

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MURRAY & POOLE ENTERPRISES LTD.,

Petitioner,

v.

INSTITUT DE CARDIOLOGIE DE MONTREAL,

Patent Owner.

Case IPR2023-01064

Patent 11,400,063

PATENT OWNER'S SUR-REPLY

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I. INTRODUCTION

Petitioner's continued attack on Dr. Tardif's groundbreaking work is a distraction that has no impact on the validity of the '063 patent. MHI produced corroborating declarations of Dr. Tardif's sole inventorship claim, which were further confirmed at Dr. Tardif and Dr. Bouabdallaoui's depositions.¹ Moreover, even if Petitioner could meet its high burden to show that Dr. Bouabdallaoui is an inventor, Patent Owner can correct inventorship, meaning EX1005 would still not qualify as prior art. Thus, even if Petitioner "succeeds" with their spurious invalidity theory, grounds 1 and 4 will ultimately fail.

Petitioner's Reply Brief and corresponding exhibits fail to show EX1006 (the COLCOT Protocol) is prior art. Rather than address the discrepancy between Petitioner's claims and the FDA website, Petitioner uses a new expert to rehash the same positions offered by librarian Cruitt. Further, EX1006 fails to disclose the key stroke-reduction and efficacy claim limitations, which gives life and vitality to the claims. Indeed, Petitioner's expert, Dr. Ridker, opined that POSAs would not rely on an FDA website summary of a study protocol, and he himself would have used a

¹ Although Petitioner informed the Board that these witnesses and depositions are critical, Petitioner did not even use half of their permitted time with either witness. EX1050 at 6:7-21, 9:10-19.

different publication. Additionally, EX1006 does not inherently disclose stroke reduction, and Petitioner's inherency position would have far-reaching policy ramifications that would eviscerate countless critical life science patents. Accordingly, ground 2 fails.

Petitioner's ground 3 analysis fails because it ignores relevant prior art that teaches away, and hand-selects references to force-fit them into its hindsight driven conclusions. Assessment of relevant prior art as a whole shows that this field was rife with unpredictability, which would not have sufficiently motivated a POSA with a reasonable expectation of success in reducing the risk of stroke or other CV events by initiating low-dose colchicine treatment within the recited days after MI. MHI has also shown that the '063 patent is nonobvious in view of unexpected results and skepticism of others. Rather than address these core issues, Petitioner focuses on a faux Section 112 analysis, alleging that the data supporting the '063 patent and published in EX1005 are a biological implausibility.

As explained herein, Petitioner has failed to meet its burden to show invalidity of the '063 patent and MHI respectfully requests the Board uphold the validity of the life-saving treatments claimed in the '063 patent.

II. EX1005 IS NOT PRIOR ART

Petitioner alleges that claims 1-26, 28, and 40-50 are anticipated by EX1005 (the Bouabdallaoui reference) or obvious over EX1005 in view of EX1016 (the

COLCRYST label), but EX1005 is not prior art as it is the inventor's own disclosure and published after the priority date. Petitioner has conceded the '063 patent is entitled to a priority date of November 15, 2019, which is more than one year before the August 2020 publication date of EX1005, and thus fails to qualify as prior art on this ground alone.² Petitioner's argument requires both that (1) the '063 patent has a priority date of November 2020 and (2) EX1005 is not the work of Dr. Tardif. *See* Reply at II. If, despite Petitioner's concession, the Board finds a later priority date applies, there is no dispute that Dr. Tardif at the very least conceived of the claimed invention and conceived of and directed the study that is described in EX1005. There is, therefore, no credible argument that EX1005 does not describe Dr. Tardif's work and was published within one year of the latest possible priority.

Petitioner alleges that EX1005 somehow includes the work of Dr. Bouabdallaoui but fails to identify what inventive contribution she made to the claims of the '063 patent. While no evidence supports naming Dr. Bouabdallaoui as an inventor, inventorship can be corrected, if necessary, under 35 U.S.C. § 256, and EX1005 would still remain the work of an inventor published within the one-year

² As discussed below, Petitioner's objections are based, *inter alia*, on a November 2019 priority date for the '063 patent.

grace period. Accordingly, regardless of the Board’s findings for inventorship, EX1005 cannot be prior art.

A. ’063 Claims 1, 8, and 28 Are Entitled to November 2019 Priority

The time-to-treatment (“TTI”) initiation limitations of claims 1, 8, and 28 are sufficiently described in the 2019 provisional application that is the basis for the priority date for the ’063 patent. *See* EX1004 and EX2067. The initiation time ranges claimed in the ’063 patent wholly overlap with those recited in claims 1, 8, and 28. EX1004 at 2:32-33; EX2067, 1; EX1001, cls. 1, 8, 28. As mentioned, Petitioner has conceded that the ’063 patent is entitled to its November 2019 priority date. Paper 23 at ¶ 24 (alleging EX2070, which was published the same day in 2020 as EX1005, is not prior art because it was published “after the priority date”).

The ’063 patent claims priority to the ’865 provisional application under 35 U.S.C. § 119(e). Petitioner’s reliance on *Baird* makes clear that the only challenge to the ’063 patent’s priority claim to the ’865 provisional application is pursuant to the requirements set forth in MPEP § 211.05. However, the facts of *Baird* are inapposite here, and Petitioner’s analysis fails to consider more relevant Federal Circuit case law.

A patentee is entitled to the priority of an earlier-filed provisional if “the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing

date.” *Merck Sharp & Dohme Corp. v. Microspherix LLC*, 814 Fed.Appx. 575, 579-580 (Fed. Cir. 2020) (quoting *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010)). Here, like in *Merck*, the provisional application disclosed ranges, and a POSA would understand that the description in the ’865 provisional application of “within 5 days” and “within 10 days” adequately supports “within about 3 days” and “within 4 to 7 days.” *Id.* at 580 (finding that disclosure of strands of 2-10 mm, 4-6 mm, and “a plurality of spacers between 0.5 mm and 50 mm” supported claims without specified strand length).

Indeed, contrary to Petitioner’s mischaracterization of Dr. Tardif’s testimony, he explained that his TTI idea arose “[a]fter... the results of... the main result of COLLOT.” EX1077 at 37:13-18. The results of COLCOT were available to Dr. Tardif and his team before November 15, 2019. *Id.* at 24:13-25:5, 51:3-11; EX1022 at 2 (“This article was published on November 16, 2019 at NEJM.org.”). Tellingly, Petitioner asserts no date for when it contends the TTI was conceived.

Moreover, Petitioner’s spurious blaze marks theory is contrary to the patent specification, which sufficiently shows possession of the claimed invention. The Board correctly found that “within 5 days” means at days 1, 2, 3, and 4, but not day 5. Thus, the ’865 provisional’s disclosure recites only one day longer than claims 1 and 8 of the ’063 patent. Paper 9 at 50. Moreover the ’865 provisional explicitly discloses treatment initiation of at least 3.2 days. EX1004 at Table 1 (showing 3.2

days after MI as within one standard deviation of the mean). Far from the forest described by Petitioner, the '865 provisional discloses four trees and the patent claims three of those trees—a well bounded limit within which a POSA could readily discern the limitation. *Compare GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, 744 F.3d 725, 731 (Fed. Cir. 2014) (finding written description where claim term does not assert coverage of yet-identified ways of achieving the desired claim result) *with Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1326-27 (Fed. Cir. 2000) (finding no written description where specification discloses calculating a ratio and provides conflicting data regarding that calculation).

Moreover, it is undisputed that the COLCOT study had a prospective endpoint of colchicine effectiveness in patients initiated within 30 days after MI. *See, e.g.*, EX1022. Nevertheless, after reviewing the results, Dr. Tardif chose to claim TTI of shorter times, including within 5 days, recognizing the shorter time frame as preferable. EX1004; EX2067. The use of the shorter time frames compared to the endpoint of 30 days clearly show that Dr. Tardif had conceived the claimed invention.

Thus, the '063 patent is properly entitled to a priority date of November 15, 2019 from the '865 provisional application.

B. Dr. Tardif Is the Sole Inventor of the '063 Patent

Petitioner here, makes a strikingly unusual demand by asking the Board to find that an individual expressly *disavowing* inventorship, must actually be a named inventor. Historically, inventorship issues arise when an unnamed inventor seeks to be named. Nonetheless, Petitioner has failed to show that Dr. Tardif is not the sole inventor of the '063 patent.

“Because a patent is presumed valid under 35 U.S.C. § 282, there follows a presumption that the named inventors on a patent are the true and only inventors.” *Gemstar-TV Guide Int’l, Inc. v. Int’l Trade Comm’n*, 383 F.3d 1352, 1381 (Fed. Cir. 2004). Rebutting this presumption requires “clear and convincing evidence that the alleged unnamed inventor was in fact a coinventor before correcting inventorship under 35 U.S.C. § 256.” *Caterpillar Inc. v. Sturman Indus., Inc.*, 387 F.3d 1358, 1377 (Fed. Cir. 2004). Similarly, determining “[w]hether a reference is a work of others for the purposes of § 102(a) is, like that of inventorship, a question of law based on underlying facts.” *Allergan, Inc. v. Apotex Inc.*, 754 F.3d 952, 969 (Fed. Cir. 2014).

Petitioner alleges that it satisfied its burden of production, and that burden shifted to MHI. Reply at 4. However, Petitioner provides no explanation of how it has met its burden of production, nor how MHI has failed to meet its burden. Despite two days of deposition testimony of Canadian citizens, Petitioner complains that it

has somehow been prejudiced in its efforts to challenge inventorship. *Id.* However, Petitioner chose to challenge the '063 patent in this venue with full knowledge of the discovery rules. Now that live testimony contradicts Petitioner's narrative on inventorship, Petitioner complains about the amount of discovery allowed in IPR proceedings. Petitioner ignores that it had a full and fair opportunity to cross-examine both individuals that Petitioner purports are inventors; indeed, Petitioner had five lawyers present at each of the depositions and voluntarily ended the depositions early. *See* EX1077, EX1078.

Additionally, Petitioner improperly conflates sufficient invention (conception and constructive reduction to practice) with completion of a post-hoc analysis. Reply at 5. Dr. Tardif clearly testified that although the COLCOT trial was designed to determine if low-dose colchicine treatment within 30 days of an MI was beneficial, he conceived the much shorter TTI and its possible benefit before completing the post-hoc analysis. EX1007 at 50:12-51:11 (testifying that the TTI invention idea was "right after... after the end of the study, which was July – I think July 2019."). The mere fact that additional brainstorming sessions occurred after the publication of EX1022 does not prove that Dr. Tardif did not conceive of the TTI invention in July

2019, only that he coordinated with colleagues about reducing his conception to practice.³

It is well-settled that “[a]n inventor may use the services, ideas, and aid of others in the process of perfecting his invention without losing his right to a patent.” *Shatterproof Glass Corp. v. Libbey-Owens Ford Co.*, 758 F.2d 613, 624 (Fed. Cir. 1985) (internal quotations omitted). This foundational principle was espoused by the Supreme Court in addressing Samuel Morse’s discussion with scientists while developing the telegraph. *O’Reilly v. Morse*, 56 U.S. 622, 111 (1853) (“And it can make no difference, in this respect, whether [the inventor] derives his information from books, or from conversation with men skilled in the science. If it were otherwise, no patent, in which a combination of different elements is used, could ever be obtained.”).

³ Ignoring all the corroborating evidence, Petitioner alleges Dr. Bouabdallaoui’s testimony is the only credible account of the origination of the TTI subgroups. But Dr. Bouabdallaoui’s testimony unequivocally supports Dr. Tardif’s sole inventorship, and both witnesses were clear that additional brainstorming sessions addressed other post-hoc analyses that is not the subject matter of or claimed in the ’063 patent. EX1077 at 42:16-43:11; EX1078 at 14:17-15:11.

“Conception exists when a definite and permanent idea of an operative invention, including every feature of the subject matter sought to be patented, is known.” *Sewall v. Walters*, 21 F.3d 411, 415 (Fed. Cir. 1994) (citing *Coleman v. Dines*, 754 F.2d 353, 359 (Fed. Cir. 1985)). In *Sewall*, the Federal Circuit affirmed the district court’s findings that Sewall’s designs simply carried out the ideas of sole inventor Walters. The facts here are analogous. Dr. Tardif conceived of the COLCOT study, which provided the support and enabling disclosure of the patent—the effectiveness of low-dose colchicine without a loading dose in patients that recently suffered an MI. Dr. Bouabdallaoui testified that she did not participate in the design or conduct of the COLCOT study. EX1078 at 44:22-45:8. Therefore, as MHI has consistently stated, Dr. Tardif was the inventor, and Dr. Bouabdallaoui and others assisted with further analysis of the underlying COLCOT study, including post-hoc analyses at Dr. Tardif’s direction. Accordingly, Dr. Bouabdallaoui does not qualify as a joint inventor. *Ethicon, Inc. v. United States Surgical Corp.*, 135 F.3d 1456, 1460 (Fed. Cir. 1998) (“One does not qualify as a joint inventor by merely assisting the actual inventor after conception of the claimed invention.”) (citing *Sewall*, 21 F.3d at 416-17).

Petitioner’s circumstantial evidence does not support naming Dr. Bouabdallaoui an inventor. The mere fact that Dr. Bouabdallaoui previously conducted post-hoc analyses, or that she contributed to writing EX1005 does not

support inventorship. Neither she, Dr. Tardif or the patent attorney who prepared and prosecuted the '063 patent believe Dr. Bouabdallaoui qualifies as an inventor. Additionally, there is **zero** evidence to suggest Dr. Bouabdallaoui was excluded from inventorship for any financial reasons or an effort to exclude her from the patent. Indeed, Dr. Tardif testified that he is not an attorney, and relied on the advice of counsel to determine who should be the properly named inventors. EX1077 at 70:11-18.

The cases Petitioner cites to support its corroboration position are inapposite to the facts here. Each case assessed whether an individual purporting to be an inventor had provided sufficient corroborating evidence of conception and reduction of practice. *See Kolcraft Enters., Inc. v. Graco Children's Prods., Inc.*, 927 F.3d 1320 (Fed. Cir. 2019); *Singh v. Brake*, 317 F.3d 1334 (Fed. Cir. 2003); *Lockheed Aircraft Corp. v. U.S.*, 553 F.2d 69 (Ct. Cl. 1977). Moreover, each case cited by Petitioner concerns pre-AIA patents (and design patents in *Kolcraft*) with the purported inventors attempting to antedate their inventions with pre-filing conception. *Id.* Contrarily, here, Dr. Bouabdallaoui has disavowed her inventorship, not asserted it. Thus, in view of the declarations of Dr. Tardif and Dr. Bouabdallaoui, MHI has satisfied the requirements for confirming inventorship.

Finally, Petitioner alleges that Tardif's assertions of self-inventorship are uncorroborated. That is incorrect. Dr. Bouabdallaoui, the individual that Petitioner

alleges was excluded as an inventor, consistently testified that she is not an inventor.
EX1078 36:17-21, 42:18-43:18.

C. Petitioner's Inventorship Position is Futile

Finally, even if the Board finds that the latest possible priority date should apply for claims 1, 8, and 28 and that Dr. Bouabdallaoui should be listed as an inventor, EX1005 is still not prior art. If it is held that Dr. Bouabdallaoui is an inventor, MHI can correct inventorship under 35 U.S.C. § 256. Even under Petitioner's reasoning, if Dr. Bouabdallaoui is an inventor, then EX1005 is the work of the inventor that was published less than one year before the latest possible priority date. Paper 7; Reply at 6.

For these reasons, even if Petitioner prevails on its priority date and inventorship theories, EX1005 cannot be prior art. Accordingly, Grounds 1 and 4 must fail.

III. GROUND 2

Claims 27, and 29-36 cannot be anticipated by the COLCOT protocol (EX1006) because Petitioner fails to prove it is prior art, Dr. Ridker testified a POSA would not rely on such a reference because it is only a summary of a protocol, it fails to disclose any results to meet the reduced stroke limitation, and Petitioner fails to show inherency.

A. Petitioner Failed to Show EX1006 is Prior Art

MHI explained why Petitioner has failed to show that EX1006 was publicly accessible prior art in the Response. Reply at 19-20. Rather than address the discrepancy between EX1006 and EX2069 showing different information from the version Petitioner relied on, Petitioner relies on the declaration of Mr. Cruitt, and another declarant testifying that Mr. Cruitt found EX1006 using the method stated in EX1072. *Id.*; EX1073.

Petitioner has still failed to meet its burden to show that EX1006 is publicly available prior art. Mr. Cruitt agrees that EX2069 refers to a July 16, 2020 upload date for the study protocol. EX1072 at ¶ 5. In response to MHI's explanation of the discrepancy in public availability evidenced by EX1006 and EX2069, Mr. Cruitt alleges that a EX2069 refers to a submission on March 6, 2017 for "the study record." *Id.* ¶ 7. Thus, Mr. Cruitt still fails to show that this is the same submission as EX1006, or that the unlinked submission in EX2069 was publicly accessible.

Additionally, Petitioner misconstrues MHI's argument regarding Dr. Ridker's reliance on this reference. MHI does not argue that EX1006 should be disregarded. Rather, MHI accurately points out that Dr. Ridker's opinions regarding EX1006 are unreliable and lack probative value based on his testimony. Response 20-21.

B. EX1006 Fails to Disclose a Reduction in Stroke

It is undisputable that EX1006 does not disclose certain claim limitations, including stroke reduction. Response 6-10, 22-30.

As an initial matter, Petitioner grossly mischaracterizes Dr. Ardehali's testimony. Dr. Ardehali *never* "admitted EX1006 teaches effective stroke treatment within about 30 days of an MI." *Compare* Reply at 11 *with* EX1076 at 119:20-121:8 (testifying about the *results* of COLCOT rather than the protocol). Petitioner similarly grossly mischaracterizes the testimony of Dr. Bouabdallaoui, who also agreed that the *results* of COLCOT showed a stroke reduction. EX1078 at 60:19-62:8.

Additionally, the stroke reduction claim limitation is limiting because it is "necessary to give life, meaning and vitality' to the claims" and describes the "essence of the invention." *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1345 (Fed. Cir. 2003); *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305 (Fed. Cir. 1999). Without the preamble of reducing stroke, claims 27 and 29-39 are reduced to nothing more than a dosage regimen that would cover treatment for any purpose or condition, even one that is wholly unrelated to reducing the risk of stroke or other cardiovascular event.

Rather than importing a limitation from the specification, MHI explained in its Response how the specification confirms the essence of the invention and its

indivisible connection to the preamble. Response at 7-8. Similarly, the prosecution history also corroborates that reducing the risk of stroke is limiting, and even the Examiner viewed the preamble as limiting. EX1002 at 399 (“The reference does not teach, show, suggest, or make obvious the instant method of ***reducing the risk of a stroke...***”) (emphasis added). Thus, even though here the prosecution needn’t evince “clear reliance on the preamble during prosecution” to impart weight, it does. *Catalina Mktg. Int’l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 809 (Fed. Cir. 2002).

Additionally, the stroke reduction limitation is not inherent from the disclosure of EX1006. Inherency must be inevitable, and “may not be established by probabilities or possibilities.” *Personal Web Techs., LLC v. Apple, Inc.*, 917 F.3d 1376, 1382-83 (Fed. Cir. 2019) (overturning finding of unpatentability because inherent disclosure taught a mere possibility) (*quoting PAR Pharma., Inc. v. TWI Pharmas., Inc.*, 773 F.3d 1186, 1195 (Fed. Cir. 2014)). Here, Petitioner has not introduced any evidence that stroke reduction is the inevitable result of following the methods disclosed in claims 27 and 29-39. Reply at 12-13. Petitioner’s conclusory attorney argument is contrary to the ’063 patent itself, which discloses that not every patient experiences a risk reduction, and it is thus not an inevitable result of the method. EX1001 at 2:4-22.

Moreover, Petitioner entirely ignores MHI's argument that low-dose administration of colchicine reduces stroke and other CV events when initiated shortly after MI. Response at 25-26. Similarly, Petitioner fails to substantively address MHI's policy argument regarding inherency in the context of clinical trials. *Id.* at 27-28. Accepting Petitioner's argument that a clinical study protocol inherently discloses every result that the eventual study may achieve would render invalid an entire field of method patents in addition to ignoring the actual law on inherency. If accepted, Petitioner's argument will stop the development of new life saving medications for important indications.

Accordingly, Petitioner has failed to show that EX1006 was publicly accessible prior art and that EX1006 discloses each limitation of claims 27, 29-39, expressly or inherently.

IV. GROUND 3

Petitioner alleges that all claims of the '063 patent are invalid as obvious over EX1007 in view of EX1006, EX1009, and EX1016. Petitioner's third ground must fail because, *inter alia*, the analysis relies on hindsight bias, fails to show a motivation to combine references, and fails to show a reasonable expectation of arriving at the claimed invention if combined.

A. The Prior Art Failed to Disclose Several Claim Limitations

Petitioner alleges that the prior art teaches all claim limitations other than TTI. Petitioner is incorrect; the invention and prior art must be considered as a whole without hindsight. *See St. Jude Med., LLC v. Snyders Heart Valve LLC*, 977 F.3d 1232, 1242-43 (Fed. Cir. 2020); *Impax Labs. Inc. v. Lannett Holdings Inc.*, 893 F.3d 1372, 1379-81 (Fed. Cir. 2018); *Millennium Pharms., Inc. v. Sandoz Inc.*, 862 F.3d 1356, 1367 (Fed. Cir. 2017); *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1085 (Fed. Cir. 2008); *Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, 724 (Fed. Cir. 1990). The prior art fails to teach several claim limitations, including in a manner that would motivate a POSA to combine the teachings with a reasonable expectation of success.

1. Nidorf, when read as a whole, would not motivate a POSA to select a daily low dose, including 0.5 mg/day.

Petitioner does not dispute that Nidorf teaches several embodiments, including preferred embodiments that a POSA would not understand as “a daily low dose.” Reply at 14. Rather than address these arguments, Petitioner merely states that one of the many embodiments disclosed was 0.5 mg daily. Reply at 14. The law is clear, a prior art reference must be considered for all it teaches, and the mere disclosure of an element may be insufficient. *St. Jude*, 977 F.3d at 1242-43 (finding no motivation to select component disclosure in prior art when it was not the

preferred or critical component disclosed in the reference); *Impax Labs.*, 893 F.3d at 1379-81 (explaining prior art must be viewed as a whole and finding that reference disclosing laundry list of treatments did not disclose nasal administration, because reference as a whole had other focus). Therefore, Petitioner’s failure to consider prior art references as a whole remains fatal. Response at 35-40.

2. The prior art fails to disclose the efficacy limitations expressly or inherently.

Rather than point to a single prior art reference that discloses the efficacy limitations, Petitioner only asserts that (1) the efficacy limitations “carry no weight” and (2) are expressly or inherently disclosed. Reply at 15.

Petitioner fails to cite to a single prior art reference that expressly discloses any of the efficacy limitations. *Id.* Instead, Petitioner merely asserts that the phrases define the result of the positively recited method steps and nothing more, and any argument to the contrary is inconsistent with the ’063 patent. *Id.* However, Petitioner never explains why the contrary—and correct—interpretation is “inconsistent with the ’063 patent” or why “MHI should be precluded for advancing such arguments.” *Id.* Such conclusory analysis is insufficient.

Contrary to Petitioner’s unsupported statements, *Allergan* is directly applicable here and to understanding the efficacy limitations. Removing the loading dose was not the only grounds for allowance. EX1002 at 398 (“There is no

motivation to delete the loading dose of [Circulation] and *treat* these patients by the method of [Am. Heart Journal].”) (emphasis added). Accordingly, Petitioner fails to sufficiently rebut MHI’s position regarding lack of efficacy disclosure in the prior art. Response at 11-13, 31, 49, 51-52.

B. A POSA Would not Have a Motivation to Shorten Nidorf’s TTI Based on the Prior Art

Petitioner alleges a POSA would have been motivated to shorten Nidorf’s TTI requiring the patient to be stable for at least 6-months after an MI to the ’063 patent’s within about 3 days after MI. Petitioner fails to show any such motivation and ignores the teaching away that a patient should be stable for a long period before initiating treatment. A POSA would not have reached the ’063 patent claims through routine optimization or in view of the unrelated ESC Guidelines. To the contrary, a POSA would be going against the grain of common knowledge in the art.

1. Petitioner fails to show how a POSA would reach the claims through routine optimization.

Petitioner’s conclusory argument that reducing the 30-day window from COLCOT, which disclosed no results, to within about 3 days based on Nidorf fails to explain why a POSA would bounce from one reference to the other. It is undisputed that EX1006 does not disclose any results for the treatment of patients initiated within 30 days before the ’063 patent’s priority date. Moreover, as Petitioner admits, EX1007 disclosed treatment with colchicine not just in stable MI

patients, but in patients that had been stable for *six months* after MI. Additionally, Petitioner again mischaracterizes the testimony of Dr. Ardehali, by alleging that he “admitted COLCOT patients were stable.” Reply at 16. Rather, Dr. Ardehali merely stated that COLCOT *included* patients that were stable. EX2001 at ¶ 40.

Petitioner’s conclusory allegation fails to explain why EX1006 (which contains no result data) and EX1007 would lead a POSA to reduce a treatment regimen from six months to three days, or from thirty days to three days. *KSR Intern. Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (explaining that obviousness cannot be sustained by conclusory statements).

The fact that the ’063 patent specification discloses other workable embodiments does not support any basis for routine optimization. Indeed, Petitioner’s reliance on Dr. Bouabdallaoui’s testimony to conclude that claiming initiation within 0 to 3 days is only “an attempt to more closely align with” a patients’ journey after MI lacks justification, as the benefits of a TTI within 3 days is actually supported by the data. Reply at 17.

Contrary to Petitioner’s argument, MHI does not assert that routine optimization does not apply to method claims. Rather, MHI has argued that the *Novartis* case, instead of Petitioner’s reliance on composition claims cases, is the apt comparison here. Response at 42. In *Novartis*, the Federal Circuit explained that “[t]o the extent the district court required a showing that a [POSA] would have

selected everolimus over other prior art compounds, it erred. The proper inquiry is whether a [POSA] would have been motivated to modify the prior art [to arrive at the claimed method of treatment].” *Novartis Pharms. Corp. v. West-Ward Pharms. Int’l Ltd.*, 923 F.3d 1051, 1060 (Fed. Cir. 2019). In that analysis, the Federal Circuit distinguished the obviousness analysis for alleged overlapping limitations in method claims compared to composition claims. Here, Petitioner fails to provide any reason why a POSA would have been motivated to exercise routine optimization to reach the ’063 patent’s claims.

2. Improving patient compliance for motivation requires hindsight.

Petitioner also alleges a POSA would have been motivated to initiate colchicine treatment in post-MI patients before the patient leaves the hospital, for example, within 3 days. Reply at 17. However, such a motivation would only occur *after* a POSA determines that initiating colchicine so early was not harmful and effective, something not done before the ’063 patent. Thus, although EX1009 discloses initiating certain drugs shortly after an MI in order to improve patient compliance, none of those drugs are colchicine.

Indeed, Petitioner’s own arguments shows that such a construct is entirely hindsight driven. Petitioner alleged that “[t]he mere lensing of the COLCOT data through a well-known TTI does not support patentability.” Reply at 18. However, before the priority date of the ’063 patent, there was no COLCOT data available.

And to the extent the Board agrees the TTI is “mere lensing,” then such “lensing” is no more than constructive reduction to practice for the entire scope of the invention, and the ’063 patent receives a priority of November 15, 2019.

Continuing its hindsight theme, Petitioner relied on Dr. Ardehali’s testimony for when patients should be on colchicine that was made in the present context, after the surprising discoveries of Dr. Tardif. EX1076 at 48:22-49:15. Thus, Petitioner’s argument does nothing more than further illustrate the surprising discovery of Dr. Tardif’s TTI with low-dose colchicine.

Finally, Petitioner’s reliance on statin labels to draw some perceived parallel is irrelevant and unsubstantiated. Reply at 19. Without support, Petitioner merely cites to three labels and makes the unfounded assertion that the FDA approves colchicine similar to statins. Because two drugs may treat similar disorders, it is not an admission from the FDA that they are similar.

Because the efficacy limitations in the ’063 patent are limiting, Petitioner’s allegation of mis-framing is incorrect. Reply at 19-20. Even so, Petitioner also includes an alternative argument based on the CANTOS study. First, EX1005 is not prior art, and without EX1005, the prior art did not provide a reasonable expectation of success.

Second, the alternative argument based on the CANTOS study concerned an entirely different agent than colchicine, yet Petitioner relies on it over other

colchicine early TTI publications. Response at 47. Confusingly, Petitioner alleges that CANTOS is relevant because it concerned the same inflammatory pathway that colchicine addresses. Reply at 20. However, that fact would not change that the other colchicine publications also concerned the same inflammatory pathway *and* used colchicine.

Dr. Ridker's position that LoDoCo, CANTOS, and COLCOT are the most germane trials because they were long-term clinical end-point studies contradicts Petitioner's other arguments. EX1075. LoDoCo was "as small study without a placebo control.... [that] was not double-blinded." EX1077 at 33:20-34:5. Petitioners have not provided evidence to rebut these facts. A POSA would have considered several other studies, including many more germane than LoDoCo and CANTOS, including for example, COPS. Response at 46-48.

C. The Relevant Art is Highly Unpredictable

Petitioner alleges there is no hindsight, yet as explained above, consistently relies on the results of post-priority studies, data, and those disclosed within the '063 patent. Reply at 15-18, 20-22. Additionally, Petitioner does not substantively address MHI's teaching away and unpredictability arguments. Therefore, Petitioner fails to appreciate the criticality of these issues to the obviousness analysis, particularly as it pertains to motivation and reasonable expectation of success. Response at 4-6, 35, 37-39, 43, 48.

V. SECONDARY CONSIDERATIONS

Petitioner alleges the claims of the '063 patent cannot have any of the alleged secondary considerations because the patent “cannot yet be said to have achieved any results.” Reply at 22. Seemingly, Petitioner incorrectly conflates a need to be on the market with a showing of secondary considerations. Not so. Moreover, Petitioner alleges that the data in EX1005 do not support unexpected results or skepticism.

Firstly, MHI properly relied on EX1005 to show unexpected results, because as explained above, it cannot be prior art, even under Petitioner’s theory. Additionally, Petitioner alleges EX1005 is a post-hoc analysis that does not statistically support unexpected results. To support its position, Petitioner relies on the Opening Declaration of Dr. Ridker and the Petition, which they purport are unrefuted. Reply at 23. Petitioner’s position is nonsensical because it is the patentee who introduces secondary considerations of nonobviousness, not the patent challenger.⁴

⁴ Petitioner consistently alleges that MHI failed to refute or address certain theories or references for secondary considerations, but each of these are from the Petition. The patentee introduces secondary considerations, not the patent challenger. The challenger, however, bears the burden of proving obviousness; a burden that Petitioner has not sustained here.

Petitioner continues its conflating of issues by explaining that the COLCOT study was designed to determine whether daily low dose colchicine initiated within 30 days of an MI was beneficial and did not have a pre-specified subgroup of 0-3 days. Petitioner then extrapolates that because post-hoc analysis is less stringent than pre-specified, EX1005 cannot show reliable results. This is exceptionally disingenuous considering Petitioner alleges EX1005 is a key prior art reference that invalidates the claims. Petition at Grounds 1 and 4. If EX1005 is not reliable, then it cannot have anticipated or obviated any claims.

Petitioner also claims that EX1005 defies biological plausibility. Again, this position entirely contradicts Petitioner's position with regard to Grounds 1 and 4. Petitioner also distorts Dr. Ardehali's testimony. Dr. Ardehali did not conclude that it would be harmful if colchicine is initiated in the middle of the 30-day window, rather Dr. Ardehali consistently testified that the sub-group analysis did not permit drawing such conclusions. EX1076 at 87:2-88:9, 89:11-90:19, 96:9-98:1, 109:15-115:9. The mere fact that the data shows a benefit across 30-days and within 3 days does not show that it defies "biological plausibility." Rather, it merely shows the data were insufficient to draw conclusions for specific days between 8-30.

Accordingly, Petitioner failed to show anticipation, obviousness, or rebut the actual secondary considerations asserted.

WORD-COUNT CERTIFICATE

Pursuant to 37 C.F.R. § 42.24(b)(1), the foregoing PATENT OWNER'S RESPONSE contains 5572 words, excluding parts of this Response exempted under § 42.24(a), as measured by the word-count feature of Microsoft Word.

Dated: August 23, 2024

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CERTIFICATE OF SERVICE

I hereby certify that on August 23, 2024, copies of the foregoing SUR-REPLY and all documents filed with it were served via electronic mail to counsel for the Petitioner, as consented to by counsel, upon the following counsel for Petitioner:

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