" and that it "has *similarities to cancers*." EX1013, 2:61-65 (emphasis added). Chen characterizes atopic dermatitis as skin abnormalities that include "1) a lowered threshold to itch stimuli, 2) a hypersensitivity to α -adrenergic agonists and to cholinergic agents, 3) a very dry hyperkeratotic skin which has decreased water holding capacity, 4) a marked tendency to produce lichenification in response to friction and scratching, and 5) a

tendency for the skin to be colonized with bacteria. *Id.*, 3:11-17. The Petition fails to address these disclosures in its own references or explain why a POSA would have ignored them as the Petition has.

2. Encube has not met its burden to demonstrate the challenged claims would have been obvious to try

Encube argues that the claimed methods would have been “obvious to try” because there was a “recognized need” for “non-steroidal topical drugs for the treatment of psoriasis,” and “a finite number of known potential tapinarof strengths and application frequencies to use when topically treating plaque psoriasis.” Pet., 32, 51, 63 (citing Sonti, Chen, and Bissonnette). Encube has not met the obvious to try standard for four reasons. First, the “recognized need” stated in the Petition was already satisfied by Bissonnette, which discloses a twice-daily non-steroidal treatment for psoriasis. Second, as already discussed, Sonti discloses nearly one million options—far more than the required “finite number of identified, predictable, solutions.” *See KSR Int’l Co. v. Teleflex, Inc.*, 550 U.S. 398, 421 (2007). Third, and also discussed above, the Petition’s reliance on Chen is misplaced because Chen does not disclose treating plaque psoriasis *with tapinarof*. EX1012, 32:10-66. Fourth, Encube relies on Bissonnette as an example of “successful” treatment while ignoring that Bissonnette administered tapinarof twice daily, not once daily. EX1008, 2. All of this undermines Encube assertion that the claims challenged in Grounds 2-4 would have been obvious to try.

3. Encube did not address known objective indicia of non-obviousness

None of Grounds 2, 3, and 4 include an analysis of objective indicia of non-obviousness, despite Encube's acknowledging the existence of the same. Objective indicia of non-obviousness "must always when present be considered en route to a determination of obviousness." *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983). And the Board has "cautioned petitioners in prior proceedings that petitions may be denied if they do not address known evidence of secondary considerations." *Stryker Corp. v. KFX Med., LLC*, IPR2019-00817, Paper 10 at 28 (P.T.A.B. Sept. 16, 2019). While a petitioner cannot address objective indicia of non-obviousness of which it is not aware or which Patent Owner has not yet presented⁸, Encube's Petition notes the patent's "surprising[] and unexpected[]" finding that once-daily application of 1% tapinarof cream was just as effective as twice-daily application. Pet., 1; EX1001, 6:52-60. Yet the Petition does not analyze, as the law requires, this surprising, unexpected finding in its obviousness arguments.

Encube's sole counter to Applicant's surprising and unexpected findings is

⁸ To be clear, this Preliminary Response is highlighting the Petition's failure to address known objective indicia and is not affirmatively presenting objective indicia of non-obviousness.

that “during prosecution the examiner cited a set of prior art by Chen et al. disclosing treating plaque psoriasis by topically applying a composition containing 1% tapinarof once a day.” Pet., 1. As already discussed, Chen discloses applying a composition containng 1% mixture of *cis* and *trans* 3,5-dihydroxy-4-isopropylstilbene, and not one containing 1% tapinarof (3,5-dihydroxy-4-isopropyl-*trans*-stilbene). Chen therefore does not undermine Applicant’s surprising and unexpected findings. The Petition does not attempt to show otherwise.

C. Additional deficiencies in Grounds 2, 3, and 4 further support denying institution

While Grounds 2, 3, and 4 all suffer from the same fundamental flaws, Grounds 2, 3, and 4 are further deficient for the following reasons.

1. Ground 2 relies on the same failed inherency argument presented in Ground 1

The Petition argues in Ground 2 that “[a]ll of the Challenged Claims (including claims 7, 10, and 21) are also obvious in view of Sonti’s teachings.” Pet., 28. Ground 2 incorporates Ground 1’s failed inherency showing that purports that disclosure of a treatment for “moderate to severe” plaque psoriasis is necessarily disclosure of a treatment for “mild” plaque psoriasis. *Id.*, 29. Encube’s own exhibits contradict this argument because they disclose that treatment of moderate to severe plaque psoriasis is not *necessarily* the same as treatment of

mild psoriasis. EX1015, 3 (Table 1); EX1006, 3 (Table 2); *see* Section V.A.1.

Nothing in Ground 2 cures this flaw. Moreover, Ground 2 fails to explain why a POSA would have allegedly been motivated to use a treatment with potential life-altering side effects (i.e., a treatment for severe psoriasis) to treat a mild form of disease, when Encube's EX1006 shows that other treatments with *no known serious risks* (i.e., a treatment for mild psoriasis) were available. EX1006, 3.

2. Grounds 2 and 4 further fail because Encube has not shown reasonable likelihood of prevailing for claims 3 and 4

Just as it did with Ground 1, the Petition's Ground 2 and 4 arguments for dependent claims 3 and 4 fail to reconcile the differences between Sonti's "physically stable" emulsion formulations and those that cause chemical degradation or are "non-uniform." Encube again picks and chooses the ingredients recited in claim 3 from at least 13 different formulations in Sonti, combining elements from Sonti's "physically stable" emulsion embodiments with other embodiments that Sonti negatively characterizes as causing "chemical degradation of the active ingredient" and as "non-uniform emulsions." Pet., 35-37; *see also* Section VI.A.3.

And Encube's Declarations do not support obviousness of claims 3 or 4. Dr. Liem relies exclusively Mr. Sudhakar's testimony for Dr. Liem's opinions on claims 3 and 4. And Mr. Sudhakar provides opinions on claims 3 and 4, but never analyzes or even mentions independent claim 1, from which claims 3 and 4

depend. Thus, both of Dr. Liem's and Mr. Sudhakar's opinions on claims 3 and 4 lack supporting facts and rationale, and neither expert's testimony should be given any weight. 37 C.F.R. § 42.65(a); *Xerox*, IPR2022-00624, Paper 9 at 15 (informative). Further, neither the Petition nor any Declaration addresses, let alone explains why a POSA would have combined ingredients from emulsions that chemically degrade the active ingredient or from non-uniform emulsions with ingredients from physically stable emulsions, or why the POSA would have reasonably expected success when doing so. *See In re Stepan Co.*, 868 F.3d 1342, 1346 n.1 (Fed. Cir. 2017) (when "selecting from large lists of elements in a single reference, there must be a motivation to make the combination and a reasonable expectation that such a combination would be successful, otherwise a skilled artisan would not arrive at the claimed combination").

3. Grounds 3 and 4 are further deficient because Bissonnette belies the purported motivation to combine

a. Encube's proffered reasons to combine Sonti and Bissonnette for claims 7 and 21 fail

Ground 3 relies on Grounds 1 "and/or" Ground 2 (Pet., 46) and likewise suffers from the same failures discussed above for Grounds 1 and 2. As already shown, Encube fails to meet its burden showing claims 7, 21, and 9-10 are

anticipated and/or obvious in view of Sonti,⁹ Encube's additional reliance on Bissonnette in Ground 3 fares no better.

Encube alleges that there “would have been good reason to combine the teachings of Sonti and Bissonnette” because “each teaches treating the *same* condition (plaque psoriasis) with the *same* amount of the *same* active compound (1% tapinarof).” Pet., 47 (emphasis in original). But Bissonnette is directed to a *twice daily* application of 1% tapinarof. EX1008, 2. The argument for claims 7 and 21 fails to mention this fact, let alone explain why a POSA would have modified that twice-daily application to once-daily application, as recited in the challenged claims. See Pet., 46-49.

Rather than address the twice-daily versus once-daily hole in its argument, Encube instead argues summarily that combining “Sonti’s teaching of treating plaque psoriasis with Bissonnette’s teachings of treating subjects with BSA affected by plaque psoriasis” would have been “just the predictable application of a known method to subjects.” Pet., 48. But, absent from the Petition is any explanation of how modifying Bissonnette’s twice-daily method in view of Sonti’s teachings would have been “predictable.” Nor has Encube explained which of

⁹ Indeed, Ground 1 does not even challenge claims 7, 10, and 21. Pet., Section VIII.

Sonti's *14 different application frequencies or 500 different amounts of tapinarof* a POSA would have combined with Bissonnette's twice-daily application.

b. Encube's reasons to combine Sonti and Bissonnette for claims 9-10 lack merit

For claims 9-10, Encube argues that because "Bissonnette [*sic*] discloses that after 12 weeks of treatment, the percent BSA affected by plaque psoriasis had decreased an average of 79.1%, from a mean of 3.3% BSA to a mean of 0.7% BSA," the "claimed decrease in BSA would have been obvious in view of the teachings of Sonti and Bissonnette." Pet., 49-50. While Encube actually acknowledges in this argument that Bissonnette teaches twice-daily application, Encube never squares that fact with the Petition's assertion that the skilled artisan would have reasonably expected the BSA reduction reported in Bissonnette to also happen when only half of the amount of tapinarof (1%, once-daily) is applied. Encube again misplaces reliance on Chen to assert obviousness because "it was also already known that once daily application was highly effective to treat mild to severe plaque psoriasis." Pet., 50. This argument is belied by the fact that Chen discloses applying a compound other than tapinarof to its Volunteers, another fact that Encube overlooks in its Petition.

c. Bissonnette itself belies the Petition's purported motivation to combine

Encube's reason for why a POSA would have been motivated to modify

Bissonnette from twice-daily to once-daily application in Ground 4 is refuted by Bissonnette's own disclosure.

Encube asserts that a POSA would have been additionally motivated to modify Bissonnette's effective twice-daily application to a once-daily application frequency for three reasons: (i) to "reduce side effect risk by reducing the body's exposure to the active compound," (ii) "to improve patient compliance with treatment recommendations," and (iii) "to reduce cost of treatment." Pet., 53. Bissonnette itself squarely contradicts the first two reasons. And the Petition does not acknowledge the contrary teachings in Bissonnette, as it must. *See In re Wesslau*, 353 F.2d 238, 241 (C.C.P.A. 1965) ("It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art."). The third reason is equally unsupported by the record.

Since the Petition cannot support that once-daily application is a viable alternative to Bissonnette's effective, twice-daily application, it has not and cannot demonstrate any motivation to modify Bissonnette. And it is Petitioner's burden to so do. *See Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367–1368 (Fed. Cir. 2016) (it is Petitioner's burden to demonstrate "that a skilled artisan would have been motivated to combine the teachings of the prior art

references to achieve the claimed invention”).

i. Bissonnette suggested reducing the concentration of tapinarof to reduce the minimal adverse events reported

Bissonnette’s disclosures belie Encube’s assertion that a POSA “would have been motivated to use the once-daily application frequency rather than twice-daily to minimize risk of side effects.” Pet., 56. Bissonnette reported that “[a]ll dermatological adverse events observed in patients randomized to WBI-1001 were either *mild* (34) or *moderate* (two) in intensity.” EX1008, 4. The Petition acknowledges that in Bissonnette, “most [adverse events] were mild,” but nonetheless asserts that “a POSA still would have been motivated to decrease the application frequency from twice to once daily to minimize the risk of such adverse events, given that the once-daily administration would have been expected to still be highly effective.” Pet., 56-57.

Yet, to the extent there were meaningful adverse events (Bissonnette reported none), Bissonnette never—contrary to the Petition—suggested reducing the frequency from twice-daily to once-daily application to minimize risk. Rather, Bissonnette suggested reducing *the concentration of tapinarof*. Indeed, Bissonnette disclosed that “WBI-1001 *at 0.5%* has been shown to be effective in treatment of atopic dermatitis, and this lower concentration *may have decreased the incidence of application site adverse drug reactions* observed in the current study.” EX1008,

5. Neither the Petition nor Encube's Declarants address this disclosure. In ignoring these teachings altogether, Encube fails to consider Bissonnette for all that it teaches, and fails to meet its burden to establish that a POSA would have had a reason to decrease the application frequency used in Bissonnette based on adverse events. *Wesslau*, 353 F.2d at 241.

ii. Bissonnette did not report patient compliance issues with twice-daily application of tapinarof

Bissonnette also contradicts Encube's assertion that a "POSA would have been motivated to use once-daily application rather than twice daily to improve patient compliance with the treatment regimen." Pet., 57. Encube's cursory assertion that it was "commonly known (and also common-sense) that patients were more likely to follow the recommended treatment regimen when the application frequency was once daily, rather than twice daily," carries no weight in the face of Bissonnette's reporting no compliance concerns with twice-daily application. *Id.*

Bissonnette disclosed that "[m]ain protocol deviations included ... *non compliance to study treatment by one patient.*" EX1008, 3 (emphasis added). That is, only one of the sixty-one patients in the study did not fully comply with the treating regimen. *Id.* Notably, the reported non-compliance was "application of study product on <80% of psoriasis plaques," and nothing to do with the number of applications per day. *Id.* Encube once again, and impermissibly, fails to consider

Bissonnette for all that it teaches, including ignoring disclosures that belie its own arguments. *Wesslau*, 353 F.2d at 241.

iii. Encube’s rationale that lower treatment cost would have motivated a POSA to use once-daily tapinarof is unsupported

In a two sentence argument relying exclusively on paragraphs from the Liem and Sudhakar Declarations, Encube asserts simply that a POSA would have been motivated to modify Bissonnette to a once-daily application “to lower treatment cost. Less frequent application uses less volume of the topical composition, resulting in lower overall treatment cost. Ex-1003, ¶338; Ex-1032, ¶86.” Pet., 57. This argument again relies on incorporation by reference to its expert declarations, providing no actual explanation or underlying evidence to support its conclusory statement. 37 C.F.R. § 42.6. Dr. Liem in EX1003, ¶338 states: “A POSA was always motivated to lower cost, *if it could be done while still maintaining treatment safety and efficacy*” (emphasis added). Mr. Sudhakar, in EX1032, ¶86, asserts that: “*Where feasible*, reducing dose frequency may offer benefits for the health care budget holder in terms of costs” (emphasis added). As already established, the Petition has failed to show that a POSA would have expected once-daily application of tapinarof would “still maintain[] treatment safety and efficacy” or be a “feasible” treatment given its flawed reliance on Chen to show as such. *See* Section IV.B.3.c.

Since the Petition's evidence does not support that once-daily application is a viable alternative to Bissonnette's effective, twice-daily application, it has not demonstrated—nor can it—that any cost savings between twice and once-daily application are significant enough to motivate a POSA to modify Bissonnette. *See Intelligent Bio-Sys.*, 821 F.3d at 1367–1368.

VII. CONCLUSION

For the reasons discussed above, the Petition fails on multiple fronts to establish a reasonable likelihood of prevailing with respect to any challenged claim. The Board should therefore deny institution.

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CERTIFICATE OF WORD COUNT (37 C.F.R. § 42.24(d))

1. This Patent Owner Preliminary Response complies with the type-volume limitation of 14,000 words, comprising 13,836 words, excluding the parts exempted by 37 C.F.R. § 42.24(a)(1).

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CERTIFICATE OF SERVICE (37 C.F.R. § 42.6(e))

I certify that the above-captioned **PATENT OWNER PRELIMINARY
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