

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.

IPR2023-01064
Patent 11,400,063 B2

Before ULRIKE W. JENKS, SHERIDAN K. SNEDDEN, and
ZHENYU YANG, *Administrative Patent Judges*.

JENKS, *Administrative Patent Judge*.

DECISION

Granting Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

On June 16, 2023, Murray & Poole Enterprises Ltd. (“Petitioner”) filed a Petition requesting an *inter partes* review of claims 1–50 (“the challenged claims”) of U.S. Patent No. 11,400,063 B2 (Ex. 1001, “the ’063 patent”). Paper 1 (“Pet.”). On October 18, 2023, Institut de Cardiologie de Montréal (“Patent Owner”) filed a Preliminary Response to the Petition. Paper 6 (“Prelim. Resp.”). With our authorization, Petitioner filed a Reply to the Preliminary Response (Paper 7, “Reply”) on December 6, 2023 and Patent Owner filed a Sur-reply (Paper 8, “Sur-reply”) to Petitioner’s Reply on December 13, 2023.

We have authority under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted “unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a). Upon considering the arguments and evidence presented in the parties’ briefs, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing the unpatentability of at least one claim challenged in the Petition. Accordingly, we institute an *inter partes* review of claims 1–50 of the ’063 patent.

A. Real Parties in Interest

Petitioner identifies Murray & Poole Enterprises Ltd., AGEPHA Pharma FZ LLC, AGEPHA Pharma USA, LLC, and UPTTON Limited, as real parties-in-interest. Pet. 72. Patent Owner identifies Institut de Cardiologie de Montréal (“MHI”) and Pharmascience Inc. as real parties-in-interest. Paper 5, 2.

B. Related Matters

The parties state that they are not aware of any related matters.
Pet. 72; Paper 5, 2.

C. The '063 Patent (Ex. 1001)

The '063 patent is titled “Early Administration of Low-dose Colchicine After Myocardial Infarctions.” Ex. 1001, code (54). The '063 patent issued from Application No. 17/097,285 (“the '285 application”), filed November 13, 2020. *Id.* at codes (21), (22). The '063 patent claims priority to Provisional Application No. 63/093,988 (“the '988 provisional application”), filed on October 20, 2020 and Provisional Application No. 62/935,865 (“the '865 provisional application”), filed on November 15, 2019. *Id.* at code (60). The '063 patent relates to “a method of treating a patient after having a myocardial infarction (MI), the method including initiating the administration of colchicine at a daily low dose to the patient within about 3 days of the MI.” *Id.* at code (57).

According to the '063 patent, “[i]nflammation appears to play an important role in atherosclerosis . . . and coronary artery disease.” *Id.* at 1:9–11. The '063 patent states that “[b]ecause acute coronary syndromes are associated with higher risks of recurrent events and exacerbated inflammation a need exists in the art for new treatment regimens.” *Id.* at 1:60–62. The '063 patent explains that “[c]olchicine is an inexpensive, orally administered, potent anti-inflammatory medication” that is indicated for the treatment of gout, familial Mediterranean fever, and pericarditis. *Id.* at 1:28–30, 1:43–47. However, the cardiovascular effects of colchicine have also been evaluated in trials in which participants were administered 0.5 mg

of colchicine once daily. *Id.* at 1:52–2:28. In one such example, trial participants with stable coronary disease were treated with colchicine at a dose of 0.5 mg once daily and had fewer cardiovascular events than those not receiving colchicine. *Id.*

In a second example, patients who had recently suffered an MI were treated with colchicine at a dose of 0.5 mg once daily and had a statistically significant lower risk of ischemic cardiovascular events than placebo; had significantly reduced rates of death from cardiovascular causes, resuscitated cardiac arrest, myocardial infarction, stroke, and urgent hospitalization for angina leading to coronary revascularization compared to placebo; and had reduced morbidity relative to placebo. *Id.* In that study, “colchicine reduced the risk of ischemic cardiovascular (“CV”) events by 23% in the post-MI setting. *Id.* at 2:41–43.

In a third example, the time to treatment initiation (“TTI”) was evaluated and patients who had recently suffered an MI were treated with colchicine at a dose of 0.5 mg once daily starting on days post-MI from 0–3, 4–7, and 8–30. In that TTI study, initiation of colchicine treatment in days from 0–3 post-MI reduced the risk of the composite primary endpoint by 48%. *Id.* at 2:43–47. The composite primary endpoint consisted of “a composite of CV death, resuscitated cardiac arrest, MI, stroke, or urgent hospitalization for angina requiring coronary revascularization.” *Id.* at 8:5–8. The invention claimed in the ’063 patent is based on the treatments used in the TTI study.

*1. Overview of Provisional Patent Application No. 63/093,988
(Ex. 1003)*

The '988 provisional application describes patients with coronary artery disease (CAD) as being at “an increased risk of cardiovascular events including death, myocardial infarction (MI), stroke, and cardiac arrest; a risk that is magnified for each subsequent cardiovascular event.” Ex. 1003, 2:3–4 (footnote omitted). “[I]nflammation has emerged as an important therapeutic target in patients with atherosclerosis.” *Id.* at 2:12–13 (footnote omitted). The '988 provisional application is directed to a contemporary meta-analysis evaluating randomized control patient trials comparing colchicine to placebo (or no colchicine) for secondary cardiovascular prevention. *Id.* at 7:21–22. “Colchicine has an established safety profile from its centuries of use to treat gout.” *Id.* at 10:5.

The colchicine trials show improvement in patients with CAD.

In patients with CAD, the addition of colchicine to standard medical therapy was associated with a statistically significant reduction in the primary composite endpoint of cardiovascular mortality, MI, ischemic stroke, and urgent coronary revascularization, compared to patients on placebo or no colchicine.

Ex. 1003, 6:8–12. “[A]ll trials showed a decrease in urgent coronary revascularizations among patients randomized to colchicine, [but] only COLCOT^[1] detected a reduction in ischemic strokes.” *Id.* 8:11–13.

The '988 provisional application explains that

[t]he anti-inflammatory properties of colchicine work through various mechanisms to inhibit the pathogenesis of CAD, and subsequently reduce the incidence of ischemic cardiovascular

¹ Colchicine Cardiovascular Outcomes Trial (COLCOT) (Ex. 1006).

events. In addition to targeting the NLRP3 inflammasome leading to the reduction of circulating levels of IL-1 β and IL-6, colchicine also inhibits cholesterol crystals that promote inflammation and plaque instability in atherosclerosis.

Ex. 1003, 9:3–7 (footnote omitted).

2. *Overview of Provisional Patent Application No.62/935,865 (Ex. 1004)*

The '865 provisional application describes colchicine as “an inexpensive, orally administered, potent anti-inflammatory medication that was initially extracted from the autumn crocus and has been used for centuries.” Ex. 1004, 1:21–22.

The '865 provisional application explains that “[i]n the Low-Dose Colchicine (LoDoCo) trial, patients with stable coronary disease treated with colchicine at a dose of 0.5 mg once daily had fewer cardiovascular events than those not receiving colchicine.” *Id.* at 1:36–38. In a different clinical trial referred to as the COLCOT “the effects of colchicine on cardiovascular outcomes as well as its long-term safety profile in patients who had recently had a myocardial infarction” was evaluated. *Id.* at 2:8–10.

The '865 provisional application describes that “the method involves administering colchicine within 5, 10, 15, 20, or 25 days of the MI.” *Id.* at 2:32–33; *see also id.* at 9 (Table 1 – Patients were enrolled a mean 13.4 $\pm$ 10.2 days after myocardial infarction). The '865 provisional application discloses that “colchicine is administered at 0.4 to 0.6 mg, and is preferably administered at 0.5 mg” daily. *Id.* at 3:12–13.

The '865 provisional application concludes that colchicine administered at a daily low dose of 0.5 mg led to a statistically significant lower risk of ischemic cardiovascular events than placebo. Death from

cardiovascular causes, resuscitated cardiac arrest, myocardial infarction, stroke, or urgent hospitalization for angina leading to coronary revascularization was also significantly lower among the patients who received 0.5 mg of colchicine than those who received placebo. Ex. 1004, 2:13–17.

D. Illustrative Claim

Claims 1, 8, and 27 are the independent claims challenged by Petitioner in this proceeding. Independent claim 27, reproduced below, is illustrative of the subject matter:

27. A method of reducing the risk of a stroke in a patient after having an MI, the method comprising initiating the administration of colchicine at a daily low dose to the patient within about 30 days of an MI.

Ex. 1001, 42:33–36.

E. Prior Art and Asserted Grounds

Petitioner asserts that claims 1–50 of the '063 patent are unpatentable based on the following grounds. Pet. 24.

Claims challenged	35 U.S.C. §	References/Basis
1–13, 17–26, 28, 40–46, 49, 50	102	Bouabdallaoui ²
27, 29–36, 39	102	COLCOT protocol ³

² Bouabdallaoui et al., *Time-to-treatment initiation of colchicine and cardiovascular outcomes after myocardial infarction in the Colchicine Cardiovascular Outcomes Trial (COLCOT)*, EUROPEAN HEART J., 41:4092–4099 (2020). Ex. 1005 (“Bouabdallaoui”).

³ “*Colchicine Cardiovascular Outcomes Trial (COLCOT) (COLCOT)*,” <https://web.archive.org/web/20171020004013/https://clinicaltrials.gov/ct2/sh>

1–50	103	Nidorf, ⁴ COLCOT Protocol, ESC Guidelines, ⁵ COLCRYS ⁶
1–26, 28, 40–50	103	Bouabdallaoui, COLCRYS

Petitioner relies upon the declaration of Paul Ridker, M.D. (Ex. 1049) to support its contentions. In addition, Petitioner relies on the Declaration of Raymond Cruitt, M.S. (Ex. 1038) and its appendices to establish the availability of the references.

II. ANALYSIS

A. Claim Construction

The Board applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). 37 C.F.R. § 100(b) (2019). Under that standard, claim terms “are generally given their ordinary and customary meaning” as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc) (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). “In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written

ow/NCT02551094. Ex. 1006 (“COLCOT protocol”); *see also* Ex. 1038, ¶¶ 15–19, 23–25.

⁴ Nidorf, US 10,206,891 B2, issued Feb. 19, 2019. Ex. 1007 (“Nidorf”).

⁵ Ibanez et al., *2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation*, EUROPEAN HEART J., 39:119–177 (2018). Ex. 1009 (“ESC guidelines”).

⁶ Package insert for COLCRYSTM (colchicine, USP) tablets for Oral use, *available at* <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&App1No=022351>. Ex. 1016 (“COLCRYS”); *see also* Ex. 1038, ¶¶ 30–32.

description, and the prosecution history, if in evidence.” *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at 1312–17).

Petitioner proposes constructions for several terms, including the preamble of claims 1–26 and 40–50 which recites “a method of treating a patient after having a myocardial infarction (MI),” the preamble of claims 27–39 which recites “reducing the risk of a stroke,” and “wherein the patient is at a lower risk of a cardiovascular event” recited in claims 8–11 and 20–23. *See* Pet. 21–24.

Patent Owner responds to Petitioner’s constructions of “reducing the risk of a stroke” and “wherein the patient is at a lower risk of a cardiovascular event,” but does not discuss Petitioner’s construction of “a method of treating a patient after having a myocardial infarction (MI)” at this time. Prelim. Resp. 16–22.

In rendering our Decision, we construe the terms raised by Petitioner and Patent Owner.

1. “*a method of treating a patient after having a myocardial infarction (MI)*”

Petitioner contends that the preamble limitation is directed to treating a patient population but there is no required clinical efficacy. Pet. 22 (citing *In re Montgomery*, 677 F.3d 1375, 1380 (Fed. Cir. 2012) (“We are skeptical that a proper interpretation of [the claim term ‘for the treatment or prevention of stroke or its recurrence’] would include an efficacy requirement”); Ex. 1048 ¶¶ 97–104).

Patent Owner does not address this limitation. *See generally* Prelim. Resp.

We agree with Petitioner that the preamble does not appear to have an efficacy requirement. Accordingly, at this stage of the proceeding, we accept Petitioner's interpretation that the preamble simply describes the patient population that is to receive treatment.

2. “*reducing the risk of a stroke*”

Petitioner contends that the limitation of “reducing the risk of a stroke” is an intended result. Pet. 23 (citing *Bristol-Myers Squibb Co. v. Ben Venue Lab's, Inc.*, 246 F.3d 1368, 1375–76 (Fed. Cir. 2001) (finding preamble language “a method for treating a cancer patient to effect regression of a taxol-sensitive tumor, said method being associated with reduced hematologic toxicity” “is only a statement of purpose and intended result”); Ex. 1049 ¶¶ 104–108).

Patent Owner contends that “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.” Prelim. Resp. 19. In addition, Patent Owner contends that in the notice of Allowability, Examiner stated that claim 27 is allowable “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.’” Prelim. Resp. 20.

If the body of the claim sets out the complete invention, and the preamble is not necessary to give “life, meaning and vitality” to the claim, “then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation.” *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305 (Fed.Cir.1999). Here, the

body of claim 27 recites “initiating the administration of colchicine at a daily low dose to the patient within about 30 days of an MI.” Ex. 1001, 42:34–36. The claim body, therefore, identifies the patient population that is to be treated with the low dose colchicine and the time frame in which to initiate treatment. The preamble, therefore, does not narrow the patient population nor change the way colchicine is administered – all that is required by the claim is that colchicine is administered to patients that have suffered a MI within a particular time period after the MI event. The step of the method is preformed the same way whether or not the patient experiences a reduction in the risk of stroke. *See, e.g., In re Hirao*, 535 F.2d 67, 70 (CCPA 1976) (“the preamble merely recites the purpose of the process; the remainder of the claim . . . does not depend on the preamble for completeness, and the process steps are able to stand alone.”); *see* Pet. 23 (“‘reducing the risk of a stroke’ does ‘not result in a manipulative difference in the steps of the claim’ and is [therefore] non-limiting.” (citing *Bristol-Myers*, 246 F.3d at 1375–76; Ex. 1049 ¶¶ 104–108)).

We agree with Petitioner that Examiner’s claim interpretation is in error. Here, the body of claim 27 defines a structurally complete invention by identifying the target population as any patient that has had a myocardial infarction (MI) and the onset of treatment using 0.5 mg colchicine within a 30-day time window. *See Rowe v. Dror*, 112 F.3d 473, 478 (Fed. Cir. 1997) (“[W]here a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation.”); *IMS Tech., Inc. v. Haas Automation, Inc.*, 206 F.3d 1422, 1434 (Fed. Cir. 2000) (“If the preamble adds no limitations to those in the body of the claim, the preamble is not

itself a claim limitation and is irrelevant to proper construction of the claim.”). The recitation of “reducing the risk of a stroke” in the preamble, therefore, does not result in a difference in the way colchicine is administered to the identified patient population. *See* Pet. 23.

We have reviewed the parties’ contentions, and determine at this stage of the proceedings that Petitioner has provided a requisite showing that the body of claim 27 describes a structurally complete invention. The preamble of claim 27, therefore, is not limiting because it simply expresses the intended result of the positively recited method step within the body of the claim. *See* Pet. 23.

3. *“wherein the patient is at a lower risk of a cardiovascular event”*

Claim 8 contains three wherein clauses: (1) “wherein the colchicine is administered without pre-loading the patient with a higher dose of colchicine before the administration at the daily low dose;” (2) “wherein the cardiovascular event is resuscitated cardiac arrest, stroke, or urgent hospitalization for angina requiring coronary revascularization;” and (3) “wherein the patient is at a lower risk of a cardiovascular event, relative to a patient not being administered colchicine.” *See* Ex. 1001, 41:50–60.

Petitioner contends that the third “wherein clause” of claim 8 – “wherein the patient is at a lower risk of a cardiovascular event” – “‘is only a statement of purpose and intended result’ that ‘does not result in a manipulative difference in the steps of the claim’ and is thus a non-limiting intended result and does not add patentable weight to the claims.” Pet. 23 (citing *Bristol-Myers*, 246 F.3d at 1375–76; *Syntex (U.S.A.) LLC v. Apotex*,

Inc., 407 F.3d 1371, 1378 (Fed. Cir. 2005); *Minton v. Nat’l Ass’n of Sec. Dealers, Inc.*, 336 F.3d 1373, 1381 (Fed. Cir. 2003)).

Patent Owner disagrees. Patent Owner argues that a wherein clause that “states a condition that is material to patentability, . . . cannot be ignored in order to change the substance of the invention.” Prelim. Resp. 20 (citing *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))). During prosecution, “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.). . . . [The] ‘wherein’ clauses were necessary to overcome the prior art.” Prelim. Resp. 21.

The first wherein clause “wherein the colchicine is administered without pre-loading the patient with a higher dose of colchicine before the administration at the daily low dose” defines the limitations of how the colchicine is administered.

The second wherein clause “wherein the cardiovascular event is resuscitated cardiac arrest, stroke, or urgent hospitalization for angina requiring coronary revascularization” defines the type of cardiovascular event encompassed by the claim.

The dispute between the parties is directed to the third wherein clause “wherein the patient is at a lower risk of a cardiovascular event, relative to a patient not being administered colchicine.” This third wherein clause simply asks for a comparison between patients receiving colchicine with a similar situated patient population not receiving the colchicine treatment.

“An intended use or purpose usually will not limit the scope of the claim because such statements usually do no more than define a context in which the invention operates.” *See Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1345 (Fed. Cir. 2003). Although “[s]uch statements often . . . appear in the claim’s preamble,” a statement of intended use or purpose can appear elsewhere in a claim. *In re Stencel*, 828 F.2d 751, 754 (Fed. Cir. 1987).

We have reviewed the parties’ contentions, and determine at this stage of the proceedings that Petitioner has provided a requisite showing that this third clause merely describes the benefit of the administration of colchicine to the identified patient population. We are not persuaded by Patent Owner’s contention that this clause is material to how the method is performed. This “wherein clause,” therefore, merely defines the result of the positively recited method steps. *See* Pet. 23; *see, e.g., Minton*, 336 F.3d at 1381 (a “whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.”).

B. Level of Ordinary Skill in the Art

Petitioner contends a person of ordinary skill in the art (“POSA”), or a “skilled cardiologist,” would have:

- An M.D. degree and be board-certified with a subspecialty in the treatment of cardiovascular disease.
- At least 3-5 years of experience, following board certification, in cardiology and cardiovascular disease treatment and sufficient clinical experience to understand standard good medical practice in patient management.
- Been familiar with acute coronary syndromes, stable coronary diseases, cardiovascular diseases, and their standard treatments,

including the acute management and long-term secondary preventions of myocardial infarction.

- Been aware of research relating to cardiovascular disease progression, including the role of inflammatory pathways in secondary cardiovascular events.

Pet. 21 (citing Ex. 1049, ¶ 89).

Patent Owner's declarant, Hossein Ardehali, M.D., Ph.D., disputes Petitioner's definition of a POSA. Ex. 2001 ¶ 12. Dr. Ardehali posits that Dr. Ridker's definition is too narrow and that "a POSA for the '063 patent would be an M.D. with training and 3-5 years of experience in treating cardiovascular disease." *Id.* Although Dr. Ardehali disagrees with Petitioner's definition of a POSA, Dr. Ardehali states that his opinions remain the same regardless of whether the Board adopts Petitioner's definition or Patent Owner's definition. *Id.*

Based on the present record, we adopt Petitioner's definition of a POSA. We further note that the prior art itself demonstrates the level of skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required "where the prior art itself reflects an appropriate level and a need for testimony is not shown") (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985)).

C. Discretionary Denial Under 35 U.S.C. § 325(d)

As a preliminary issue, Patent Owner urges the Board to exercise discretion to deny institution of *inter partes* review under 35 U.S.C. § 325(d). Prelim. Resp. 2–16. Petitioner opposes. Pet. 62–71.

1. Legal Standard

Section 325(d) provides that the Director⁷ may “reject the petition” if “the same or substantially the same prior art or arguments previously were presented to the Office.” The Board analyzes this issue under a two-part framework:

(1) [determining] whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office; and (2) if either condition of [the] first part of the framework is satisfied, [determining] whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims.

Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH, IPR2019-01469 Paper 6, 8 (PTAB Feb. 13, 2020) (precedential) (footnote omitted). “If a condition in the first part of the framework is satisfied and the petitioner *fails* to make a showing of material error, the Director generally will exercise discretion not to institute *inter partes* review.” *Id.* at 8–9 (emphasis added).

In analyzing whether the same or substantially the same art or arguments were previously presented to the Office, we consider factors including: (i) the similarities and material differences between the asserted art and the prior art previously presented to the Office; (ii) the cumulative nature of the asserted art and the prior art previously evaluated by the Office; and (iii) the extent of the overlap between the arguments made before the Office and the manner in which the petitioner relies on the prior art or the patent owner distinguishes the prior art. *Id.* at 8–10; *see also Becton*,

⁷ The Board institutes trial on behalf of the Director. 37 C.F.R. § 42.4(a).

Dickinson & Co. v. B. Braun Melsungen AG, IPR2017-01586, Paper 8, 17–18 (Dec. 15, 2017) (precedential as to § III.C.5, first paragraph) (“*Becton, Dickinson*”).

In analyzing whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims, we consider factors including: (iv) the extent to which the asserted art was evaluated by the Office, including whether the prior art was the basis for rejection during examination; (v) whether the petitioner has pointed out sufficiently how the Office erred in its evaluation of the asserted prior art; and (vi) the extent to which additional evidence and facts presented in the petition warrant reconsideration of prior art or arguments. *Advanced Bionics*, 8–10; *Becton, Dickinson*, 17–18.

2. Analysis

a. Part 1: Whether the same or substantially the same art or arguments were presented previously to the Office

The first part of the *Advanced Bionics* framework requires us to determine whether the Petition advances the same or substantially the same art or arguments that were previously presented to the Office. *Advanced Bionics*, 8. For the reasons explained below, we determine that the same or substantially the same art was previously presented, and thus, the first part of the framework is satisfied.

Petitioner relies on five references in its asserted grounds of unpatentability: Bouabdallaoui (Ex. 1005), COLCOT protocol (Ex. 1006), Nidorf (Ex. 1007), ESC guidelines (Ex. 1009), and COLCRYST (Ex. 1016). Pet. 24. Petitioner acknowledges that “Bouabdallaoui (EX1005) was submitted via IDS” but argues that Examiner did not substantively address

the reference on the record. Pet. 63. According to Petitioner, “Bouabdallaoui is prior art to all challenged claims not entitled to an effective filing date earlier than November 13, 2020, i.e., at least claims 1–26, 28 and 40–50.” Pet. 65.

Petitioner argues that during prosecution of the ’063 patent, Patent Owner listed the COLCOT protocol on an IDS (*see* Ex. 1002, 358) but actually submitted a non-prior art version “retrieved from the Clinicaltrial.gov website on March 15, 2021, that differs from the 2015 version.” Pet. 63 (citing Ex. 1002, 315–323, 326); *compare* Ex. 1006 with Ex. 1002, 316–323. Petitioner contends that “this non-prior art was never addressed on the record.” Pet. 63.

Petitioner additionally cites Nidorf (Ex. 1007), ESC guidelines (Ex. 1009), and COLCRYs (Ex. 1016) and asserts that these references were not submitted to the office and are not cumulative with “references ‘extensively evaluated during examination’ or were ‘the basis for rejection.’” Pet. 68. Petitioner acknowledges that “another Nidorf patent (EX1018)” was submitted to the office but asserts that the reference was not discussed by Examiner. Pet. 68 n.9.

Patent Owner responds that “Petitioner does not dispute that Bouabdallaoui was provided to the Examiner.” Prelim. Resp. 3, *see also id.* at 8 (citing Ex. 1002, 76, 175-182). Additionally, Patent Owner contends that Bouabdallaoui is not prior art because “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.” Prelim. Resp. 5.

Patent Owner contends that the COLCRYS disclosure of colchicine tablets relied on by Petitioner is cumulative to information already before Examiner. Prelim. Resp. 9, *see also id.* at 16 (“Colcrys is cumulative at best and also irrelevant as it relates to another condition (gout) and not the claimed condition.”). Patent Owner contends that “[t]he Exhibit that Petitioner relies upon is merely an earlier version of the Protocol that was provided to the Examiner,[] and the earlier and later versions are substantively the same. (*Compare* EX1006 with EX1002 at 315-323.)” Prelim. Resp. 10.

Patent Owner acknowledges that “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.” Prelim. Resp. 15. Patent Owner contends that both Nidorf 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.” *Id.*

Patent Owner contends that “[t]he 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.” Prelim. Resp. 15, *see also id.* at 15–16 (“The Guideline teachings are too general and would not be applicable to treatment with colchicine, which is not mentioned in the Guidelines at all.”).

There can be no dispute that Bouabdallaoui and the COLCOT protocol were before the Office. Bouabdallaoui and the COLCOT protocol were listed on an IDS, initialed by Examiner and listed on the face of the

'063 patent as a considered-reference. Ex. 1001, code (56); Ex. 1002, 306, 358. Specifically, Examiner certified that all references listed in the IDS “except where lined through” were considered, and Bouabdallaoui and the COLCOT protocol are not lined through. Ex. 1002, 306, 358. Patent Owner further argues that “the COLCOT Protocol is substantially similar to the COLCOT Protocol the Examiner reviewed.” Prelim. Resp. 11; *compare* Ex. 1006 *with* Ex. 1002, 315–323.

On the other hand, Nidorf, ESC guidelines, and COLCRYST were not, themselves, before the Office during examination of the application that issued as the '063 patent and therefore are not the “same art” previously presented to the Office. *Advanced Bionics*, 13–14. But, Patent Owner argues, art substantially similar to these references was before the Office during examination. *See* Prelim. Resp 2–16.

As to Nidorf, Patent Owner acknowledges that the “specific Nidorf patent cited by Petitioner was not before the Examiner, [but] a related Nidorf patent (EX1018) was before the Examiner with substantially the same disclosure” and both rely on the same priority applications. Prelim. Resp. 15; (*compare* Ex. 1007, (63), (30) *with* Ex. 1018, (86), (30)). We further note that Example 1 of the Nidorf patent before Examiner contains a substantially similar disclosure as Example 1 of the Nidorf patent cited in the Petition. *Compare* Ex. 1007, 17:60–20:10 *with* Ex. 1018, 17:30–19:27. The protocol discloses administering 0.5 mg/day of colchicine to patients receiving standard secondary prevention therapies including aspirin and high dose statins. *Compare* Ex. 1007, 18:2–6 *with* Ex. 1018, 17:31–35. Based on our review of these disclosures at this stage of the proceeding, Patent Owner has

sufficiently shown that substantially similar art was before Examiner during prosecution.

As to ESC guidelines, Patent Owner argues that “[t]he 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.” Prelim. Resp. 15. The guidelines discuss management and treatment of patients after a myocardial infarction, but do not specifically address using colchicine in therapy. *See generally* Ex. 1009.

Hennessy relied on by Examiner teaches the use of colchicine after a myocardial infarction. Ex. 1028, abstract; Ex. 1002, 306 (IDS initialed by Examiner), 348–349. Hennessy discloses administering 0.5 mg once daily colchicine to adult patients “if they had sustained a type 1 acute MI (by the 3rd universal definition[]) within the prior 7 days.” Ex. 1028, 2. Hennessy also teaches that colchicine can be administered in conjunction with standard treatment. *See* Ex. 1028, 7 (“In the Low Dose Colchicine (LoDoCo) study, treatment with 0.5 mg colchicine per day in addition to standard treatment in patients with stable [coronary heart disease] significantly reduced the risk of developing an acute coronary syndrome, an out of hospital cardiac arrest or non-cardioembolic stroke.”) (footnote omitted). Hennessy, therefore, teaches treatment after myocardial infarction, and based on our review of the disclosure at this stage of the proceeding, we find that Patent Owner has sufficiently shown that the ESC guidelines is substantially similar to art before Examiner during prosecution.

As to COLCRYS, Patent Owner argues that this is “cumulative of information already before the Examiner.” Prelim. Resp. 15. COLCRYS is

prescribing information for colchicine tablets, specifically, 0.6 mg tablets. Ex. 1016, 4. Hennessy discloses administering 0.5 mg once daily colchicine to adult patients “if they had sustained a type 1 acute MI (by the 3rd universal definition[]) within the prior 7 days.” Ex. 1028, 2.

Having considered the record, acknowledging Petitioner’s point that Nidorf, ESC guidelines, and COLCRY5 was not actually of record during prosecution, we agree with Patent Owner that Nidorf, ESC guidelines, and COLCRY5 each is cumulative to the teaching in Hennessy relied on by the Examiner for administering low-dose colchicine (0.5 mg daily) to patients following an acute myocardial infarction (MI), and, therefore, is “substantially the same art” as that previously presented to the Office. *Advanced Bionics*, 8.

We also agree with Patent Owner that ESC guidelines “are too general and do not relate at all to treating the specific patients identified in the claims with colchicine.” Prelim. Resp. 15. Patent Owner contends that ESC “Guidelines relate to treatment using high intensity statins, which are a different class of drugs compared to colchicine.” Prelim. Resp. 35 (citing Ex. 2001 ¶ 48). Here, Hennessy also teaches that colchicine can be administered in conjunction with standard treatment. *See* Ex. 1028, 7 (“In the Low Dose Colchicine (LoDoCo) study, treatment with 0.5 mg colchicine per day in addition to standard treatment in patients with stable [coronary heart disease] significantly reduced the risk of developing an acute coronary syndrome, an out of hospital cardiac arrest or non-cardioembolic stroke.”) (footnote omitted). The ESC guidelines are directed to the administration of statins, therefore, are cumulative to the teachings in Hennessy as previously presented to the Office and considered by Examiner.

For these reasons, we determine that all the references that Petitioner asserts in the Petition (i.e., Bouabdallaoui, COLCOT protocol, Nidorf, ESC guidelines, and COLCRY5) are the same or substantially the same art that were previously presented to the Office. Accordingly, we determine that the first part of the *Advanced Bionics* framework is satisfied.

b. *Part 2: Whether the Petitioner Demonstrates Material Error*

Next, we consider “whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims.” *Advanced Bionics*, 8. Patent Owner argues that “[t]he Examiner also did not make any material error in evaluating the prior art, or even determining the closest prior art.” Prelim. Resp. 9. Patent Owner contends that “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.” *Id.* at 11–12.

During prosecution, Examiner identified Hennessy as being the closest prior art. *See* Ex. 1002, 348–349, 399. Hennessy describes treating a patient population that has had a recent myocardial infarction (MI). The patient population described in Hennessy received 0.5 mg of colchicine once a day and describes the population as adults 18 years or older that have had a MI event within the prior 7 days. *See* Ex. 1028, 2 (“[a]dult (>18 years old) patients were eligible for enrolment if they had sustained a type 1 acute MI (by the 3rd universal definition[]) within the prior 7 days.”). Hennessy teaches that the “[r]eadmission rates [for their patient population] were significantly lower in the colchicine treated patients but [recognizes that] the numbers are small.” Ex. 1028, 6. This comports with the “Low Dose

Colchicine (LoDoCo) study, treatment with 0.5 mg colchicine per day in addition to standard treatment in patients with stable [coronary heart disease] CHD significantly reduced the risk of developing an acute coronary syndrome, an out of hospital cardiac arrest or non-cardioembolic stroke.”
Ex. 1028, 7.

In the notice of allowability, Examiner asserts that the closest prior art also appears to be [Hennessy (Ex. 1028)] *American Heart Journal* (September 2019), Vol. 215, pp. 62-69, outlined above. The reference 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.

Ex. 1002, 399 (footnote omitted).

Here, Examiner in the notice of allowance specifically finds that Hennessy does not address the risk of stroke in the patient population receiving colchicine as a reason for allowing the claim. For the reasons discussed above (*see* II.A.i), we agree with Petitioner that Examiner’s claim interpretation is in error because it requires reading the “reducing the risk of a stroke” as a claim limitation into the claim rather than reading this limitation as an intended result of treating the same patient population – those having suffered a myocardial infarction – with the same active ingredient – colchicine. For these reasons, we determine that Petitioner has sufficiently shown that the Office erred in a manner material to the patentability of challenged claims. Accordingly, we determine that the second part of the *Advanced Bionics* framework is also satisfied.

3. *Summary*

For the reasons discussed above, we determine that part one of the two-part framework of *Advanced Bionics* is satisfied. However, we find that Examiner made a material error in claim interpretation of claim 27 and as such, we find the Petitioner has sufficiently established how Examiner made a material error. Consequently, part two of the *Advanced Bionics* framework is also satisfied. Thus, we decline to exercise our discretion pursuant to 35 U.S.C. § 325(d) to deny institution of trial.

D. Anticipation by COLCOT Protocol

Petitioner contends that claims 27, 29–36, and 39 are unpatentable as anticipated over COLCOT protocol. Pet. 29–34. Patent Owner opposes because the COLCOT protocol was before the Examiner and because the COLCOT protocol does not disclose the reduction of risk of stroke. Prelim. Resp. 10–14, 22–23.

1. Overview of COLCOT Protocol (Ex. 1006)

COLCOT protocol is a copy of a webpage from ClinicalTrials.gov in which the Colchicine Cardiovascular Outcomes Trial (COLCOT) is described. Ex. 1006, 1.

According to COLCOT protocol, “[a]therosclerosis is the most common cause of myocardial infarction, stroke and peripheral arterial disease. Research has clearly demonstrated that inflammation plays a key role in the initiation, progression and manifestations of atherosclerosis.” *Id.* at 4. COLCOT protocol explains that “[c]olchicine is an inexpensive, yet potent, anti-inflammatory drug approved for acute use in patients with gout and chronic use in patients with Familial Mediterranean Fever” and

“[c]onsiderable work has highlighted the potential of colchicine in the treatment of cardiovascular diseases mediated by pro-inflammatory processes,” such as coronary artery disease (CAD). *Id.*

COLCOT protocol explains that “[t]he study evaluates whether long-term treatment with colchicine reduces rates of cardiovascular events in patients after myocardial infarction.” *Id.* at 1. In the study, patients who suffered an acute MI within the last 30 days received either 0.5 mg/day colchicine or a matching placebo for about 2 years or until “the target of 301 primary endpoints has been reached.” *Id.* The primary outcome measures in the study include cardiovascular death, resuscitated cardiac arrest, acute myocardial infarction, stroke, and hospitalization for angina requiring coronary revascularization. *Id.* at 2.

2. Claim 27

Petitioner contends that COLCOT protocol anticipates claim 27. Pet. 29–32. Patent Owner opposes. Prelim. Resp. 10–14, 22–23. Specifically, Patent Owner contends that the COLCOT protocol “does not disclose the reduction of risk of stroke.” *Id.* at 22.

Based upon our review of the parties’ arguments and supporting evidence in the current record, we determine that Petitioner has shown a reasonable likelihood that claim 27 is anticipated by COLCOT protocol.

The target patient population in the COLCOT protocol are patients that “have suffered a documented acute myocardial infarction within the last 30 days.” Ex. 1006, 1; Pet. 30–32; Ex. 1049 ¶¶ 125–132. In other words, patients that suffered a myocardial infarction *more than 30 days ago* are excluded from the study. The COLCOT protocol, therefore, includes patients that had a documented myocardial infarction, but that the

myocardial infarction event was less than 30 days from the start of treatment. This meets the target population of claim 27 that administers colchicine to patients “within about 30 days of an MI.” *See* Ex. 1001, 42:35–36.

The COLCOT protocol instructs to sort patients into either a treatment or placebo group. Ex. 1006, 1. The treatment group will receive “colchicine (0.5 mg per day) . . . for an estimated 2 years period.” Ex. 1006, 1; Pet. 30–32; Ex. 1049 ¶¶ 125–132. The treatment group, therefore, meets the limitation of claim 27 that administers “low dose” colchicine to patients. *See* Ex. 1001, 42:36, *see also id.* at 42:50–53 (describing that colchicine is administered at 0.5 mg once per day).

For the reason discussed above (*see* II.A.2), at this stage of the proceeding, we find that the preamble of claim 27 is not limiting because it simply expresses the intended result of the positively recited method step within the body of the claim. The step of the method is performed the same way whether or not the patient experiences a reduction in the risk of stroke. *See, e.g., In re Hirao*, 535 F.2d at 70 (“the preamble merely recites the purpose of the process; the remainder of the claim . . . does not depend on the preamble for completeness, and the process steps are able to stand alone.”); *see also Bristol-Myers*, 246 F.3d at 1375–76 (“the expression ‘[a] method for treating a cancer patient to effect regression of a taxol-sensitive tumor, said method being associated with reduced hematologic toxicity’ in the preambles . . . is only a statement of purpose and intended result. The expression does not result in a manipulative difference in the steps of the claim.”).

Furthermore, by treating the same patient population with the same drug – low dose colchicine – we agree with Petitioner that the result of lowering the risk of stroke is an inherent feature of the treatment method taught in COLCOT protocol. *See Bristol-Myers Squibb Co.*, 246 F.3d at 1376 (“Newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent.”); *see also Prometheus Labs., Inc. v. Roxane Labs., Inc.*, 805 F.3d 1092, 1099–01 (Fed. Cir. 2015) (finding that it would have been obvious to treat the claimed subpopulation of irritable bowel syndrome patients based on common practices in the field).

For these reasons, we determine that Petitioner has shown a reasonable likelihood that claim 27 is anticipated by the COLCOT protocol.

3. *Claims 29–36 and 39*

Claims 29–36 and 39 depend directly or indirectly from claim 27. Ex. 1001, 42:40–57, 42:62–63. Petitioner provides citations to the COLCOT protocol and explains where each of dependent claims 29–36 and 39 are disclosed by the reference. Pet. 32–34. Petitioner supports its assertions with the testimony of Dr. Ridker. *Id.* (citing Ex. 1049, ¶¶ 133–139). Patent Owner argues the claims as a group and does not provide arguments for the dependent claims separate from those discussed above with respect to claim 27. Prelim. Resp. 10–14, 22–23.

We are persuaded, for the reasons stated in the Petition, which findings we adopt as our own for the purpose of institution, that Petitioner’s arguments and evidence have established a reasonable likelihood that each limitation of claims 29–36 and 39 are anticipated by the COLCOT protocol. *See* Pet. 32–34.

E. Obviousness over Nidorf, COLCOT Protocol, ESC Guidelines, and COLCRYS

Petitioner contends that claims 1–50 are unpatentable as obvious over Nidorf, COLCOT protocol, ESC guidelines, and COLCRYS. Pet. 34–54. Patent Owner opposes. Prelim. Resp. 23–37.

1. Overview of Nidorf (Ex. 1007)

Nidorf is titled “Method of Treating Cardiovascular Events Using Colchicine Concurrently with an Antiplatelet Agent” and issued on February 19, 2019. Ex. 1007, codes (45), (54). Nidorf relates to “[m]ethods of treating and/or preventing a cardiovascular event in a patient, the method comprising orally administering a colchicine to a patient who is receiving concurrent treatment with at least one antiplatelet agent.” *Id.* at code (57). According to Nidorf, “[c]olchicine is an anti-inflammatory drug with a long history in human medicine, used for the symptomatic treatment of inflammatory diseases, most prominently gout,” but also familial Mediterranean fever and Behçet’s disease. *Id.* at 6:19–21; *see id.* at 1:19–28. Colchicine has also been proposed to be effective in therapy for cardiovascular diseases such as recurrent and acute pericarditis, post-pericardiotomy syndrome (PPS), and atherosclerotic vascular disease. *Id.* at 1:29–2:33.

Nidorf’s method includes treating and/or preventing a cardiovascular event in a patient, such as acute coronary syndrome, out-of-hospital cardiac arrest, and/or noncardioembolic ischemic stroke, by administering a composition comprising an effective amount of colchicine to a patient who is receiving concurrent treatment with at least one antiplatelet agent, such as aspirin. *Id.* at 2:56–3:6. In some embodiments, the amount of colchicine in the composition is 0.5 mg or 0.6 mg, but the amount of colchicine “will vary

depending upon the host treated and the particular mode of administration.”

Id. at 14:46–49; *see id.* at 2:56–3:6.

Nidorf’s composition may be administered orally, parenterally, by inhalation, or topically as a single dose, multiple doses, or over an established period of time, and the dosage regimen can be adjusted to provide the desired therapeutic or prophylactic response. *Id.* at 13:55–57, 14:49–53. Nidorf states that its composition can be administered with a single dose or up to 10 doses, given once daily or up to 10 times per day, but preferably once per day as a single dose. *Id.* at 15:31–38. Nidorf also explains that its composition can be administered regularly for long periods of time, including from a period of weeks to up to 10 years, depending on the severity of disease, the overall health of the patient, any additional medications the patient is taking, and whether the treatment is prophylactic or not. *Id.* at 15:39–58.

2. Overview of ESC Guidelines (Ex. 1009)

ESC guidelines is titled “2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation.” Ex. 1009, 1. ESC guidelines defines acute myocardial infarction (AMI) as a condition with evidence of myocardial injury (i.e., “an elevation of cardiac troponin values with at least one value above the 99th percentile upper reference limit”) with necrosis consistent with myocardial ischaemia. *Id.* at 6. ESC guidelines provides treatment and management guidance for emergency care of AMI and hospitalization, reperfusion therapy, post-discharge care, and complications. *Id.* at 2–3. ESC guidelines also discusses how to assess the quality of care and areas for future research. *Id.* ESC guidelines was developed by selected experts in the field who “undertook a

comprehensive review of the published evidence for management of [AMI] according to ESC Committee for Practice Guidelines (CPG) policy” and “[a] critical evaluation of diagnostic and therapeutic procedures was performed, including assessment of the risk–benefit ratio.” *Id.* at 5.

3. *Overview of COLCRYS (Ex. 1016)*

COLCRYS is a package insert from “COLCRYSTM (colchicine, USP) tablets for Oral use.” Ex. 1016, 1. COLCRYS states that the tablets are indicated for use to treat gout flares and Familial Mediterranean fever (FMF). *Id.* COLCRYS may be given on a long-term basis for treating FMF, but “the safety and efficacy of repeat treatment in gout flares has not been evaluated.” *Id.* at 2 (emphasis omitted). It is thought that COLCRYS works by “interfer[ing] with the intracellular assembly of the inflammasome complex present in neutrophils and monocytes that mediates activation of interleukin-1 β .” *Id.* at 9.

To treat gout flares, COLCRYS should be administered at a dosage of “1.2 mg (2 tablets) at the first sign of a gout flare followed by 0.6 mg (1 tablet) one hour later.” *Id.* at 1. “The maximum recommended dose for treatment of gout flares is 1.8 mg over a 1 hour period.” *Id.* at 2.

To treat FMF, COLCRYS should be administered at the total daily dose in one or two divided doses and increased or decreased “as indicated and as tolerated in increments of 0.3 mg/day, not to exceed the maximum recommended daily dose.” *Id.* at 1. For adults and children older than 12 years, the daily dosage is 1.2–2.4 mg. *Id.* For children 6 to 12 years, the daily dosage is 0.9–1.8 mg. *Id.* For children 4 to 6 years, the daily dosage is 0.3–1.8 mg. *Id.*

4. *Analysis*

A patent claim is unpatentable under 35 U.S.C. § 103 if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). “An obviousness determination requires finding both ‘that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.’” *CRFD Research, Inc. v. Matal*, 876 F.3d 1330, 1340 (Fed. Cir. 2017) (quoting *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367–1368 (Fed. Cir. 2016)).

a. *Claim 27*

Petitioner contends that claim 27 is unpatentable as obvious over Nidorf, COLCOT protocol, ESC guidelines, and COLCRYST. Pet. 34–35, 44–46. Patent Owner opposes. Prelim. Resp. 23–37.

For the reasons discussed above with respect to claim 27, we determine that Petitioner has shown a reasonable likelihood that claim 27 is anticipated by the COLCOT protocol. *See above* II.D.ii; *see Realtime Data, LLC v. Iancu*, 912 F.3d 1368, 1373 (Fed. Cir. 2019) (“[I]t is well settled that a disclosure that anticipates under § 102 also renders the claim invalid under § 103, for anticipation is the epitome of obviousness.”) (internal quotations and citations omitted).

Furthermore, by treating the same patient population with the same drug – low dose colchicine – we agree with Petitioner that the result of

lowering the risk of stroke is an inherent feature of the treatment method taught in COLCOT protocol. *See Bristol-Myers Squibb Co.*, 246 F.3d at 1376 (“Newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent.”); *see also Prometheus Labs.*, 805 F.3d at 1099–01 (finding that it would have been obvious to treat the claimed subpopulation of irritable bowel syndrome patients based on common practices in the field).

i. Summary

Based upon our review of the parties’ arguments and supporting evidence in the current record, we determine that Petitioner has shown a reasonable likelihood that claim 27 is unpatentable as obvious over the combination of Nidorf, COLCOT protocol, ESC guidelines, and COLCRYS.

b. Claim 1

Petitioner contends that claim 1 is unpatentable as obvious over Nidorf, COLCOT protocol, ESC guidelines, and COLCRYS. Pet. 34–44. Patent Owner opposes. Prelim. Resp. 23–37. Specifically, Patent Owner argues that the Petition fails to address: (a) the removal of a pre-loading dose; (b) applying the claimed method to patients who have already been provided a percutaneous intervention; and (c) administration of colchicine within the first 3 days after an MI. *Id.* at 25–26.

i. A method of treating a patient after having a myocardial infarction (MI)

Petitioner contends that based on the teachings of Nidorf, COLCOT protocol, ESC guidelines, and COLCRYS, a person of ordinary skill in the art at the time the invention was made would have been motivated to start “secondary preventive therapy in post-MI coronary artery disease patients.”

Pet. 34 (citing Ex. 1007; Ex. 1006), 36 (citing Ex. 1007, 20:3–5; Ex. 1049, ¶¶ 68, 145–146).

Nidorf describes adding “0.5 mg/day of colchicine to standard secondary prevention therapies including aspirin and high dose statins reduces the risk of cardiovascular events in patients with objectively diagnosed and clinically stable coronary disease.” Ex. 1007, 18:2–6.

The COLCOT protocol similarly describes treating “[p]atients who have suffered a documented acute myocardial infarction within the last 30 days” with colchicine at a dose of 0.5 mg/day and that those patients “are treated according to the national guidelines and after having completed any planned percutaneous revascularization procedures associated with their initial infarction.” Ex. 1006, 1.

ESG guidelines teaches the management of patients having suffered acute myocardial infarctions. *See generally* Ex. 1009. ESG guidelines include instructions for emergency care and reperfusion therapies. *See* Ex. 1009, 8–24. ESG guidelines also includes instructions for the administration of secondary therapies such as antithrombic therapies including aspirin, dual antiplatelet therapy, beta-blockers, lipid-lowering therapy, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, and mineralocorticoid/aldosterone receptor antagonists. *Id.* at 31–35.

Based upon our review of the parties’ arguments and supporting evidence in the current record, we determine that Petitioner has shown a reasonable likelihood that the combination of Nidorf, COLCOT protocol, and ESC guidelines teach methods for “treating a patient after having a myocardial infarction (MI)” as recited in claim 1.

ii. the method comprising initiating the administration of colchicine at a daily low dose to the patient

Petitioner contends that Nidorf teaches “administering colchicine as secondary preventative therapy for ‘patients with objectively diagnosed and clinically stable coronary disease,’ including patients who had an MI.” Pet. 36 (citing Ex. 1007, 20:3–5; Ex. 1049 ¶¶ 68, 145–146). “COLCOT Protocol also teaches initiating colchicine treatment within 30 days post-MI.” *Id.* (citing Ex. 1006, 1 (targeting “patients after myocardial infarction”); Ex. 1049 ¶¶ 78, 146).

Based upon our review of the parties’ arguments and supporting evidence in the current record, we determine that Petitioner has shown a reasonable likelihood that the combination of Nidorf and COLCOT protocol teach “the administration of colchicine at a daily low dose to the patient” as recited in claim 1.

iii. wherein the colchicine is administered without pre-loading the patient with a higher dose of colchicine before the administration at the daily low dose

Petitioner contends that the prior art teaches low dose colchicine administration without a pre-loading dose. Specifically, Petitioner contends that “Nidorf’s disclosure that LoDoCo administered 0.5 mg/daily colchicine without a preloading dose” and that COLCOT protocol “similarly discloses administering 0.5 mg/daily colchicine without a preloading dose.” Pet. 37 (citing Ex. 1007, 18:18–24; Ex. 1006, 2; Ex. 1049 ¶¶ 143, 146).

Patent Owner argues that the Petition fails to address “the removal of a pre-loading dose.” Prelim. Resp. 25. Patent Owner argues that “the limitation ‘without pre-loading the patient with a higher dose of colchicine’ was critical for overcoming the prior art.” *Id.* at 27 (citing Ex. 1002, 331,

383–87, 396, 398). Patent Owner argues that “Petitioner and its expert, Dr. Ridker, erroneously asserts that the prior art taught low-dose colchicine without a pre-loading dose.” *Id.* at 26, *see also id.* at 28 (a person of ordinary skill in the art “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.)”).

We have reviewed the Nidorf and COLCOT protocols and agree with Petitioner that these protocols do not recite administering a pre-loading dose to the patients. *See* Pet. 37 (citing Ex. 1007, 18:18–24; Ex. 1006, 2; Ex. 1049 ¶¶ 143, 146); Ex. 1049 ¶¶ 44–56, 67. This is supported by Petitioner’s declarant, Dr. Ridker, finding that Nidorf and the COLCOT protocol administer 0.5 mg/day to a patient with no mention of including a pre-loading dose in these protocols. Ex. 1049 ¶¶ 67 (“Nidorf describes the ‘LoDoCo’ trial that ‘assess[ed] the therapeutic effects’ of colchicine in ‘patients with cardiovascular disease’ by administering 0.5 mg/day of colchicine without a preloading dose to patients with clinically stable coronary disease.”)(footnote omitted), 79 (“COLCOT Protocol describes administering a 0.5 mg tablet of colchicine once per day to the patients.”)(footnote omitted), 146.

We are not persuaded by Patent Owner’s argument that Nidorf and COLCOT should be interpreted as necessarily including a pre-loading dose. *See* Prelim. Resp. 27 (“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.”). Just because Patent Owner’s declarant can direct us to references that utilized a pre-loading dose

in their colchicine administration protocols does not persuade us that any other clinical protocol that does not recite such a pre-loading should be interpreted as including such a dose. *See* Ex. 2001 ¶¶ 38 (citing Ex. 2010, Ex. 2008), 56 (citing Ex. 1040; Ex. 2009). At this point in the proceeding there is insufficient evidence in the record to suggest that clinicians routinely *do not* follow clinical protocols, from which to conclude that we should interpret Nidorf and COLCOT protocol as including a pre-loading dose.

Based upon our review of the parties’ arguments and supporting evidence in the current record, we determine that Petitioner has shown a reasonable likelihood that the combination of Nidorf and COLCOT protocol teach the administration of colchicine without a pre-loading dose as recited in claim 1.

iv. within about 3 days of the MI

Petitioner’s declarant acknowledges that Nidorf does not teach initiating the treatment “within about 3 days” of the myocardial infarction. Ex. 1049 ¶ 145. Petitioner’s declarant finds that COLCOT provides a 30-day window in which to start the colchicine therapy, and this would include starting therapy within 3 days of the myocardial infarction. *Id.* Petitioner contends that “[i]nitiation times within this prior art range are presumptively obvious and not overcome here by any unexpected results or evidence of criticality. *E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1006 (Fed. Cir. 2018) (“presumption of obviousness” for values within prior art range).” Pet. 38–39. Petitioner contends that this is supported by “ESC Guidelines teaches initiating secondary preventative therapy at or prior to post-MI hospitalization discharge, corresponding to around day 2 or 3 post-MI.” Pet. 39 (citing Ex. 1009, 24, 30, 33; Ex. 1049 ¶ 159) (footnote

omitted). Petitioner contends “that initiating treatment in stabilized post-MI patient at or before hospitalization discharge would potentially provide increased compliance and earlier prevention of secondary cardiovascular events.” Pet. 42 (citing Ex. 1009, 33; Ex. 1008, 6; Ex. 1049 ¶ 171).

Patent Owner contends that Petitioner did not explain why a person of ordinary skill in the art at the time the invention was made “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.” Prelim. Resp. 33–34. Patent Owner contends that Petitioner presented only conclusory arguments with respect to the start of colchicine treatment and provides no evidence why early treatment, such as 3 days after a myocardial infarction would have been effective. *See id.* at 34–35 (citing Ex. 2001 ¶¶ 45–49).

Here, Petitioner provides an adequate showing that COLCOT protocol suggests treating patients within 30 days of the myocardial infarction, and this would include treating patient within 3 days of the event. *See* Pet. 38–41; *see* Ex. 1006, 1 (“Patients who have suffered a documented acute myocardial infarction within the last 30 days, are treated according to the national guidelines and after having completed any planned percutaneous revascularization procedures associated with their initial infarction will receive either colchicine (0.5 mg per day).”). COLCOT protocol inclusion criteria requires that the patient have a documented myocardial infarction and treatment needs to start before 30 days has elapsed. *See* Ex. 1006, 1. The range for administration of colchicine in the COLCOT protocol, therefore, is reasonably interpreted to be from day 0 through day 30. *Id.*; Ex. 1049 ¶ 150.

We find no error with Petitioner’s interpretation that COLCOT protocol teaches a range for starting colchicine administration. *See* Pet. 38–39.

Petitioner further supports the position for the early administration of secondary preventative therapies with the declaration by Dr. Ridker. *See* Pet. 39–40; Ex. 1049 ¶¶ 147–153. Petitioner’s declarant avers that “[i]n my experience, a 3-day post-MI hospitalization stay was common in 2019 as it is today. Consistent with common medical practice . . . that pre-discharge management included the administration of secondary preventive therapy (in particular statins, which had been approved for this indication) to ‘increase patient adherence after discharge’ and provide ‘early and sustained clinical benefits.’” Ex. 1049 ¶ 148 (citing Ex. 1009, 24 (“A short hospital stay implies limited time for proper patient education and up-titration of secondary prevention treatments.”), 33 (“Therefore, statins are recommended in all patients with AMI . . . Lipid-lowering treatment should be started as early as possible, as this increases patient adherence after discharge, and given as high-intensity treatment, as this is associated with early and sustained clinical benefits.”) (footnote omitted). Petitioner’s declarant further avers that before 2019, multiple other clinical trials initiating low dose colchicine in MI patients early post-MI had been already registered, initiated, or completed. Ex. 1049 ¶ 49.

Based upon our review of the parties’ arguments and supporting evidence in the current record, we determine that Petitioner has shown a reasonable likelihood that the combination of Nidorf and COLCOT protocol teach the administration of colchicine within 0–30 days of the myocardial infarction, thereby overlapping with the administration between 0–3 day of the myocardial infarction as recited in claim 1.

v. *wherein percutaneous coronary intervention was performed for treating the patient's MI.*

Petitioner contends that a patient population including those that had received percutaneous coronary intervention (PCI) is taught by COLCOT protocol. Pet. 37 (citing Ex. 1006, 2, 5; Ex. 1049 ¶¶ 23, 78).

Patent Owner contends that “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.” Prelim. Resp. 31 (citing *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)).

Here, COLCOT protocol discloses that the relevant patient population includes patients that had received percutaneous coronary intervention (PCI) therapy. COLCOT protocol describes the patient population as “[p]atients who have suffered a documented acute myocardial infarction within the last 30 days, are treated according to the national guidelines *and* after having completed any planned percutaneous revascularization procedures associated with their initial infarction will receive . . . colchicine (0.5 mg per day) . . . for an estimated 2 year[] period.” Ex. 1006, 1 (emphasis added). COLCOT protocol, therefore, discloses a genus of patients having experienced a myocardial infarction, and further identifies a subgroup (species) of patients that have had myocardial infarction *and* have received percutaneous coronary intervention (PCI) therapy. COLCOT protocol discloses that both populations are treated the same way – they are

administered 0.5 mg/day of colchicine starting within 30-days of the myocardial infarction.

In *In re Petering*, our reviewing court found that in some circumstances species claims were unpatentable over prior art that was directed to a genus:

It is our opinion that one skilled in this art would, on reading the [prior] patent, *at once envisage each member of this limited class*, even though this skilled person might not at once define in his mind the formal boundaries of the class as we have done here . . . [W]e think that one with ordinary skill in this art, with . . . [the reference genus patent] before him, *would also have before him those subspecies*.

In re Petering, 301 F.2d 676, 681–82 (1962) (emphases added). “[T]he question under 35 USC 103 is not merely what the references expressly teach but what they would have suggested to one of ordinary skill in the art at the time the invention was made.” *Merck & Co. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989).

Here, the COLCOT protocol teaches treating patient having had a myocardial infarction by administering 0.5 mg/day of colchicine starting within 30-days of the myocardial infarction, and it does not treat patients that received percutaneous coronary intervention (PCI) therapy differently from those that did not get PCI treatment. The method disclosed in the COLCOT protocol, therefore, administers colchicine the same way regardless of whether the patient did or did not undergo a percutaneous revascularization procedure.

Based upon our review of the parties’ arguments and supporting evidence in the current record, we determine that Petitioner has shown a reasonable likelihood that COLCOT protocol teach the administration of

colchicine to patients that have had a documented myocardial infarction and endured percutaneous revascularization procedure, and thereby encompasses this limitation of claim 1.

vi. Summary

Based upon our review of the parties' arguments and supporting evidence in the current record, we determine that Petitioner has shown a reasonable likelihood that claim 1 is unpatentable as obvious over the combination of Nidorf, COLCOT Protocol, ESC Guidelines, and COLCRYS.

c. Claim 8

Petitioner contends that claim 8 is unpatentable as obvious over Nidorf, COLCOT protocol, ESC guidelines, and COLCRYS. Pet. 34–44. Patent Owner opposes. Prelim. Resp. 23–37.

i. A method of treating a patient after having a myocardial infarction (MI),

Based upon our review of the parties' arguments and supporting evidence in the current record in conjunction with the reasons discussed above (*see* § II.E.4.b.i), we determine that Petitioner has shown a reasonable likelihood that the combination of Nidorf, COLCOT protocol, and ESC guidelines teach “[a] method of treating a patient after having a myocardial infarction (MI)” as recited in claim 8.

ii. the method comprising initiating the administration of colchicine at a daily low dose to the patient

Based upon our review of the parties' arguments and supporting evidence in the current record in conjunction with the reasons discussed above (*see* § II.E.4.b.ii), we determine that Petitioner has shown a

reasonable likelihood that the combination of Nidorf and COLCOT protocol teach a “method comprising initiating the administration of colchicine at a daily low dose to the patient” as recited in claim 8.

- iii. wherein the colchicine is administered without pre-loading the patient with a higher dose of colchicine before the administration at the daily low dose,*

Based upon our review of the parties’ arguments and supporting evidence in the current record in conjunction with the reasons discussed above (*see* § II.E.4.b.iii), we determine that Petitioner has shown a reasonable likelihood that the combination of Nidorf and COLCOT protocol teach the administration of colchicine without a pre-loading dose as recited in claim 8.

- iv. within about 3 days of the MI*

Based upon our review of the parties’ arguments and supporting evidence in the current record in conjunction with the reasons discussed above (*see* § II.E.4.b.iv), we determine that Petitioner has shown a reasonable likelihood that the combination of Nidorf and COLCOT protocol teach the administration of colchicine within 0–30 days of the myocardial infarction, thereby overlapping with the administration between 0–3 day of the myocardial infarction as recited in claim 8.

- v. wherein the patient is at a lower risk of a cardiovascular event, relative to a patient not being administered colchicine*

For the reason discussed above (*see* § II.A.3), at this stage of the proceeding, we find that the wherein clause “wherein the patient is at a lower risk of a cardiovascular event, relative to a patient not being administered colchicine” of claim 8 is not limiting because it simply

expresses the intended result of the positively recited method step within the body of the claim.

The method steps are preformed the same way whether or not the patient experiences a lower risk of a cardiovascular event. *See, e.g., In re Hiraio*, 535 F.2d at 70 (“the preamble merely recites the purpose of the process; the remainder of the claim . . . does not depend on the preamble for completeness, and the process steps are able to stand alone.”)

We have reviewed the parties’ contentions, and determine at this stage of the proceedings that Petitioner has provided a requisite showing that this third clause merely describes the benefit of the administration of colchicine to the identified patient population. This “wherein clause,” therefore, merely defines the result of the positively recited method step of administering colchicine to patients after suffering MI. *See* Pet. 23; *see, e.g., Minton*, 336 F.3d at 1381 (a “whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.”).

Based upon our review of the parties’ arguments and supporting evidence in the current proceeding, we determine that Petitioner has shown a reasonable likelihood that the combination of Nidorf and COLCOT protocol teach the recited purpose “the patient is at a lower risk of a cardiovascular event, relative to a patient not being administered colchicine” as recited in claim 8.

- vi. *wherein the cardiovascular event is resuscitated cardiac arrest, stroke, or urgent hospitalization for angina requiring coronary revascularization.*

Petitioner contends that Nidorf teaches this limitation. Pet. 37–38 (citing Ex. 1007, 18:31–34, 18:65–67, 19: 6–14, 19:55–59, 19:63–64; Ex. 1049 ¶¶ 28, 39, 68, 69, 143).

Patent Owner contends that the art does not provide motivation to administer colchicine to patients that have already been provided a percutaneous intervention. *See* Prelim. Resp. 31–33.

Nidorf teaches that “[t]his trial demonstrates that the addition of colchicine 0.5 mg/day to standard therapy in patients with stable coronary disease significantly reduces the risk of a cardiovascular event, including an ACS, out of hospital cardiac arrest and non-cardio-embolic ischemic stroke.” Ex. 1007, 21:55–59, *see id.* at 22:12–24 (claims 1–3).

An acute coronary syndrome (ACS) was defined as either (a) Acute Myocardial Infarction (AMI), as evidenced by acute ischemic chest pain associated with a rise in serum troponin above the upper limit of normal or (b) Unstable Angina (UA), as evidenced by a recent acceleration of the patient’s angina unassociated with a rise in serum troponin but associated with angiographic evidence of a change in the patient’s coronary anatomy.

Ex. 1007, 19:6–14.

COLCOT protocol teaches administration of 0.5 mg colchicine per day to patients that suffered an MI “and after having completed any planned percutaneous revascularization procedures associated with their initial infarction.” Ex. 1006, 1.

Based upon our review of the parties’ arguments and supporting evidence in the current record, we determine that Petitioner has shown a

reasonable likelihood that at least the combination of Nidorf and COLCOT protocol teaches treating patients with the identified cardiovascular event as encompassed by claim 8.

vii. Summary

Based upon our review of the parties' arguments and supporting evidence in the current record, we determine that Petitioner has shown a reasonable likelihood that claim 8 is unpatentable as obvious over Nidorf, COLCOT protocol, ESC guidelines, and COLCRYS.

d. Claims 2–7, 9–26, and 28–50

Claims 2–7, 9–26, and 28–50 depend directly or indirectly from claim 1, claim 8, or claim 27. Ex. 1001, 41:37–49, 41:61–42:32, 42:37–43:20. Petitioner provides citations in Nidorf, COLCOT protocol, ESC guidelines, and COLCRYS where each of dependent claims 2–7, 9–26, and 28–50 are disclosed by the references. Pet. 46–54. Petitioner supports its assertions with the testimony of Dr. Ridker. *Id.* (citing Ex. 1049, ¶¶ 181–216). Patent Owner argues the claims as a group and does not provide arguments for the dependent claims separate from the independent claims discussed above. Prelim. Resp. 23–37.

We are persuaded, for the reasons stated in the Petition, which findings we adopt as our own for the purpose of institution, that Petitioner's arguments and evidence have established a reasonable likelihood that each limitation of claims 2–7, 9–26, and 28–50 are unpatentable as obvious over Nidorf, COLCOT protocol, ESC guidelines, and COLCRYS. *See* Pet. 46–54.

e. *Summary*

Based upon our review of the parties' arguments and supporting evidence in the current record, we determine that Petitioner has shown a reasonable likelihood that claims 1–50 are unpatentable as obvious over the combination of Nidorf, COLCOT protocol, ESC guidelines, and COLCRYS.

F. *Anticipation by Bouabdallaoui*

Petitioner contends that claims 1–13, 17–26, 28, 40–46, 49, and 50 are unpatentable as anticipated by Bouabdallaoui. Pet. 24–29. Patent Owner opposes asserting that Bouabdallaoui is not prior art. Prelim. Resp. 3–8, 22–23, 39–40; *see generally* Sur-reply. Petitioner disagrees. *See generally* Reply.

1. *Overview of Bouabdallaoui (Ex. 1005)*

Bouabdallaoui is a journal article titled “Time-to-treatment initiation of colchicine and cardiovascular outcomes after myocardial infarction in the Colchicine Cardiovascular Outcomes Trial (COLCOT).” Ex. 1005, 1. Bouabdallaoui lists the inventor of the '063 patent, Jean-Claude Tardif, as the second author of the article. *Id.* Bouabdallaoui relates to building on the results of the COLCOT protocol “to determine whether time-to-treatment initiation (TTI) influences the beneficial impact of colchicine” administered after MI. *Id.*

According to Bouabdallaoui, “[m]yocardial infarction (MI) is associated with an acute exacerbation of cardiovascular (CV) inflammation superimposed on the chronic atherosclerosis-related inflammatory process.” *Id.* at 2 (footnote omitted). Bouabdallaoui reports that “[c]olchicine is an inexpensive, orally administered, potent anti-inflammatory medication”

shown to significantly reduce the risk of ischaemic CV events by 23% compared with placebo when given daily at a dose of 0.5 mg within the first 30 days after MI in COLCOT. *Id.*

In Bouabdallaoui’s study, the COLCOT data were reassessed using three different cut-offs for TTI (0–3 days post-MI, 4–7 days post-MI, and 8–30 days post-MI) to determine the association between early initiation of colchicine therapy and clinical outcomes. *Id.* at 2–3. The authors found that compared to placebo, “early initiation of low-dose colchicine within the first 3 days after MI is associated with a reduction of 48% in the risk of the primary endpoint consisting of a composite of CV death, resuscitated cardiac arrest, MI, stroke, or urgent hospitalization for angina requiring coronary revascularization.” *Id.* at 5. The authors also found that “[t]he secondary efficacy endpoint consisting of a composite of CV death, resuscitated cardiac arrest, MI, or stroke was also significantly reduced by 45% with early initiation of low-dose colchicine,” and “[t]he benefits were more marked when treatment was initiated within the first 3 days after MI, as compared with between Days 4 and 30, supporting the strategy of in-hospital initiation of colchicine in order to improve CV outcomes post-MI.” *Id.*

2. Analysis

a. Prior art status of Bouabdallaoui

Petitioner contends that claims 1-26, 28, and 40-50 of the ’063 patent are not entitled to an effective filing date earlier than November 13, 2020. Pet. 19. Specifically, Petitioner contends that the limitation of administering colchicine “within about 3 days of the MI” (claims 1–26 and 40–50) or “within 4 to 7 days of the MI” (claim 28) are not described in the ’988 provisional application of October 20, 2020, or the ’865 provisional

application of November 15, 2019. *Id.* Petitioner, therefore, asserts that Bouabdallaoui is available prior art to claims 1–26, 28, and 40–50. *See* Pet. 24, 54.

Patent Owner asserts that “[t]he ’063 patent is entitled to a priority date of November 15, 2019.” Prelim. Resp. 3.

The ’063 patent claims priority to Provisional Application No. 63/093,988 (“the ’988 provisional application”), filed on October 20, 2020 and Provisional Application No. 62/935,865 (“the ’865 provisional application”), filed on November 15, 2019. Ex. 1001, code (60). We have reviewed these provisional applications and agree with Petitioner that the “within about 3 days of the MI” limitation as recited in independent claims 1 and 8 is not readily apparent from the disclosure of the ’998 and ’865 provisional applications.

Claims found in a later-filed application are entitled to the filing date of an earlier application if, inter alia, the disclosure in the earlier application provides an adequate written description of the later-filed claims under 35 U.S.C. § 112, first paragraph. *See Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1158 (Fed. Cir. 1998) (discussing requirements of claiming benefit of priority date of earlier application under 35 U.S.C. § 120). “[A] claim complies with 35 U.S.C. § 120 and acquires an earlier filing date if, and only if, it could have been added to an earlier application without introducing new matter.” *Studiengesellschaft Kohle M.B.H. v. Shell Oil Co.*, 112 F.3d 1561, 1564 (Fed. Cir. 1997).

The ’063 patent describes that the “method includes administering colchicine *within 3 days* of the myocardial infarction (for example, at 1 day or 2 days).” Ex. 1001, 4:12–14 (emphasis added), *see also* 4:6–12

(describing “within 5 days of the myocardial infarction (for example, at 1 day, 2 days, 3 days, or 4 days) . . . within 4 days of the myocardial infarction (for example, at 1 day, 2 days, or 3 days).” In another part, the ’063 patent describes that the method includes “the administration of colchicine at a daily low dose to the patient *within about 3 days* (e.g., 1 day, 2 days, and 3 days) of the MI.” Ex. 1001, 5:37–39 (emphasis added). Therefore, when the range in the ’063 patent is defined to be “within” a particular numerical value the end points are not included, on the other hand when a range is defined to be “within about” a particular numerical value the end point is included. Based on these disclosures in the ’063 patent “within about 3 days” would encompass administration of colchicine up to day 3 after the initial myocardial infarction but this range would not encompass a time point beyond day 3. This is consistent with our interpretation above (*see* §§ II.E.b.iv and II.E.C.iv) the limitation of “within about 3 days of the MI” is reasonably construed to mean a range from 0–3 days but would not extend beyond 3 days.

The ’865 provisional application describes that “the method involves administering colchicine within 5, 10, 15, 20, or 25 days of the MI.” Ex. 1004, 2:32–33, *see also id.* at 9 (Table 1 – Patients were enrolled a mean 13.4 ± 10.2 days after myocardial infarction). The disclosure “within 5 days” means administration of colchicine at 1 day, 2 days, 3 days, or 4 days, but would not encompass day 5. Given these disclosures in the ’865 provisional application, there appears to be support for a range of up to 30 days, 10 days, 5 days and possibly up to 3.2 days by way of the experimental data table. *See* Ex. 1004, 9 (Table 1). Administration at 3.2 days is beyond day 3 and is, thereby, not encompassed within the meaning of “within about 3 days” as

disclosed in the '063 patent. The '865 provisional application also does not provide a reason to select administration within about 3 days (i.e. at days 1, 2, or 3) or the specific range of with 4–7 days.

The Federal Circuit has explained that “[t]he disclosure of a broad range of values does not by itself provide written description support for a particular value within that range.” *General Hospital Corp. v. Sienna Biopharms. Inc.*, 888 F.3d 1368, 1372 (Fed. Cir. 2018) (quoting *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000) (allows “one skilled in the art . . . [to] ‘immediately discern the limitation at issue in the claims.’)). We agree with Petitioner at this stage of the proceeding, that the '865 provisional application does not appear to provide sufficient blaze marks from which to pick the discrete values presently claimed – “within about 3 days of the MI” (claims 1-26 and 40-50) or “within 4 to 7 days of the MI” (claim 28). *See id.* at 1326 (“one cannot disclose a forest in the original application, and then later pick a tree out of the forest and say here is my invention.”).

Next, Patent Owner asserts that Bouabdallaoui “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.” Prelim. Resp. 1. “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.” *Id.* at 39. Specifically, Patent Owner contends that “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).” *Id.*

Patent Owner asserts “that the main and corresponding author of Bouabdallaoui is Dr. Tardif, the named inventor of the '063 patent.” Prelim. Resp. 3. “Dr. Tardif conceived of the COLCOT study to investigate his idea regarding early intervention with colchicine for specific patients that had experienced myocardial infarction. . . . Dr. Tardif drafted the COLCOT study protocol, obtained the funding for the study, and was the study's primary principal investigator.” *Id.* at 7 (citing Ex. 2011 ¶¶ 16–18), *see also id.* at 39. “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.” *Id.* at 5–6 (citing Ex. 2011 ¶¶ 19, 20 27, 28). “The other authors worked under the direction of Dr. Tardif 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.” *Id.* at 8.

In the Reply, Petitioner contends that “Patent Owner provides no evidence from any other co-authors disclaiming contribution to the relevant subject matter.” Reply 2–3 (citing MPEP § 2153). Specifically, Petitioner contends that Patent Owner has not provided supporting information from Dr. Bouabdallaoui to support the position that they were working under the direction of Dr. Tardif. *Id.* at 3. “Most notably, Dr. Tardif only contends that he was the ‘primary author’ not the sole author.” *Id.* at 3 (citing Ex. 2011 ¶¶ 28 (“The data generated from the clinical study that was included in Bouabdallaoui was collected, provided to me, and was analyzed at my direction.”), 29 (“The co-authors of Bouabdallaoui had the complete

information regarding the results of the COLCOT study only because I provided it to them.”)).

Patent Owner responds that “Petitioner falsely claims Bouabdallaoui is the ‘lead’ author (as opposed to the first-named one), the article clearly lists Dr. Tardif as the corresponding author.” Sur-reply 2. Furthermore, Patent Owner contends that “[t]he COLCOT protocol lists Dr. Tardif as the sole principal investigator. As the principal investigator, Dr. Tardif was responsible for conducting the study and its results that underly Bouabdallaoui.” *Id.* Dr. Tardif also provided “[t]he clinic agreements [that] make clear that MHI and Dr. Tardif are responsible for the overall conduct of the study and compiling the data, and own the data and associated IP and control any publication rights.” *Id.* at 4 (citing Ex. 2012–2015). Finally, Dr. Tardif’s use of “the services of a statistician to perform statistical analyses that yielded surprising results does not make the statistician an inventor.” Sur-reply 5. “One that is following directions is merely a technician, not an inventor.” *Id.* (citing *Mattor v. Coolegem*, 530 F.2d 1391, 1395 (CCPA 1976)).

The relevant language of 35 U.S.C. § 102 reads as follows:

(a) NOVELTY; PRIOR ART.—A person shall be entitled to a patent unless—

(1) the claimed invention was patented, *described in a printed publication*, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention; or

* * *

(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.

35 U.S.C. § 102 (emphasis added).

“[A]uthorship of an article by itself does not raise a presumption of inventorship with respect to the subject matter disclosed in the article.” *In re Katz*, 687 F.2d 450, 455 (1982). There is nothing in Bouabdallaoui that states that the reference is describing the sole work of Dr. Tardif, therefore, there is some ambiguity created with the reference. Although the submission, of disclaiming affidavits or declarations co-authors would be ideal, they are not required by the statute or Rule 132. *See id.*

The issue presented is whether the declaration submitted by Dr. Tardif (Ex. 2011) provides sufficient information that allows us to conclude that the Bouabdallaoui reference is not “by another.” Dr. Tardif avers that COLCOT protocol was a large-scale clinical study, that required recruitment of many different facilities that ultimately entered into an agreement with Montreal Heart Institute (MHI). Ex. 2011 ¶ 19. “These agreements show that the

investigators were part of the multi-site study, and that MHI had overall supervision and responsibility for the COLCOT study.” *Id.* (citing Ex. 2012–2015).

Exhibits 2012–2015 each disclose an agreement for a clinical research study entitled Colchicine Cardiovascular Outcomes Trial (COLCOT) sponsored by the Montreal Heart Institute. *See* Ex. 2012, 1; Ex. 2013, 2; Ex. 2014, 1; Ex. 2015, 1. A review of these exhibits identifies the Montreal Heart Institute as the sponsor but does not otherwise identify Dr. Tardif as the principal investigator. *See generally* Ex. 2012–2015. Bouabdallaoui lists 18 clinical centers in addition to the Montreal Heart Institute, however, Exhibits 2012–2015 provide the agreements for only 4 of the listed centers. *Compare* Ex. 1005, 1 *with* Ex. 2012–2015.

We recognize that the Bouabdallaoui reference lists Dr. Tardif as the corresponding author. Ex. 1005, 1; *see* Sur-reply 3 (“it is well understood in the industry that a ‘corresponding author’ is the individual that is responsible for the article, speaks on behalf of the other authors, and is responsible for edits, agreements, and publishing the article. (EX2011, ¶27.) This is corroborated by Dr. Ardehali. (EX2001, ¶¶30-31.)”). A corresponding author may well be responsible for communication between the authors and the journal publication. However, listing of a corresponding author in reference, without more, does not sufficiently persuade us that Dr. Tardif is the sole inventor of the subject matter described in the reference.

The Bouabdallaoui reference lists a total of 7 authors that are associate with the Montreal Heart Institute. Dr. Tardif in his declaration only explains his relationship with one of those authors –Dr. Bouabdallaoui. *See* Ex. 2011 ¶¶ 28, 29. Dr. Tardif explains that “Dr. Bouabdallaoui was

relatively early in her career and I had her listed as the first author on the publication to acknowledge her assistance in conducting the trial as well as to provide a ‘first author’ publication for her CV.” *Id.* ¶ 29. Being early in one’s career does not sufficiently persuade us that Dr. Bouabdallaoui did not contribute to the invention.

Dr. Tardif also explains the work relationship with Marie-Claude Guertin. “I . . . instructed Marie-Claude Guertin, a statistician employed by MHICC with whom I had worked in the past, to perform a data analysis at my direction and to report the results to me.” Ex. 2011 ¶ 20. This explanation in the declaration appears to sufficiently support Patent Owner’s position that Marie-Claude Guertin was working as a technician for Dr. Tardif and reasonably not be considered an inventor to the ’063 patent.

Based upon our review of the parties’ arguments and supporting evidence in the current record, we determine that the issue whether the Bouabdallaoui reference *is* or *is not* the work “by another” will benefit from development during trial.

b. *Claims 1–13, 17–26, 28, 40–46, 49, and 50*

Petitioner provides citations in the Petition where each of the claimed elements are disclosed by the Bouabdallaoui reference. Pet. 24–29, 54. Petitioner supports its assertions with the testimony of Dr. Ridker. *Id.* (citing Ex. 1049 ¶¶ 109–122). Patent Owner argues the claims as a group and does not provide arguments for the dependent claims separate from those discussed above. Prelim. Resp. 2–8, 22–23.

Based upon our review of the parties’ arguments and supporting evidence in the current record, we determine that *if* Bouabdallaoui qualifies as prior art as argued by Petitioner, then we are persuaded, for the reasons

stated in the Petition, which findings we adopt as our own for the purpose of institution, that Petitioner's arguments and evidence have established a reasonable likelihood that each limitation of claims 1–13, 17–26, 28, 40–46, 49, and 50 are anticipated by Bouabdallaoui. *See* Pet. 27–29.

G. Obviousness over Bouabdallaoui and COLCRYS

Petitioner contends that claims 1–26, 28, and 40–50 are unpatentable as obvious over Bouabdallaoui and COLCRYS for the same reasons discussed above (*see* § II.F.1.a). Pet. 54. Patent Owner opposes. Prelim. Resp. 23–25, 37–38.

Based upon our review of the parties' arguments and supporting evidence in the current record, we determine that *if* Bouabdallaoui qualifies as prior art as argued by Petitioner, then we are persuaded, for the reasons stated in the Petition, which findings we adopt as our own for the purpose of institution, that Petitioner's arguments and evidence have established a reasonable likelihood that each limitation of claims 1–26, 28, and 40–50 are unpatentable as obvious over Bouabdallaoui and COLCRYS. *See* Pet. 54.

III. CONCLUSION

After considering the evidence and arguments presented in the current record, we determine that Petitioner has demonstrated a reasonable likelihood of success in proving that at least one challenged claim of the '063 patent is unpatentable. We therefore institute trial on all challenged claims under all the grounds raised in the Petition. *See PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018) (indicating that a decision whether to institute an *inter partes* review "require[s] a simple yes-or-no institution choice respecting a petition, embracing all challenges included in

the petition.”); 37 C.F.R. § 42.108. At this stage of the proceeding, we have not made a final determination with respect to claim construction or the patentability of any of the challenged claims.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review of claims 1–50 of the ’063 patent is instituted with respect to all grounds set forth in the Petition; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial commencing on the entry date of this Decision.

IPR2023-01064
Patent 11,400,063 B2

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