

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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LABORATORY CORPORATION OF AMERICA HOLDINGS,  
Petitioner,

v.

QUEST DIAGNOSTICS INVESTMENTS LLC,  
Patent Owner.

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IPR2019-01517  
Patent 7,972,867 B2

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Before SUSAN L. C. MITCHELL, JENNIFER MEYER CHAGNON, and  
AVELYN M. ROSS, *Administrative Patent Judges*.

CHAGNON, *Administrative Patent Judge*.

DECISION

Denying Petitioner's Request for Rehearing of Decision Denying Institution  
*37 C.F.R. § 42.71(d)*

## I. INTRODUCTION

Laboratory Corporation of America Holdings (“Petitioner”) filed a Request for Rehearing under 37 C.F.R. § 42.71(d). Paper 12 (“Reh’g Req.”). Petitioner’s Request for Rehearing seeks reconsideration of the Decision Denying Institution of *inter partes* review of claims 21–28 and 31 of U.S. Patent Number 7,972,867 B2 (Ex. 1001, “the ’867 patent”). Paper 11 (“Dec.”). Pursuant to the panel’s authorization, Quest Diagnostics Investments LLC (“Patent Owner”) filed an Opposition to Petitioner’s Request for Rehearing (Paper 13, “Opp.”) and Petitioner filed a Reply to Patent Owner’s Opposition (Paper 14, “Reply”).

As explained below, we have considered the arguments presented by Petitioner in its Request for Rehearing, as well as the parties’ arguments in the Opposition and Reply, but we discern no reason to modify the Decision Denying Institution. Accordingly, we *deny* Petitioner’s Request for Rehearing.

## II. STANDARD OF REVIEW

The party challenging a decision in a request for rehearing bears the burden of showing the decision should be modified. 37 C.F.R. § 42.71(d). A request for rehearing “must specifically identify all matters the party believes the Board misapprehended or overlooked, and the place where each matter was previously addressed.” *Id.* Upon a request for rehearing, the decision on a petition will be reviewed for an abuse of discretion. 37 C.F.R. § 42.71(c). An abuse of discretion may be indicated if a decision is based on an erroneous interpretation of law, if a factual finding is not supported by substantial evidence, or if the decision represents an unreasonable judgment

in weighing relevant factors. *Arnold P'ship v. Dudas*, 362 F.3d 1338, 1340 (Fed. Cir. 2004).

### III. ANALYSIS

Our Decision Denying Institution determined that Petitioner did not demonstrate a reasonable likelihood of success in showing that independent claim 21 would have been obvious in view of the asserted combination of Voyksner,<sup>1</sup> Watson,<sup>2</sup> and Rainbow,<sup>3</sup> and we did not institute *inter partes* review. *See* Dec. 14–21. In its Request for Rehearing, Petitioner contends that our determination not to institute an *inter partes* review is improper for three reasons. First, Petitioner argues that we misapprehended the teachings of the '867 patent. Reh'g Req. 4–7. Second, Petitioner argues that we overlooked Petitioner's argument explaining why one of ordinary skill would have applied Voyksner's method to measuring 25-hydroxyvitamin D<sub>2</sub> (25(OH)D<sub>2</sub>). *Id.* at 8–12. Third, Petitioner argues that we overlooked Petitioner's argument as to selecting a protonated, dehydrated precursor ion of 25(OH)D<sub>2</sub>. *Id.* at 12–14. We address each of these arguments in turn.

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<sup>1</sup> Voyksner, R. D. and Lee, H., *Improvements in LC/Electrospray Ion Trap Mass Spectrometry Performance Using an Off-Axis Nebulizer*, 71 Anal. Chem. 1441–47 (1999) (Ex. 1004).

<sup>2</sup> Watson, D. and Setchell, K. D. R., *Analysis of Vitamin D and Its Metabolites Using Thermospray Liquid Chromatography/Mass Spectrometry*, 5 Biomed. Chromatography 153–60 (1991) (Ex. 1007).

<sup>3</sup> Rainbow, S., et al., *The Analysis of Vitamin D Analogues by Atmospheric Pressure Ionization Coupled to Triple Quadrupole Mass Spectrometry*, Poster No. M-045, Proc. 51st ASMS Conference on Mass Spectrometry and Allied Topics, Montreal, Canada (June 8–12, 2003) (Ex. 1008).

*A. Whether the Board misapprehended the '867 patent's teachings as to the importance of the specific precursor ion*

Petitioner contends “the Board erroneously focused on why a [person of ordinary skill in the art] would have been motivated to select the specific precursor ion of  $395.30 \pm 0.5 \text{ m/z}$ ,” rather than addressing Petitioner’s argument as to “why a [person of ordinary skill in the art] would have been motivated to modify Voyksner’s method to detect  $25(\text{OH})\text{D}_2$  (which would necessarily generate the precursor ion of  $395.30 \pm 0.5 \text{ m/z}$ ).” Reh’g Req. 4–5. Petitioner contends Patent Owner mischaracterized the text of the ’867 patent causing the Board to focus on the importance of selecting certain **fragment** ions rather than specific **precursor** ions. *Id.* at 5–6 (citing Patent Owner’s Preliminary Response (Paper 7, “Prelim. Resp.”) 22; Ex. 1001, 10:60–11:1, 11:46–12:20). Petitioner argues that the text cited by Patent Owner does not support that “‘25-hydroxyvitamin D2 can be converted into a *variety* of different precursor ions’ or that ‘only some [precursor ions] may be useful in a mass spectrometric method.’” *Id.* at 6 (citing Dec. 18, emphasis Petitioner’s).

We are not persuaded by Petitioner’s argument that we misapprehended the disclosure of the ’867 patent.<sup>4</sup> The cited portion of the ’867 patent states that:

Generally, the fragment ions that represent dehydrations or deaminations of the precursor ion are not specific fragment ions for a particular analyte. For example, MS/MS performed to detect  $25\text{OHD}_2$  by selecting for a precursor ion at  $413 \text{ m/z}$  (i.e. the protonated and hydrated ion) and detecting a fragment ion of  $395 \text{ m/z}$  (representing a dehydration of the  $413 \text{ m/z}$

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<sup>4</sup> We address below Petitioner’s arguments about “why a [person of ordinary skill in the art] would have been motivated to modify Voyksner’s method to detect  $25(\text{OH})\text{D}_2$ ” (Reh’g Req. 5). *See* Section III.B.

precursor ion) would not be able to distinguish 25OHD<sub>2</sub> from 1 $\alpha$ (OH)D<sub>2</sub> which would form the same precursor and fragment ions. Therefore a 395 m/z fragment ion is not a specific fragment ion for 25OHD<sub>2</sub> or 1 $\alpha$ (OH)D<sub>2</sub>. Accordingly, in preferred embodiments of the invention, MS/MS is performed such that at least one fragment ion of a vitamin D metabolite is detected that does not represent only a loss of one or more water molecules and/or a loss of one or more ammonia molecules from the precursor ion.

Ex. 1001, 10:58–11:6. We recognize that the 395 m/z ion being detected in this portion of the '867 patent is the fragment ion. *See* Reh'g Req. 6. But, the preferred embodiments of the '867 patent describe tuning the first quadrupole to select for a least two different 25-hydroxyvitamin D<sub>2</sub> **precursor** ions—395.30 m/z (i.e., the protonated and dehydrated precursor ion) and 413 m/z (i.e., the protonated and hydrated precursor ion). *Id.* at 11:46–12:20. And, fragment ions are derived from precursor ions. *See* Opp. 6; Ex. 1001, 8:59–9:9 (describing the MS/MS technique, and indicating that precursor ions are fragmented to yield fragment ions). Thus, contrary to Petitioner's assertion (Reh'g Req. 6), the '867 patent describes at least one other precursor ion for 25(OH)D<sub>2</sub> than the claimed ion of 395.30 m/z, namely an ion of 413 m/z, which is consistent with Patent Owner's argument that "25-hydroxyvitamin D<sub>2</sub> can be converted to a variety of different precursor ions" (Prelim. Resp. 22).

*B. Whether the Board overlooked Petitioner’s argument as to why one skilled in the art would have applied Voyksner’s method to measure 25(OH)D<sub>2</sub>*

*1. Whether the Board misapprehended Petitioner’s arguments regarding using Voyksner’s methods for other vitamin D metabolites*

Petitioner contends the Board “misapprehended Petitioner’s arguments by focusing only on whether a [person of ordinary skill in the art] would have *a priori* selected the protonated, dehydrated precursor ion of 25(OH)D<sub>2</sub>.” Reh’g Req. 8 (citing Dec. 15–20). Petitioner contends “by using Voyksner’s method for measuring 25(OH)D<sub>2</sub>, the method would have necessarily led a [person of ordinary skill in the art] to detect and select an ion having an  $m/z$  of  $395.30 \pm 0.5$  (the protonated, dehydrated ion of that metabolite).” *Id.* at 10; *see also* Ex. 1002 ¶ 57. Petitioner contends this argument is supported by an expert opinion and should be afforded greater weight than Patent Owner’s argument, which is not supported by an expert opinion. *See* Reh’g Req. 7. Petitioner contends that “relying on its expert’s testimony, [] one of ordinary skill in the art would have known how to select any precursor ion/fragment pair for any analyte.” *Id.* (citing Pet 29–30; Ex. 1002 ¶¶ 29, 31, 59).

We are not persuaded by Petitioner’s argument. As discussed in the Decision, we considered Petitioner’s arguments based on Dr. Fitzgerald’s testimony that “the selection of precursor and fragment ions was often simply determined by the selected equipment, the conditions for ionization, and the relative abundance of the ions and the specificity of the ions for the analyte of interest.” Dec. 17 (citing Pet. 29–30; Ex. 1002 ¶¶ 59–61). We also considered Dr. Fitzgerald’s testimony that “the recited  $m/z$  of  $395.30 \pm 0.5$  merely indicates the expected value for a protonated, dehydrated

precursor of 25-hydroxyvitamin D<sub>2</sub> having a molecule weight of 412.7 g/mol.” *Id.* (citing Pet. 27; Ex. 1002 ¶ 57). Petitioner’s arguments explain what a skilled artisan *could have* done, i.e., select an appropriate precursor ion. However, as discussed in the Decision, the Petition, even when considered along with Dr. Fitzgerald’s testimony, “does not describe specifically *why* one of ordinary skill in the art would have selected the specific precursor ion” (Dec. 19), when as discussed above, multiple precursors are possible.<sup>5</sup> *See Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1073 (Fed. Cir. 2015) (“[O]bviousness concerns whether a skilled artisan not only *could have made* but *would have been motivated to make* the combinations or modifications of prior art to arrive at the claimed invention.”).

As to weighing the evidence, “[t]he Board has broad discretion to assign weight to be accorded expert testimony.” Office Patent Trial Practice Guide 35 (84 Fed. Reg. 64,280 (Nov. 21, 2019)). “Expert testimony [] cannot take the place of a disclosure in a prior art reference, when that disclosure is required as part of the unpatentability analysis.” *Id.* at 36. In the Decision, we reviewed and assessed the persuasiveness of Dr. Fitzgerald’s testimony in light of the other factual evidence in the record, including the cited prior art and the disclosure of the ’867 patent. We found that “[i]t is not in dispute that none of the cited references include the claimed protonated and dehydrated precursor ion of 25-hydroxyvitamin D<sub>2</sub>

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<sup>5</sup> Petitioner’s arguments here presuppose that the asserted combination shows that one of ordinary skill in the art would have been motivated to use Voyksner’s method to measure 25(OH)D<sub>2</sub> in the first instance. As discussed below, we are not persuaded by Petitioner’s showing in this regard. *See* Section III.B.2.

with a m/z ratio of  $395.30 \pm 0.5$ .” Dec. 18–19. Dr. Fitzgerald’s testimony cannot take the place of the required disclosure that is not taught by the art.<sup>6</sup> Accordingly, we found unpersuasive Petitioner’s contentions and Dr. Fitzgerald’s supporting testimony regarding the pertinent limitation. *Id.* at 18–20.

2. *Whether the Board overlooked Petitioner’s arguments as to the motivation to combine the references*

Petitioner contends the Board “overlooked at least four arguments that a [person of ordinary skill in the art] would have used the method of Voyksner to detect 25(OH)D<sub>2</sub>.” Reh’g Req. 10. These arguments include: (1) Rainbow teaches using tandem mass spectrometry to measure 25(OH)D<sub>2</sub>, 25(OH)D<sub>3</sub>, and 1,25(OH)D<sub>2</sub>; (2) Vitamin D<sub>2</sub> and D<sub>3</sub> have similar structures whereby the same methods would be suitable to analyze both compounds; (3) a person of ordinary skill in the art would have known that Voyksner’s methods would have been suitable for other Vitamin D metabolites which form protonated, dehydrated ions during ionization; and (4) Vitamin D metabolites, such as 25-hydroxyvitamin D, serve as markers for plasma levels of vitamin D. *Id.* at 10–12.

We are unpersuaded that we misapprehended or overlooked Petitioner’s position or cited evidence. At the outset, we note that our Decision expressly addressed Petitioner’s arguments as to the motivation to combine the asserted references. *See* Dec. 16–17. Nonetheless, we have reconsidered our determination in light of Petitioner’s Request for Rehearing. Petitioner’s arguments can be summarized as: the combined

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<sup>6</sup> Petitioner does not argue that the prior art inherently teaches this limitation. *See* Reply 3.

prior art teaches determining the presence or amount of 25-hydroxyvitamin D<sub>2</sub> in a sample. However, as discussed in the Decision, claim 21 “requires more than merely determining the presence or amount of 25-hydroxyvitamin D<sub>2</sub> in a sample.” *Id.* at 18. Petitioner does not argue that our interpretation of the plain meaning of claim 21 is incorrect or that we should disregard the step of generating “protonated and dehydrated precursor ion of said 25-hydroxyvitamin D<sub>2</sub> with a mass to charge ratio (m/z) of 395.30±0.5.” *See id.* Accordingly, we are not persuaded that we overlooked Petitioner’s arguments.

Further, we agree with Patent Owner that the Petition lacks sufficient explanation of *why* a person of ordinary skill in the art “would have chosen to [specifically] investigate 25-hydroxyvitamin D<sub>2</sub> using Voyksner’s methods in the first place, particularly since Voyksner only discusses ‘*di*hydroxyvitamin *D*<sub>3</sub>’ for the purposes of evaluating the orientation of certain mass spectrometry equipment.” Opp. 5 (citing *Arendi S.A.R.L. v. Apple Inc.*, 832 F.3d 1355, 1362–63 (Fed. Cir. 2016) (noting that it is error to accept general knowledge in the art without evidence on the record for limitations that are “*not evidently and indisputably* within the common knowledge of those skilled in the art”) (emphasis in original)).

*C. Whether the Board overlooked Petitioner’s arguments as to the selection of a protonated, dehydrated precursor ion of 25(OH)D<sub>2</sub>*

Petitioner contends that we overlooked the arguments that: “(1) the selection of a precursor ion/fragment pair was generally known in the art, and (2) that a [person of ordinary skill in the art] would have selected the protonated, dehydrated precursor of 25(OH)D<sub>2</sub> based on what was known in the art about vitamin D’s structure and characteristics.” Reh’g Req. 12–13.

We are unpersuaded that we misapprehended or overlooked Petitioner's position or cited evidence as to the selection of a protonated, dehydrated precursor ion of 25(OH)D<sub>2</sub>. Again, Petitioner argues that a person of ordinary skill in the art *could have* selected the protonated, dehydrated precursor of 25(OH)D<sub>2</sub>, but “does not explain sufficiently *why* a person of ordinary skill in the art would specifically choose the protonated, dehydrated 25-hydroxyvitamin D<sub>2</sub> as a precursor.” Dec. 18.

Disagreement with the Board's analysis and conclusions is not a sufficient basis on which to request rehearing. It is not an abuse of discretion to have made an analysis or conclusion supported by the evidence of record with which a party simply disagrees. We are not persuaded that the Decision misapprehended or overlooked any arguments or evidence presented by Petitioner. Accordingly, we did not abuse our discretion in determining that the Petitioner did not adequately establish a reasonable likelihood of prevailing on the proposed combination of Voyksner, Watson, and Rainbow.

#### IV. CONCLUSION

For the foregoing reasons, Petitioner has not demonstrated that we abused our discretion, or that we misapprehended or overlooked any issue, in denying institution of *inter partes* review in this case.

#### V. ORDER

Accordingly, it is ORDERED that Petitioner's Request for Rehearing is *denied*.

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