

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MURRAY & POOLE ENTERPRISES, LTD.,
Petitioner,
v.

INSTITUT DE CARDIOLOGIE DE MONTREAL,
Patent Owner,

Case IPR2023-01064
Patent No. 11,400,063

PATENT OWNER'S PRELIMINARY RESPONSE

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I. INTRODUCTION

The Board should deny institution of the Petition because Petitioner merely seeks to reargue positions already evaluated and disposed of by the Examiner under the guise of “new references.” But Petitioner’s references are not new, and in some cases not even prior art. Petitioner’s main reference for Grounds 1 and 4—the Bouabdallaoui reference (EX1005)—is not prior art because it was published within the one-year grace period for filing an application and, as Petitioner neglects to inform the Board, is a disclosure from the inventor himself as the lead author who had responsibility for the reference and its publication. Grounds 2 and 3 rely on references that are substantively the same as material before the Examiner, and arguments that are driven by hindsight.

In addition to relying on a primary reference that is not even prior art, Petitioner ignores the very unexpected and surprising results discovered by the inventor, namely that the administration of colchicine reduced the risk of stroke, and that it could be beneficially administered to certain patients who had myocardial infarction (MI) and a percutaneous intervention within 3 days of having an MI without the use of a pre-loading dose of colchicine. Petitioner ignores these important limitations and the surprising result, but the Examiner expressly relied on the unexpected results in allowing the claims. The Board should deny institution and not disturb the thorough work performed by the

Examiner, who evaluated and considered the very same or cumulative prior art references and arguments during prosecution.

II. THE BOARD SHOULD EXERCISE ITS DISCRETION UNDER 35 U.S.C. §325(d) TO DENY INSTITUTION OF THE PETITION

The Board should exercise its discretion and deny institution of the petition because the same or substantially the same references relied on by Petitioner were before the examiner, including the Bouabdallaoui reference which is not even prior art. *See* 35 U.S.C. §325(d). Petitioner's contentions that the Examiner erred in evaluating the closest prior art or the teachings of the prior art are demonstrably wrong. It speaks volumes that Petitioner relies on references it should know are not prior art and that are cumulative of cited patents in its own patent family.

The Board's decision in *Advanced Bionics* streamlined the analysis first proposed in *Becton* for determining whether the Board should exercise its discretion in denying institution under §325(d). *See, e.g., Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 (PTAB Feb. 13, 2020); *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 (PTAB Dec. 15, 2017). Generally, the Board evaluates whether the same or substantively the same art or argument was previously before the Examiner and, if so, whether the petitioner has demonstrated material error by the Examiner. *Advanced Bionics*, Paper 6 at 10. Here, the same or substantially the same references and arguments were presented to the Examiner, and the Examiner

made no error in review.

A. Grounds 1 and 4¹: Bouabdallaoui is not prior art and was before the Examiner; COLCRYs is cumulative of disclosed references.

Petitioner does not dispute that Bouabdallaoui was provided to the Examiner, but argues that the Examiner erred in not considering it the closest prior art or consider its alleged teachings that were missing from the prior art. Of course, the Examiner did not further evaluate Bouabdallaoui because it is not prior art. Petitioner neglects to mention that the main and corresponding author of Bouabdallaoui is Dr. Tardif, the named inventor of the '063 patent. The '063 patent is entitled to a priority date of November 15, 2019. But even if the Board accepted Petitioner's priority date, Bouabdallaoui was published on August 29, 2020, which is less than 3 months before the filing of the '285 application that issued as the '063 patent. (*Compare* EX1001 at 1 at (22) *with* EX1005 at 1.) It is disingenuous for Petitioner to ignore Dr. Tardif's involvement in Bouabdallaoui and claim the article is anticipatory prior art that was ignored by the Examiner.

¹ Petitioner mentions COLCRYs in the heading for its section on Grounds 1 and 2, but Petitioner did not raise COLCRYs as an anticipatory reference for Ground 1 or 2. We therefore address Grounds 1 and 4 together as Ground 4 relates to the combination of Bouabdallaoui and COLCRYs.

Therefore, Bouabdallaoui is not prior art as it is a publication of the invention or substantively the same subject matter by the inventor or by another who obtained the subject matter disclosed directly or indirectly from the inventor within one year of the application date. 35 U.S.C. §§102(b)(1)(A) and (B).

1. Bouabdallaoui is not prior art, and therefore cannot be the closest prior art.

Petitioner's Grounds 1 and 4 fail as the Bouabdallaoui reference is not prior art under 35 U.S.C. §102(b)(1)². Petitioner fails to mention that Dr. Jean-Claude Tardif, who is the named inventor on the '063 patent, provided the pertinent information and in fact is the corresponding author of Bouabdallaoui. Dr. Tardif's publication of Bouabdallaoui and the subject matter described therein falls within the one-year grace period permitted to inventors to file a patent application, and therefore Bouabdallaoui is not prior art.

Even without the grace period, Petitioner is wrong that the '063 patent is not entitled to priority to provisional application number 62/935,865 ("the '865 application") filed on November 15, 2019 for all of the claims. While additional

² Because the applications relating to the '063 patent were filed after March 16, 2013, the version of 35 U.S.C. §102 that was enacted as part of the America Invents Act ("AIA") applies.

details regarding the COLCOT trial were provided in the '285 application that issued as the '063 patent, the '865 application disclosed that very same COLCOT trial as well as the subject matter claimed in the '063 patent.

But even assuming the '063 patent is not accorded its earliest priority date, Bouabdallaoui still is not prior art. AIA §102(b) provides a prior art exception for any publication disclosing the invention or the subject matter of the invention that an inventor makes or is made from information obtained directly or indirectly from the inventor:

(b) Exceptions.

(1) Disclosures made 1 year or less before the effective filing date of the claimed invention. A disclosure made 1 year or less before the effective filing date of a claimed invention shall not be prior art to the claimed invention under subsection (a)(1) if—

(A) the disclosure was made by the inventor or joint inventor or by another who obtained the subject matter disclosed directly or indirectly from the inventor or a joint inventor; or

(B) the subject matter disclosed had, before such disclosure, been publicly disclosed by the inventor or a joint inventor or another who obtained the subject matter disclosed directly or indirectly from the inventor or a joint inventor.

Both exceptions apply here with respect to Bouabdallaoui.

Previous clinical studies that involved the use of colchicine with patients that had experienced myocardial infarction were too small and suffered from several other defects. (EX1001 at 1:52-59; EX2011 at ¶15.) Dr. Tardif conceived of the COLCOT study to investigate his idea regarding early intervention with colchicine for specific patients that had experienced myocardial infarction. (EX2011 at ¶¶16-

17.) Dr. Tardif drafted the COLCOT study protocol, obtained the funding for the study, and was the study's primary principal investigator. (*Id.* at ¶¶16-18.) He could not, however, conduct the clinical study by himself; no clinician does. So Dr. Tardif himself recruited other clinicians to participate in his study and to provide to him data relating to the primary and secondary evaluated outcomes. (*Id.* at ¶19.) He obtained confidentiality agreements with these clinicians and their respective clinics. As the primary principal investigator, Dr. Tardif was ultimately responsible for the conduct of the study as well as the collection and reporting on the results of the study. (*Id.* at ¶¶19-20.) In fact, Dr. Tardif and MHI expressly retained all IP rights in the study and its results, and controlled publication of any such data. (*Id.*) Based on that data that Dr. Tardif accumulated, he was able to file the '063 patent.

Even using Petitioner's August 29, 2020 publication date for Bouabdallaoui, there is no question Bouabdallaoui was published within one year of the filing of the November 13, 2020 filing date for the '285 application that issued as the '063 patent. There is no question Dr. Tardif was the lead investigator on the COLCOT study, that is independently corroborated by Petitioner's own Exhibit 1006 at page 6. There is no dispute that Bouabdallaoui relates to the COLCOT clinical study that Dr. Tardif organized and was the lead investigator. (EX2011 at ¶25.) There is no question that Dr. Tardif is the corresponding author of Bouabdallaoui (EX 1005

at 1), which means that he is the primary author and speaks on behalf of all Bouabdallaoui named authors regarding the article. (EX2011 at ¶¶27-28; *see also* EX2001 at ¶31.) In fact, Dr. Bouabdallaoui is an employee of MHI with Dr. Tardif. (*See* EX1005.) Therefore, no credible argument can be made that Bouabdallaoui is prior art because it is a disclosure by Dr. Tardif himself within the one-year prior art exception under 35 U.S.C. §102(b)(1)(A), (B). Petitioner's failure to disclose Dr. Tardif's involvement in Bouabdallaoui and the fact that he is listed as the corresponding author of the article is at best disingenuous.

To the extent Petitioner's position is that additional authors on Bouabdallaoui somehow removes the article from the exception provided under §102(b)(1), the Petition provides no support for such a proposition and the statute in fact says the contrary. The exception under §102(b)(1) also applies if the disclosure of the invention or subject matter of the invention is "by another who obtained the subject matter disclosed directly or indirectly from the inventor...." 35 U.S.C. §102(b)(1)(A), (B). Disclosure is by the inventor Dr. Tardif himself, and there is no question that the co-authors of Bouabdallaoui obtained the subject matter of the disclosure directly or indirectly from inventor Dr. Tardif. The clinical investigators provided the data and information to Dr. Tardif and his team, who analyzed the results and published his findings in the Bouabdallaoui article. (EX2011 at ¶¶19-20, 27-28.) Dr. Tardif chose to list Dr. Bouabdallaoui as the first

author of the publication to provide a colleague that he had mentored with a professional accolade for her CV. (*Id.* at ¶29.) The other co-authors were included in the article because of their clinical testing contributions to the study, not because they conceived of the invention. (*Id.*) The other authors worked under the direction of Dr. Tardiff following his clinical study protocol and provided data to Dr. Tardif to evaluate his hypothesis and were given information from him that constitutes the subject matter of the Bouabdallaoui article. This is clearly within the exception provided in 35 U.S.C. §§102(b)(1)(A), (B). Stripping an inventor of a patent for recruiting others to collect data to clinically support a discovery and then acknowledging their contributions by including them as co-authors on a scientific publication ignores the realities of how clinical investigation and discovery works, and would stifle innovation.

For the above reasons, Bouabdallaoui is not prior art and therefore the Board should deny institution of Grounds 1 and 4.

2. Bouabdallaoui and COLCRYS were before the Examiner.

The Board can also exercise its discretion and deny Grounds 1 and 4 because Bouabdallaoui and COLCRYS are not new references. It is undisputed that Bouabdallaoui was in fact before the Examiner. (EX1002 at 76, 175-182.) In addition, COLCRYS is cumulative of information provided to the Examiner and not relevant to the claims at issue. COLCRYS is a commercial colchicine tablet

product that is indicated for the treatment of gout, and which is a completely different indication than the subject matter of the instant claims. Petitioner relies on COLCRYS for its disclosure of colchicine tablets, but several other references that were before the Examiner disclosed administration of colchicine tablets. (*See, e.g.*, EX1002 at 317, EX1028 at 2.) Therefore, COLCRYS is cumulative of information already before the Examiner. *See Gardner Denver v. Utex Indus., Inc.*, IPR2020-00333, Paper 12 at 13-14 (PTAB Aug. 5, 2020) (denying institution finding newly asserted references are no more relevant than examined references); *Sandoz, Inc. v. Acerta Pharma B.V.*, IPR2023-00478, Paper 17 at 15-16 (PTAB Aug. 7, 2023) (denying institution finding reference cumulative where cited reference related to “twice daily” limitation in disclosing administration “2 to 4 times per day”).

The Examiner also did not make any material error in evaluating the prior art, or even determining the closest prior art. The Examiner properly determined Bouabdallaoui is not prior art. Moreover, the Examiner’s rejections in view of the actual prior art shows that the Examiner recognized what was disclosed in the prior art, and recognized that the Applicant properly presented claims and arguments that distinguished the prior art. Specifically, Applicant included claim limitations that the patient had completed a percutaneous intervention or that the administration of colchicine was made within 3 days of myocardial infarction. (*See, e.g.*, EX1002 at 383-388.) Applicant further demonstrated objective indicia of

nonobviousness, including unexpected results. (*Id.* at 398-99.) The record demonstrates that the Examiner evaluated the same argument Petitioner makes now, along with evidence provided by the inventor, and agreed that the superior, surprising and unexpected results justified issuing the claims over the prior art. *See Sandoz*, IPR2023-00478, Paper 17 at 19-20.

Because Bouabdallaoui is not prior art and was before the Examiner already, and Colcrys is cumulative of information already before the Examiner, the Board should exercise its discretion and deny institution of Grounds 1 and 4.

B. Ground 2: COLCOT Protocol was before the Examiner

Petitioner's Ground 2 is limited to anticipation of claims 27, 29-36, and 39 based on the COLCOT Protocol. Petitioner tries to create an issue regarding the COLCOT Protocol, but the Protocol was also clearly before the Examiner and therefore does not warrant the Board's re-review.

The Exhibit that Petitioner relies upon is merely an earlier version of the Protocol that was provided to the Examiner,³ and the earlier and later versions are substantively the same. (*Compare* EX1006 with EX1002 at 315-323.) In fact, key portions are identical including a description of the sponsor of the study and

³ While Petition states that the EX1006 Protocol is from 2015, it is actually from at least March 8, 2017.

location (Montreal Heart Institute), the stated purpose of the study including the condition being investigated and the treatment regimen, the study design, the primary and secondary outcomes, the detailed description of the study, and the inclusion criteria. (*Id.*) The exclusion criteria in the two documents are insubstantially different. (*Compare* EX1006 with EX1002 at 320-321.) The only difference Petitioner points to is the identification of Montreal Heart Institute as a hospital in its COLCOT Exhibit Protocol, but that is irrelevant to patentability and adds nothing because the Montreal Heart Institute was already identified as the Sponsor and location for the study in the Protocol that the inventor provided to the Examiner. In any event, the disclosure in the newly asserted art and the art evaluated by the Examiner do not need to “be identical or entirely cumulative, only [] substantially same” to satisfy the standard under *Advanced Bionics*. See *Dropworks, Inc. v. The University of Chicago*, IPR2021-00100, Paper 9 at 13-14 (PTAB May 14, 2021). Here, the COLCOT Protocol is substantially similar to the COLCOT Protocol the Examiner reviewed, and Petitioner has not met its burden to show otherwise. Petitioner therefore cannot meet the first factor under *Advanced Bionics*, which justifies the Board exercising discretionary denial of this ground for the petition.

Even if the Board looked to the second factor under *Advanced Bionics*, it would see the Examiner did not err in evaluating the COLCOT Protocol as neither

version of the protocol discloses key limitations of the claims that eventually issued, including the claim limitation that early intervention with colchicine reduces the risk of stroke. *See Albany Int’l Corp. v. Kimberly-Clark Worldwide, Inc.*, PGR2021-00019, Paper 22 at 15-17 (PTAB June 22, 2021) (exercising discretion to deny institution where portion of reference no more pertinent to claims than portion indicated by examiner). Petitioner focuses on the assertion that the Protocol has the same dosing regimen as the claims, but the challenged claims in Ground 2 are method claims with specific uses and features that go beyond just a dosing regimen. Dr. Tardif discovered the surprising reduction in risk of stroke under the claimed method.

Petitioner’s argument improperly relies on hindsight; Dr. Tardif had to complete his study in order to satisfy the written description and enablement requirements to learn and demonstrate what was before then unknown and unknowable. Petitioner tries to disguise its blatant hindsight analysis by arguing that the reduction in the risk of stroke, which is a requirement of claim 27 and its dependent claims, is either not a limitation of the claims or, in the alternative, that it is an inherent result from the Protocol. As discussed below in section III.A., the preamble here is limiting as the claimed “reducing the risk of stroke” was relied on for patentability and indeed was key in differentiating the claims from the prior art. Petitioner’s inherency argument would mean that patent applicants could never

claim medical treatments, even after conducting substantial clinical trials to discover new and useful methods, because every medical treatment would be argued as an inherent property. Petitioner simply has not proven that the risk of stroke would be necessarily reduced in every single patient and do not have data to show inherency. Therefore, inherency is not proper here.

Further, the Examiner did not err in determining that Hennessey, and not the COLCOT Protocol, was the closest prior art. The COLCOT Protocol was nothing more than an untested hypothesis and the surprising reduction in the risk of stroke was not even identified in the Protocol as a possible outcome. Instead, Hennessey was the closest prior art reference because it addressed the disease condition. In any event, the Examiner addressed substantively the same arguments regarding the prior art raised by Petition here. For example, Petitioner claims that Bouabdallaoui and COLCOT Protocol might be closer prior art because they make no mention of a pre-loading dose and the claims do not have a pre-loading dose. But that does not make it closer prior art. Hennessey also makes no mention of using a pre-loading dose of colchicine. *See Dropworks*, Paper 9 at 13-14 (holding “Petitioner has not sufficiently distinguished the new secondary references from those previously presented to the Office.”) Petitioner’s position that two different references should be “closest prior art,” demonstrates that there is some level of subjectivity in the decision. At the end of the day, however, Petitioner’s arguments are irrelevant as

Bouabdallaoui is not prior art and both it and COLCOT Protocol were before the Examiner.

Because the COLCOT Protocol was before the Examiner and because the Examiner did not err in finding Hennessey as the closest prior art in view of the deficiencies of the COLCOT Protocol, the Board should exercise its discretion and deny institution of Ground 2.

C. Ground 3: The references are the same or cumulative to what was before the Examiner, and provide no new supporting evidence.

Petitioner is disingenuous in arguing the cited references were not before the Examiner and that there is “new supporting evidence” that saves the challenge from discretionary denial. All of the references in the Petition were before the Examiner or are cumulative of information already before the Examiner. As shown above, the COLCOT Protocol was already before the Examiner and COLCRY⁴ is

⁴ The term “colcrys” was also used as part of the international search report that was attached to the WO2014/066944 (Nidorf) reference that was provided to the Examiner, and therefore was before the Examiner. (EX1002 at 82, 126.) *See Sandoz*, IPR2023-00478, Paper 17 at 13-14 (finding Examiner was aware of reference because it was cited in an international search report provided to Examiner).

cumulative of information already before the Examiner. The ESC Guidelines were not themselves cited, but Petitioner ignores the fact that they are too general and do not relate at all to treating the specific patients identified in the claims with colchicine. Additionally, while the specific Nidorf patent cited by Petitioner was not before the Examiner, a related Nidorf patent (EX1018) was before the Examiner with substantially the same disclosure. In fact, Petitioner calls Nidorf '281 “another Nidorf patent” (Petition at 68, n.9) even though both patents claim priority from the same foreign applications and both are subject to a terminal disclaimer in view of the same U.S. patent (*compare* EX1007 at 1 at (*), (63), (30) *with* EX1018 at 1 at (*), (86), (30)). They are therefore cumulative.

Petitioner's reliance on prior art references that are cumulative or do not disclose key claimed elements does not constitute “new supporting evidence.” “If 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; *see also Sandoz*, IPR2023-00478, Paper 17 at 19-20. Here, Petitioner relies on references that don't address key claimed limitations, are not prior art, or are irrelevant. Simply because Nidorf or COLCOT Protocol are silent regarding a pre-loading dose of colchicine does not mean a POSA would understand and conclude a pre-loading dose is unnecessary or beneficial to omit. The Guideline teachings are too general and would not be

applicable to treatment with colchicine, which is not mentioned in the Guidelines at all. And Colcrys is cumulative at best and also irrelevant as it relates to another condition (gout) and not the claimed condition. Petitioner further relies on Dr. Ridker's declaration, but that declaration relates to other references not disclosed in the asserted combination for Ground 3 and therefore cannot be relied on to show any claim is reasonably likely invalid. Moreover, as seen below, Dr. Ridker's analysis is based on hindsight and ignores both the lack of motivation for the limitations of the claims as well as the surprising results that Dr. Tardif achieved.

Therefore, for these reasons, the Board should exercise its discretion and deny institution as to Ground 3.

* * *

For all the above reasons, the Board should exercise its discretion and deny the Petition.

III. PETITIONER'S CONSTRUCTIONS ARE INCORRECT AND IGNORE THE INTRINSIC EVIDENCE.

Petitioner's claim construction arguments ignore the fact that the preambles in the patent claims are limiting as they provide the basis for the claims and their issuance, and provide the antecedent basis for limitations in the claims. Petitioner plainly is construing the claims to bolster its invalidity position and not with any basis in any law on claim construction.

A. The preamble phrase “reducing the risk of stroke in a patent after having an MI” is limiting: it provides the purpose of the claim and was relied on for allowance.

Regardless of the construction standard applied, Petitioner is wrong that “reducing the risk of stroke” is not a limitation of claim 27 and its dependent claims. The determination of whether the preamble is a claim limitation is “resolved only on review of the entirety of the patent to gain an understanding of what the inventors actually invented and intended to encompass by the claim.” *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257 (Fed. Cir. 1989); *Catalina Mktg. Int’l v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002). “A claim’s preamble may be limiting ‘if it recites essential structure or steps, or if it is ‘necessary to give life, meaning, and vitality’ to the claim.’” *Sanofi Mature IP v. Mylan Labs., Ltd.*, 757 Fed. Appx. 988, 992 (Fed. Cir. 2019) (*citing Catalina Mktg.*, 289 F.3d at 808 (*quoting Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305 (Fed. Cir. 1999))). “A preamble may provide context for claim construction, particularly, where as here, that preamble’s statement of intended use forms the basis for distinguishing the prior art in the patent’s prosecution history.” *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1362 (Fed. Cir. 2004) (*citing Catalina Mktg.*, 289 F.3d at 809). “Clear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art may indicate that the preamble is a claim limitation because the

preamble is used to define the claimed invention.” *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1347 (Fed. Cir. 2002).

First, it is clear the term “reducing the risk of stroke” is an indication of what Dr. Tardif invented and is necessary to give “life, meaning, and vitality” to the claim. In *Sanofi*, the Federal Circuit reversed the Board’s construction finding the preamble for a “method of increasing survival” not limiting. *Sanofi*, 757 Fed. Appx. at 989-990, 993. The court relied on a previous decision which found that the preamble term “[a] method of treating or preventing macrocyticmegaloblastic anemia” limited the claim because it articulated the “purpose for which the method must be performed.” *Id.* at 993 (*quoting Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003)). Both decisions are similar to the preamble language of claim 27 here. The term “reducing the risk of stroke” is the very purpose of the claimed method. The ’063 patent claims other methods, but claim 27 is different because it is a method of reducing risk of stroke in a patient after having MI, and the preamble is “‘necessary to give life, meaning, and vitality’ to the claim.” *Sanofi*, 757 Fed. Appx. at 992. Because the purpose of performing the claim method is reducing the risk of stroke in patients that had MI, the preamble term is limiting.

Relatedly, when the entire preamble is properly considered it is clear it provides the antecedent basis for a later portion of the claim. Specifically, the

claim term “to the patient within about 30 days of an MI” relies on the preamble “reducing the risk of a stroke *in a patient after having an MI*” for antecedent basis. Here, the *Rapoport* case cited by *Sanofi* is instructive. In *Rapoport*, the court found that the preamble “[a] method for treatment of sleep apnea” is limiting because it serves as the antecedent basis for the term “to a patient in need of such treatment” later in the claim. *Rapoport v. Dement*, 254 F.3d 1053, 1059 (Fed. Cir. 2001). The court “concluded that the most natural interpretation of ‘[a] method for treatment of sleep apneas’ in this context was that the method—administering a certain compound—must be practiced to achieve the purpose stated in the preamble.” *Sanofi*, 757 Fed. Appx. at 992 (*discussing Rapoport*, 254 F.3d at 1058-61). Similarly here, the administering of low dose colchicine to a patient within about 30 days of MI must be practiced in order to achieve the purpose stated in the preamble of reducing the risk of stroke in those patients that have suffered an MI. Petitioner ignores the full preamble, but that is improper for a claim construction analysis. Therefore, because the preamble states the purpose of the invention of claim 27 and provides the antecedent basis for the administration step in the claim, the preamble is limiting.

Second, the applicant and the examiner relied on the preamble limitation of “reducing the risk of stroke in a patient after having MI” to differentiate the claim from the prior art, a critical fact that Petitioner ignores. Specifically, in the Notice

of Allowability, the Examiner stated that claim 29 (which was later re-numbered to be claim 27) should be allowed because the prior art “does not teach, show, suggest or make obvious the instant method of reducing the risk of a stroke in a patient having had a myocardial infarction by the administration of daily low dose colchicine within about 30 days of the myocardial infarction.” (EX1002 at 399.) It is clear the Examiner recognized that the claimed reduced risk of stroke in post-MI patients differentiated claim 27 from the prior art. In fact, Petitioner admits as much as it contends that the other limitations of the claim—e.g., administering low dose colchicine to a patient within 30 days of an MI—were already taught by the prior art.

B. The phrase “wherein the patient is at a lower risk of a cardiovascular event” in claims 8-11 and 20-23 is limiting because it was material to patentability.

Petitioner is incorrect that the term “wherein the patient is at a lower risk of a cardiovascular event” is a non-limiting intended result entitled to no patentable weight. Where, as here, a wherein clause “states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention.” *Allergan Sales, LLC v. Sandoz, Inc.*, 935 F.3d 1370, 1376 (Fed. Cir. 2019) (quoting *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329 (Fed. Cir. 2005)).

In *Allergan*, the court found the “wherein” clause limiting because both the applicant and the Examiner relied on the “wherein” clause as limitations to

differentiate the invention from the prior art. *Allergan*, 935 F.3d at 1375-76; *see also Horizon Pharma, Inc. v. Dr. Reddy's Labs., Inc.*, No. 15-3324 (SRC), 2018 U.S. Dist. LEXIS 196702 at *8-*9 (D.N.J. Nov. 19, 2018) (applying preamble claim construction law to find wherein clauses limiting where applicant clearly treated them as such during prosecution). The same is true here. Dr. Tardif argued that his study showed a reduction in risk of specific cardiovascular risks with early administration of colchicine, which is different from and not disclosed in the prior art. (EX1002 at 331-332.) However, the Examiner did not allow the claims over the prior art until the applicant submitted original dependent claim 9 in independent form and included two interrelated “wherein” clauses, which indicates that the wherein clause should be considered limiting because it was used for patentability. (*Id.* at 382-88, 397.) The first is the “wherein” clause addressed by Petitioner: “wherein the patient is at a lower risk of a cardiovascular event relative to a patient not being administered colchicine.” The second “wherein” clause specifies the cardiovascular events for which risk was reduced. In allowing the claims, the Examiner specifically stated that the prior art “does not teach[,] show[,] suggest[,] or make obvious the cardiovascular events: resuscitated cardiac arrest, stroke, or urgent hospitalization for angina requiring coronary revascularization.” (*Id.* at 398-99.) Thus, both “wherein” clauses were necessary to overcome the prior art.

Moreover, the “wherein” clause addressed by Petitioner also provides the antecedent basis for the “the cardiovascular event” portion of the second wherein clause, and therefore is a limitation for that additional reason. *See Rapoport*, 254 F.3d at 1059. Without the first “wherein” clause, there would be no “cardiovascular event” otherwise described in the claim and the reference to cardiovascular events in the second “wherein” clause would make no sense. Thus, for this additional reason, the “wherein” clause should be construed as limiting.

IV. PETITIONER FAILED TO DEMONSTRATE ANTICIPATION FOR GROUNDS 1 AND 2

Petitioner’s Ground 1 for anticipation based on Bouabdallaoui must fail because Bouabdallaoui is not prior art under 35 U.S.C. §§102(b)(1)(A) and (B) as discussed in section II.A. Since Dr. Tardif is the primary author and therefore the disclosure is by him or another based on information provided by him and is within one year of at least the US application, Bouabdallaoui cannot anticipate any claims of the ’063 patent. Therefore, the Board should not institute the Petition based on Ground 1.

Petitioner’s Ground 2 for anticipation based on the COLCOT Protocol also must fail. Not only was the COLCOT Protocol before the Examiner (*see* Section II.B.), but the Protocol does not disclose several of the key limitations required by challenged claims 27, 29-36, and 39. For example, the COLCOT Protocol does not disclose the reduction of risk of stroke, which as seen above (Section III.A.) is a

limitation of claim 27 and the claims that depend therefrom. For at least this reason, the Board should not institute on Ground 2 of the Petition.

V. PETITIONER’S OBVIOUSNESS ARGUMENTS ARE CONCLUSORY AND HINDSIGHT DRIVEN

Grounds 3 and 4 of the Petition fail not only because of their use of references that are not prior art under 35 U.S.C. § 102, but also because Petitioner’s arguments rely on improper conclusory and hindsight-driven analysis. Petitioner fails to show either (1) that a POSA would have been motivated to combine the cited prior art references and (2) that a POSA would have had a reasonable expectation of success in achieving the claims of the ’063 patent.

Petitioner bears the burden to establish a reasonable likelihood that the claims of the ’063 patent are obvious. 35 U.S.C. § 314(a); *Harmonic, Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (holding that an IPR petitioner has the burden to show “with particularity why the patent it challenges is unpatentable”). The Supreme Court made clear that obviousness “cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR Int’l Co. v. Teleflex, Inc.*, 550 U.S. 398, 418 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)); see also *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016) (“To satisfy its burden of proving obviousness, a petitioner cannot employ mere conclusory statements.”); *SFC Co. v.*

LG Chem. Ltd., IPR2020-00178, Paper 16, at 38-39 (PTAB May 29, 2020)

(denying institution where Petitioner relied on conclusory statements and failed to supply sufficient reason to combine references). As shown below, Petitioner's obviousness arguments are deficient from both a legal and a substantive perspective. And the deficiencies that lead to Petitioner falling short in making a *prima facie* obviousness showing are further magnified in its insufficient arguments on objective indicia of nonobviousness.

A. Petitioner's obviousness arguments are legally deficient and the Board should deny institution.

Petitioner's expert declaration simply repeats the same conclusory arguments in the Petition without explanation of the factual foundations for those conclusions. The Board has consistently recognized that expert testimony merely repeating the same arguments as the Petition is given little or no weight because it "adds little to the analysis." *Alliance Indus. Corp. v. Gebo Cermex USA, Inc.*, IPR2019-01647, Paper 9, at 27 (PTAB Mar. 24, 2020); *see also InfoBionic, Inc. v. Braemar Mfg., LLC*, IPR2015-01704, Paper 11, at 14-15 (PTAB Feb. 16, 2016) (denying institution and rejecting expert testimony because it merely repeated the petition's conclusory arguments). Because Dr. Ridker's declaration simply repeats the conclusory statements in the Petition, he fails to address any reason a POSA would combine the asserted prior art references, fails to address limitations that were vital to overcoming the prior art, and lacks any support for his alleged POSA

expectations. *See* EX1049. Conclusory expert opinion does not satisfy Petitioner’s burden. *TQ Delta, LLC v. CISCO Sys., Inc.*, 942 F.3d 1352, 1359 (Fed. Cir. 2019) (restating that “conclusory expert testimony is inadequate to support an obviousness determination”).

The Petition also fails to address whether a POSA would combine the asserted prior art to arrive at the claimed invention. A “patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *KSR*, 550 U.S. at 420. At most, that is all Petitioner has attempted to show. The Petition fails to show that the invention “as a whole” would have been obvious. *See Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1086 (Fed. Cir. 2008) (“The determination of obviousness is made with respect to the subject matter as a whole, not separate pieces of the claim.”); *accord Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1383 (Fed. Cir. 1986) (“Focusing on the obviousness of substitutions and differences instead of the invention as a whole... [is] a legally improper way to simplify the difficult determination of obviousness.”). Petitioner’s failure to consider the claimed combination as a whole renders its Petition legally deficient.

B. Ground 3: The Petition contains several substantive deficiencies and therefore an obvious finding is not reasonably likely.

The Petition also has several substantive deficiencies as it fails to meaningfully address several key claim limitations, including: (a) the removal of a

pre-loading dose; (b) applying the claimed method to patients who have already been provided a percutaneous intervention; (c) administration of colchicine within the first 3 days after an MI; and (d) the method resulting in a reduction of the risk of stroke. Because the Petition does not show these limitations would have been obvious in the context of the challenged claims, it is not reasonably likely that even one claim would have been obvious and the Board should deny institution.

1. The prior art does not provide a reasonable expectation of successfully using colchicine without a higher pre-loading dose, and there was no motivation to delete the loading dose.

With respect to claims 1-26 and 40-50, Petitioner fails to provide any non-conclusory basis for its assertion that the prior art disclosed low dose colchicine treatment without a higher pre-loading dose. Petitioner also failed to argue that a POSA would have been motivated to omit the pre-loading dose and have had a reasonable expectation of success in achieving the claimed invention without a pre-loading dose of colchicine.

Petitioner and its expert, Dr. Ridker, erroneously asserts that the prior art taught low-dose colchicine without a pre-loading dose. Specifically, Petitioner relies on Nidorf and the COLCOT Protocol to support its position. Petition at 37. But, neither reference teaches treating a patient with colchicine at a low dose without a pre-loading dose. Rather, each reference is silent regarding a pre-loading dose, which is not the same as an affirmative teaching to omit an established pre-

loading dose. However, the limitation “without pre-loading the patient with a higher dose of colchicine” was critical for overcoming the prior art. (EX1002 at 331, 383-87, 396, 398.)

When the prior art does not disclose a limitation, or there is no apparent reason to modify that prior art in a manner that meets the claims, the claimed invention is likely non-obvious. *See, e.g., Univ. Strathclyde v. Clear-Vu Lighting LLC*, 17 F.4th 155, 160-62 (Fed. Cir. 2021) (reversing Board’s IP decision because limitation “without using a photosensitizing agent” was not in the prior art and Petitioner did not provide a reason to modify the prior art in such a way).

Similarly, here, Nidorf and COLCOT Protocol disclose methods of treating patients with lower colchicine doses, however, neither discusses, nor provides any suggestion that a POSA could remove the standardized pre-loading dose and still effectively treat patients. *See Palo Alto Networks, Inc. v. Finjan, Inc.*, 777 Fed.Appx. 501, 506 (Fed. Cir. 2019) (upholding the Board’s finding that a teaching that might serve the claimed function is not establishing that a POSA would understand that as a teaching or suggestion). Consistent with the findings of the Board and Federal Circuit in *Palo Alto*, here there is no evidence that Nidorf and the COLCOT Protocol’s silence on a pre-loading dose would teach or suggest to a POSA that a patient could be treated without it, even if those studies might have served the function of removing a pre-loading dose, which neither even states.

Importantly, the COLCOT Protocol was before the Examiner, and the Examiner found, *inter alia*, that the “without pre-loading” limitation overcame the prior art. (EX1002 at 398.) Although the Nidorf reference cited by Petitioner was not before the examiner, another Nidorf patent with the same parent application (and thus shared specification) was before the Examiner. (*See* section III.C.) Similarly, that reference was overcome by specifically excluding pre-loading colchicine in the claimed invention. Thus, the same or substantively the same information and arguments were before the Examiner (*see id.*), and the applicant was able to overcome those challenges to the claims.

Therefore, Petitioner does not sufficiently address this critical limitation, and there is no evidence presented that removing the pre-loading dose would motivate a POSA to combine teachings in the prior art to arrive at the claimed invention.

Contrary to Petitioner’s conclusory arguments, colchicine’s efficacy without a higher pre-loading dose was unexpected. Petitioner alleges that Nidorf and COLCOT taught administering 0.5 mg/day colchicine without a pre-loading dose. Petition at 37. However, that is not correct. Neither Nidorf nor COLCOT teach administering 0.5 mg/day colchicine without a pre-loading dose. In fact, a POSA would have understood from other “lower dose” colchicine studies published at the time that a pre-loading dose was necessary to reduce side effects. (EX2001 at ¶38.)

In addition, the patients in Nidorf were not administered low dose colchicine

until they were stable; a POSA would not have understood that they could omit the pre-loading dose for non-stable patients because for such patients the inflammation was likely severe. (*Id.* at ¶39.) At best, these references are *silent* regarding a pre-loading dose, which does not mean that they teach omitting the standard pre-loading dose established in the prior art. (*Id.* at ¶40.)

Tellingly, Dr. Ridker’s declaration fails to even mention this issue, seemingly because the required negative limitation is not in fact present in the prior art. (*See* EX1049 at Sec. VIII.A.1.-2.) The expert’s repetition of conclusory statements does not help Petitioner meet its burden under *KSR*. *See, e.g., TQ Delta*, 942 F.3d at 1359 (“This court’s opinions have repeatedly recognized that conclusory expert testimony is inadequate to support an obviousness determination on substantial evidence review.”) (collecting cases).

Petitioner and its expert also neglect to present any argument as to why a POSA would have had a reasonable expectation of success in achieving the results of the claimed invention without the use of a pre-loading dose. (EX2001 at ¶41.) This exclusion is another fatal flaw to Petitioner’s argument. The expectation of success is not implied by showing the presence of individual limitations, or even a showing of a motivation to combine references. *Eli Lilly and Co. v. Teva Pharma. Int’l GmbH*, 8 F.4th 1331, 1344 (Fed. Cir. 2021). Just as the Board and the Federal Circuit found in *Eli Lilly*, Petitioner cannot carry its burden without such a

showing. *Eli Lilly*, 8 F.4th at 1344. Moreover, both Hennessy and the COLCOT Protocol were before the Examiner—and did not expressly disclose the use of a pre-loading dose—and the Examiner still issued the claims over those references. (EX2001 at ¶42.)

In addition, the Petitioner did not even show a motivation to combine certain teachings of the prior art to remove the pre-loading dose, because no such teaching existed. (EX2001 at ¶41.) Even if Petitioner could have shown that Nidorf and the COLCOT Protocol’s silence meant affirmatively disclosing removing the pre-loading dose, there was no motivation to combine with the other teaching to arrive at the claimed invention. *Purdue Pharma L.P. v. Depomed, Inc.*, 643 Fed.Appx. 960, 965 (Fed. Cir. 2016) (citing *KSR*, 550 U.S. at 418 (affirming Board’s finding that mere existence of claim elements is not sufficient to show obviousness, there must also be prior art that would have prompted a POSA to arrive at the claimed invention)). Petitioner has not introduced any such evidence, and cannot because it is not in the prior art.

The Board should deny institution and uphold the Examiner’s conclusion that “[o]ne of ordinary skill would not have found it obvious to treat the myocardial infarction patients of *Circulation* (2015), 132(15), pp. 1395-1403, who have also been treated with primary percutaneous coronary intervention, following the method of *American Heart Journal* (September 2019), Vol. 215, pp. 62-69 –

that is, without a pre-loading dose of colchicine. There is no motivation to omit the loading dose of *Circulation* (2015), 132(15), pp. 1396-1403 and treat these patients by the method of *American Heart Journal* (September 2019), Vol. 215, pp. 62-69.” (EX1002 at 398.) Petitioner fails to provide any new evidence that requires revisiting the Examiner’s evaluation.

2. The prior art does not provide a motivation to administer low-dose colchicine to patients who have also already been provided a percutaneous intervention.

With respect to claims 1-7, 9, 12-19, 21, and 24-26, Petitioner does not identify any arguments showing a motivation to administer low-dose colchicine to patients who have been treated with a percutaneous intervention. Rather, Petitioner and its expert again rely on improper, conclusory, hindsight-based arguments that are unsupported by the evidence.

Petitioner erroneously alleges that the prior art taught low-dose colchicine treatment for patients already provided with a percutaneous intervention following an MI. Petition at 37. The prior art does not disclose this inventive aspect of the claims. And the mere existence of patients who received a low dose of colchicine following percutaneous intervention is not sufficient to show a motivation for treating patients with low-dose colchicine following those procedures. *Forest Labs., LLC v. Sigmapharm Labs., LLC*, 918 F.3d 928, 934 (Fed. Cir. 2019) (finding mere presence of claimed limitations in prior art insufficient to show

obviousness because there was no reason to combine the teachings that would lead a POSA to the claimed invention with a reasonable likelihood of success).

The Petition relies on Nidorf, which discusses the stratification of baseline characteristics in the LoDoCo study, including “coronary angioplasty.” However, Petitioner provides no evidence, nor explanation for why that is a disclosure of a motivation to treat patients who have already received a percutaneous intervention. The mere fact that certain individuals in the study fell into that category is insufficient to show a motivation for treating such patients with low-dose colchicine. Notably, Nidorf and LoDoCo do not discuss any benefit or provide any explanation of these patients other than describing participant baseline characteristics.

Similarly, the COLCOT Protocol fails to teach a motivation to administer low-dose colchicine treatment for patients who had already completed a percutaneous intervention following an MI. (EX2001 at ¶43.) As Petitioner admits, the COLCOT Protocol merely required that participants with a *planned* percutaneous revascularization procedure first complete that procedure. That requirement was plainly a safety measure included within the study to limit any negative consequences to the patients. (*Id.*)

In addition, there was no reasonable expectation of success for removing the pre-loading dose. As the Examiner found, and as discussed above, not only was

there no motivation to omit the use of a pre-loading dose when combining low-dose colchicine treatment with post-percutaneous intervention, the fact that many other colchicine studies at the time used a pre-loading dose would have taught away from the claims. (EX1002 at 398-99.) It follows, then, that there was also no reasonable expectation of successfully treating such patients without a pre-loading dose. (EX2001 at ¶44.) Petitioner has not introduced any new evidence to disturb either conclusion.

3. It was unexpected that administration of colchicine within first 3 days following an MI would reduce risk of cardiovascular events.

Petitioner again relies merely on conclusory statements that a POSA would have expected a reduction in the risk of a cardiovascular event if a patient is treated with low-dose colchicine according to the patented claims. These unsubstantiated arguments are insufficient to establish obviousness of claims 1-26 and 40-50. *KSR*, 550 U.S. at 418 (holding that obviousness “cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)); see also *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016) (“To satisfy its burden of proving obviousness, a petitioner cannot employ mere conclusory statements.”)).

Petitioner provides no argument for why a POSA would have extrapolated

the purported success of treatment 30 or 60 days after MI to reasonably expect successful reduction of cardiovascular events with treatment initiated after 3 days according to the claimed methods.

Petitioner first alleges that because Nidorf disclosed a reduction in the risk of cardiovascular events with low-dose colchicine initiated at least 6 *months* after MI, a POSA would have expected a low-dose colchicine treatment initiated 3 *days* after MI would also reduce the risk of cardiovascular events. Petition at 42; *see also* EX1049 at ¶167. Notably, other than the conclusory statement, neither Petitioner nor its expert provides any evidence or argument for why a POSA would have that expectation. (EX2001 at ¶¶45-46.) As explained above, such conclusory statements are insufficient to show obviousness.

Petitioner then alleges based on the “inflammation hypothesis” of CANTOS and the COLCOT Protocol⁵, a POSA would have known low-dose colchicine is effective 30 days after MI stabilization, and that a POSA would have expected a similar outcome with low-dose colchicine treatment initiated within 3 days of MI.

⁵ Petitioner and Dr. Ridker talk extensively about the Deftereos reference, however the Petition did not assert Deftereos as an invalidating reference and not of the Grounds for invalidity rely on Deftereos. Therefore, arguments about that reference are improper.

Petition at 43. Again, Petitioner fails to provide any evidence for why a POSA would have expected the same success with low-dose colchicine if administered within 3 days as opposed to within 30 days of MI. (EX2001 at ¶¶47, 49.)

Petitioner relies on the ESC Guidelines, however those Guidelines relate to treatment using high intensity statins, which are a different class of drugs compared to colchicine. (EX2001 at ¶48.) A POSA would not have reasonably expected statins would provide anti-inflammatory response at a 0.5 mg strength and therefore would not expect any improvement in reducing cardiovascular events. (*Id.*) Thus, simply because an early intervention may have worked with one drug does not mean a POSA would reasonably expect it would work for a completely different drug.

Importantly, for all of these allegations, Petitioner fails to acknowledge the claimed invention as a whole. (EX2001 at ¶46.) The '063 patent does not claim initiating colchicine within 3 days alone, rather, it claims initiating within 3 days on a low-dose without any pre-loading dose, and only in patients that had their MI treated with a percutaneous intervention. The references that Petitioner relies on *never* combine these inventive aspects in the manner claimed, and never lead a POSA to expect success in doing so. (*Id.* at ¶¶48-49.)

4. The prior art does not provide a motivation to combine references that reduced the risk of stroke, nor a reasonable expectation that administration of colchicine would result in reduced stroke.

Petitioner also alleges that claim 27-39 would have been obvious over Nidorf in view of COLCOT and ESC Guidelines. However, Petitioner's argument is noticeably devoid of any motivation to combine these references to arrive at the claimed invention. (EX2001 at ¶50.)

The Petition merely lists how each limitation of claim 27 is allegedly present in the prior art, however, Petitioner does not even attempt to provide an argument for why a POSA would combine these references to arrive at claim 27. Petition at 44-45. It is well-settled that showing obviousness requires more than identifying the existence of the claim limitations in the prior art. *Forest Labs.*, 918 F.3d at 934 (finding mere presence of claimed limitations in prior art insufficient to show obviousness because there was no reason to combine the teachings that would lead a POSA to the claimed invention with a reasonable likelihood of success). Like *Forest Labs.*, Petitioner here has not identified any reason to combine the teaching of the prior art to arrive at the claimed invention. (EX2001 at ¶51.) Such a failure is fatal to Petitioner's request for institution.

Moreover, a POSA would not have reasonably expected from the asserted prior art that administration of colchicine within 30 days after MI would result in a reduced risk in stroke. (EX2001 at ¶52.) COLCRYST teaching administering

colchicine for different indications than those of the '063 patent and makes no mention of administration within 30 days of an MI to reduce stroke. (*Id.*) The ESC Guidelines provide general teachings regarding intervention following MI, but is not specific to colchicine or any benefits with respect to stroke. (*Id.* at ¶53.) In fact, the ESC Guidelines taught that drugs that have similar effects as colchicine, such as certain antiarrhythmics, are contraindicated for certain patients who have had an MI, and therefore a POSA would not have had a reasonable expectation of success in using colchicine with such patients. (*Id.*) Nidorf is a small-scale study that was not placebo controlled, and contains no teaching about administering colchicine within 30 days of an MI to reduce the risk of stroke. (*Id.* at ¶54.) And the COLCOT Study does not show that administration within 30 days following an MI reduces the risk of stroke, just that stroke was an endpoint that was being evaluated in the study. (*Id.* at ¶55.)

Petitioner also has not shown that a POSA would have a reasonable expectation of success in reducing the risk of stroke by administering colchicine within 30 days of a MI (EX2001 at ¶56), and therefore the Petition should not be instituted.

C. Ground 4: An obviousness finding is not reasonably likely

Ground 4 in the Petition relies on a combination of references that includes Bouabdallaoui, which as shown above is not prior art. Section II.A. Therefore, the

Petitioner is not likely to be able to demonstrate obviousness with respect to claims 1-26, 28, and 40-50, and the Petition should not be instituted.

D. The dependent claims are non-obvious

As discussed above, the independent claims are each non-obvious and Petitioner failed to present evidence sufficient to warrant institution. Because the independent claims are non-obvious, each dependent claim therefrom is also non-obvious, as they incorporate all of the elements of the independent claims. Further, Petitioner did not make a particularized showing regarding the obviousness of the various additional limitations required by the dependent claims in the context of the claims as a whole. Therefore, the Board should exercise its discretion to deny institution on these specious arguments.

E. Petitioner's objective evidence arguments are deficient

Even if a patent challenger has established a prima facie case of obviousness, the patentee still may produce objective evidence of non-obviousness. *Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd.*, 719 F.3d 1346, 1354 (Fed. Cir. 2013). Objective indicia of non-obviousness must be considered under the *Graham* factors before a determination of obviousness can be made. *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966); *Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1358 (Fed. Cir. 2013) (“Objective indicia of nonobviousness play a critical role in the obviousness analysis.”). “The objective indicia of non-

obviousness play an important role as a guard against the statutorily proscribed hindsight reasoning in the obviousness analysis.” *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1328 (Fed. Cir. 2016) (collecting cases).

As described above, Petitioner has not established a prima facie showing of obviousness. Thus, the '063 patent is not obvious and the Board should exercise its discretion to deny institution. Moreover, Petitioner's arguments regarding the lack objective indicia of non-obviousness are also deficient.

1. Bouabdallaoui is not prior art

Petitioner relies yet again on Bouabdallaoui, this time to argue that certain claims of the '063 patent were not unexpected. But as patentee has repeatedly explained, Petitioner is incorrect in categorizing Bouabdallaoui as prior art. Dr. Tardif organized the COLCOT study and was the lead investigator. Dr. Tardif is also the corresponding, or main author, and speaks on behalf of all Bouabdallaoui named authors regarding that publication. (*See* Section II.A.) Thus, even if we use Petitioner's November 13, 2020 alleged priority date, Bouabdallaoui was published on August 29, 2020, and was a disclosure by Dr. Tardif (the named inventor) less than one year before Petitioner's alleged priority date. Bouabdallaoui is not prior art under 35 U.S.C. § 102(b)(1)(A), (B), and there is no valid argument to the contrary. Therefore, Petitioner's allegations of no unexpected benefits from the claimed inventions because of the disclosure in Bouabdallaoui is legally incorrect

and a fatal flaw in the Petition.

2. The claimed inventions resulted in an unexpected benefit

Petitioner confusingly conflates its arguments regarding the unexpected benefit of treatment following the claimed regimen with a continuation of its prima facie obviousness case. Petition at 56. Petitioner also improperly views the “within about 3 days of the MI” in isolation rather than in the context of the claims as a whole. As the patent specification clearly shows, it was a surprising benefit that administering colchicine in a low dose, with no pre-loading dose, in patients that underwent a percutaneous intervention saw a 25% reduction in the risk of a future cardiovascular event when the treatment was acutely administered (within 3 days of the MI).

Rather than present any real argument to address this unexpected benefit conferred by the claimed regimen, Petitioner and its expert merely chalk the results up to “a play of chance.” Petition at 57. Petitioner and its expert advance pure speculation here based on the data in the '063 patent. Petitioner also asserts there are no unexpected results to support claims 27 and 28. As explained above, Petitioner has not established a prima facie obviousness case of these claims. Regardless, Petitioner merely relies upon the patent’s specification to support its argument that there was no unexpected benefit. This speculative approach is insufficient, and is a weak written description argument under 35 U.S.C. §112

disguised as a secondary considerations argument, which is improper in an *inter parties* review proceeding.

The '063 patent plainly demonstrates that the inventor was able to achieve not only a way to treat specific patients by administering a low dose of colchicine within 3 days of having a myocardial infarction, but also to reduce the risk of stroke in a patient after having a myocardial infarction. (EX2001 at ¶¶57-58.) For the claims requiring the administration within 3 days, Petitioner ignores the actual differences that were shown in the specification when colchicine is administered within 3 days following a myocardial infarction for certain patients, and instead try to incorporate a statistical difference limitation into the claims. But no such limitation exists, and it is inappropriate for Petitioner to incorporate a limitation simply to try to demonstrate a lack of a secondary consideration. For the claims regarding a reduction in the risk of stroke, Petitioner stated without any basis or citation that the data does not show an improved stroke reduction. However, the claim limitation is reducing the risk of a stroke not improved stroke reduction. Petitioner once again try to incorporate limitations that are not present in the claims to manufacture an obviousness argument. For example, Petitioner improperly introduces a statistically significant reduction limitation for the risk of stroke, which is not present in the claims. A reduced risk can be clinically significant while not being statistically significant. Again, that Petitioner needs to add

limitations speaks volumes as to its secondary considerations arguments.

Moreover, the '063 patent claims a benefit to patients that was not previously disclosed. Dr. Tardif showed that for certain patients there was a 25% reduction in future cardiovascular events, including stroke. (EX2001 at ¶57.) Tardif further showed that surprisingly there was a 62% reduction in the risk of stroke for patients administered low-dose colchicine according to claims 27-39. (*Id.* at ¶59.) The Examiner recognized these surprising and unexpected benefits in allowing the claims to issue. (*Id.*; *see also* EX1002 at 398-99.)

Petitioner failed to show a *prima facie* case of obviousness, but also failed to show there are no unexpected results with respect to the claims of the '063 patent.

3. The patent data are commensurate with the claim scope

Tellingly, Petitioner asserts that the patentee failed to show any unexpected benefit because the patent data are not commensurate with the claim scope, but offers no argument on this point. Confusingly, Petitioner only cites to its expert's declaration for support of this allegation, which to the extent the expert provides support it is an impermissible argument for invalidity under 35 U.S.C. § 112. (EX1049 at ¶¶ 220-248.) Arguments under Section 112 are not grounds for institution, and these positions should be disregarded.

VI. CONCLUSION

For the foregoing reasons, Petitioner has not provided any sufficient grounds upon which the Board should institute review. Moreover, Petitioner's arguments further evidence the non-obviousness of the claims of the '063 patent, as concluded by the Examiner. Respondent, therefore, respectfully request the Board deny institution of review and find the '063 not unpatentable for obviousness.

VII. MANDATORY NOTICES UNDER 37 C.F.R. § 42.8

A. Real Parties-in-Interest (37 C.F.R. § 42.8(b)(1))

Institut de Cardiologie de Montréal ("MHI") is the assignee and owner of the entire title and interest in "the '063 patent" and the real party-in-interest in this proceeding. Pharmascience Inc. is the exclusive licensee of the '063 patent and is also a real party-in-interest.

B. Lead and Backup Counsel and Service Information (37 C.F.R. §§ 42.8(b)(3), (4))

Lead Counsel	Backup Counsel
Sailesh K. Patel, Reg. No. 46,982 Sailesh.patel@afslaw.com ArentFox Schiff LLP 233 S. Wacker Dr. Suite 7100 Chicago, Illinois 60606 Tel: 312-258-5698	Imron T. Aly, Reg. No. 48,706 Imron.aly@afslaw.com ArentFox Schiff LLP 233 S. Wacker Dr. Suite 7100 Chicago, Illinois 60606 Tel: 312-258-5523

Please address all correspondence to counsel at the addresses above.

Respondent consents to electronic service by email at the above email addresses.

VIII. CERTIFICATION UNDER 37 C.F.R. § 42.24(d)

Pursuant to 37 C.F.R. § 42.24(a)(1)(i), the foregoing PATENT OWNER'S PRELIMINARY RESPONSE contains 10,186 words, excluding parts of this Preliminary Response exempted under § 42.24(a), as measured by the word-count feature of Microsoft Word.

Respectfully submitted,

Dated: October 18, 2023

By: /Sailesh K. Patel/
Sailesh K. Patel, Reg. No. 46,982
Imron T. Aly, Reg. No. 48,706
ArentFox Schiff, LLP
233 S. Wacker Dr., Suite 7100
Chicago, IL 60606
(312) 258-5500

Counsel for Patent Owner

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