

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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NOVARTIS PHARMACEUTICALS CORPORATION,  
Petitioner,

v.

REGENTS OF THE UNIVERSITY OF MICHIGAN AND UNIVERSITY  
OF SOUTH FLORIDA,  
Patent Owner.

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IPR2023-01346  
Patent 10,633,344 B2

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Before JEFFREY N. FREDMAN, MICHAEL J. FITZPATRICK, and  
SHERIDAN K. SNEDDEN, *Administrative Patent Judges*.

Opinion for the Board filed by *Administrative Patent Judge* SNEDDEN.

Opinion dissenting filed by *Administrative Patent Judge* FITZPATRICK.

SNEDDEN, *Administrative Patent Judge*.

DECISION  
Granting Institution of *Inter Partes* Review  
35 U.S.C. § 314; 37 C.F.R. § 42.4

## I. INTRODUCTION

### *A. Background and Summary*

Novartis Pharmaceuticals Corporation (“Petitioner”) filed a Petition requesting an *inter partes* review of claims 10, 11, and 18 of U.S. Patent No. 10,633,344 (“the ’344 patent,” Ex. 1001). Paper 4 (“Pet.”). University of South Florida and Regents of The University of Michigan (“Patent Owner”) did not file a Preliminary Response.

To institute an *inter partes* review, we must determine that the information presented in the Petition shows “a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a) (2018). The Supreme Court has held that a decision to institute under 35 U.S.C. § 314 may not institute on less than all claims challenged in the petition. *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1359–60 (2018). After considering the information presented in the Petition, we determine that Petitioner has demonstrated a reasonable likelihood of success in proving that at least 1 of the challenged claims of the ’344 patent is unpatentable.

### *B. Real Parties in Interest*

Petitioner asserts that Novartis Pharmaceuticals Corporation is the real party in interest. Pet. 72.

### *C. Related Matters*

Petitioner indicates that the ’344 patent is asserted against Petitioner in *Regents of the Univ. of Mich. v. Novartis Pharm. Corp.*, 3:2-cv-04913-AMO (N.D. Cal.), filed August 29, 2022. Pet. 72.

Petitioner has also filed a petition for *inter partes* review in IPR2023-01347 against the ’344 patent. Paper 3.

*D. The '344 patent (Ex. 1001)*

The '344 patent discloses “binary phase compositions comprising one or more pharmaceutical entities and methods for producing such compositions.” Ex. 1001, Abstract. In particular, “[t]he subject invention relates to the application of the concepts of crystal engineering towards the design of new pharmaceutical phases that contain more than one molecular component.” Ex. 1001, 3:9–11. The '344 patent describes “crystal engineering,” noting that “[t]he ability of crystalline self-assemblies to be built from a bottom-up approach could provide an exceptional control of the design of new phases at a molecular level.” *Id.* at 2:1–4. The '344 patent describes that “novel crystalline assemblies can afford improved drug solubility, dissolution rate, stability and bioavailability.” *Id.* at 3:26–28.

The '344 patent claims “a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of co-crystal.” *Id.* at 25:18–20. The co-crystal is a “supramolecular synthon,” which “refers to the sum of the components of a multi-component noncovalent interaction.” *Id.* at 9:66–67, 10:1. The supramolecular synthon is “formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and at least one co-former.” *Id.* at 25:21–23. The '344 patent details that APIs may include “aspirin, one or more members of the profen series (e.g., ibuprofen and flurbiprofen), carbamazepine, phenytoin and acetaminophen.” *Id.* at 3:17–19. The API must have a “first chemical functionality that permits formation of API homosynthons through non-covalent hydrogen bonding.” *Id.* at 25:24–26. The '344 patent describes co-formers as “solvent molecules, other drug molecules, GRAS compounds, or approved food additives.” *Id.* at 3:35–37. The co-former must have “a second chemical functionality

complementary to the first chemical functionality via non-covalent hydrogen bonding.” *Id.* at 25:28–30. Importantly, the API’s first chemical functionality is by one of three functional groups: (i) a carboxamide, (ii) a carbonyl, or (iii) an amine. *Id.* at 25:38–39.

*E. The Challenged Claims*

Petitioner challenges claims 10, 11 and 18, which are reproduced below.

10. [10a] A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of [10b] a co-crystal comprising supramolecular synthons, each supramolecular synthon formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and at least one co-former,

[10c] wherein the API has a first chemical functionality that permits formation of API homosynthons through non-covalent hydrogen bonding when the API is in its pure form,

[10d] wherein the co-former has a second chemical functionality complementary to the first chemical functionality via non-covalent hydrogen bonding,

[10e] wherein said co-former is a solid at room temperature and atmospheric pressure when the co-former is in its pure form,

[10f] wherein supramolecular synthons are formed via non-covalent hydrogen bonding between the first chemical functionality of the API and the second chemical functionality of the co-former, and

[10g] wherein the first chemical functionality is (i) a carboxamide, (ii) a carbonyl, or (iii) an amine.

11. The pharmaceutical composition of claim 10, wherein the supramolecular synthon comprises a heterosynthon dimer formed by non-covalent hydrogen bonding of the API to the co-former.

18. The pharmaceutical composition of claim 10, wherein the first chemical functionality is a carboxamide.

Ex. 1001, 25:18–39, 25:40–43, 26:22–23.

*F. Evidence*

Petitioner relies upon information that includes the following.

Ex. 1004, Hickey et al., “Performance Comparison of a Co-Crystal of Carbamazepine with Marketed Product,” 67 EUR. J. PHARM. & BIOPHARM. 112–119 (2007) (“Hickey”).

Ex. 1005, Almarsson, US Pat. No. 7,927,613 B2, published April, 19, 2011 (“Almarsson”).

Ex. 1006, Martindale, The Complete Drug Reference (37<sup>th</sup> ed. 2011) (“Martindale”).

Petitioner also relies on the Declaration of Robin D. Rogers, Ph.D. (Ex. 1002) and Leah Appel, Ph.D. (Ex. 1003) to support its contentions.

*G. Asserted Grounds of Unpatentability*

Petitioner asserts that claims 10, 11 and 18 would have been unpatentable on the following grounds:

| Ground | Claim(s)<br>Challenged | 35 U.S.C. § <sup>1</sup> | Reference(s)/Basis            |
|--------|------------------------|--------------------------|-------------------------------|
| 1      | 10, 11, 18             | 102(b)                   | Hickey                        |
| 2      | 10, 11, 18             | 102(b)/103(a)            | Almarsson                     |
| 3      | 10, 11, 18             | 103(a)                   | Almarsson, Hickey, Martindale |

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<sup>1</sup> The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112-29, 125 Stat. 284, 287–88 (2011), amended 35 U.S.C. § 103, effective March 16, 2013. Because the application leading to the ’344 patent claims priority to an application filed before March 16, 2013, we apply the pre-AIA version of 35 U.S.C. § 103.

*H. Effective Filing Date of the Challenged Claims*

Pursuant to 35 U.S.C. § 120, a patent application is entitled to assert priority to the filing date of a prior application only “for an invention disclosed [in the prior application] in the manner provided by” 35 U.S.C. § 112. This requires that the earlier application provides written description support for the invention claimed by the later application. *See Paice LLC v. Ford Motor Co.*, 881 F.3d 894, 906 (Fed. Cir. 2018); *PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1306–11 (Fed. Cir. 2008); *Augustine Medical, Inc. v. Gaymar Indus., Inc.*, 181 F.3d 1291, 1302–03 (Fed. Cir. 1999). The test for sufficiency of a written description under 35 U.S.C. § 112, ¶ 1, is whether the earlier application’s disclosure “reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.” *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). The written description “test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art.” *Id.*

As articulated in *Ariad*, “an adequate written description requires a precise definition, such as by structure, formula, chemical name, physical properties, or other properties, of species falling within the genus sufficient to distinguish the genus from other materials.” *Ariad*, 598 F.3d at 1350 (citations omitted). One test of whether a claimed genus finds adequate support involves identifying in the specification “either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can ‘visualize or recognize’ the members of the genus.” *Ariad*, 598 F.3d at 1350 (citing *Regents of the Univ. of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997)).

The '344 patent issued from U.S. application Ser. No. 14/179,862 (“the ’862 application”), filed on February 13, 2014, which claims priority to U.S. application Ser. No. 10/378,956, filed Mar. 3, 2003, and to U.S. Provisional Application Ser. No. 60/360,768, filed Mar. 1, 2002 (collectively, “the Priority Applications”). Ex. 1501, at [21], [22], [60], [63]. Petitioner contends that “Patent Owner[] will be unable to meet their burden of production of showing written description and enablement support for claim 16 as of the 2002/2003 filing dates of the Priority Applications, as required by 35 U.S.C. §§ 112 and 120 (pre-AIA).” Pet. 11. “As a result, the earliest possible priority date [for the challenged claim] is the February 13, 2014 filing date of the ’862 application.” *Id.* at 12. More specifically, Petitioner contends that the Priority Applications lack adequate written description support for the full scope of claimed co-crystals. *Id.* at 11–17. We will assess Petitioner’s contentions in relation to independent claim 10 in detail.

Claim 10 is directed to a pharmaceutical composition comprising a co-crystal comprising supramolecular synthons, where each supramolecular synthon is formed from stoichiometric amounts of at least one API and at least one co-former. Ex. 1001, 25:18–23. Claim 10 recites that the API has a first chemical functionality (either a carboxamide, a carbonyl, or an amine) that permits formation of API homosynthons through non-covalent hydrogen bonding when the API is in its pure form. Claim 10 further recites that the co-former has a second chemical functionality complementary to the first chemical functionality via non-covalent hydrogen bonding. In short, the co-former’s second chemical functionality must be complementary to either a carboxamide, carbonyl, or amine functionality of an API via non-covalent hydrogen bonding.

According to Petitioner, “[t]he challenged claims are extremely broad [because] [t]hey are not limited to a specific co-crystal, or even a small group of co-crystals.” Pet. 12. In particular, Petitioner contends that the recited API and co-former are each selected from a large genus of potential APIs and co-formers, respectively. Pet. 12 (“the API may be selected from a large genus of potential APIs and the co-former from a large genus of potential co-formers”) (citing Ex. 1002 ¶¶ 69–74). Here, we note that the ’344 patent discloses “concepts of crystal engineering” to create “new pharmaceutical solid phases” using “cocrystal formers that are complementary [with an API] in the sense of supramolecular chemistry, i.e., they form supramolecular synthons with pharmaceutical molecules or ions.” Ex. 1001, 3:29–34, 4:10–12. The API may be any API having a carboxamide, carbonyl, or amine functionality. *Id.* at 25:38–39. The ’344 patent describes co-formers as “solvent molecules, other drug molecules, GRAS compounds, or approved food additives.” Ex. 1001, 3:35–37; *see* also *id.* at 8:35–38 (“The identified co-crystal formers can be, for example, a different API, a GRAS compound, a food additive, a low toxicity organic, or a metal-organic complex.”). The ’344 patent discloses that a GRAS is a compound “Generally Regarded as Safe by the Food and Drug Administration (FDA),” and is preferably a non-pharmaceutical entity. *Id.* at 9:21–26. Thus, taken together, the ’344 patent discloses that the co-former recited in the Challenged Claims may be one of a solvent molecule, a pharmaceutical entity, a non-pharmaceutical entity, a food additive, a low toxicity organic, or a metal-organic complex. Petitioner asserts that there are no structural features common to all embodiments of the challenged claims “because the challenged claims do not limit the structure of the API (beyond specifying the first chemical functionality) or the co-former of the claimed

co-crystals, let alone their structures when combined into a co-crystal.” Pet. 13 (citing Ex. 1002 ¶¶ 69, 75).

Petitioner also asserts that “[t]he Priority Applications fail to provide a representative number of species to support the breadth of the challenged claims.” *Id.* (citing Ex. 1002 ¶¶ 69, 75–82). Furthermore, Petitioner asserts that “no Example in the Priority Applications involves a co-crystal where the API has a first chemical functionality that is a carbonyl.” Pet. 13 (citing Ex. 1002 ¶ 76). Petitioner argues that “there are only ten Examples where the API has a carboxamide or amine and the co-former is solid, as required by the challenged claims.” Pet. 13 (citing Ex. 1002 ¶¶ 76–77). Specifically, Example 2 discloses a co-crystal with “hydrogen bonding of adjacent phenytoin molecules between the carbonyl and the amine closest to the tetrahedral carbon.” Ex. 1001, 12:44–46. Example 7 discloses a co-crystal with “hydrogen bonded carboxamide homodimers that crystallize in the space group C2/c.” *Id.* at 16:24–26. Examples 8, 9, and 14 disclose co-crystals with “hydrogen bonded carboxamide homodimers.” *Id.* at 17:13–14, 18:1–2, 21:3–4. Example 10 discloses a molecule where “[e]ach hydrogen on the CBZ 1 amine is hydrogen bonded to a carbonyl group of a different 2,6-pyridinedicarboxylic acid moiety.” *Id.* at 18:53–55. Example 12 discloses a co-crystal with “hydrogen bonded carboxamide-carboxylic heterodimers.” *Id.* at 20:1–2. Example 15 discloses a co-crystal with “hydrogen bonded carboxamide-carboxylic heterodimers between the carbamazepine moieties and the butyric acid moieties.” *Id.* at 21:36–38. Example 16 discloses a co-crystal with “hydrogen bonded carboxamide homosynthon.” *Id.* at 22:1–2. Example 17 discloses a co-crystal with a “hydrogen bonded carboxamide homodimers between two carbamazepine moieties and carboxylic acids homodimers between two formamide

moieties.” *Id.* at 22:38–41. According to Petitioner, “[t]hese ten Examples (involving only three different APIs with a carboxamide or amine and no examples of an API with a carbonyl first chemical functionality) are not representative of all APIs and co-formers that provide co-crystals encompassed by the challenged claims.” Pet. 15–16 (citing Ex. 1002 ¶¶ 76–78). Petitioner asserts that “the Priority Applications do not provide any correlation between the structure of any given co-former or its ‘second chemical functionality’ and the function required by the claims.” *Id.* at 16 (citing Ex. 1002 ¶¶ 77–78, 80–82).

Petitioner also asserts that, in the ’344 patent, “no Example involves a co-crystal where the API has a first chemical functionality that is a carbonyl and at most there are ten examples with an API having a carboxamide or amide first chemical functionality and a solid co-former (Examples 1, 2, 7–11, 13, 14, 19),” which “are insufficient to guide a POSA in practicing the full scope of broad claims 10, 11 and 18.” Pet. 30 (citing Ex. 1002 ¶¶ 76–77, 79, 127–30).

Based on the preliminary record, we are persuaded by Petitioner’s contention that claims 10, 11, and 18 do not comply with the written description requirement for the reasons set forth in the Petition (Pet. 11–16), summarized above. More specifically, on the current record, we do not recognize the ’344 patent to disclose a representative number of co-formers having the necessary features complementary to the recited carboxamide, carbonyl, or amine functionality. That is, we do not understand the ’344 patent to disclose structural features common to the recited co-formers such that a POSA could “visualize or recognize” the members of the claimed genus. *Ariad*, 598 F.3d at 1350. We recognize that a POSA’s perspective is key to the written description inquiry and many factors may inform the

adequacy of a specification's disclosure, including existing knowledge in the field and the content of the prior art. *See Ariad*, 598 F.3d at 1351. On the current record, however, we do not find evidence that a POSA would have considered the recited “second chemical functionality compl[e]mentary to the first chemical functionality via non-covalent hydrogen bonding” to form a supramolecular synthon a concept that was well-known in the art.

Accordingly, in view of the above, we preliminary determine that the effective filing date for claims 10, 11, and 18 is February 13, 2014, the filing date the '344 patent.<sup>2</sup>

## II. ANALYSIS

### *A. Principles of Law*

“In an [*inter partes* review], 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) (requiring *inter partes* review petitions to identify “with particularity . . . the evidence that supports the grounds for the challenge to each claim”)). This burden of persuasion never shifts to Patent Owner. *See Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015) (discussing the burden of proof in *inter partes* review).

To anticipate a claim under 35 U.S.C. § 102, “a single prior art reference must expressly or inherently disclose each claim limitation.” *Finisar Corp. v. DirecTV Group, Inc.*, 523 F.3d 1323, 1334 (Fed. Cir. 2008).

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<sup>2</sup> We note that Petitioner additionally challenges the Priority Applications for lack of enablement. Having found that the '344 patent lacks written description support for all Challenged Claims, however, we need not address Petitioner's enablement challenge in order to decide whether to institute.

Accordingly, “the dispositive question regarding anticipation [i]s whether one skilled in the art would reasonably understand or infer from the [prior art reference’s] teaching’ that every claim element was disclosed in that single reference.” *Dayco Prods., Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 1368 (Fed. Cir. 2003) (quoting *In re Baxter Travenol Labs.*, 952 F.2d 388, 390 (Fed. Cir. 1991)).

A claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which that subject matter pertains. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved based on underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness, if present. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

In analyzing the obviousness of a combination of prior art elements, it can be important to identify a reason that would have prompted one of skill in the art “to combine . . . known elements in the fashion claimed by the patent at issue.” *KSR*, 550 U.S. at 418. A precise teaching directed to the specific subject matter of a challenged claim is not necessary to establish obviousness. *Id.* Rather, “any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.” *Id.* at 420. Accordingly, a party that petitions the Board for a determination of unpatentability based on obviousness of a combination of prior art teachings must show that “a skilled artisan would have been motivated to combine the

teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.” *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1381 (Fed. Cir. 2016) (internal quotation marks and citations omitted). Under the proper inquiry, “obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success.” *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007).

We analyze the asserted grounds of unpatentability in accordance with these principles.

#### *B. Claim Construction*

We interpret a claim “using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b).” 37 C.F.R. § 42.100(b) (2019). Under this standard, we construe the claim “in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” *Id.*

Petitioner proposes constructions for the terms “active pharmaceutical ingredient (API)”, “API homosynthons”, “carbonyl”, “carboxamide”, “co-former”, “heterosynthon dimer”, and “supramolecular synthon.” Pet. 9–10. According to Petitioner, “[t]he parties agree that co-former is used synonymously with co-crystal former and that a co-former is a component of a co-crystal.” *Id.* at 9. Petitioner represents that the proposed constructions have been agreed to between the parties in parallel litigation, or agreed upon such that “the disputed portions are not relevant to the issues raised in this Petition.” *Id.* at 8. We have reviewed each of these constructions and adopt

Petitioner’s proposed construction for the purposes of this Decision. Petitioner’s construction aligns with the plain words of the claim, is consistent with the prosecution history of the ’344 patent, and finds support in the uncontroverted testimony of Dr. Rogers. Ex. 1002 ¶¶ 55–64; Ex. 1016, 256–58, 261–63.

Petitioner construes the term “co-crystal” to mean “a multiple-component, single crystalline phase, having a fixed stoichiometry of its component compounds.” *Id.* at 10. Petitioner states that the proposed construction of the term “co-crystal” is “currently disputed in parallel litigation; however, because the claims are unpatentable under Patent Owners’ constructions, Petitioner adopts those constructions solely for the purpose of this Petition.” *Id.* at 8. We adopt Petitioner’s proposed construction of “co-crystal” for the purposes of this Decision.

No other terms require express construction. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Ltd.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (per curiam) (claim terms need to be construed “only to the extent necessary to resolve the controversy”) (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)). To the extent further discussion of the meaning of any claim term is necessary to our decision, we provide that discussion below in our analysis of the asserted grounds of unpatentability.

*C. Level of Ordinary Skill in the Art*

Petitioner asserts that a person of ordinary skill in the art (“POSA”) at the time of the invention

would have had a Ph.D. in chemistry or a related field with at least two years of experience in solid state chemistry, including experience preparing multiple-component crystalline solids and

evaluating their single crystal structures. Alternatively, a POSA would have had a Ph.D. in chemistry, pharmacy, or a related field with at least two years of experience in formulation of pharmaceutical compositions, and the POSA would consult with others having ordinary experience in other disciplines, such as solid-state chemistry, including experience preparing multiple-component crystalline solids and evaluating their single crystal structures.

Pet. 7–8.

Because Petitioner’s presently unopposed definition is consistent with the ’344 patent and the prior art of record, we adopt that definition in deciding whether to institute trial. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1354–55 (Fed. Cir. 2001); *In re GPAC Inc.*, 57 F.3d 1573, 1579–80 (Fed. Cir. 1995); *In re Oelrich*, 579 F.2d 86, 91 (CCPA 1978).

*D. Ground 1: Asserted Anticipation of Claims 10, 11, and 18 by Hickey*

Petitioner asserts that Hickey anticipates claims 10, 11, and 18. Pet. 33–45. To support its contentions, Petitioner directs our attention to the disclosure of Hickey and provides a detailed claim analysis addressing how Hickey discloses each element of claims 10, 11, and 18. *Id.* (citing Ex. 1002). Petitioner contends that Hickey qualifies as prior art to the ’344 patent “[b]ecause the challenged claims are not entitled to a 2002/2003 priority date.” *Id.* at 33.

In view of the following, we determine that Petitioner has demonstrated a reasonable likelihood of prevailing on this ground. We start with an overview of the asserted prior art, Hickey.

*1. Hickey (Ex. 1004)*

Hickey discloses the use of carbamazepine as a co-crystal “that is suitable for drug development.” Ex. 1004, 118. Hickey notes that

“[c]arbamazepine, an important anti-epileptic agent that has been in use for over 30 years, is an example of a water-insoluble drug that has a high dose requirement ( $>100$  mg/day) for therapeutic effect.” Ex. 1004, 112. Hickey details a co-crystal of carbamazepine and saccharin, including “a performance comparison of the co-crystal to the marketed form of carbamazepine (Tegretol<sup>®</sup>, containing carbamazepine form 3).” Ex. 1004, 113. Hickey concludes that “[t]he present study illustrates the utility of a co-crystal as a type of material that is suitable for drug development.” Ex. 1004, 118. Particularly, Hickey notes that “[t]he benefits of using the carbamazepine: saccharin co-crystal include (i) relative lack of polymorphism and equivalent chemical stability to the anhydrous polymorph, (ii) favorable dissolution properties and suspension stability, and (iii) comparable oral absorption profile in dogs compared with the commercial immediate release product.” *Id.*

## 2. Independent Claim 10

Turning now to the claims, we discuss independent claim 10 in detail.

*a) [10a] A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of [a co-crystal]*

Petitioner asserts that Hickey discloses a “pharmaceutically acceptable carrier” by describing the preparation of alpha-lactose monohydrate (lactose) into a capsule. Pet. 42 (citing Ex. 1004, 115, 118; Ex. 1002 ¶¶ 186–88). Petitioner further argues that the described composition would have also been understood to include a co-crystal as Hickey disclosed the capsule to contain “‘200 mg of carbamazepine,’ i.e., the same amount of carbamazepine included in the commercial Tegretol product.” Pet. 42–43 (citing Ex. 1004, 112, 115, 118; Ex. 1002 ¶¶ 187–88;

Ex. 1003 ¶¶ 58–59). Petitioner asserts that the capsules were reported to be a “‘viable alternative’ to Tegretol” and thus, a person of ordinary skill in the art would have concluded “that the Hickey capsules included an amount of co-crystal that was therapeutically effective as an anti-epileptic.” Pet. 43 (citing Ex. 1004, 112–13, 115, 118; Ex. 1002 ¶¶ 186–89; Ex. 1003 ¶¶ 57, 59–60).

Based on Petitioner’s argument and evidence, we are persuaded that Petitioner has shown sufficiently for purposes of this Decision that Hickey discloses the subject matter of the preamble of claim 10.

*b) [10b] a co-crystal comprising supramolecular synthons, each supramolecular synthon formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and at least one co-former*

Petitioner notes that “Hickey discloses a 1:1 co-crystal of carbamazepine and saccharin.” Pet. 35 (citing Ex. 1004, 113–15. Petitioner argues that Hickey’s description of carbamazepine meets the “agreed-upon API definition.” Pet. 36 (citing Ex. 1004, 112). Further, Petitioner argues that “[a] POSA would understand that saccharin is a co-former in the co-crystal because it is complementary to, and forms a co-crystal with, carbamazepine.” Pet. 36 (citing Ex. 1004, 113–15). Therefore, Petitioner asserts that “[t]he carbamazepine/saccharin co-crystal qualifies as a co-crystal under the ‘344 patent.” Pet. 37.

Based on Petitioner’s argument and evidence, we are persuaded that Petitioner has shown sufficiently for purposes of this Decision that Hickey discloses this element of claim 10.

- c) [10c] Wherein the API has a first chemical functionality that permits formation of API homosynthons through non-covalent hydrogen bonding when the API is in its pure form*  
*[10g] wherein the first chemical functionality is a carboxamide*

Petitioner asserts Hickey discloses these claim limitations by describing carbamazepine. Pet. 40 (citing Ex. 1002 ¶ 173). Petitioner argues that carbamazepine discloses limitation [10c] because “[t]he carboxamide on one carbamazepine hydrogen bonds with the carboxamide of an adjacent carbamazepine to form an API homosynthon, i.e., a synthon between identical and complementary chemical functionalities (the carboxamide groups) of the API (carbamazepine).” Pet. 39 (citing Ex. 1005, figure 50A, 6:38–40, 6:47–61; Ex. 1002 ¶¶ 171–73).

Based on Petitioner’s argument and evidence, we are persuaded that Petitioner has shown sufficiently for purposes of this Decision that Hickey discloses these elements of claim 10.

- d) [10d] wherein the co-former has a second chemical functionality complementary to the first chemical functionality via non-covalent hydrogen bonding*  
*[10f] wherein the supramolecular synthons are formed via non-covalent hydrogen bonding between the first chemical functionality of the API and the second chemical functionality of the co-former*

Petitioner argues that “saccharin has a second chemical functionality . . . that forms non-covalent hydrogen bonds with the first chemical functionality (carboxamide) of the API (carbamazepine).” Pet. 40–41 (citing Ex. 1004, 113; Ex. 1002 ¶¶ 166–67, 174–75, 180–81). Further, Petitioner notes the “same non-covalent hydrogen bonding between the first chemical functionality of the API and the second chemical functionality of the co-

former gives rise to supramolecular synthons. Pet. 41 (citing Ex. 1002 ¶¶ 166–67, 180–82).

Based on Petitioner’s argument and evidence, we are persuaded that Petitioner has shown sufficiently for purposes of this Decision that Hickey discloses these elements of claim 10.

*e) [10e] wherein said co-former is a solid at room temperature and atmospheric pressure when the co-former is in its pure form*

Petitioner asserts the co-former disclosed in Hickey, saccharin, meets the claim limitation. Petitioner notes that saccharin “has a melting point of 228.8 °C” and thus, “saccharin is a solid at room temperature and atmospheric pressure when in its pure form.” Pet. 41–42.

Based on Petitioner’s argument and evidence, we are persuaded that Petitioner has shown sufficiently for purposes of this Decision that Hickey discloses this element of claim 10.

### *3. Conclusion*

In view of the foregoing, we determine that Petitioner has demonstrated a reasonable likelihood of showing that Hickey discloses all limitations of claim 10 and thus that claim 10 is anticipated by Hickey. Claims 11 and 18 depend from claim 10. Having reviewed Petitioner’s arguments asserting that claims 11 and 18 are anticipated by Hickey (Pet. 38–40, 43–45), we also determine that Petitioner has demonstrated a reasonable likelihood of prevailing on its assertions as to those dependent claims.

*E. Ground 2: Asserted Anticipation or Obviousness of Claims 10, 11, and 18 over Almarsson*

Petitioner asserts that claims 10, 11, and 18 are anticipated by Almarsson. Pet. 45–62. To support its contentions, Petitioner directs our attention to the disclosure of Almarsson and provides a detailed claim analysis addressing how Almarsson discloses each element of claims 10, 11, and 18. *Id.* at 45–62 (citing Ex. 1002). Petitioner also asserts, in the alternative, that claims 10, 11, and 18 would have been obvious over Almarsson. *Id.* Petitioner contends that Almarsson qualifies as prior art to the '344 patent “[b]ecause the challenged claims are not entitled to a 2002/2003 priority date.” *Id.* at 45.

For the reasons explained below, we determine that Petitioner has demonstrated a reasonable likelihood of prevailing on these grounds. We start with an overview of the asserted prior art, Almarsson.

*1. Almarsson (Ex. 1005)*

Almarsson is a patent that “relates to co-crystal API-containing compositions, pharmaceutical compositions comprising such APIs, and methods for preparing the same.” Ex. 1005, 1:28–30. Though Almarsson does not claim relation to the '344 patent, all three inventors of the '344 patent are listed as inventors on Almarsson. *Id.* at [75]. Almarsson notes that “variation of the crystalline state of an API is one of many ways in which to modulate the physical properties thereof.” *Id.* at 1:49–51. Almarsson discloses “a co-crystal pharmaceutical composition comprising an API compound a co-crystal former, such that the API and co-crystal former are capable of co-crystallizing from a solid or solution phase under crystallization conditions.” *Id.* at 2:12–15.

Almarsson's example 1 discloses "1:1 carbamazepine:saccharin co-crystals (Form I)." *Id.* at 32:20. Almarsson's example 2 discloses "1:1 carbamazepine:nicotinamide co-crystals." *Id.* at 32:31. Almarsson's example 3 discloses "1:1 carbamazepine:trimesic acid co-crystals (Form I)." *Id.* at 32:41. Almarsson's example 24 discloses "[a]cetaminophen:4,4'-bipyridine:water (1:1:1 stoichiometry)." *Id.* at 36:65. Almarsson's example 25 discloses "[p]heny[t]oin:[p]ydridone (1:1 stoichiometry)." *Id.* at 37:27. Almarsson's example 26 discloses "[a]spirin (acetylsalicylic acid):4,4'-bipyridine (2:1 stoichiometry)." *Id.* at 38:10–11. Almarsson's example 27 discloses "[i]buprofen:4,4'-[b]ipyridine (2:1 stoichiometry)." *Id.* at 38:50. Almarsson's example 28 discloses "[f]lurbiprofen:4,4'-bipyridine (2:1 stoichiometry)." *Id.* at 39:30. Almarsson's example 29 discloses "Flurbiprofen:trans-1,2-bis(4-pyridyl) ethylene (2:1 stoichiometry)." *Id.* at 40:9–10. Almarsson's example 30 discloses "[c]arbamazepine:p-[p]hthalaldehyde (1:1 stoichiometry)." *Id.* at 40:57. Almarsson's example 31 discloses "[c]arbamazepine:nicotinamide (Form II) (1:1 stoichiometry)." *Id.* at 41:37. Almarsson's example 32 discloses "[c]arbamazepine:saccharin (Form II) (1:1 stoichiometry)." *Id.* at 42:22. Almarsson's example 33 discloses "[c]arbamazepine:2,6-pyridinedicarboxylic acid (2:3 stoichiometry)." *Id.* at 43:7–8. Almarsson's example 34 discloses "[c]arbamazepine:5-nitroisophthalic acid (1:1 stoichiometry)." *Id.* at 43:42. Almarsson's example 35 discloses "[c]arbamazepine: 1.3.5.7-adamantane tetracarboxylic acid (1:1 stoichiometry)." *Id.* at 44:22. Almarsson's example 36 discloses "[c]arbamazepine:benzoquinone (1:1 stoichiometry)." *Id.* at 44:55. Almarsson's example 37 discloses "[c]arbamazepine:trimesic Acid (Form II) (1:1 stoichiometry)." *Id.* at 45:19.

2. *Independent Claim 10*

Turning now to the claims, we discuss independent claim 10 in detail.

- a) *[10a] A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of [a co-crystal]*

Petitioner asserts that “Almarsson discloses a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a 1:1 carbamazepine/saccharin co-crystal.” Pet. 55. Petitioner acknowledges that “[c]laims 19 and 20 of Almarsson do not expressly reference the use of a therapeutically effective amount of the carbamazepine/saccharin co-crystal . . . however, that claim limitation would be taught or at least obvious in view of Almarsson’s teachings alone.” Pet. 55 (citing Ex. 1002 ¶¶ 247–52; Ex. 1003 ¶¶ 33, 63–66). Petitioner notes that Almarsson’s specification discloses a pharmaceutical composition with “a desired amount of API per dose” and “predetermined amount of the API.” Pet. 55 (citing Ex. 1005, 21:39-52). Thus, Petitioner asserts that “[a] POSA would understand these Almarsson references . . . teach, or at least render obvious, a therapeutically effective amount of the disclosed carbamazepine/saccharin co-crystal.” Pet. 56 (citing Ex. 1002 ¶¶ 246–52; Ex. 1003 ¶¶ 33, 64).

Based on Petitioner’s argument and evidence, we are persuaded that Petitioner has shown sufficiently for purposes of this Decision that Almarsson discloses this element of claim 10.

- b) *[10b] a co-crystal comprising supramolecular synthons, each supramolecular synthon formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and at least one co-former*

Petitioner asserts that Almarsson discloses a co-crystal of “carbamazepine and saccharin.” Pet. 48 (citing Ex. 1005, CITE – CLAIMS

19, 20). Petitioner argues that “[t]he carbamazepine/saccharin co-crystal of Almarsson Example 32 qualifies as a co-crystal under the ’344 patent.” Pet. 49. Petitioner notes that “[t]he Almarsson carbamazepine/saccharin co-crystal likewise contains supramolecular synthons.” Pet. 49. Additionally, Petitioner asserts that “Almarsson specifically identifies carbamazepine as an API” and “Almarsson further identifies saccharin as a co-crystal former.” Pet. 50. Thus, Petitioner argues that “Almarsson discloses in Example 32 a co-crystal comprising supramolecular synthons formed from 1:1 stoichiometric amounts of the API carbamazepine and the co-former saccharin, meeting limitation [10b].” Pet. 51 (citing Ex. 1002 ¶¶ 220, 229).

Based on Petitioner’s argument and evidence, we are persuaded that Petitioner has shown sufficiently for purposes of this Decision that Almarsson discloses this element of claim 10.

*c) [10c] wherein the API has a first chemical functionality that permits formation of API homosynthons through non-covalent hydrogen bonding when the API is in its pure form*

*[10g] wherein the first chemical functionality is a carboxamide*

Petitioner argues that “Figure 50A of Almarsson depicts the crystal structure of carbamazepine in pure form and shows that carbamazepine has a first chemical functionality that permits formation of API homosynthons through non-covalent hydrogen bonding.” Pet. 52 (citing Ex. 1005, Figure 50A).

Based on Petitioner’s argument and evidence, we are persuaded that Petitioner has shown sufficiently for purposes of this Decision that Almarsson discloses these elements of claim 10.

- d) [10d] wherein the co-former has a second chemical functionality complementary to the first chemical functionality via non-covalent hydrogen bonding*
- [10f] wherein the supramolecular synthons are formed via non-covalent hydrogen bonding between the first chemical functionality of the API and the second chemical functionality of the co-former*

Petitioner asserts that Almarsson's "[s]accharin has a second chemical functionality that forms non-covalent hydrogen bonds with the first chemical functionality (carboxamide) of the API (carbamazepine), and the second chemical functionality of saccharin is therefore complementary to the first chemical functionality of carbamazepine." Pet. 52–53 (citing Ex. 1002 ¶¶ 226, 234–35). Further, Petitioner asserts "[t]hat same non-covalent hydrogen bonding between the first chemical functionality of the API and second chemical functionality of the co-former gives rise to supramolecular synthons." Pet. 53 (citing Ex. 1002 ¶¶ 227–28, 234–35, 240–42).

Based on Petitioner's argument and evidence, we are persuaded that Petitioner has shown sufficiently for purposes of this Decision that Almarsson discloses these elements of claim 10.

- e) Wherein said co-former is a solid at room temperature and atmospheric pressure when the co-former is in its pure form*

Petitioner asserts Almarsson's co-former, saccharin, meets the limitation because "saccharin has a melting point of 228.8 °C, and is therefore a solid at room temperature and atmospheric pressure." Pet. 54.

Based on Petitioner's argument and evidence, we are persuaded that Petitioner has shown sufficiently for purposes of this Decision that Almarsson discloses this element of claim 10.

### 3. Conclusion

In view of the foregoing, we determine that Petitioner has demonstrated a reasonable likelihood of showing that Almarsson discloses all limitations of claim 10 and thus, that claim 10 is anticipated by Almarsson. Claims 11 and 18 depend from claim 10. Having reviewed Petitioner's arguments asserting that claims 11 and 18 are anticipated by Almarsson (Pet. 51, 59–62), we also determine that Petitioner has demonstrated a reasonable likelihood of prevailing on its assertions as to those dependent claims.

Furthermore, because anticipation is the epitome of obviousness, Petitioner has also demonstrated a reasonable likelihood of showing claims 10, 11, and 18 would have been obvious over Almarsson. *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed.Cir.1983) (“a disclosure that anticipates . . . also renders the claim invalid under § 103, for anticipation is the epitome of obviousness” (citations and internal quotation marks omitted)); *see also Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1357 n. 21 (Fed.Cir.1998) (a disclosure that anticipates also renders a claim obvious); *In re Pearson*, 494 F.2d 1399, 1402 (CCPA 1974) (anticipation is “the ultimate . . . obviousness”) (citations and internal quotation marks omitted); *In re Kalm*, 54 C.C.P.A. 1466, 378 F.2d 959, 962 (1967) (“Necessarily, a description in a reference which is insufficient as a matter of law to render a composition of matter obvious to one of ordinary skill in the art would a fortiori be insufficient to ‘describe’ the composition as that term is used [for purposes of establishing anticipation], a complete description being but the ultimate or epitome of obviousness.”).

*F. Ground 3: Asserted Obviousness of Claims 10, 11, and 18 over the Combination of Almarsson, Hickey, and Martindale*

Petitioner also asserts, in the alternative, that claims 10, 11, and 18 would have been obvious over the combination of Almarsson, Hickey, and Martindale. Pet. 45–62. We provided an overview of Almarsson and Hickey hereinabove. Before addressing Petitioner’s analysis, we additionally provide an overview of Martindale.

*1. Martindale (Ex. 1006)*

Martindale aims “to summarise clinically useful information on all drugs and medicines around the world.” Ex. 1006, preface v. Martindale discloses carbamazepine, describing carbamazepine as “a dibenzazepine derivative with antiepileptic and psychotropic properties.” *Id.* at 518. Additionally, Martindale discloses carbamazepine as a treatment “to control secondarily generalized tonic-clonic seizures and partial seizures, and in some primary generalised seizures.” *Id.*

*2. Discussion*

Petitioner asserts that “the POSA would also have looked to references like Hickey and Martindale to determine therapeutically effective amount of this Almarsson co-crystal.” Pet. 56 (citing Ex. 1002 ¶¶ 253–58; Ex. 1003 ¶ 67). Thus, Petitioner argues that “[a] POSA would have been motivated to combine these two additional references in view of their overlapping subject matter.” Pet. 56 (citing Ex. 1002 ¶¶ 259–61; Ex. 1003 ¶ 76).

As discussed above, Petitioner has already demonstrated a reasonable likelihood that it will prevail on its asserted anticipation grounds. *See supra* Sections II.D, II.E. Accordingly, we institute trial on all challenged claims and all asserted grounds of unpatentability, including the grounds based

additionally on the combination of Almarsson, Hickey, and Martindale. *See SAS Inst. Inc. v. Iancu*, 138 S. Ct. 1348, 1359–60 (2018) (holding that a decision to institute under 35 U.S.C. § 314 may not institute on fewer than all claims challenged in the petition); Patent Trial and Appeal Board, Consolidated Trial Practice Guide, 5 (Nov. 2019), available at <https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf> (“In instituting a trial, the Board will either (1) institute as to all claims challenged in the petition and on all grounds in the petition, or (2) institute on no claims and deny institution. The Board will not institute on fewer than all claims or all challenges in a petition.”).

### III. CONCLUSION

Petitioner has, at this stage, established a reasonable likelihood of prevailing in showing that at least one of the challenged claims is unpatentable. This determination is, however, based on a preliminary record. We will make a final determination on the patentability of the challenged claims, as necessary and applying the preponderance of the evidence standard, based on a fully developed record through trial. *See In re NuVasive*, 842 F.3d 1376, 1380–81 (Fed. Cir. 2016) (noting in the context of an *inter partes* review that “there is a significant difference between a petitioner’s burden to establish a ‘reasonable likelihood of success’ at institution, and actually proving invalidity by a preponderance of the evidence at trial”) (quoting 35 U.S.C. § 314(a) and comparing § 316(e)).

Any argument not raised in a timely Patent Owner Response to the Petition, or as permitted in another manner during trial, shall be deemed waived. *See In re NuVasive*, 842 F.3d at 1380–81 (holding Patent Owner waived an argument addressed in the Preliminary Response by not raising

the same argument in the Patent Owner Response). In addition, nothing in this Decision authorizes Petitioner to supplement information advanced in the Petition in a manner not permitted by the Board's Rules.

#### IV. ORDER

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review of claims 10, 11, and 18 of the '344 patent is hereby instituted on the grounds set forth in the Petition, commencing on the entry date of this Order, and pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial.

FURTHER ORDERED that the trial will be conducted in accordance with a separately issued Scheduling Order.

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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NOVARTIS PHARMACEUTICALS CORPORATION,  
Petitioner,

v.

REGENTS OF THE UNIVERSITY OF MICHIGAN AND UNIVERSITY  
OF SOUTH FLORIDA,  
Patent Owner.

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IPR2023-01346  
Patent 10,633,344

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FITZPATRICK, *Administrative Patent Judge*, dissenting.

A petition for an *inter partes* review must “[p]rovide a statement of the precise relief requested for each claim challenged,” which “statement must identify . . . [h]ow the challenged claim is to be construed” and “[h]ow the construed claim is unpatentable.” 37 C.F.R. § 42.104(b)(3)–(4); *see also Hologic, Inc. v. Enzo Life Sciences, Inc.*, No. IPR2018-00019 (PTAB April 18, 2018), Paper 17 at 9–10 (“Because the Petition does not map the challenged claims, as Petitioner considers them to be correctly construed, to the asserted prior art, there is not a reasonable likelihood that Petitioner would prevail with respect to any challenged claim.”). The Petition does not comply with these requirements. Instead, the Petition explains how the

challenged claims would be unpatentable if they are given a different construction, namely one that Petitioner considers to be erroneous.

Independent claim 10 recites, and dependent claims 11 and 18 incorporate by reference, the term “co-crystal.” As for that term, the Petition states: “Although Petitioner disagrees with Patent Owners’ construction [in district court] of the term ‘co-crystal,’ solely for purposes of this Petition, Petitioner adopts Patent Owner’s proposal: ‘A multiple-component, single crystalline phase, having a fixed stoichiometry of its component compounds.’” Pet. 10 (citing Ex. 1018, 7–11; Ex. 1002 ¶65).

Exhibit 1018 is a Joint Claim Construction and Prehearing Statement filed June 6, 2023 in *Regents of the Univ. of Mich. v. Novartis Pharm. Corp.*, Case No. 3:2-cv-04913-AMO(N.D. Cal.). In it, Petitioner advocates for a clearly narrower construction for the term “co-crystal.” Ex. 1018, 7.

Exhibit 1002 is a Declaration of Robin D. Rodgers, Ph.D., in which Dr. Rodgers testifies:

. . . In the district court litigation, the Parties dispute the meaning of the term “co-crystal” and whether it is indefinite, but for the purpose of this declaration, *Petitioner’s counsel has asked me to adopt Patent Owners’ proposed construction* that “co-crystal” means “[a] multiple-component, single crystalline phase, having a fixed stoichiometry of its component compounds.”

Ex. 1002 ¶65 (emphasis added).

If Patent Owner’s construction in the related lawsuit is erroneous, Petitioner should respond accordingly there. At the Board, a petitioner should bring a petition for an *inter partes* review asserting unpatentability based on a construction the petitioner seeks. A petitioner should not seek an *inter partes* review, as was done here, based *exclusively* on a construction it considers erroneous but “adopts” “solely for purposes of this Petition.”

Pet. 10.

To be clear, it is not my view that a petitioner is prohibited from challenging the patentability of claims based on a construction with which it disagrees. It may do so in the alternative. *See Hologic, Inc. v. Enzo Life Sciences, Inc.*, No. IPR2018-00019 (PTAB April 18, 2018), Paper 21 at 6 (“Where a petitioner is concerned that the Board may not adopt what it believes is the proper claim construction, it may choose to offer alternative constructions and demonstrate unpatentability under each construction.”).

However, a petition must meet the requirements of 37 C.F.R. § 42.104(b)(3) and (4). Because the Petition fails to meet these requirements, I dissent from the Board’s Decision to institute.

IPR2023-01346  
Patent 10,633,344 B2

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