

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CURIO BIOSCIENCE, INC.,
Petitioner

v.

PROGNOSYS BIOSCIENCES INC. AND 10X GENOMICS, INC.,
Patent Owner

Case IPR2024-01289
Patent 10,480,022

**PATENT OWNER'S RESPONSE TO PETITIONER'S
REQUEST FOR REHEARING**

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Pursuant to the Board's Order (Paper 1), Patent Owner submits this Response to Petitioner's Request for Rehearing (Paper 11, "RR") of the Board's Decision Denying Institution (Paper 10, "DDI").

I. INTRODUCTION

Petitioner continues the pattern of misdirection that Patent Owner identified in its Preliminary Response. Patent Owner Preliminary Response ("POPR"), 1–4. At the outset, Petitioner mischaracterizes the Board's factual findings. This is evident in Petitioner's "quotation" of the Board's DDI that omits significant portions of the Board's analysis of Ground 2 (alleged obviousness over Cantor in view of Armani).

The following is a snippet of Petitioner's Rehearing Request:

There, the Board concluded that "Armani [] fails to disclose determining a spatial location of the nucleic acids within a tissue sample because the sample itself is lysed and therefore fails to retain the spatial information of the sample nucleic acids within the tissue sample." Decision at 24. This is a simple misapprehension of

RR, 1. But here is what the Board actually said: "Thus, *the combination of Cantor and Armani likewise* fails to disclose determining a spatial location of the nucleic acids within a tissue because the sample itself is lysed and therefore fails to retain the spatial information of the sample nucleic acids within the tissue sample." DDI,

24.* Read in full, nothing about that sentence constitutes a clearly erroneous factfinding or legal error.

Petitioner also mischaracterizes the arguments it presented in the Petition to make new arguments about Ground 2 in the Rehearing Request. The Board should not consider Petitioner's new arguments. But even if it did, nothing in those new arguments show that the Board's DDI should be modified because the Board's ultimate conclusion on Ground 2—that Petitioner failed to show a reasonable likelihood of unpatentability—is correct. The Board should deny Petitioner's Rehearing Request.

II. STANDARD OF REVIEW

Petitioner has the burden to show that the Board's DDI should be modified. 37 C.F.R. §42.71(d). When rehearing a decision on a petition, the Board reviews the decision for an abuse of discretion. An abuse of discretion occurs when a “decision was based on an erroneous conclusion of law or clearly erroneous factual findings,” or the Board committed “a clear error of judgment.” *PPG Indus. Inc. v. Celanese Polymer Specialties Co.*, 840 F.2d 1565, 1567 (Fed. Cir. 1988) (citations omitted). Applying that standard, the Board should deny the Rehearing Request.

* Emphasis added throughout unless stated otherwise.

III. ARGUMENT

Petitioner contends that the Board should reconsider its DDI for three reasons. RR, 1–2. First, Petitioner contends that the Board misapprehended the teachings of Armani. *Id.*, 1. Second, Petitioner contends that the Board “relied on an implicit and unstated claim construction that added an additional ‘no lysing’ limitation not found in the claims.” *Id.* And third, Petitioner contends that the Board engaged in “anticipation reasoning” for a ground based on obviousness. *Id.*, 1–2. None of these contentions hold water.

A. The Board should disregard Petitioner’s new arguments about Ground 2

The Board cannot “rehear” arguments that Petitioner did not expressly make before. This is why the Board’s rules expressly require a party dissatisfied with a decision to specifically identify “the place where each matter was previously addressed.” 37 C.F.R. §42.71(d). But here, Petitioner cannot (and does not) specifically identify where it made several of its arguments about the combination of Cantor and Armani (Ground 2) because it never made those arguments before.

Instead, Petitioner rewrites Ground 2. RR, 6-8. Petitioner now contends that it relied on Cantor only for “each physical element.” *Id.*, 6. And after a long discussion of Armani absent from the Petition, Petitioner contends that it relied on “Armani’s microwell-based nucleic acid amplification techniques for spatial

analysis of nucleic acids in tissue sections.” *Id.*, 7–8. Thus, Petitioner contends, Ground 2 was based on Armani’s “techniques for spatial analysis of nucleic acids in a tissue section” where Armani’s “fluorescence-based” detection method is replaced with Cantor’s “sequencing techniques for detection.” *Id.* Not so.

In the Petition, Petitioner argued that “Ground 2 incorporates the analysis of Ground 1.” Pet., 49. Petitioner then relied on Armani for two purposes: first, to “provide[] further evidence of a POSA’s motivation and reasonable expectation of success in using *Cantor’s device and methods* to determine the spatial location of biological molecules, including mRNA, in a tissue sample,” and second, to “provide[] additional information rendering obvious *the step of contacting the plurality of beads with a tissue section* such that the *binding agents interact with nucleic acids of the tissue sample.*” *Id.*

As to the first purpose (motivation and reasonable expectation of success), Petitioner argued that Armani “expressly motivated” a POSA to use “Cantor’s device and methods *in the manner they are disclosed – to detect nucleic acids from a tissue sample*, while specifically using the identification probes to *identify the location* at which beads were provided.” Pet., 53. Put differently, Petitioner did not rely on Armani to teach any missing claim limitation here, but as evidence allegedly showing that a POSA would have been motivated to use Cantor’s device and methods as is (i.e., “in the manner they are disclosed”). *Id.* Indeed, Petitioner

(confusingly) labeled “specifically using the identification probes to identify the location at which beads were provided” a “mental step”— highlighting that Petitioner did not rely on Armani for any claim limitation here. *See id.* (“Armani expressly motivates this mental step....”).

As to the second purpose (combination allegedly rendering the claimed step of “contacting the plurality of beads with a tissue sample such that the binding agent interacts with the biological molecule” obvious), Petitioner argued that a POSA would have (1) provided Cantor’s bead array with beads disposed in wells “as expressly contemplated by Cantor,” (2) contacted the array with a tissue slice “as disclosed by both Cantor and Armani,” (3) pressed the tissue sample into the wells and lysed the tissue “as described by Armani,” and then (4) proceeded with nucleic acid extension, amplification, and detection according to the “steps disclosed by Cantor.” Pet., 51–52. Put differently, Petitioner relied on Armani to teach contacting Cantor’s bead array a tissue sample, pressing that tissue sample into Cantor’s bead array with beads disposed in wells, and lysing the tissue. *Id.*

The Board correctly recognized Petitioner’s uses of Armani in the DDI and rejected them. *See* DDI, 23–24 (describing Petitioner’s assertions as to Ground 2). As to the first purpose (motivation and reasonable expectation of success), the Board correctly recognized that using Cantor’s device and methods “in the manner they are disclosed” would **not** have led to spatial location information because Cantor’s

device and methods are directed to bulk analysis, not spatial analysis. *See, e.g.*, DDI, 23 (“we are not persuaded that Cantor teaches or suggests contacting a tissue sample with beads at known locations to obtain spatial information of a biological molecule within the tissue sample”). Petitioner cannot seriously dispute this finding, which is supported by both the plain language of Cantor and Dr. Cantor’s testimony. *See, id.*, 21 (stating that “we are persuaded by the testimony of Dr. Cantor” (citing EX2002, ¶¶17, 19); *see also, id.*, 22 (“Cantor provides no teaching, however, regarding how to use a tissue sample with the probes and methods described in Cantor to identify where the target nucleic acids of Cantor were spatially located within the tissue sample itself.”)).

Turning to the second purpose (rendering obvious the claimed step of “contacting the plurality of beads with a tissue sample such that the binding agent interacts with the biological molecule”), the Board correctly determined that Armani “did not cure the deficiencies of Cantor.” DDI, 24. The Board agreed with Patent Owner that, even if a POSA combined the teachings of Armani and Cantor as described in the Petition, “the spatial location of the biological molecules cannot be determined” because the target nucleic acids are non-uniformly distributed in the tissue sample but Cantor’s bead collections are not repeated. DDI, 24–25 (quoting POPR, 77).

Rather than challenging *that finding*, however, Petitioner suggests that the Board erred because Ground 2 relied on *Armani* for “determining the location of a nucleic acid in a tissue sample because the presence of fluorescence in a given well indicates that the nucleic acid was present at that location of the tissue sample.” RR, 7. But the Board is not responsible for deciding a ground of unpatentability that Petitioner never presented. And here, contrary to Petitioner’s arguments otherwise, Ground 2 as presented in the Petition started and ended with Cantor. Ground 2 relied on *Cantor’s* bead array, with beads disposed in wells “as expressly contemplated by Cantor.” Pet., 51. Indeed, in discussing the motivation to combine Cantor and Armani, Petitioner stated that “Cantor’s protocols *facilitate the capture*, amplification, and detection of mRNA by sequencing.” *Id.*, 52.

Petitioner’s new theory of unpatentability—that the Petition relied on Cantor only for its sequencing techniques—cannot be squared with Petitioner’s statement bridging pages 51 and 52 of the Petition. There, Petitioner set forth each references’ contribution to Ground 2’s theory of unpatentability: “A POSA would have found it obvious to combine the teachings of Cantor and Armani by providing Cantor’s bead array with the plurality of beads disposed in wells (as expressly contemplated by Cantor), contacting that array with a tissue slice as disclosed by both Cantor and Armani, and then pressing the tissue sample into the wells and lysing the tissue as described by Armani.” Pet. 51–52.

Moreover, even in characterizing its reliance on Cantor's sequencing technique, Petitioner contradicts its earlier position. Petitioner argued in the Petition that "using sequencing as a detection method" as in Cantor "would allow a POSA to *simply pool the contents of all wells together* in a multiplexed sequencing procedure, where the data can then be deconvoluted and spatially mapped based on the read out of location-correlated identification sequences." Pet., 53. But now, Petitioner argues that "according to the proposed combination," nucleic acid sequencing occurs "in *each of the microwells* of the array" because sequencing in the individual wells "retains and provides spatial information." RR, 9. Petitioner cannot have it both ways. *See, e.g., Micron Tech., Inc. v. Yangtze Memory Techs. Co.*, IPR2024-00910, Paper 15, 5 (PTAB Apr. 22, 2025) ("A request for rehearing is not an opportunity to supplement a petition.").

At bottom, Petitioner's attempts to rewrite Ground 2 only highlight that the Petition failed to explain, with sufficient clarity and particularity, how the challenged claims would have been obvious over Cantor in view of Armani. *See Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1369 (Fed. Cir. 2016) ("It is of the utmost importance that petitioners in the IPR proceedings adhere to the requirement that the initial petition identify 'with particularity' the 'evidence that supports the grounds for the challenge to each claim.'" (quoting 35 U.S.C. §312(a)(3))). The Board has no responsibility to search the record and piece together

what arguments and evidence may support Petitioner's theory of unpatentability. 37 C.F.R. §42.71(d); *see also SAS Inst., Inc. v. Iancu*, 584 U.S. 357, 363 (2018) (“in an inter partes review the petitioner is master of its complaint”). The Board should decline “rehear” Petitioner new theory here.

B. The Board did not misapprehend Armani’s teachings and Petitioner has failed to show otherwise

The Board provided a detailed summary of Armani. DDI, 12–14. For example, the Board explained that Armani discloses a 2-D map “to show correlation with the spatial area of a tissue sample for assessing the status of multiple genes within tissue sections and ‘yielding a molecular map that directly correlates with the histology of the sample.’” *Id.*, 12 (quoting EX1022, 3526). The Board’s description of Armani is consistent with both the teachings of Armani and Patent Owner’s overview provided in the Preliminary Response. POPR, 17–19. Petitioner argues, however, that the Board misapprehended the teachings of Armani. *E.g.*, RR, 8–9. Specifically, Petitioner argues that the Board found that Armani’s 2-D PCR technique cannot provide spatial information because Armani’s samples are lysed. *Id.* (citing DDI, 24). But it is Petitioner that misapprehends the Board’s finding, not the other way around.

To begin, Petitioner misquotes the Board’s analysis. For example, Petitioner writes that “*Armani* unambiguously contradicts the Board’s conclusion that *it* ‘fails

to disclose determining a spatial location....” RR, 11 (quoting DDI, 24). But what the Board said in the DDI was that “the *combination of Cantor and Armani likewise* fails to disclose determining a spatial location of the nucleic acids within a tissue because the sample itself is lysed and therefore fails to retain the spatial information of the sample nucleic acids within the tissue sample.” DDI, 24.

To be clear, the Board did *not* say that *Armani* fails to disclose determining a spatial location in a vacuum. The Board said that *Petitioner’s combination of Cantor and Armani* fails to do so because combining Armani with Cantor, as Petitioner urged, still resulted in bulk (not spatial) analysis. This is clear from the Board’s parenthetical quotation from the POPR right after: “Cantor says nothing about placing beads in a ‘known location’ on a substrate because Cantor’s beads contact a sample nucleic acid, which itself has no spatial information.” *Id.* (citing POPR, 41).

And nothing Petitioner relied on in Armani fixes the problem the Board identified. Again, Petitioner stated in the Petition that it would have been “obvious to combine the teachings of Cantor and Armani by *providing Cantor’s bead array* with the plurality of beads disposed in wells (as expressly contemplated by Cantor).” Pet. 51. Cantor does not place beads in a “known location” on a substrate, and Petitioner made no argument in the Petition (unlike in its Rehearing Request) that Armani compensates for that. Instead, as Patent Owner explained in the POPR,

Petitioner’s combination of Cantor and Armani “*still presumes* that a POSA would construct Petitioner’s array with beads at known locations”—i.e., the beads disposed in wells of a multi-well plate. POPR, 76 (citing Pet., 50–51; EX2002, ¶¶179). But as Dr. Cantor testified, a POSA would have had *no* reason to determine the location of a bead because that information would have been completely irrelevant to Cantor’s bulk-analysis methods. POPR, 52 (citing EX2002, ¶¶152-158).

Moreover, even if the Board erred specifically as to Armani’s factual teachings about lysis (which it did not), the Board should not institute *inter partes* review here. The Board’s *ultimate conclusion on obviousness*—that “Ground 2 still suffers from the same flaws as Ground 1: because the target nucleic acids are non-uniformly distributed in the tissue sample and the probes of Cantor’s bead collections are not repeated” (DDI, 24–25)—is correct. Patent Owner explained in the POPR, based on Dr. Cantor’s testimony, that Petitioner’s obviousness grounds were doomed by the presence of different probes on each bead. POPR, 56 (citing EX2002, ¶160). Patent Owner explained that contacting Petitioner’s bead array with a tissue sample would not necessarily result in the spatial analysis due to non-uniform distribution of nucleic acids in a tissue sample and Cantor’s non-repeating probes. *Id.*, 63–68. Patent Owner also provided illustrations showing so. *Id.*, 64–67. Patent Owner explained that nothing in Armani changed that result due to—again—non-uniform distribution of nucleic acids in a tissue sample and Cantor’s

non-repeating probes. *Id.*, 76–77. Petitioner does not argue otherwise or take on any of Patent Owner’s illustrations in its Rehearing Request. Thus, because the Board’s ultimate conclusion is correct, it need not rehear its DDI.

C. The Board did not conduct a stealth claim construction

Petitioner devotes much of its Rehearing Request to a theory that the Board conducted a stealth claim construction—one that “required nucleic acid analysis to occur on the tissue sample without lysis.” Req. Reh’g, 11–13. But this theory directly flows from Petitioner’s misquotation and mischaracterization of the Board’s actual factual findings about the *combination* of Cantor and Armani. *See id.*, 11 (arguing that “[t]h The Board’s factual misapprehension of Armani was further compounded by the Board’s implicit claim construction.”). The Board should reject this argument accordingly. Even so, the Board’s rules state that a Petitioner must explain “[h]ow the *construed* claim is unpatentable” where needed. 37 C.F.R. §42.104(b)(4). Nothing in *PLR Worldwide*—a nonprecedential decision by a former Director cited in the Rehearing Request—abrogates the Board’s rules and Petitioner’s responsibilities. *See* RR, 11 (citing *PLR Worldwide Sales Ltd. v. Flip Phone Games Inc.*, IPR2024-00133, Paper 12 (Vidal Aug. 22, 2024)). Nor could it, because in that case the former Director simply disagreed with the panel majority about the meaning of “non-promotional background object” and remanded the case to the panel. Paper 12, 7.

D. The Board knows well the differences between anticipation and obviousness

Finally, Petitioner argues that the Board erroneously conflated the requirements of anticipation and obviousness by “adopting Patent Owner’s contention that ‘Cantor says nothing about placing beads in a known location.’” RR, 14 (quoting DDI, 24). According to Petitioner, the Board’s finding “improperly focused on the express teachings of Cantor alone, rather than the modifications motivated by the prior art and presented in the Petition.” *Id.* (citing Pet. 53; EX1100, ¶242). Petitioner contends that the Board’s finding is incorrect based on the teachings of Cantor, knowledge in the art, and Dr. Puglisi’s testimony. *Id.*, 13–14 (citing Pet., 39–42, EX1100, ¶¶65–70, 90, 165–173).

This is yet another new argument in the guise of “legal error,” and the Board should reject it. First, Petitioner simply disagrees with the Board’s findings about Cantor. RR, 13 (quoting DDI, 24). But disagreement is not enough to establish reversible error. *See, e.g., Kelonia Therapeutics, Inc. v. Interius Biotherapeutics, Inc.*, PGR2024-00008, Paper 15, 3 (PTAB Oct. 1, 2024) (“A rehearing request is not an opportunity for the requesting party...merely to express disagreement with the underlying decision.”). Second, nothing in the Board’s finding about Cantor is incorrect. As Dr. Cantor himself explained, Cantor teaches the use of substrates to facilitate handling and processing. EX2002, ¶¶69, 152–155; POPR, 50–51.

Dr. Cantor’s testimony is supported by plain language of Cantor, which states that “[t]he array can be arranged on any substrate suitable for sequence analysis or manufacture processes described herein.” EX1031, 17–18; *see also* POPR, 50–51. As Patent Owner and Dr. Cantor further explained, that Cantor says nothing about placing beads in a known location on a substrate makes sense because Cantor’s methods relate to ***bulk analysis***, not spatial analysis. POPR, 41, 50–54. The Board found Dr. Cantor’s testimony about Cantor’s methods being drawn to bulk analysis rather than spatial analysis persuasive (DDI, 21), and no new arguments in Petitioner’s Rehearing Request (RR, 14) can change that. *See, e.g., Elbit Sys. of Am., LLC v. Thales Visionix, Inc.*, 881 F.3d 1354, 1358 (Fed. Cir. 2018) (“The PTAB is entitled to weigh the credibility of the witnesses.” (quotation omitted)).

E. Institution of a flawed petition is unwarranted

Finally, the Board is never required to institute *inter partes* review. *See Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) (“[T]he PTO is permitted, but never compelled, to institute an IPR proceeding.”). Petitioner does not challenge the Board’s findings and conclusions about Ground 1 (obviousness over Cantor) or Ground 3 (anticipation by Frisen). *See generally* RR. Instead, Petitioner goes all in on Ground 2—ironically, the Ground that it explained ***the least*** in the Petition. Petitioner’s analysis in the Petition for Ground 2 covered fewer than six pages. *Compare* Pet., 49–54 (Ground 2), *with id.*, 21–49 (Ground 1)

and 54–72 (Ground 3). And for all challenged claims other than claim 1 in Ground 2, Petitioner’s arguments were just **one sentence** (claims 4–7, 11–15, 17, 19, 27–29) or **two sentences** (claims 2 and 3). Pet. 53–54.

Petitioner’s showing as to most of the claims challenged in Ground 2 falls far short of meeting its burden to identify, with particularity, evidence sufficient to show the unpatentability of those claims. 35 U.S.C. §312(a)(3). It would not be an efficient use of the Board’s time and resources to institute even if the Petitioner met the reasonable likelihood as to **one out of three** grounds and on **one out of seventeen** claims. *See Adaptics Limited v. Perfect Co.*, IPR2018-01596, Paper 20, 17 (PTAB Mar. 6, 2019) (informative) (“Even when a petitioner demonstrates a reasonable likelihood” of prevailing with respect to at least one patent claim, institution of review “remains discretionary.”); *Deeper, UAB v. Vexilar, Inc.*, IPR2018-01310, Paper 7, 42–43 (PTAB Jan. 24, 2019) (informative); *Chevron Oronite Co. v. Infineum USA L.P.*, IPR2018-00923, Paper 9, 10 (PTAB Nov. 7, 2018) (informative).

IV. CONCLUSION

Petitioner has not carried its burden of demonstrating that the Board misapprehended or overlooked any matters, and therefore abused its discretion, in denying institution of *inter partes* review of the challenged claims of the ’022 patent. Accordingly, the Board should deny Petitioner’s Rehearing Request.

Respectfully submitted,

Date: May 2, 2025

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e)(4) and 42.205(b), the undersigned certifies that on May 2, 2025, a complete and entire copy of this Patent Owner's Preliminary Response and accompanying exhibits were provided by email to Petitioner by serving the correspondence email address of record as follows:

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