

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MICROBIOTICA, LIMITED,
Petitioner

v.

BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM,
Patent Owner

Case PGR2023-00026
U.S. Patent No. 11,395,838

**PATENT OWNER PRELIMINARY RESPONSE
UNDER 37 C.F.R. § 42.207(a)**

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PATENT OWNER'S EXHIBIT LIST

Exhibit No.	Description
2001	Declaration of Wendy S. Garrett, M.D., Ph.D.
2002	<i>Curriculum Vitae</i> of Wendy S. Garrett, M.D., Ph.D.
2003	Nardinocchi <i>et al.</i> , “Interleukin-17 and interleukin-22 promote tumor expression in human nonmelanoma skin cancer,” <i>European Journal of Immunology</i> , 45:922-931 (March 2015)
2004	Vetizou <i>et al.</i> , “Anticancer immunotherapy by CTLA-4 blockade relies on the gut microbiota,” <i>Science</i> , 350(6264):1079-1084 (November 2015)
2005	Sivan <i>et al.</i> , “Commensal <i>Bifidobacterium</i> promotes antitumor immunity and facilitates anti-PD-L1 efficacy,” <i>Science</i> , 350(6264):1084-1089 (November 2015)
2006	Ye <i>et al.</i> , “The Role and Regulation of Human Th17 Cells in Tumor Immunity,” <i>The American Journal of Pathology</i> , 182(1):10-20 (January 2013)
2007	He <i>et al.</i> , “IL-17 promotes tumor development through the induction of tumor promoting microenvironments at tumor sites and myeloid derived suppressor cells,” <i>Journal of Immunology</i> , 184(5):2281-2288 (March 2010)
2008	Brandt <i>et al.</i> , “An overview of fecal microbiota transplantation: techniques, indications, and outcomes,” <i>Gastrointestinal Endoscopy</i> , 78(2):240-249 (May 2013)
2009	Vindigni <i>et al.</i> , “Fecal Microbiota Transplantation,” <i>Gastroenterology Clinics of North America</i> , 46(1):171-185 (March 2017)
2010	Youngster <i>et al.</i> , “Oral, frozen fecal microbiota transplant (FMT) capsules for recurrent <i>Clostridium difficile</i> infection,” <i>BMC Medicine</i> , 14:134 (September 2016)

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2011	Khan <i>et al.</i> , “Antioxidants Keep the Potentially Probiotic but Highly Oxygen-Sensitive Human Gut Bacterium <i>Faecalibacterium prausnitzii</i> Alive at Ambient Air,” <i>PLOS One</i> , 9(5):e96097 (May 2014)
2012	U.S. Patent Application Publication No. 2016/0193257 A1 to Honda <i>et al.</i> , published July 7, 2016 (“Tokyo”)
2013	Kuzu <i>et al.</i> , “Current State of Animal (Mouse) Modeling in Melanoma Research,” <i>Cancer Growth and Metastasis</i> , 8(Suppl 1):81-94 (October 2015)
2014	Dankort <i>et al.</i> , “Braf ^{V600E} cooperates with <i>Pten</i> loss to induce metastatic melanoma,” <i>Nature Genetics</i> , 41(5):544-552 (May 2009)
2015	Segata <i>et al.</i> , “Metagenomic biomarker discovery and explanation,” <i>Genome Biology</i> , 12(6):R60 (June 2011)
2016	Hadrup <i>et al.</i> , “Effector CD4 and CD8 T Cells and Their Role in the Tumor Microenvironment,” <i>Cancer Microenvironment</i> , 6(2):123-133 (August 2013)
2017	Peske <i>et al.</i> , “Control of CD8 T-cell Infiltration into Tumors by Vasculature and Microenvironment,” <i>Advanced Cancer Research</i> , 128:263-307 (June 2015)
2018	Chaput <i>et al.</i> , “Baseline gut microbiota predicts clinical response and colitis in metastatic melanoma patients treated with ipilimumab,” <i>Annals of Oncology</i> , 28(6):1368-1379 (June 2017)
2019	Baruch <i>et al.</i> , “Fecal microbiota transplant promotes response in immunotherapy-refractory melanoma patients,” <i>Science</i> , 371(6529):602-609 (February 2021)
2020	Davar <i>et al.</i> , “Fecal microbiota transplant overcomes resistance to anti-PD-1 therapy in melanoma patients,” <i>Science</i> , 371(6529):595-602 (February 2021)

Exhibit No.	Description
2021	Wang <i>et al.</i> , “IL-17 can promote tumor growth through an IL-6-Stat3 signaling pathway,” <i>The Journal of Experimental Medicine</i> 206(7):1457-1464 (July 2009)
2022	Wang <i>et al.</i> , “IL-17 Enhances Tumor Development in Carcinogen-Induced Skin Cancer,” <i>Cancer Research</i> , 70(24):10112-10120 (December 2010)
2023	Villarino <i>et al.</i> , “Composition of the gut microbiota modulates the severity of malaria,” <i>Proceedings of the National Academy of Sciences</i> , 113(8):2235-2240 (February 2016)
2024	Xin <i>et al.</i> , “Isolation, identification and characterization of human intestinal bacteria with the ability to utilize chloramphenicol as the sole source of carbon and energy,” <i>FEMS Microbiology Ecology</i> , 82(3):703-712 (December 2012)
2025	Milojević, S., “Nature, Science, and PNAS Disciplinary profiles and impact,” <i>Scientometrics</i> , 123:1301-1315 (May 2020)
2026	“Management Team,” Microbiotica Limited, accessible at https://microbiotica.com/about/management-team/ , accessed August 21, 2023
2027	“Microbiotica Announces Clinical Trial Collaboration with MSD to Evaluate MB097 in Combination with KEYTRUDA® (pembrolizumab) in a Phase 1b Clinical Trial in Melanoma,” Microbiotica Limited Press Release, April 12, 2023, accessible at https://microbiotica.com/microbiotica-announces-clinical-trial-collaboration-with-msd-to-evaluate-mb097-in-combination-with-keytruda-pembrolizumab-in-a-phase-1b-clinical-trial-in-melanoma/ , accessed August 21, 2023

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I. INTRODUCTION

The Petition for Post-Grant Review of U.S. Patent No. 11,359,838 B2 (“Petition”), filed by Microbiotica, Limited (“Petitioner”), suffers from multiple fundamental flaws that warrant denying institution of trial.

First, the Board should deny institution because Petitioner relies on a demonstrably incorrect claim construction that undermines all Grounds. *See* Section II. Petitioner’s construction of the terms “isolated” and “purified” disregards the fundamental claim construction principle that a patentee can override the plain and ordinary meaning of a claim term by being its own lexicographer. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312, 1327 (Fed. Cir. 2005) (en banc). Here, the ’838 Patent explicitly defines the terms “isolated” and “purified.” EX1001, 28:40-66. Rather than apply these explicit definitions, Petitioner offers its own allegedly plain and ordinary meaning for these terms. But even that construction is contravened by law, because it is supported only by extrinsic evidence. *Id.* at 1316. Petitioner’s flawed claim construction infects each of the Grounds for each claim, and the petition contains no arguments applying the correct claim construction. Having blatantly violated fundamental principles of claim construction, Petitioner has failed to meet its burden to show that it is more likely than not that at least one *construed claim* is unpatentable. 37 C.F.R. §§ 42.204(b)(3)-(4).

Second, the Board should deny institution under 35 U.S.C. § 325(d) because Petitioner relies solely on art and arguments that are the same or substantially the same as considered by the Examiner, and Petitioner does not meet its burden to demonstrate material error by the Examiner. Record evidence shows that Petitioner’s “Section 112” Grounds 1-3 merely retread the same claim-breadth arguments that the Examiner fully addressed during prosecution. EX1002, 43-49, 89; EX2001, ¶¶79-88, Table A and B. Yet Petitioner fails to explain, and provides no testimony on, how its “Section 112” Grounds 1-3 are not the same or substantially the same as the arguments the Examiner considered. Petitioner fares no better on demonstrating material error, as it merely asserts—again without testimony—that the Examiner failed to “consider and identify” the “Section 112 issues” raised in the Petition. Reviewing similar facts, the Board has denied institution on several occasions where the Examiner considered the same § 112 arguments proffered by Petitioner (e.g., both Examiner and Petitioner considered written description) or substantially the same § 112 arguments proffered by Petitioner (e.g., Examiner considered enablement and Petitioner challenged written description). *See, e.g., Novartis Pharms. Corp. v. Plexxikon, Inc.*, IPR2018-01287, Paper 17, at 6-16 (P.T.A.B. Jan. 16, 2019); *Triplet Therapeutics, Inc. v. Board of Supervisors of Louisiana State University and Agricultural and Mechanical College*, PGR2021-00059, Paper 12, at 33-39 (P.T.A.B. Sept. 8, 2021). Petitioner

makes no mention of these decisions.

The Petition also advances the same or substantially the same art presented to the Office during prosecution. Indeed, two of the three references Petitioner relies upon for its obviousness Grounds 4-5—Gajewski and Miquel—were presented to or cited by the Examiner, respectively, and *considered* during prosecution. EX1002, 116, 126, 170; EX2001, ¶¶98-100, Table E. And the third reference—Honda—is entirely cumulative to Tokyo (EX2012), which the Examiner also *considered* during prosecution. EX1002, 125, 169; EX2001, ¶¶89-93, Table C. Yet, Petitioner and Dr. Robinson omit any discussion of Tokyo, and thus fail to explain why Honda is not cumulative to Tokyo.

Not only do Petitioner and Dr. Robinson fail to meaningfully grapple with—let alone distinguish—the extensive prosecution history, but Petitioner’s application of *Advanced Bionics* fails as a matter of law. For example, Petitioner argues that “the Examiner never applied or discussed Gajewski,” that its argument based on Miquel “was not previously before the Office,” and that thus “the conditions of the first part of the *Advanced Bionics* framework are not met.” Petition, 86-87. Whether the Office *applied* or *discussed* a cited reference, or whether an *argument* regarding a cited reference was before the Office, is *not* the standard under *Advanced Bionics*. The relevant inquiry is whether the cited art is the same or substantially the same as art previously *presented to* the Office, either

by the Applicant, such as in an Information Disclosure Statement (IDS), or cited by the Examiner. *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6, at 7-8 (P.T.A.B. Feb. 13, 2020) (precedential).

And there is no evidence of Examiner error here. Petitioner’s material-error arguments at most amount to a mere disagreement with the Examiner over whether the Examiner should have rejected the claims over the Petition’s art combinations. The Petition is a classic example of the type of recycled and rehashed arguments that *Advanced Bionics* and 35 U.S.C. § 325(d) ward against.

Third, the Board should deny institution because Petitioner fails to meet its burden to demonstrate that a person of ordinary skill in the art (“POSA”) would have had a reason to combine Honda and Gajewski (Ground 4) or Honda, Gajewski, and Miquel (Ground 5) with a reasonable expectation of success. For example, Petitioner fails to establish that a POSA would have started with Honda’s “Th17-inducing bacterial compositions” given that the art taught that Th17 cells *promote* tumor growth—the opposite of what Petitioner alleged a POSA would have sought to achieve. EX2021, Abstract; EX2022, 10113; EX2003, 927; EX2001, ¶¶42-44. Petitioner also does not establish that a POSA would have thought Gajewski’s *Ruminococcus* to “be useful” for “skin cancer tumors” (Petition, 68), given Gajewski’s teaching that “the presence or increased level of,”

e.g., *Ruminococcus* actually “*potentiates* cancer/tumor growth.”¹ EX1012, 22:6-9; EX2001, ¶¶45-46. Gajewski overlooked *Ruminococcus* all-together and concluded that *Bifidobacterium*, not *Ruminococcus*, showed an anti-cancer effect (EX1012, 49, FIGs. 8A-D; EX2001, ¶¶47-49), further undermining Petitioner’s alleged reasons to combine Honda and Gajewski.

Petitioner also fails to establish that a POSA would have had a reasonable expectation of success in view of the unpredictability in the art. Before September 27, 2016, POSAs were aware of the “complexity” in the field regarding which gut bacteria were positively associated with skin cancer treatments, and none of the studies pointed to the Ruminococcaceae family, anyhow. EX1007, 26; EX2001, ¶¶50-53. Petitioner failed to establish that a POSA would have reasonably expected any success with Ruminococcaceae in the face of the “complexity” taught in the art. EX2001, ¶53; EX2004, Abstract; EX2005, Abstract.

Fourth, the Board should deny institution because Petitioner does not establish that Patent Owner lacked possession of the claimed methods as of the filing date of the ’838 Patent. Petitioner repeatedly insists on an actual reduction to practice in humans, contrary to the demands of the written description law. *Alcon Research Ltd. v. Barr Laboratories, Inc.*, 745 F.3d 1180, 1190 (Fed. Cir. 2014).

¹ Emphasis is added throughout, unless expressly specified.

Petitioner complains that the claims are directed to a genus of methods, but fails to show that the species exemplified in the specification (e.g., clinical data from human patients, a mouse melanoma model) are not representative of the claimed genus, because Petitioner fails to address the predictability of the science and the technological knowledge of a POSA as of the relevant date.

Fifth, the Board should deny institution because Petitioner fails to show that practicing the claimed methods would require undue experimentation. Petitioner did not use the *Wands* factors framework in its analysis, and the arguments that Petitioner proffered rely only on the conclusory and unsupported testimony of its expert. Petition, 36; EX1003, ¶120; *Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 9 (P.T.A.B. Aug. 24, 2022). While Dr. Robinson summarily alleges that practicing the claimed methods would require “considerable” experimentation, he never proffers any reasons as to why *undue* experimentation would be required, particularly in light of the high level of skill in the art. EX2001, ¶¶26,70-71. *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996) (even a “considerable amount of experimentation is permissible, if it is merely routine”).

Sixth, the Board should deny institution because Petitioner ignored the fundamental principle of patent law that “*the claims* measure the invention” (*see United Carbon Co. v. Binney & Smith Co.*, 317 U.S. 228, 232 (1942)). Instead, Petitioner argued that Patent Owner’s definition of “isolated or purified” leaves a

POSA “without any understanding as to the metes and bounds of *these two claim limitations*” (Petition, 57), but this is contrary to the law. *Id.* Additionally, Petitioner failed to prove that a POSA would have been unable to ascertain the metes and bounds of the claims. For example, Petitioner failed to establish that patent’s express definitions of “isolated” and “purified” fail to “inform those skilled in the art about the scope of the invention with reasonable certainty.” *See Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S.Ct. 2120, 2129 (2014). Petitioner also failed to prove that a POSA would not have understood with reasonable certainty the meaning of the term “bacteria belonging to the family Ruminococcaceae,” because Petitioner did not assess what this term meant—or show any ambiguity in its scope—as of the September 27, 2017 filing date, the relevant date for this analysis. *Id.* at 2130. Petitioner’s arguments regarding the scope of Ruminococcaceae in 2006, 2009, and 2019 are irrelevant. *Id.*

The Board has discretion to deny institution of petitions, particularly in circumstances where efficiency, conservation of limited resources, and fairness are a concern. *See, e.g., Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11, at 6 (P.T.A.B. Mar. 20, 2020) (precedential) (“[T]he Board takes a holistic view of whether efficiency and integrity of the system are best served by denying or instituting review.”). Additionally, institution is only authorized when the petition “demonstrate[s] that it is more likely than not that at least 1 of the claims

challenged in the petition is unpatentable.” 35 U.S.C. § 324(a); 37 C.F.R.

§ 42.208(c). If the Board chooses to institute, the review must proceed “on all of the challenged claims and on all grounds of unpatentability asserted for each claim.” 37 C.F.R. § 42.208(a). Here, because the petition utilizes incorrect claim construction, repeats arguments already addressed during prosecution, and is based on legally and factually flawed arguments, the principles of efficiency, conservation of resources, and fairness would best be served by denying institution.

II. PETITIONER’S CONSTRUCTION OF “ISOLATED OR PURIFIED” VIOLATES THE WELL-ESTABLISHED AXIOM IN PATENT LAW THAT PATENTEE CAN BE ITS OWN LEXICOGRAPHER, LEAVING THE PETITION DEFICIENT UNDER 37 C.F.R. § 42.204(B)(3)-(4)

Petitioner’s construction of the terms “isolated or purified” disregards the fundamental claim construction principle that “[a] patentee is free to be his own lexicographer,” overriding the “ordinary meaning.” *Phillips*, 415 F.3d at 1312, 1327; *Mentor Graphics Corp. v. EVE-USA, Inc.*, 851 F.3d 1275, 1294 (Fed. Cir. 2017); *Alloc, Inc. v. Int’l Trade Comm’n*, 342 F.3d 1361, 1368 (Fed. Cir. 2003). As the Petitioner acknowledges, the ’838 Patent explicitly defines “isolated or purified.” EX1001, 28:40-67; Petition, 14. Yet, contrary to controlling precedent, Petitioner dismisses the patent’s explicit definition because it, allegedly, “deviates from the plain and ordinary meaning.” Petition, 14. Petitioner’s claim construction

is contravened by *Phillips*, 415 F.3d at 1316 (“the inventor’s intention, as expressed in the specification, is regarded as dispositive”). Even Petitioner’s proffered “plain and ordinary meaning” is contravened by law, because it is supported only by extrinsic evidence (*see* EX1022 and EX1023, both undated; EX1003) (Petition, 50-51; EX1002, ¶147). *See 3M Innovative Props. Co. v. Tredegar Corp.*, 725 F.3d 1315, 1326-28, (Fed. Cir. 2013) (rejecting the use of extrinsic evidence to construe claim terms clearly defined in the specification).

Petitioner’s faulty claim construction undermines the entire petition because all of the grounds rely upon an improper construction of these terms that appear in all challenged claims. As such, Petitioner has failed to meet its burden to establish unpatentability of the challenged claims. *Medicines Co. v. Mylan, Inc.*, 853 F.3d 1296, 1308 (Fed. Cir. 2017) (“our rules place an affirmative burden on petitioners to ‘set forth: . . . How the challenged claim is to be construed.’ . . . This burden continues by requiring petitioners to adequately explain ‘[h]ow the *construed claim* is unpatentable’”).

III. PETITIONER SET THE LEVEL OF A PERSON OF ORDINARY SKILL IN THE ART (“POSA”) TOO LOW

Patent Owner submits that because the ’838 Patent relates to methods of reducing or delaying growth of skin cancer tumors in subjects, the level of skill of a POSA in this field is high. EX2001, ¶25. A POSA for the ’838 Patent typically would have an advanced degree, such as an M.D. or a Ph.D., with experience and

training in oncology, have several years of experience with administering oncology treatments to subjects and evaluating results of such treatments, and have experience or knowledge in microbiome science and its modulation, inclusive of studies that involve stool microbiome profiling, as well as experience in, or knowledge of, related research and development of bacterial-based cancer treatments. EX2001, ¶¶26-27. A POSA may also have worked as part of a multi-disciplinary team and drawn upon not only his or her own skills, but also taken advantage of certain specialized skills of others in the team, to solve a given problem. For example, such a team may include a clinician, an immunologist, microbiologist, bioinformatician, molecular biologist, manufacturing specialist, and/or pharmaceutical formulator. *Id.*

Petitioner’s attempt to lower the skill level of a POSA—“a basic Bachelor’s degree with four to five years of relevant work experience” or “a Masters or Ph.D. but having fewer years of experience” (Petition, 21)—is a thinly veiled attempt to distort the perspective of a POSA that should be used to assess patentability of the challenged claims. It is settled law that § 112(a) must be assessed in view of the relative skill of those in the art. *See Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1363 (Fed. Cir. 2006) (written description is “judged from the perspective of one of ordinary skill in the art”); *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (“[p]atents are written to enable those skilled in the art to practice the invention”).

A POSA “comes to the patent with the knowledge of what has come before,” and the specification need only include enough “to convince a person of skill in the art” of the sufficiency of description. *See LizardTech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005).

But by lowering a POSA’s skill level to “a basic Bachelor’s degree” or “a Masters or Ph.D” with *fewer* than four to five years of experience, Petitioner overstates the amount of guidance needed in the specification to describe and enable the claimed methods. *Id.* And Petitioner has not shown that a POSA with the proper skill level would need the guidance Petitioner says is lacking in the specification, failing to meet its burden under 35 U.S.C. § 322(a)(3).²

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

Petitioner fails to meet its burden to show that the Petition’s grounds do not contain “the same or substantially the same prior art or arguments previously . . . presented to the Office,” or that the Office materially erred during examination. Instituting trial here would simply rehash arguments that are the same or substantially the same as those previously addressed by the Examiner, eviscerating the deference owed to the Office’s previous patentability assessment. *Advanced*

² Patent Owner affirms that all arguments on all grounds presented herein apply regardless of which party’s POSA definition is used.

Bionics, LLC, Paper 6, at 7-8. The petition fails to meaningfully grapple with—let alone distinguish—the extensive prosecution history. Nor does it identify a cognizable material error in the prosecution history, even though the burden to do so plainly lay with Petitioner.

For example, neither Petitioner nor Dr. Robinson make any effort to explain how its “Section 112” Grounds 1-3 are not the same or substantially the same arguments that were previously considered by the Examiner during prosecution. EX2001, ¶79. Petitioner feebly asserts: “the Examiner did not address the detailed Section 112 issues raised in this Petition.” Petition, 87. And Dr. Robinson provided *no testimony* on this issue. As such, Petitioner failed to meet its burden under the first prong of *Advanced Bionics*. Petitioner’s attempt to show material error is similarly deficient, as Petitioner offered only the bald statement that the Examiner failed to “consider and identify” the “Section 112 issues” raised in the Petition. Petitioner’s assessment of the factual record again was unsupported by testimony. *Advanced Bionics* requires more of Petitioner. *Advanced Bionics*, Paper 6, at 10-11 (stating that “the petitioner’s required showing of material error must overcome persuasively [disagreement with a] specific finding of record” by the Office). Yet, Petitioner offers nothing beyond naked conclusions.

The Petition fares no better on Grounds 4 and 5, where Petitioner errs in applying the first prong of *Advanced Bionics* to Gajewski, Miquel, and Honda.

Petition, 86. Here, the art is the same (Gajewski and Miquel) or substantially the same (Honda) as the art considered during prosecution, so *Advanced Bionics* requires identifying a material error by the Examiner. *Advanced Bionics*, Paper 6, at 8. Petitioner concluded otherwise, asserting that it did not need to demonstrate material error because the Office did not consider its art “combinations.” Petition, 86-87 (asserting that “the Examiner never *applied or discussed* Gajewski” and the “*argument* [concerning Miquel] was not previously before the Office”). But *Advanced Bionics* is very clear: the first prong is satisfied when the same or substantially the same art was presented to the Office. *Advanced Bionics*, Paper 6, at 8. And neither Petitioner nor Dr. Robinson provide any analysis of Honda in view of the prosecution record, which clearly applied the same disclosure in Tokyo (EX2012) as Petitioner relies on from Honda. EX2001, ¶¶89-97, Tables C and D. Petitioner’s material-error argument similarly mischaracterizes the Examiner as “failing to identify and consider these references and the arguments” in the Petition. Petition, 87. This is patently false.

As discussed below, and supported by record evidence, the Petition relies on art and arguments that are the same or substantially the same as considered by the Examiner, and Petitioner does not demonstrate material error by the Examiner. The Board should thus exercise its discretion to deny institution for review. Should the Board reach a different determination under § 325(d) on any of Petitioner’s

grounds—despite the significant overlapping issues to those already considered by the Office—instituting trial based on evidence or arguments directed to a subset of grounds would not be an efficient use of the Board’s time and resources. Even a subset of Petitioner’s grounds sufficiently implicate § 325(d)’s statutory purpose, which would be undermined by institution.

A. The Board should deny institution because the Petition presents the same “Section 112” arguments as in prosecution and fails to identify any material error

The Board applies the *Becton, Dickinson* factors broadly to “any situation in which a petition relies on the same or substantially the same art or arguments previously presented to the Office.” *Advanced Bionics*, Paper 6, at 10 (referring to *Becton, Dickinson & Cp. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 (P.T.A.B. Dec. 15, 2017) (precedential as to § III.C.5, first paragraph). Here, Petitioner merely packaged the same “Section 112” arguments in its written description ground (Ground 1) as considered by the Examiner, and repackaged the same or substantially the same arguments for enablement (Ground 2) and definiteness (Ground 3) as considered by the Examiner. This is all fatal to Petitioner’s burden of showing its arguments are not the same or substantially the same under § 325(d) and error material to patentability.

1. The Examiner considered the same written description arguments presented in Ground 1

The Examiner raised a lack of written description rejection for the same

reasons as now set forth by Petitioner—its complaint regarding the breadth of the claims. Petition, 31 (“[T]he specification simply cannot support the *broad breadth* of the Challenged Claims.”). The Examiner expressly considered the same arguments raised in the Petition.

For example, the Examiner’s analysis states that while “the specification [] provides support for reduc[ing] implanted melanoma tumor growth in germ-free mice by direct injection of a fecal microbiota sample (FMT) to said tumor..., it does not necessarily provide[] support for ‘**administering to the subject a composition comprising** one or more isolated or purified population of bacteria belonging to the family of *Ruminococcaceae*’ for treating **cancer** or reducing or delaying **tumor growth** in a subject in need thereof, as required by [then-pending] claim 44³.” EX1002, 89; EX2001, ¶80. The Examiner reviewed Patent Owner’s response and required deleting “treating cancer,” and changing “tumor growth” to “growth of a **skin cancer tumor**” before withdrawing the written description

³ Then-pending claim 44 referred to a “method of treating cancer or reducing or delaying tumor growth in a subject in need thereof, comprising administering to the subject a composition comprising one or more isolated or purified population of bacteria belonging to the family Ruminococcaceae” and corresponds to claim 1 as granted with the ’838 Patent after amendment. EX2001, ¶81, Table A.

rejection and allowing the claims. EX1002, 11-19; EX2001, ¶¶82, 84-85.

Patent Owner's expert Wendy S. Garrett, M.D., Ph.D., a board-certified medical oncologist at Dana-Farber Cancer Institute and Brigham Women's Hospital and a tenured Professor of Medicine at Harvard Medical School, reviewed the '838 Patent prosecution history. EX2001, ¶¶12-23. As Dr. Garrett confirms (EX2001, ¶83, Table B), each bolded feature considered by the Examiner squarely aligns with Petitioner's complaints about claim breadth: “**‘administering’**, **‘subject’**, **‘composition’**, and **‘skin cancer tumor’** [allegedly] have such limitless range that the scope of the Challenged Claims are entirely untethered from any reasonable construction of PO's purported ‘invention’ described in the specification.” Petition, 31-32; *see id.*, 42 (alleging that “[t]he over breadth of Claim 1 is further compounded by PO's use of the **‘comprising’** transition”).

Satisfied with Patent Owner's claim amendment and responsive arguments, the Examiner withdrew any issues related to breadth of claim 1. EX1002, 11-19; EX2001, ¶82. By characterizing the Examiner's written description analysis of a claim the Examiner deemed broader than issued claim 1 as failing to “address the detailed Section 112 issues raised in this Petition directed to written description,” Petitioner mischaracterizes record evidence.

The Board has denied institution in comparable circumstances, and should do so here as well. In *Novartis Pharmaceuticals Corp. v. Plexxikon, Inc.*, the

Examiner withdrew rejections related to compliance with the written description requirement after patent owner amended the claims to a subgenus of compounds. IPR2018-01287, Paper 17, at 6-10 (P.T.A.B. Jan. 16, 2019). Petitioner raised both written description and enablement challenges, arguing that the patent “discloses enormous genera of chemical compounds which cover an effectively incalculable number of compounds,” but only three examples. *Id.* at 10-11. The Board declined to institute trial, concluding that petitioner’s arguments were substantially same as those raised by the Examiner. *Id.* at 12-16.

Here, complaining similarly of claim breadth (“entirely untethered from any reasonable construction of PO’s purported ‘invention’ described in the specification,” Petition, 31-32; EX2001, Table B), Petitioner asks the Board to follow the same path as the Examiner in its Ground 1. Yet, as described above, Ground 1 of the Petition raises arguments that are the same as and cumulative to the written description arguments the Examiner and Patent Owner resolved during examination. Petitioner must demonstrate an error material to patentability by the Examiner to avoid discretionary denial. *Advanced Bionics*, Paper 6, at 8–9 and n.10.

2. Petitioner fails to demonstrate an error material to patentability in its written description (Ground 1) analysis

Petitioner failed to meet its burden to show that the Examiner erred in a manner material to patentability in allowing the challenged claims. To “support”

material error by the Office, Petitioner makes the same banal remark for Ground 1 (and Grounds 2 and 3): “[i]n failing to identify and consider [the “detailed”] Section 112 issues [raised in the Petition], the Examiner materially erred.” Petition, 87-88. Not only does the Petition’s general reference to “Section 112 issues” force the Board on a hunting expedition in search of them, but, in fact, Petitioner describes no material error. *Novartis Pharms. Corp.*, Paper 17, at 14 (denying institution where the Petition and declaration present no “argument distinguishing the Office’s previous decisions on substantially the same issues or [] provide a compelling reason why we should readjudicate substantially the same arguments considered by the Examiner during prosecution”).

At most, the Petition presents *only a disagreement* with the Examiner’s findings. “[I]f the alleged error is a disagreement with a specific finding of record by the Office, then ordinarily the Petitioner’s required showing of material error must overcome *persuasively* that specific finding of record.” *See Advanced Bionics*, Paper 6, at 10-11. However, a generic statement intended to address why the Examiner “materially erred” in finding the claims compliant with the § 112 requirements falls far short of persuasive. *Pharmacosmos A/S v. American Regent, Inc.*, PGR2020-00009, Paper 17, at 26 (P.T.A.B. Aug. 14, 2020) (finding insufficient a material error showing where petitioner presents a general statement that the Examiner failed to identify and consider its arguments).

And a disagreement, even if supported by additional evidence or facts presented with a Petition, is insufficient to demonstrate error where, as here, the core of Petitioner’s argument—purported “broad breadth of the Challenged Claims” illustrated by analysis of certain claim terms—mirrors the arguments made and considered by the Examiner. *See, e.g., Aquestive Therapeutics, Inc. v. Neurelis, Inc.*, IPR2019-00450, Paper 8, at 21-22 (P.T.A.B. Aug. 1, 2019) (denying institution where petitioner offered a new declaration with additional detail and argument not considered by the Examiner but which addressed the *same* art considered by the Examiner). Petitioner offers no compelling reason to reconsider the Examiner’s decision simply because, as shown above, the Petition looks at the same claim terms evaluated during examination.

The facts presented above show that Petitioner has failed to “demonstrate[] that the Office erred in a manner material to the patentability of the challenged claims.” The Board should deny trial.

3. The Petition repackages substantially the same written description arguments to argue insufficient enablement of the claims in Ground 2

Under Ground 2 (enablement), Petitioner merely refers to the arguments presented under Ground 1 (written description) relying on the same complaint about breadth of the claims. Petition, 47 (“[T]he specification, considered as a whole, fails to enable a POSA to formulate *any composition* of bacteria belonging

to the Ruminococcaceae family, that can be *administered through any means* possible, at *any concentration*, in *any type of subject*, and is safe and effective at treating *any type of skin cancer tumor*. § VII.A.⁴ Thus, in view of the foregoing, a POSA would conclude that the '838 Patent specification fails to teach a POSA how to make and use the *full scope* of the claimed invention...). EX2001, ¶83, Table B. Thus, Petitioner relies on the same arguments it raises to challenge written description to challenge enablement of the claims. And Petitioner makes no attempt to argue (or support with testimony) that its enablement challenge arguments are not substantially the same as those considered by the Examiner during examination. Petition, 87-88 (summarily stating that “the Examiner did not address the detailed Section 112 issues raised in this Petition directed to ... enablement”); EX2001, ¶79. The Board has repeatedly denied institution where the petition simply repackages a § 112 rejection previously considered by the Office under an alternative § 112 ground.

For example, in *Starbucks Corp. v. Ameranth, Inc.*, the Board concluded that Petitioner’s enablement arguments were substantially similar to the written

⁴ Petitioner refers to the entire 17 pages of § VII.A discussing written description as supporting its enablement challenge, without specifically applying any evidence to an enablement framework.

description arguments previously considered by the Office. CBM2017-00053, Paper 7, at 14-15 (P.T.A.B. Dec. 4, 2017). The Board denied institution, stating that Petitioner’s “arguments as to whether the [claims] are supported properly by the [patent’s] disclosures ... require an analysis of the description of the [claimed invention] in order to determine the adequacy of the disclosures,” as previously before the Office. *Id.* at 15.

In *Pharmacosmos A/S v. American Regent, Inc.*, the Board found “substantial overlap between arguments” where although “the Examiner never issued a written description rejection during prosecution ... many of the issues involved in Petitioner’s claim construction and enablement arguments (which were previously before the Office), overlap with issues Petitioner raises in connection with written description.” PGR2020-00009, Paper 17, at 20-21. As to prong 2 of *Advanced Bionics*, the Board found no material error where the petition did not “present specific arguments as to why the Office materially erred” and the written description issues overlapped with “claim construction, enablement, and indefiniteness arguments . . . previously before the Office.” *Id.* at 27.

More recently, the Board denied institution where petitioner presented *substantially the same* written description arguments as those previously considered by the Office in the context of enablement. *Triplet Therapeutics, Inc.*, Paper 12, at 33-37. Under the first prong of *Advanced Bionics*, the Board

concluded that “[a]s with the Examiner’s rejections[], Petitioner’s arguments are *based on a broad reading of the claims* as interpreted by the ordinarily skilled artisan, and would require us to analyze whether [there] is sufficient support in the specification for the entire scope of the challenged claims.” *Id.* at 37. Moving to the second prong of *Advanced Bionics*, the Board faulted petitioner for making no attempt to distinguish “the *Novartis*⁵ and *Starbucks* cases finding that issues similar to those addressed here were substantially similar for the purposes of the exercise of discretion to deny review” and for not “provid[ing] a compelling reason why we should readjudicate substantially the same arguments considered by the Examiner during prosecution.” *Id.* at 39.

As outlined above, the Examiner previously considered Petitioner’s written description arguments. Petitioner premised its written description challenge on the same claim-breadth issue considered during prosecution. And the Petition’s enablement challenge relies on the same broad reading of the claims and would require the same analysis over the scope of the claims. As in *Starbucks*,

⁵ As discussed above, the Board denied institution under § 325(d) in *Novartis* because petitioner’s written description arguments were substantially the same as the Examiner’s rejection overcome during examination by amending the claims to a subgenus of compounds. IPR2018-01287, Paper 17, at 14-15.

Pharmacosmos A/S, and *Triplet*, the “arguments in both cases require an analysis of the description of the [claimed invention] in order to determine the adequacy of the disclosures” (*Starbucks*, CBM2017-00053, Paper 7, at 15) and must therefore be substantially the same arguments considered by the Examiner. The Petition makes no attempt to explain why its claim-breadth arguments that the Examiner and Patent Owner resolved during prosecution are not substantially the same.

And the Petition makes no effort to distinguish any Board decision denying institution under the same circumstances or provide a compelling reason to “readjudicate substantially the same arguments considered by the Examiner during prosecution.” *Triplet Therapeutics, Inc.*, PGR2021-00059, Paper 12 at 39; *see* Petition, 87-88 (asserting material error only for “fail[ure] to identify and consider” vague “Section 112 issues”).

4. Petitioner presents no error material to patentability in its enablement (Ground 2) analysis

As with its written description arguments, Petitioner fails to meet its burden to show a material error, supporting discretionary denial under § 325(d). *Advanced Bionics*, Paper 6, at 8-9. Petitioner merely states that “[i]n failing to identify and consider [the “detailed”] Section 112 issues [presented in the Petition], the Examiner materially erred.” Petition, 87-88. A general statement that the Examiner failed to identify and consider petitioner’s arguments and evidence is insufficient to show material error. *Pharmacosmos*, Paper 17, at 26.

Dispositive here, as in *Triplet*, is that the Petition makes no effort to distinguish any Board decision denying institution under the same circumstances or provide a compelling reason to “readjudicate substantially the same arguments considered by the Examiner during prosecution.” *Triplet*, Paper 12, at 39; *see* Petition, 87-88 (asserting material error only for “fail[ure] to identify and consider” vague “Section 112 issues”). The Examiner extensively considered the same issues of claim scope discussed in the Petition, and Petitioner has not substantively addressed how the Examiner erred. A mere disagreement based on the core argument about breadth of claims is insufficient to demonstrate material error. *See Aquestive*, Paper 8, at 21-22. The Board should deny institution.

5. Petitioner presents cumulative definiteness arguments under Ground 3

Petitioner anchors its definiteness arguments in Ground 3 to the *same* underlying theme of claim breadth that permeates Grounds 1 and 2. *See, e.g.*, Petition, 48 (“[T]he ‘*isolated*’ and ‘*purified*’ claim limitations, . . . fail to reasonably inform a POSA *about the scope* of the claimed invention.”), 49 (“This is the definition of indefiniteness, and, in addition, gives rise to lack of enablement *across the breadth of the claims.*”), 54 (referring to “unbridled breadth” of the term *isolated*), 59 (referring to “*scope* of the *Ruminococcaceae* taxonomic family”). EX2001, ¶83, Table B. Yet the Petition fails to address whether its complaints about breadth for the claim terms “*isolated*,” “*purified*,” and “*bacteria belonging to*

the family Ruminococcaceae” are the same or substantially the same as considered by the Examiner during prosecution. EX2001, ¶79. As outlined below and confirmed by Dr. Garrett, they are. EX2001, ¶¶79-88, Table A and B.

The Petition generically asserts that “the Examiner did not address the detailed Section 112 issues” directed to “indefiniteness.” Petition, 87-88. However, in the context of § 112, the Examiner considered whether the specification “provide[s] support for ‘administering to the subject a composition comprising one or more **isolated** or **purified** population of **bacteria belonging to the family of *Ruminococcaceae***’.” EX1002, 89; EX2001, ¶80, Table A and B. Indeed, an Examiner must evaluate definiteness of claims under § 112(b) when determining “whether the specification meets the criteria of 35 U.S.C. 112(a) ... with respect to the claimed invention.” M.P.E.P. § 2173; *see* M.P.E.P. Foreword (stating that the Manual “outlines the current procedures which the examiners are required or authorized to follow”). Thus, when determining that then-pending claim 44 did not satisfy the written description requirement for administering “a composition comprising one or more **isolated** or **purified** population of bacteria belonging to **the family of *Ruminococcaceae***,” M.P.E.P. § 2173 required the Examiner to evaluate the definiteness of the claim vis-à-vis its terms. Petitioner now asks the Board to follow substantially the same path worn by the Examiner in assessing the claims under § 112.

In addition, the Examiner unquestionably considered the claim terms “isolated” and “purified” during prosecution. For example, when applying Miquel as prior art, the Examiner explained that it discloses use of a “composition comprising at least one *isolated or purified* population of bacteria *Faecalibacterium prausnitzii* (administering *Faecalibacterium prausnitzii* to mice ...).” EX1002, 116 (citing Abstract, which discusses administering *F. prausnitzii* strain A2-165 and its culture supernatant); EX2001, ¶86.

Further, Petitioner attacks definiteness of claim 1 because a “taxonomic definition is ... subject to change over time,” and “‘bacteria belonging to the family Ruminococcaceae’ is a moving target.” Petition, 58, 59. To support its argument, Petitioner relies on references dated 2006, 2009, and 2019. Petitioner’s arguments conjure a red herring because, as discussed in § IX.C, definiteness is assessed from the standpoint of a POSA *at the time of the patent application*, and the Petition presents no such controversy as of September 2017. While the Examiner following M.P.E.P. § 2173 during prosecution would not have misapplied the law as Petitioner does, the Examiner considered that bacterial taxonomy may change. For example, the Examiner pointed to “p. 255 left-hand column last paragraph” of Miquel, which discusses reclassification of *Faecalibacterium prausnitzii* in 2002. EX1002, 116; EX2001, ¶87. Thus, the Examiner considered the same or substantially the same argument Petitioner now

raises.

Petitioner also made no effort to address the Examiner's consideration of the terms isolated, purified, and bacteria belonging to the family Ruminococcaceae, or the cumulativeness of its definiteness challenge to arguments considered during prosecution. EX2001, ¶79. As shown above, the first prong of *Advanced Bionics* is met. *See Pharmacosmos A/S*, Paper 17, at 20 (finding substantial overlap between petitioner's written description arguments and those previously before the Office related to claim construction and enablement even though "the Examiner never issued a written description rejection during prosecution").

6. Petitioner presents no error material to patentability in its definiteness (Ground 3) analysis

Similar to its other "Section 112" challenges, Petitioner does not meet its burden of demonstrating material error through a general allegation that the Examiner failed to "identify and consider . . . Section 112 issues." Petition, 87-88. Vague reference to "Section 112 issues" of definiteness is no substitute for demonstrating that the Examiner committed an error in a manner material to patentability when conducting its definiteness analysis.

Here, as above with respect to written description and enablement, Petitioner's dissatisfaction with the granted claims centers on a core argument about breadth of the claims. But Petitioner's dissatisfaction cannot substitute for persuasively overcoming the specific findings of record. *Advanced Bionics*, Paper

6, at 10-11; Petition, 87-88. The Examiner resolved any issues of claim breadth when evaluating the definiteness (as well as written description and enablement) of the claims during prosecution—Petitioner provides no sufficient reason to readjudicate substantially the same arguments. At best, even “[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 Board should deny institution.

B. The Board should deny institution because the Petition relies on the same or substantially the same art and fails to present material error

The Petition presents two grounds of obviousness: Ground 4 (Honda in view of Gajewski for claims 1-3 and 5-18) and Ground 5 (Honda in view of Gajewski and Miquel for claim 4). None of it is new, as the Examiner considered Gajewski and Miquel. And Honda is substantially the same as Tokyo (EX2012), which the Examiner also considered during prosecution. The Petition omits any analysis of Honda in view of the prosecution record and feigns material error through misstatement that the Examiner failed “to identify and consider these references.” Petition, 87. As discussed in more detail below, denial of institution is warranted.

1. The Examiner previously considered Miquel and Gajewski during prosecution

Patent Owner submitted a complete copy of Gajewski to the Examiner, which the Examiner considered. EX1002, 126, 170 (Ref. Des. B33); EX2001, ¶98.

Further, the Examiner made Miquel of record, relying on it to reject several pending claims (EX1002, 116; EX2001, ¶99, Table E). Petitioner admits as much. Petition, 30, 86. Thus, the Petition’s reliance on the same art meets the first prong of *Advanced Bionics*.

However, despite Petitioner’s admission that it relied on the same art as before the Office, Petitioner asserts that 1) “the Examiner never applied or discussed Gajewski” and 2) its argument based on Miquel “was not previously before the Office.” Petition, 86-87. Petitioner misapplies the law.

Whether the Office *applied or discussed* Gajewski and whether the *argument* based on Miquel was before the Office is not the standard under *Advanced Bionics*. Rather 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” either by applicant, such as in an Information Disclosure Statement (IDS), or cited by the Examiner. *Advanced Bionics*, Paper 6, at 7-8; *see also Biocon Pharma Ltd. v. Novartis Pharms. Corp.*, IPR2020-01263, Paper 12, at 9 n.4 (P.T.A.B. Feb. 16, 2021) (“Because we determine that the ‘same or substantially the same prior *art*’ was presented previously to the Office, we *need not reach* whether the ‘same or substantially the same *arguments*’ were presented previously to the Office.”); *Janssen Biotech, Inc. v. United States*, IPR2021-01484, Paper 10, at 29 (P.T.A.B. Mar. 2, 2022) (emphasizing that “part one of the

Advanced Bionics framework requires **only** that the same or substantially the same art **or** substantially the same arguments were previously presented to the Office” (bold emphases added)).

Because Applicant previously presented Gajewski to the Office and the Examiner made Miquel of record, the Board can proceed directly to the second prong of *Advanced Bionics*.

2. Honda is cumulative of Tokyo, which was previously considered by the Examiner

Petitioner asserts that Honda “was not cited, applied by, or disclosed to, the Examiner during prosecution of the ’838 Patent” (Petition, 30), but fatally omits any analysis of Honda’s disclosure relative to art previously presented to the Examiner. EX2001, ¶91. This inquiry is mandated by § 325(d). *See Advanced Bionics*, Paper 6, at 8, 13, 19 (finding three of the four references cited by Petitioner cumulative over references cited in an IDS); *Bio-Rad Lab ’ys, 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 [similarities or] material differences” from art presented in an IDS).

Petitioner and Dr. Robinson should have compared Honda’s disclosure to that of Tokyo’s (EX2012). Applicant submitted a complete copy of Tokyo during prosecution, which the Examiner considered. EX1002, 125, 169 (Ref. Des. A1); EX2001, ¶90. As confirmed by Dr. Garrett (EX2001, ¶¶89-93, Table C), Tokyo

presents the same or substantially the same disclosure relied on by Petitioner in Honda. For example, Petitioner argues that “Honda is directed to a method for treating, reducing the severity of, or preventing ... cancer, by orally administering to an individual in need thereof of, a composition comprising bacteria within the family Ruminococcaceae.” Petition, 60. Tokyo also discloses pharmaceutical compositions comprising bacteria belonging to the family Ruminococcaceae (*see*, for example, EX2012, ¶¶28, 32, 39), that such compositions can be “administered orally to an individual in need thereof” (*id.*, ¶46), and that “condition[s] for which the bacterial composition is a potential treatment” include cancer, where treatment includes “reducing adverse effects or prevention” (*id.*, ¶¶95-97, 132). *Compare* EX1011, ¶¶21, 55, 57-60, 64 (Petition, 61-62, discussing how to formulate, dose, and administer) *with* EX2012, ¶¶46, 99, 100-103, 117 (same); EX1011, ¶¶23, 42, 63 (Petition, 61, discussing how to isolate and purify bacteria) *with* EX2012, ¶¶81, 85, 113, 138, 183, 184 (same); EX1011, ¶2 (Petition, 60, discussing how gut commensal bacteria influence host immune response) *with* EX2012, ¶3 (same). EX2001, Table C.

Petitioner also argues that “Honda is directed to compositions of human-derived bacteria that induce proliferation of Th17 cells.” Petition, 60. Tokyo provides corresponding disclosure: “commensal microorganisms influence... **accumulation of unique lymphocytes** in mucosal tissues, including... IL-17-

producing CD4-positive T cells (**Th17**).” EX2012, ¶3. Tokyo administered human fecal suspensions orally to germ-free mice (including mouse #A1), which resulted in “**significant accumulation of IL-17-expressing CD4+ cells (namely, Th17 cells)**.” EX2012, ¶¶55, 56, 251, FIGs. 1E and 1F. Analysis of mouse #A1 cecal contents identified bacteria belonging to the family of Ruminococcaceae. EX2012, ¶77, Table 1B (identifying *inter alia* *Anaerotruncus colihominis* in the mouse #A1 sample). Tokyo refers to *Anaerotruncus colihominis* throughout its specification. *See, e.g.*, EX2012, ¶¶35, 39. According to Petitioner, “Honda teaches that compositions . . . can be administered to humans, including bacteria within the purported family Ruminococcaceae,” with Honda “identifying . . . *Anaerotruncus colihominis*.” Petition, 60-61; EX2001, ¶92, Table C.

The extensive disclosure overlap between Honda and Tokyo is not surprising given that *all* inventors listed on the face of Honda are also listed on the face of Tokyo. EX2001, ¶93. Neither Petitioner nor Dr. Robinson discuss the substantial similarity between Honda and Tokyo (or any other reference cited during prosecution). EX2001, ¶91. Petitioner cannot deny that Honda is “substantially the same” as Tokyo under the first prong of *Advanced Bionics*.

3. Petitioner presents no error material to patentability in its obviousness (Ground 4 and 5) arguments

The Petition asserts that the Board need not address the second prong of *Advanced Bionics*. Petition, 87. Petitioner misapplies the law. Where the Examiner

considered the same art (Gajewski and Miquel) or substantially the same art (Tokyo) during prosecution, a petitioner must demonstrate “the Office erred in a manner material to the patentability of challenged claims.” *Advanced Bionics*, Paper 6, at 8. Here, Petitioner’s assertion of material error—that the Examiner’s “fail[ure] to identify and consider [any combination of Honda, Gajewski and Miquel] and the arguments as presented in the Petition”—similarly misses the mark. Petition, 87.

First, as shown above, the Examiner identified and considered Gajewski, Miquel, and Tokyo during prosecution, and Honda’s disclosure is cumulative to the latter’s. The mere absence of a rejection based on a particular combination of references does not evidence material error and does not provide a basis to institute review. *See Fortinet Inc. v. British Telecommunications Public Limited Co.*, IPR2019-01326, Paper 8, at 9 (P.T.A.B. Jan. 7, 2020) (denying institution where “Petitioner does not explain how its Ground [] argument was not previously before the Office, apart from merely using a different reference ... [and] also fails to describe *any* difference between [the references] that would provide a reason to obtain a different result from the obviousness analysis previously performed by the Examiner” (emphasis in original)); *Dorco Co. v. The Gillette Co.*, IPR2017-00500, Paper 7, at 15-16 (P.T.A.B. June 21, 2017) (denying institution where Petitioner merely “substituted” references for their obviousness argument without identifying

features not disclosed by the art cited during prosecution); *Ivantis, Inc. et al. v.*

Sight Sciences, Inc., IPR2022-01533, Paper 14, at 19 (P.T.A.B Mar. 27, 2023)

(“To the extent Petitioner equates Examiner’s silence in discussing relevant prior art to a material error ..., we are not persuaded.”).

Second, Petitioner mischaracterizes the prosecution history in asserting that the Examiner “fail[ed] to identify and consider . . . the arguments presented in the Petition.” Petition, 87. In fact, not only does Petitioner rely on the same or substantially same art, but Petitioner’s arguments are the same or substantially same as those considered during prosecution. For example, while asserting that its Miquel argument was not before the Office (*id.*), a side-by-side comparison shows that the Examiner considered the *same argument* during prosecution, as shown below and confirmed by Dr. Garrett (EX1002, 116; EX2001, ¶¶99-100, Table E).

Petitioner’s Miquel argument	Examiner’s Miquel argument
“Miquel is applied... to show that [F]aecalibacterium prausnitzii is the most abundant bacterium in feces of healthy adults.” Petition, 87, and also 71.	“Faecalibacterium prausnitzii is the most abundant bacteria in the intestinal microbiota.” EX1002, 116.

<p>“A POSA would have... recognized the major role these butyrate producing bacteria play in the physiology of the human gut, including the ‘numerous beneficial effects for health through... reduction of cancer progression’ as taught by Miquel.” Petition, 71-72.</p>	<p>Miquel “further teach[es] beneficial effects of butyrate-producing <i>Faecalibacterium prausnitzii</i> for health and reduction of cancer progression.” EX1002, 116.</p>
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Further, the Office acting as International Searching Authority (ISA) cited both Gajewski and Tokyo in the International Search Report (ISR). EX1002, 177-178, 667-668; EX2001 ¶¶95, 98. The ISA cited Gajewski as a category “X” document⁶ and indicated that the “**entire document**” contains “relevant passages” to multiple claims, including then-pending claim 44. EX1002, 177-178, 667-668; EX2001, ¶98. The ISA also cited Tokyo as a category “X” document against then-pending claim 44, and as a category “Y” document⁷ against several claims

⁶ See definition of category “X” documents in the ISR. EX1002, 177, 667 (“document of **particular relevance**; the claimed invention cannot be considered novel or... to involve an inventive step when the document is taken alone”).

⁷ See definition of category “Y” documents in the ISR. EX1002, 177, 667 (“document of **particular relevance**; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art”).

dependent therefrom. EX1002, 177, 667; EX2001, ¶95.

Further, the ISA asserted in the Written Opinion *inter alia* that then-pending claim 44 lacks novelty over Tokyo. EX1002, 191, 647; EX2001, ¶96. The ISR and Written Opinion were cited and considered by the Examiner. EX1002, 127, 171 (Ref. Des. C8); EX2001, ¶97. Then-pending claim 44 entered U.S. national examination without amendment, was examined during prosecution, and corresponds to claim 1 of the '838 Patent after amendment.⁸ EX2001, ¶95.

Dr. Garrett confirms that Petitioner now presents the same or substantially the same arguments with respect to Honda as the ISA set forward in the Written Opinion with respect to Tokyo (cumulative to Honda). EX2001, ¶¶96, 97, Table D. *See Ivantis*, Paper 14, at 16-20 (finding that a reference cited by Petitioner is cumulative to a reference cited by the ISA and applied in its Written Opinion “for

⁸ The amendments changed “treating or preventing cancer” (then-pending claim 44) to “reducing or delaying growth of a skin cancer tumor” (claim 1 as granted with the '838 Patent) and bacteria belonging to “the class Clostridia, class Mollicutes, order Clostridiales, family Ruminococcaceae and/or genus *Faecalibacterium*” (then-pending claim 44) to bacteria belonging to “the family Ruminococcaceae” (claim 1 as granted with the '838 Patent). EX1002, 620; EX1001, 189:2-6.

challenging the novelty of similar pending claims”).

Petitioner’s Honda argument	ISA’s Tokyo argument
“Honda is directed to a method for treating, reducing the severity of, or preventing... cancer , by orally administering to an individual in need thereof of, a composition comprising bacteria within the family Ruminococcaceae.... ” Petition, 60.	“Tokyo discloses a method of treating or preventing cancer... in a subject comprising administering to the subject a composition (a pharmaceutical preparation for oral administration...) comprising... bacteria... belonging to... family Ruminococcacea[e] ”; “Tokyo discloses the administration of the gut bacteria to treat or ameliorate cancer. ” EX1002, 191, 193, 647, 649.
“Honda teaches specific methods for ‘isolating or purifying’ the desired intestinal commensal bacteria. ” Petition, 74.	Tokyo discloses “methods of identifying and culturing intestinal commensal bacteria, isolated from humans.” EX1002, 191 and 647.
“Honda teaches a variety of excipients, carriers, and other additives useful for formulating a pharmaceutically acceptable preparation for oral ingestion. ” Petition, 62.	Tokyo discloses “a pharmaceutical preparation for oral administration compris[ing] an additional component that enables efficient delivery of the bacterial composition... to the colon.” EX1002, 191 and 647.
“While Honda teaches the use of <i>Ruminococcus</i> for treatment of diseases and cancer, it does not specifically identify a subset of cancers for which it is useful [including skin cancer].” Petition, 68.	“Tokyo discloses the method of claim 44 [referring to cancer in general], but Tokyo does not disclose wherein the cancer is a skin cancer. ” EX1002, 193 and 649.

Not only did Petitioner (and its expert) omit any comparison between Tokyo and Honda, they also failed to address highly relevant discussion of Tokyo in the

Written Opinion. EX2001, ¶¶91, 97. Petitioner should not be excused for its egregious disregard for the Written Opinion’s application of Tokyo and the substantial similarity of that analysis to Honda. *See Albany Int’l Corp. v. Kimberly-Clark Worldwide, Inc.*, PGR2021-00019, Paper 22, at 25 (P.T.A.B. June 22, 2021) (denying institution as “Petitioner fails to address the substantive discussion of [a reference] in the ISA’s written opinion”).

And, similarly, neither Petitioner nor Dr. Robinson even acknowledged that the ISA identified Gajewski as being “of particular relevance” in its *entirety* to then-pending claim 44. EX2001, ¶98. Petitioner merely submitted that “Gajewski was supplied by the Applicant along with over 75 other references” (Petition, 86) and that the Examiner erred by “failing to identify and consider” Gajewski (*id.*, 87), which turns a blind-eye to the entire prosecution history. *See Bio-Rad Lab’ys, Inc.*, Paper 21, at 8 (denying institution because “the Petition does not include a substantive discussion of the prosecution history”).

Petitioner’s incomplete review of the record and application of the law is insufficient to meet its burden under *Advanced Bionics*. As with its “Section 112 issues,” Petitioner, at bottom, merely disagrees with the Examiner allowing claims over disclosure in Tokyo (cumulative to Honda), Gajewski, and Miquel. But disagreement is an insufficient reason to institute trial, particularly where reasonable minds may disagree. *Advanced Bionics*, Paper 6, at 9; *see generally*

PowerOasis, Inc. v. T-Mobile USA, Inc., 522 F.3d 1299, 1304 (Fed. Cir. 2008)

(explaining that examiners are presumed to do their job, understand the cited references, and issue only valid patents). And although Dr. Robinson’s declaration was not before the Office during prosecution, Dr. Robinson did not provide “additional evidence or facts that warrant reconsideration of the Examiner’s decision.” *See Apotex Inc. v. Celgene Corp.*, IPR2018-00685, Paper 8, at 26 (P.T.A.B. Sept. 27, 2018); *also Dynaenergetics US, Inc. v. Geodynamics, Inc.*, PGR2018-00065, Paper 8, at 27-28 (P.T.A.B. Nov. 15, 2018).

Petitioner bears the burden of demonstrating an error material to patentability by the Examiner, but falls woefully short in its attempt to cobble together obviousness grounds not previously considered. The Board should deny trial and not reward Petitioner with a free pass to reexamine facets of art thoroughly considered by the Examiner.

V. GROUND 4: PETITIONER FAILS TO SATISFY ITS BURDEN OF DEMONSTRATING THAT ANY CHALLENGED CLAIM WOULD HAVE BEEN OBVIOUS

A. Petitioner failed to establish that a POSA would have had a reason to combine Honda and Gajewski

1. Petitioner ignored the art that taught a cancer-inducing property of Th17 cells

Petitioner touts Honda for being directed to “compositions of human-derived bacteria that induce proliferation of Th17 cells” and alleges that “a POSA would be motivated to apply Honda’s more generalized teachings relating to ‘cancer’

treatment to the specific cancers recited in Gajewski.” Petition, 60, 68. But Petitioner fails to establish that a POSA would have started with Honda’s “Th17-inducing bacterial compositions” when the art taught that Th17 cells *promote* tumor growth—the opposite of what Petitioner alleged a POSA would have sought to achieve. EX2021, Abstract; EX2022, 10113; EX2003, 927; EX2001, ¶¶42-44.

Specifically, Petitioner’s obviousness argument does not address the conflicting observations in the field before the September 2016 priority date that “the presence of Th17 cells in tumors has been associated with both favorable and unfavorable prognoses.” EX2022, 10112; EX2001, ¶43. For example, Petitioner ignored Wang I’s report that “Th17 cells *promote tumor growth*” of melanoma in mice. EX2021, Abstract, FIG. 1, 1459; EX2001, ¶43. Petitioner also ignored that Wang II showed that IL-17, a pro-inflammatory cytokine produced by Th17 cells, “is an important tumor-promoting element in [] skin carcinogenesis” and that “Th17 responses can *enhance carcinogenesis*.” EX2006, 10-11; EX2022, 10113; EX2001, ¶43. Nardinocchi’s observation that IL-17 promotes tumor development in human nonmelanoma skin cancer is also not mentioned or reconciled in the petition. EX2003, 927; EX2001, ¶43.

Because Petitioner failed to prove that a POSA would have started with a composition that induces proliferation of Th17 cells—which *promote* cancer—to arrive at methods for *reducing or delaying growth of* cancer, Petitioner failed to

meet its burden to establish obviousness of the claimed methods. *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”).

2. Petitioner failed to consider Gajewski for all that it teaches vis-à-vis modulating microbiome to affect tumor growth

Petitioner also argues that a POSA would have combined Honda and Gajewski because Gajewski teaches that *Ruminococcus* “would be useful” for “skin cancer tumors.” Petition, 68. But Petitioner ignores Gajewski’s teaching of the opposite: that “the presence or increased level of,” e.g., *Ruminococcus*, “*potentiates* cancer/tumor growth, spread (e.g., malignancy).” EX1012, 22:6-9; EX2001, ¶¶45-46. Petitioner also ignores Gajewski’s teaching “modulating levels of one or more commensal microbes,” which includes *Ruminococcus*, by “*decreasing* levels” of the microbe. EX1012, 2:14-15; EX2001, ¶46. In ignoring these teachings altogether, Petitioner fails to consider the reference for all that it teaches, and fails to establish that a POSA would have had a reason to administer *Ruminococcaceae* to reduce or delay tumor growth. *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.”).

Petitioner points to the data in Gajewski as allegedly teaching that “bacteria belonging to the genera *Ruminococcus*” were associated with anti-tumor activity (Petition, 64), but Petitioner is working backwards from the claimed methods to select *Ruminococcus* from the data. EX2001, ¶47. First, according to Petitioner and Dr. Robinson, “bacteria belonging to the genera *Ruminococcus*” were found among “15 taxa” that were “significantly increased” in animals having anti-tumor immune responses. Petition, 64; EX1003, ¶173. Dr. Robinson and Petitioner are both wrong: Gajewski identifies “51 taxa,” not “15,” that were associated with an anti-tumor response. EX1012, 49:3-5; EX2001, ¶47. And Petitioner did not explain how or why a POSA would have chosen *Ruminococcus* from Gajewski’s list of 51. *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”).

Petitioner also fails to show why a POSA would have chosen to administer *Ruminococcus* to reduce or delay skin cancer tumor growth, when Gajewski concludes that of the 51 potential anti-skin cancer taxa identified, only *Bifidobacterium* “showed a positive association with anti-tumor T cell responses.”

EX1012, 49:7-9, FIGs. 8A-D; Petition, 64; EX2001, ¶48. As Dr. Garrett explains, a POSA would have understood Gajewski to suggest administering *Bifidobacterium*, not *Ruminococcus*, to reduce tumor growth. EX2001, ¶¶48-49. In view of Gajewski's conclusion, Petitioner's selection of *Ruminococcus* to reduce or delay skin cancer tumor growth can be reached only through hindsight.

Because Petitioner failed to explain why a POSA would have selected *Ruminococcus* as "useful" for "skin cancer tumors" when Gajewski taught to select *Bifidobacterium*, Petitioner failed to meet its burden to establish obviousness of the claimed methods. *In re Young*, 927 F.2d 588, 591 (Fed. Cir. 1991); *Novo Nordisk A/S v. Caraco Pharma. Lab'ys, Ltd.*, 719 F.3d 1346, 1365 (Fed. Cir. 2013) ("it is necessary to consider prior art that supports unobviousness of the claimed invention, as well as that which weighs against it").

B. Petitioner failed to establish a reasonable expectation of success in view of the prior art

Petitioner argues that a POSA would have had a reasonable expectation of success because "it was state of the art to modify bacterial microbiomes for purposes of treating cancer." Petition, 69. But Petitioner fails to assess the actual state of the art before September of 2016 related to modulating the gut microbiome as a skin cancer treatment. As Dr. Garrett explains, the few studies that looked at the connection between the gut microbiome and anti-skin cancer response before September of 2016 *overlooked* Ruminococcaceae family as useful for skin cancer

treatments, and identified bacteria *other than* Ruminococcaceae for such treatments. EX2001, ¶50; EX2004, Abstract; EX2005, Abstract.

For example, Vetizou analyzed the composition of the gut microbiome in patients with metastatic melanoma, and found that the bacterial species that were positively associated with anti-cancer effects belong to the *Bacteroides* genus (“*B. fragilis* and/or *B. thetaiotaomicron*”) and the Burkholderiales order, i.e., bacteria other than Ruminococcaceae. EX2004, Abstract, FIG. 3; EX2001, ¶51. As Dr. Garrett explains, a POSA would have understood that the human gut microbiome examined in Vetizou contained bacteria from the family Ruminococcaceae because these bacteria are found in significant numbers in the human gut microbiota. EX1014, 3; EX2001, ¶51; *see also* EX2004, FIG. 4. Yet, Vetizou did not associate Ruminococcaceae with any anti-cancer effects. EX2001, ¶51. Therefore, a POSA would have concluded from Vetizou that the anti-skin-cancer properties of the gut microbiome are associated with the *Bacteroides* genus (and not Ruminococcaceae). *Id.*, ¶51.

Like Vetizou, Sivan also failed to suggest that Ruminococcaceae has anti-skin-cancer properties. Instead, and in contrast to Vetizou, Sivan identified the genus of *Bifidobacterium* (species *B. breve*, *B. longum*, and *B. adolescentis*) as “the only” bacterial taxa having “positive association with antitumor T cell responses” in a mouse melanoma model. EX2005, Abstract, 1085, FIG. 3; EX2001, ¶52. Sivan

used gut microbiome from JAX mice, which, as Dr. Garrett explains, naturally contains *Bacteroides* and Ruminococcaceae bacteria. EX2005, 1085; EX2001, ¶52; EX2023, FIG. S6C. But Sivan did not observe a positive association between Ruminococcaceae or *Bacteroides* and the anti-skin-cancer response. EX2001, ¶52. Based on Sivan's data, a POSA would have concluded that the anti-skin-cancer properties of the gut microbiome are associated with the *Bifidobacterium* genus (and not *Bacteroides* or Ruminococcaceae). EX2001, ¶52.

The field also noted the discrepancy between the results of the Vetizou and Sivan studies before September of 2016: “they differ with respect to the specific bacteria identified as causing [anticancer] effects,” and further noted that “there is a complexity here that must be addressed in future studies.” EX1007, 1262; EX2001, ¶53. Petitioner failed to establish, however, that a POSA would have reasonably expected any success in reducing or delaying a skin cancer tumor growth by administering Ruminococcaceae, when Ruminococcaceae was not known to be associated with an anti-skin cancer response before September 2016. EX2001, ¶53. Nor has Petitioner shown that a POSA would have had a reasonable expectation of success in the face of the unpredictability and “complexity” expressly declared in the prior art. *Id.*, ¶53.

Petitioner argues that a POSA would have had a reasonable expectation of success because both Honda and Gajewski demonstrated a delay in tumor growth

through “enhance[ing] induction and infiltration of tumor-specific CD8* T cells”⁹ (Petition, 69), but Petitioner ignores the unpredictability in the art related to CD8* T cells induction by Th17 cells. As discussed in Section V.A.1, the art before September 2016 taught that Th17 cell do not always induce tumor-specific CD8* T cells, but can instead *promote* tumor growth and *inhibit* CD8+ T cell infiltration into tumors. EX2021, Abstract (“Th17 cells promote tumor growth” of melanoma in mice); EX2022, 10113 (“Th17 responses can enhance carcinogenesis”); EX2003, 927; EX2007, Abstract (“IL-17 inhibited CD8 T cell infiltration”); EX2001, ¶54. Petitioner failed to explain why a POSA would have reasonably expected that a Ruminococcaceae composition, which Honda shows to increase infiltration of Th17 cells, would reduce or delay skin cancer tumor growth in view of the *opposite* teachings in the art. EX2001, ¶¶54-55.

Because Petitioner disregarded the unpredictability and inconsistent observations that riddled the field of bacteria-based skin cancer treatment before September of 2016, Petitioner failed to meet its burden of proving that a POSA would have arrived at the claimed methods with a reasonable expectation of

⁹ CD8+ T lymphocytes have antitumor effect to directly attack the tumor cells. EX2016, 124; EX2001, ¶58.

success. *Osi Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1385 (Fed. Cir. 2019)

(“hope that a potentially promising drug will treat a particular cancer is not enough to create a reasonable expectation of success in a highly unpredictable art”); *see also Eli Lilly & Co. v. Teva Pharma. Int’l GmbH*, 8 F.4th 1331, 1348 (Fed. Cir. 2021) (it is, “at all times, [Petitioner]’s burden to show that the claims would have been obvious, including that a skilled artisan would have had a reasonable expectation of success in achieving the claimed invention”).

VI. GROUND 5: PETITIONER FAILS TO SATISFY ITS BURDEN OF DEMONSTRATING THAT CLAIM 5 WOULD HAVE BEEN OBVIOUS

Ground 5, challenging dependent claim 4, differs from Ground 4 only by the addition of Miquel, and Petitioner does not allege that Miquel adds anything to the Honda/Gajewski combination beyond showing that “*faecalibacterium prausnitzii* is the most abundant bacterium in feces of healthy adults.” Petition, 87. Therefore, for the same reasons discussed for Ground 4, Petitioner failed to establish that a POSA would have had a reason to combine Honda, Gajewski, and Miquel to arrive at the methods of claim 4 with a reasonable expectation of success. EX2001, ¶56.

VII. GROUND 1: PETITIONER FAILS TO SATISFY ITS BURDEN OF DEMONSTRATING THAT ANY CHALLENGED CLAIM LACKS WRITTEN DESCRIPTION SUPPORT

A. Petitioner improperly demanded an actual reduction to practice (“ARTP”) from Patent Owner; the law does not require an ARTP

Petitioner alleges that Patent Owner is not entitled to the scope of the

claimed methods because Patent Owner “did not *create* a single composition, *administered* in any way” (Petition, 32),¹⁰ but Petitioner’s repeated insistence on creating and administering a composition is an insistence on an ARTP in humans, contrary to the demands of the written description law. *Alcon Research Ltd.*, 745 F.3d at 1190 (“[t]here is no requirement that the disclosure contain ‘either examples or an actual reduction to practice.’”). And the law certainly does not require an ARTP in humans. Yet, Petitioner wrongly deems it “critical[]” that the patent contains no disclosure of a composition comprising isolated or purified Ruminococcaceae “*administered* to a human.” Petition, 33.

By improperly requiring proof that the claimed method “was, or could be, achieved by the inventors” (*id.*, 2), Petitioner did not follow the law. Written

¹⁰ The ARTP-based alleged deficiency argument permeates the entire written description ground. *See, e.g.*, Petition, 2 (“the only ‘working examples’ ... was that of an aliquot of unprocessed human feces ... orally gavaged into a mouse”), 33 (“the patent contains no disclosure of a single ‘composition’ ... administered to a human”), 35 (“no clinical trials were performed and no human was administered either butyrate or a fecal matter transplant”), 38 (“[n]o human was orally ‘administered’ any unprocessed fecal composition”).

description is “not about whether the patentee has proven to the skilled reader that the invention works, or how to make it work;” it is about “whether the skilled reader of the patent disclosure can recognize that what was claimed corresponds to what was described.” *See Alcon Research*, 745 F.3d at 1191. Petitioner failed to assess the specification under this legal standard. For example, Petitioner admits that the specification lists a “host of different compositions that could potentially be formulated” and “list of ingredients that could potentially be used to create such formulations” (Petition, 36), but Petitioner faults the description because it “fails to disclose a single such composition that was *actually created*.” *Id.* Petitioner also admits that the specification provides a description of various routes of administration, but again complains that “[n]o human was orally ‘administered’ any unprocessed fecal composition.” *Id.*, 38.

By requiring an ARTP, Petitioner failed to meet its burden in assessing whether the disclosure “allows one skilled in the art to visualize or recognize the identity of the subject matter purportedly described,” which is “all that the written description requirement demands.” *Alcon Research*, 745 F.3d at 1190-1191; *see also Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (“the hallmark of written description is disclosure”).

B. Petitioner failed to show that the species exemplified in the specification are not representative of the claimed genus

1. Petitioner ignored actual clinical data in the '838 Patent; Petitioner's assessment of the disclosure is incomplete

Petitioner argues that “the only experiments conducted with human patients involved the *characterization* of gut and buccal microbiome of metastatic melanoma patients” (Petition, 33 (emphasis original)), but Petitioner blatantly ignores actual clinical results described in the '838 Patent. In doing so, Petitioner fails to fully assess “the scope of the inventor’s contribution to the field of art as described in the patent specification,” and Petitioner’s written description ground must fail. *See Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005).

For example, Petitioner ignored that Example 1 assessed actual *clinical responses* associated with Ruminococcaceae abundance in human melanoma patients. EX1001, 154:12-20, FIG. 3E, Table 6; EX2001, ¶58. According to Example 1, patients with a high abundance of Ruminococcaceae had “a significantly prolonged PFS [progression-free survival] versus those with low abundance.” EX1001, 154:12-20, FIG. 3E, Table 6; EX2001, ¶58. Further, there was “a higher density of CD8+ T lymphocytes” in the immune cells that infiltrate tumor tissue and in the systemic circulation prior to administering any anti-tumor therapy of responders versus non-responders. EX1001, 156:9-157:9, FIGs. 4A-D, 18-22; EX2001, ¶58. As explained in Section V.A.2, higher density of CD8+ T

lymphocytes indicates anti-tumor activity. EX2001, ¶58; EX2016, 124; EX2017, 3.

Because Petitioner ignored the clinical results reported in the '838 Patent, Petitioner failed to show that a POSA would not have recognized that inventors invented what is claimed, given these results. *See Falko-Gunter Falkner*, 448 F.3d at 1363 (written description is “judged from the perspective of one of ordinary skill in the art”). EX2001, ¶58. And Petitioner’s faulty POSA definition adds to their erroneous analysis by using too low of a skill level for a POSA. As such, Petitioner failed to meet its burden, and its written description ground must fail.

2. Petitioner did not demonstrate that the mouse melanoma model used in the '838 Patent is not predictive of other subjects and other types of skin cancer

Petitioner admitted that the specification “investigated the effects of altering the microbiome on tumor growth in mice,” but failed to substantiate its complaint that mouse models constitute a “limited disclosure.” Petitioner, 33-45. “The predictability or unpredictability of the science is relevant to deciding how much experimental support is required to adequately describe the scope of an invention.” *Capon*, 418 F.3d at 1360. Here, Petitioner also did not provide *any* evidence of unpredictability, only a conclusory remark that Patent Owner “invited more research to determine the potential value in humans.” Petition, 34; EX1003, ¶116. By failing to address the predictability of the science, Petitioner has failed to meet its burden.

Contrary to Petitioner’s assertions, the art taught that mouse models of melanoma are, indeed, “[t]he most widely used preclinical model[s]” for skin cancer, such as melanoma. EX2013, Abstract, 82; EX2001, ¶59. Indeed, the “well-established” model of injectable murine melanoma that Patent Owner used in its pre-clinical experiments “allow[s] for the interaction of melanoma cells with competent T-cells and B-cells found naturally in the human melanoma microenvironment.” EX2013, 84; EX2001, ¶59. The mouse model is also a “validated [] model” that “recapitulates key pathophysiological aspects of the human disease.” EX2014, 544, 550; EX2001, ¶59. As such, the field considered the mouse model that the ’838 Patent used to be “clinically relevant” in humans, and Petitioner did not provide any evidence to the contrary. EX2013, 84; EX2001, ¶59. Petitioner’s argument that mouse experiments constitute “limited disclosure” is unsubstantiated and should be dismissed.

Petitioner also alleged lack of possession “of a method of treating every type of ‘skin cancer tumor’” because “PO did not conduct any experiments” demonstrating the claimed methods “would be effective” for anything other than “murine melanoma.” Petition, 44. But as established, written description is “not about whether the patentee has proven to the skilled reader that the invention works, or how to make it work.” *See Alcon Research*, 745 F.3d at 1191; *see also Fresenius Kabi USA, LLC v. Coherus Biosciences, Inc.*, PGR2019-00064, Paper

10, at 11–18 (P.T.A.B. Mar. 19, 2020) (“there is no legal requirement that a patent must include test results or working examples demonstrating stability for every possible composition that is covered by the claims”).

In any event, Petitioner failed to explain why melanoma is not representative of other claimed skin cancer tumors. Petitioner has not denied, and cannot deny, that the specification discloses that administering FMT abundant in Ruminococcaceae resulted in a statistically significant ($p=0.04$) delay in melanoma tumor growth by day 14 in mice (“FMT1”). EX1001, 182:7-50, Example 4, FIG. 25B; EX2001, ¶¶60-61. The specification also discloses that Patent Owner “validate[d]” their FMT1 findings by “using stools from different [] patients” (“FMT3”), as well as showed that FMT “enhances response to α PDL-1 therapy” (“FMT2”). EX1001, 182:62-65; 184:27-30, Example 4, FIGs. 28A-C, 32A-C; EX2001, ¶¶60-62. Petitioner complained only that the FMT2 and FMT3 experiments allegedly lacked “statistical significance.” Petition, 44-45. But Petitioner failed to show that a POSA would have “doubt[ed] the truth or accuracy” of the statistically-significant results with FMT1. *See In re Marzocchi*, 439 F.2d 220, 224 (C.C.P.A. 1971); EX2001, ¶¶63-64. Nor did Petitioner “back up assertions of its own with acceptable evidence or reasoning which is inconsistent with” the FMT1 results. *In re Marzocchi*, 439 F.2d. at 224; EX2001, ¶¶64. Therefore, the Board should reject Petitioner’s criticism of the mouse melanoma

model experiments.

Petitioner alleges that the exclusion of “uveal melanoma” from the mouse experiments somehow evidences lack of possession. Petition, 45. But this argument, too, is not grounded in any legal principle. “It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim.” *See Capon*, 418 F.3d at 1359.

3. Petitioner’s expert misrepresented the data in the ’838 Patent that show a positive association of Ruminococcaceae with tumor reduction

Dr. Robinson alleges that the patent’s experimental results cannot be “ascribed to bacteria particularly from the family Ruminococcaceae” (EX1003, ¶115; Petition, 34), but the data in the specification belie Dr. Robinson’s allegation. EX2001, ¶65. First, Dr. Robinson does not, and cannot, dispute that the ’838 Patent demonstrates that the gut microbiota from responders was differentially enriched in Ruminococcaceae bacteria.¹¹ EX1001, FIGs. 2C-E;

¹¹ As Dr. Garrett explains, the experimental methods used by Patent Owner represent the state of the art in the field. EX2001, ¶65. Patent Owner used linear discriminant analysis of effect size (LEfSe) to identify the taxonomic differences between responders and non-responders. EX1001, 153:28-34; EX2001, ¶65. LEfSe is a trusted method to “detect bacterial organisms and functional characteristics

EX2001, ¶65. At most, Dr. Robinson points to Tables 1 and 2 as allegedly showing that “bacteria from the family Ruminococcaceae were found in both the ‘responder’ and ‘non-responder’ fecal samples.” EX1003, ¶¶115, 132-133; Petition, 34. But Dr. Robinson does not establish that the presence of some Ruminococcaceae species in non-responders undermines the observation that the gut microbiome from responder patients was “significantly enriched” with Ruminococcaceae on all taxonomic levels. *See* EX1001, 153:12-42, 154:4-11, 153:37-46, FIGs. 2C-F, 3D, Tables 4-5; EX2001, ¶¶65-66. In contrast, Dr. Garrett explains that “a POSA would have understood the ’838 Patent to disclose the gut microbiota of responder patients were clearly enriched for Ruminococcaceae on all taxonomic levels.” EX2001, ¶65-66.

In any event, the law does not require “that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim.” *See Capon*, 418 F.3d at 1359; *see also In re Angstadt*, 537 F.2d 498, 504 (C.C.P.A. 1976) (“The examples, both operative and inoperative, are the best guidance this art permits, as far as we can conclude from the record”). Thus, the presence of species of Ruminococcaceae in non-responders does not undermine

differentially abundant between two or more microbial environments.” EX2015, 3; EX2001, ¶65.

the sufficiency of the support for the claims of the '838 Patent.

C. Petitioner failed to assess the scientific and technological knowledge of a POSA as of the filing date of the '838 Patent

1. Petitioner used the wrong date for the § 112 analysis

Petitioner admittedly performed the analysis of what the specification would have conveyed to a POSA “as of September 27, 2016” (Petition, 31-32; EX1003, ¶112), which further undermines its lack of description arguments. To meet its burden to establish unpatentability under § 112, Petitioner needed to analyze the sufficiency of the '838 Patent disclosure as of September 27, 2017,¹² the filing date of the application that matured into the '838 Patent. EX1001, Face page; *see Reiffin v. Microsoft Corp.*, 214 F.3d 1342, 1345-46 (Fed. Cir. 2000) (holding that the written description requirement of 35 U.S.C. § 112 requires a court to examine disclosures in the specification of the continuing application’s patent, not that of the ancestor application).

Here, September 27, 2016, the date that Petitioner used for *all* its grounds, is the filing date of the ancestor application (Provisional Application No. 62/400,372). Patent Owner does not dispute that September 27, 2016, is the date that should be used when assessing patentability of the claims of the '838 Patent

¹² Patent Owner affirms that all arguments on Grounds 1-3 presented herein apply regardless of which date is used.

under § 103. But the burden here is on Petitioner, and it was wrong to assess unpatentability under § 112 based on the priority date, rather than the actual filing date. *Reiffin*, 214 F.3d at 1345-46.

Petitioner's use of the wrong date undermines its written description ground, because Petitioner failed to consider that the state of the art, and therefore the level of disclosure needed, changed between September 27, 2016, and September 27, 2017. *See Capon*, 418 F.3d at 1357 (“[t]he descriptive text needed to meet [the written description] requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence”). The following is but one example of such a change and its relevance to Petitioner's written description ground:

Petitioner alleged that “bacteria from the ‘family of Ruminococcaceae’ lacks written description support” because “certain species of bacteria from the claimed ‘Ruminococcaceae’ family were found only in stool of ‘non-responder’ patients.” *Petition*, 41. This finding, according to Petitioner, would have made a POSA understand that “at least several species of Ruminococcaceae would not result in the claimed ‘reduction’ or ‘delay’ in skin cancer tumor growth.” *Id.* Petitioner made this allegation from the perspective of a POSA as of September 2016. But as explained above, the field before September 2016 did not associate Ruminococcaceae with an anti-skin cancer response (EX2004, Abstract; EX2005,

Abstract; EX2001, ¶53), and therefore a 2016 POSA would not have “come to the patent with the knowledge” of Ruminococcaceae’s anti-skin cancer effect. *See LizardTech, Inc.*, 424 F.3d at 1345. But a POSA in 2017, assessing the specification of the ’838 Patent, would have had the benefit of Chaput, which confirmed a positive association between bacteria from the family Ruminococcaceae and skin cancer treatment in humans. EX2018, Abstract, 1370; EX2001, ¶66. Petitioner failed to establish that a POSA would not have understood that the inventors invented what is claimed, in view of Chaput and the disclosure in the specification. EX2001, ¶66. For this additional reason, Petitioner’s written description ground should fail.

2. By failing to consider existing knowledge in the field, Petitioner improperly burdened Patent Owner with re-describing known prior art concepts

Petitioner spent pages criticizing the ’838 Patent specification for allegedly not disclosing the minutia of different technical details (“excipients,” “route of administration,” “concentration” (Petition, 36-39)). But, Petitioner’s and Dr. Robinson’s demand that Patent Owner spell out every detail of the claimed methods exceeds the scope of the written description requirement. *See LizardTech, Inc.*, 424 F.3d at 1345 (“it is unnecessary to spell out every detail of the invention in the specification”); *see also Immunex Corp. v. Sandoz Inc.*, 964 F.3d 1049, 1064 (Fed. Cir. 2020) (“a patent specification need not re-describe known prior art

concepts”). Because Petitioner completely ignored a POSA’s knowledge related to the concepts of bacteria-based formulation and administration, Petitioner’s arguments as to the sufficiency of the specification fall short. EX2001, ¶67.

Indeed, a POSA (both in 2016 and in 2017) would have had knowledge of many technical details related to bacteria-based formulation and administration. For example, the prior art would have provided a POSA with answers to the following questions asked and answered in references such as Brandt and Vindigni: “How is FMT performed?”; “How should donors and recipients be screened?”; “Which route of administration is best?”; “Which diluent should be used?”; “How much stool is needed?”; etc. EX2008; EX2009; EX2001, ¶68. References such as Youngster would have taught a POSA about techniques related to “oral” FMT. EX2010; EX2001, ¶68. And references such as Khan would have informed a POSA how to culture anaerobic bacteria, such as Ruminococcaceae. EX2011; EX2001, ¶¶67-68. But as Dr. Garrett confirms, Dr. Robinson has not acknowledged such knowledge in the art. EX2001, ¶69.

Given the existing knowledge in the art related to bacteria-based formulation and administration, Patent Owner did not have to re-describe the concepts Petitioner alleges are missing from the ’838 Patent specification, e.g., determining excipients that are “best suited.” *Immunex Corp.*, 964 F.3d at 1064. In view of the extensive knowledge in the art concerning formulating and administering bacteria-

based compositions, and in light of the disclosures in the specification, Petitioner failed to show that a POSA would have been unable to recognize that the inventors invented the claimed methods of reducing or delaying growth of a skin cancer tumor by administering Ruminococcaceae.

Ultimately, “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). It was therefore Petitioner’s burden to explain whether the disclosure of the ’838 Patent would have allowed a POSA “to visualize or recognize the identity of the subject matter purportedly described” in view the scientific knowledge as of September 27, 2017. *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 968 (Fed. Cir. 2002). Petitioner failed to do so, and Ground 1 fails.

VIII. GROUND 2: PETITIONER FAILS TO SATISFY ITS BURDEN OF DEMONSTRATING THAT ANY CHALLENGED CLAIM LACKS ENABLEMENT

A. Petitioner failed to show that practicing the claimed methods would have required undue experimentation

Petitioner argues that “the ’838 Patent specification fails to teach a POSA how to make and use the full scope of the claimed invention without considerable experimentation” (Petition, 47), but Petitioner has failed to demonstrate that any experimentation would have been “undue.” See *Falko-Gunter Falkner*, 448 F.3d at

1365 (agreeing with the Board that “the mere fact that the experimentation may have been difficult and time consuming does not mandate a conclusion that such experimentation would have been considered to be ‘undue’ in this art”); *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996) (even a “considerable amount of experimentation is permissible, if it is merely routine”).

Although Petitioner offers arguments that some experimentation would have been needed, Petitioner does not even allege that the experimentation would have been *undue* in view of the *Wands* factors. *In re Wands*, 858 F.2d at 737. Indeed, Petitioner did not even mention the *Wands* factors. Petition, 47. Instead, Petitioner relied on the same arguments for both written description and enablement. *Id.* As with Petitioner’s flawed lack of written description argument, Petitioner’s lack of enablement argument failed to assess the state of the prior art and the knowledge of a POSA as of September 27, 2017. Therefore, Petitioner failed to show that any experimentation would have been undue as of the relevant date. *See In re Wands*, 858 F.2d at 737 (“it is well established that enablement requires that the specification teach ***those in the art*** to make and use the invention without undue experimentation”). And Petitioner’s faulty POSA definition adds to their erroneous analysis, because Petitioner’s POSA’s skill level is too low given that the invention relates to reducing or delaying growth of skin cancer tumors. EX2001, ¶¶25-27.

In any event, none of the arguments Petitioner offers shows the need for undue experimentation. For example, Petitioner argues that “determining which excipients or combinations of excipients are best suited for a robust formulation requires a comprehensive pre-formulation strategy that includes a host of experimentation and testing.” Petition, 36. But the only evidence Petitioner cites to support this allegation is Dr. Robinson’s declaration, which, in turn, is conclusory and unsupported on this point. EX1003, ¶120. Indeed, Dr. Robinson’s declaration merely repeats, *verbatim*, the conclusory assertion for which it is offered to support (*compare* Petition, 36, last paragraph, *and* EX1003, ¶120) and does not offer any additional evidence to support the stated conclusion. Therefore, Dr. Robinson’s testimony is entitled to little to no weight. *See* 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 Xerox Corp.*, Paper 9, at 15 (“the cited declaration testimony is conclusory and unsupported, adds little to the conclusory assertion for which it is offered to support, and is entitled to little weight”); *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”); *Cephalon, Inc. v. Watson Pharm., Inc.*, 707 F.3d 1330, 1339 (Fed. Cir. 2013) (“[u]nsubstantiated statements indicating that experimentation would be

‘difficult’ and ‘complicated’ are not sufficient”).

Petitioner’s allegation that “[c]ultivating and formulating bacteria into pharmaceutically acceptable compositions can also present myriad issues” (Petition, 25) also does not give rise to a conclusion that undue experimentation would be required. As Dr. Garrett explains, a POSA would have understood that practicing the claimed methods does not require “cultivating” Ruminococcaceae. EX2001, ¶71. As the ’838 Patent discloses, a composition comprising an isolated Ruminococcaceae can be obtained from “human fecal suspension ... using a 100 µm strainer” (EX1001, 184:65-185:2), and Dr. Garrett confirms that this was a routine practice. EX2001, ¶71; EX2008, 240; EX2010, 2; EX2009, 172, Table 1, 180. And Petitioner did not establish that *any* experimentation would have been required to simply follow a routine practice in the field. In any event, Petitioner and its expert admitted that a POSA would have known that “the bacterial product can be purified and concentrated,” or obtained using “serial dilutions of fecal content samples cultured by plating under a [sic] strictly anaerobic conditions.” Petition, 61; EX1003, ¶167. A POSA would have also known “how to formulate and administer the compositions,” according to Petitioner. Petition, 61; EX1003, ¶167. Thus, Petitioner failed to prove that undue experimentation would have been required to practice the claimed methods in view of the knowledge and experience in the art Petitioner admits a POSA would have had.

B. Petitioner ignored post-filing date data confirming that the claimed method can be practiced in humans by following the guidance in the specification

Post-filing date publications¹³ show that a POSA could have practiced the methods claimed in the '838 Patent at the time of filing without undue experimentation. *See In re Brana*, 51 F.3d 1560, 1566–67 n.19 (Fed. Cir. 1995) (post-filing data that pertains to the accuracy of a statement already in the specification “does not render an insufficient disclosure enabling, but instead goes to prove that the disclosure was in fact enabling when filed”); *see also Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1372–76, 1378–79 (Fed. Cir. 2017) (post-filing evidence should be considered if it is “relevant to determining if the claims were enabled as of the priority date”). Petitioner did not address any post-filing date data that assessed the methodology claimed in the '838 Patent.

For example, Petitioner failed to assess a 2021 publication titled “Fecal microbiota transplant promotes response in immunotherapy-refractory melanoma patients” (“Baruch”), authored by Dr. Erez Baruch and Dr. Jennifer Wargo, a named inventor on the '838 Patent. EX2019; EX2001, ¶¶72-73. As Dr. Garrett

¹³ Patent Owner contends that post-filing publications are not necessary to refute Petitioner’s arguments for Ground 2, but post-filing data confirms the Patent’s compliance with § 112.

explains, a POSA would have understood that Baruch discloses administering FMT from human donors with high relative abundances of, e.g., Ruminococcaceae to patients with metastatic melanoma. EX2019, Abstract, 4, FIG. S8; EX2001, ¶¶72-73. A POSA would have appreciated that Baruch reported “clinical responses in three patients,” including “a complete resolution of all lesions” (i.e., reduction of tumor size). EX2019, FIG. 1; EX2001, ¶73. A POSA would have further appreciated that Baruch followed the FMT procedure described and claimed in the ’838 Patent (EX1001, Example 5), and the paper does not mention any experimentation that would have been considered undue. EX2001, ¶73; EX2019, 1 (“FMT was then performed by means of both a colonoscopy (protocol day 0) and the administration of oral stool capsules”). Dr. Wendy confirms that the FMT by colonoscopy, as well by administering oral stool capsules would have been routine. EX2001, ¶68.

Similarly, Davar’s 2021 article titled “Fecal microbiota transplant overcomes resistance to anti-PD-1 therapy in melanoma patients” also confirmed that the claimed method can be practiced in humans without undue experimentation using the methods described in the ’838 Patent. EX2020; EX2001, ¶74. As Dr. Garrett explains, Davar “evaluated the safety and efficacy of responder-derived fecal microbiota transplantation (FMT) together with anti-PD-1 in patients with PD-1-refractory melanoma.” EX2020, Abstract; EX2001, ¶74. A

POSA would have understood that Davar’s study “provided clinical benefit in 6 of 15 patients,” such as “complete response (CR),” “partial response (PR),” and “stable disease (SD).” EX2020, 1; EX2001, ¶74. As Dr. Garrett explains, a POSA would have appreciated that Davar also followed the FMT procedure described and claimed in the ’838 Patent (EX1001, Example 5), and also did not mention any experimentation that would have been considered undue. EX2001, ¶74; EX2020, 1.

Notably, both Baruch and Davar were published in *Science*, one of the world’s top scientific journals. EX2025, Abstract; EX2001, ¶75. Dr. Garrett confirms that a POSA would have known about these studies. EX2001, But Dr. Robinson did not discuss either Baruch or Davar in his declaration. EX2001, ¶75.

In sum, Petitioner failed to meet its burden to show that a POSA would have require undue experimentation to practice the claimed invention. *In re Wands*, 858 F.2d at 736–37. Ground 2, therefore, must fail.

IX. GROUND 3: PETITIONER FAILS TO SATISFY ITS BURDEN TO DEMONSTRATE THAT ANY CHALLENGED CLAIM IS INDEFINITE

A. Petitioner wrongly applied the “plain and ordinary” meaning to the terms “isolated” and “purified” in arguing indefiniteness

Petitioner’s proffered plain and ordinary meaning of the terms “isolated” and “purified” (Petition 49-50) is in violation of the basic principle of claim

construction that allows an inventor to be its own lexicographer. *See Phillips*, 415 F.3d at 1316; *see also* Section III, above. Patent Owner acted as their own lexicographer in defining the terms “isolated” and “purified,” Petitioner conceded this much (Petition, 53-54), and therefore Patent Owner’s definition controls. *See CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002) (a “claim term will not receive its ordinary meaning if the patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in either the specification or prosecution history”). As such, the argument that the terms “isolated” and “purified” are “ambiguous to a POSA” because the plain and ordinary meanings of these terms are “inconsistent with the patent record” (Petition, 49) is wrong as a matter of law.

B. Petitioner failed to demonstrate that the claims do not sufficiently define the metes and bounds of the invention

Petitioner complains that the definitions in the specification for “isolated” and “purified” create “ambiguity” because they allegedly are “overlapping” and “circular.” Petition, 56. But Petitioner did not show that any alleged overlap or circularity would prevent the “patent’s claims, viewed in light of the specification and prosecution history, [from] inform[ing] those skilled in the art about the scope of the invention with reasonable certainty.” *See Nautilus, Inc.*, 134 S.Ct. at 2129. Indeed, Petitioner’s complaint that “the two limitations collapse onto themselves” (Petition, 56) does not support a conclusion that the claims do not “define the area

conveyed,” even if the terms “isolated” and “purified” bear an overlap in meaning. *See In re Vamco Machine and Tool, Inc.*, 752 F.2d 1564, 1577 n.5 (Fed. Cir. 1985) (patent claims “are not technical descriptions of the disclosed inventions but are legal documents like the descriptions of lands by metes and bounds in a deed which define the area conveyed but do not describe the land”); *see also Nautilus, Inc.*, 134 S.Ct. at 2129 (“The definiteness requirement, so understood, mandates clarity, while recognizing that absolute precision is unattainable”).

Petitioner’s indefiniteness allegations continue with an argument that the term “isolated” is ambiguous because the ’838 Patent uses the phrase “by the hand of man” as part of its definition for this term. Petition, 54-55. But a POSA would have no difficulty in recognizing that a composition that is made “by the hand of man” is one that is distinct from a naturally occurring composition. EX2001, ¶77. Moreover, the term a “hand of man” is a known term in patent law jurisprudence. *See, e.g., Diamond v. Chakrabarty*, 100 S.Ct. 2204, 2207 (1980) (“Congress intended statutory subject matter to ‘include anything under the sun that is made by man’”). A “patent is a legal instrument,” and is to be construed “like other legal instruments, according to its tenor.” *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 388 (1996). Petitioner fails to show that the use of the phrase “hand of man” in the context of the challenged ’838 Patent—a legal instrument—precludes an understanding of the scope of the claims.” *Id.*

Further, the fundamental principle of patent law is that “*the claims* measure the invention,” not, as Petitioner argued, isolated “claim limitations.” (Petition, 57). *See United Carbon Co.*, 317 U.S. at 232. Petitioner’s assertion that Patent Owner’s definition of “isolated or purified” leaves a POSA “without any understanding as to the metes and bounds of these two claim limitations” (Petition, 57) is based solely on Dr. Robinson’s testimony. But Dr. Robinson’s testimony is merely a *verbatim* restatement of the petition’s conclusory assertions and does not offer *any* supporting evidence. *Compare* Petition, 57 and EX1003, ¶159; EX2001, ¶77. Therefore, Dr. Robinson’s testimony is entitled to little to no weight. *See* 37 C.F.R. § 42.65(a); *Xerox Corp.*, Paper 9, at 15.

C. Petitioner failed to show that a POSA would not have understood the meaning of “bacteria belonging to the family Ruminococcaceae”

In arguing that the claims are indefinite because “‘bacteria belonging to the family Ruminococcaceae’ is a moving target,” Petitioner relies on three references, dated 2006, 2009, and 2019. Petition, 58-59. As Dr. Garrett explains, none of the references Robinson cites shows any ambiguity regarding the scope of Ruminococcaceae as of *the actual filing date of the ’838 patent*. EX2001, ¶78. By pointing to art from irrelevant years, Petitioner fails to establish that the term

“Ruminococcaceae” would have been unclear to a POSA *in September of 2017*,¹⁴.

35 U.S.C. § 112; *see also Nautilus, Inc.*, 134 S.Ct. at 2130 (“the definiteness inquiry trains on the understanding of a skilled artisan *at the time of the patent application*, not that of a court viewing matters *post hoc*”). Thus, Petitioner failed to meet its burden to show that a POSA would not have understood with reasonable certainty the metes and bounds of a claim reciting “Ruminococcaceae.”

X. THE BOARD SHOULD GIVE DR. ROBINSON’S DECLARATION LITTLE TO NO WEIGHT, BECAUSE IT IS BIASED

Petitioner’s sole declarant, Dr. Robinson, is also Petitioner’s Senior Vice President of Research. EX1003, ¶21. Rather than retain an *independent* expert and compensate them for their time, Petitioner used its own employee to serve as its expert. As discussed below, Dr. Robinson is no ordinary employee, rather he oversees Petitioner’s research programs in the very scope of the challenged patent. Petitioner cannot dispute that its employed-expert is an interested witness, and the Board should give little to no weight to his testimony. “In assessing the probative value of an expert opinion, we must consider,” *inter alia*, “the interest of the expert in the outcome of the case[.]” *EC Data Systems, Inc. v. J2 Global, Inc.*, Appeal No.

¹⁴ For the same reason, Petitioner failed to establish that the term “Ruminococcaceae” would have been unclear to a POSA in September of 2016, the earliest claimed priority date here. EX2001, ¶78.

2014-008203, 2014 WL 7171966, at *4 (P.T.A.B. Dec. 15, 2014). An expert who “was employed by [the proffering party] when he provided the expert opinion ... has a substantial interest in the outcome of the case” that must be weighed in assessing the probative value of the testimony. *Ex Parte Magna Electronics, Inc.*, Appeal No. 2013-004164, 2014 WL 2360424, at *3 (P.T.A.B. May 28, 2014); *see also EC Data Systems, Inc.*, 2014 WL 7171966 at *5 (“[The testifying expert] was employed by Patent Owner when he provided the expert opinion and, therefore, has a substantial interest in the outcome of the case.”). Indeed, the Federal Circuit has noted that “the opinion testimony of a party having a direct interest in the pending litigation is less persuasive than opinion testimony by a disinterested party.” *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 294 (Fed. Cir. 1985).

Though Dr. Robinson claims that his “compensation or employment is in no way dependent on the outcome of this post grant review,” Petitioner’s website suggests that Dr. Robinson nonetheless has an interest in the outcome of his employer’s challenge to the ’838 Patent. Petitioner’s website reveals that Dr. Robinson is “responsible for understanding how the microbes interact with and impact the host, *as well as the company’s immuno-oncology program.*” EX2026, 8. Indeed, Dr. Robinson admittedly “has responsibility for the discovery research across [Petitioner’s] company from overall strategy to developing the microbiome

analysis platform and discovery projects.” EX1003, ¶21. And, Petitioner announced that it will conduct clinical trials that involve administering Petitioner’s consortium of bacterial strains [known as MB097] in combination with anti-PD-1 antibodies [known as KEYTRUDA] to melanoma patients: Microbiotica’s website’s Media Centre announces, “Microbiotica will conduct a phase 1b clinical trial to evaluate the safety and tolerability, and initial signs of clinical activity of its live biotherapeutic product, MB097, in combination with KEYTRUDA® (pembrolizumab), [an] anti-PD-1 therapy, in melanoma patients with primary resistance to an anti-PD-1-containing immunotherapy.” EX2027, 1. Dr. Robinson’s feigned lack of interest in the outcome of the challenge to the ’838 Patent strains credulity.

Given Dr. Robinson’s bias, it is unsurprising that his testimony distorts how a POSA would have viewed the prior art. For example, Dr. Robinson ignored clearly relevant papers related to his obviousness testimony, e.g., papers that teach that “Th17 cells *promote* tumor growth” in mice having melanoma. EX2021, Abstract; EX2022, 10113; EX2003, 927; EX2001, ¶43. Similarly, Dr. Robinson offered a distorted view of Gajewski, omitting Gajewski’s teaching that “the presence or increased level of,” e.g., *Ruminococcus*, “*potentiates* cancer/tumor growth, spread (e.g., malignancy).” EX1012, 22:6-9; EX2001, ¶46. And Dr. Robinson failed to discuss either Baruch or Davar, which were published in the

premier journal *Science*, validating the methodology of the '838 Patent. EX2019; EX2020; EX2001, ¶75.

In sum, Dr. Robinson has a direct and substantial interest in the outcome of this case that must be weighed against the probative value of his testimony. The Board has previously given “little weight” to testimony offered by similarly biased witnesses in the proffering party’s employ: “[W]e give little weight to Mr. Mattsson’s testimony because Mr. Mattsson is not a disinterested witness.” *Informatica Corp. v. Protegrity Corp.*, CBM2015-00021, Paper 38, at 12, 52 (P.T.A.B. May 31, 2016). Likewise, here, the Board should give no or “little weight” to Dr. Robinson’s testimony. *Ashland Oil, Inc.*, 776 F.2d at 294.

XI. CONCLUSION

The Petition fails to show that is more likely than not that any of the challenged claims is unpatentable under 35 U.S.C. §§ 103 or 112 and, therefore, the Board should deny institution.

Respectfully submitted,

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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 18,700 words, comprising 16,436 words, excluding the parts exempted by 37 C.F.R. § 42.24(a)(1).

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Respectfully submitted,

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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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