

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BIO-RAD LABORATORIES, INC.,
Petitioner,

v.

CALIFORNIA INSTITUTE OF TECHNOLOGY,
Patent Owner.

IPR2024-01178
U.S. PATENT NO. 10,770,170

**PETITIONER'S REQUEST FOR REHEARING OF THE BOARD'S NON-
INSTITUTION DECISION UNDER 37 C.F.R. § 42.71(d)**

TABLE OF CONTENTS

	Page
I. INTRODUCTION	1
II. BRIEF SUMMARY OF THE BOARD’S ERROR	2
III. STANDARD OF REVIEW	3
IV. ARGUMENT.....	4
A. Denying Institution Of Grounds 6-10 Based On Saxonov’s Status As Non-Prior Art Requires Careful Analysis Because It Is Undisputed That Almost All Of Saxonov Is Prior Art.....	5
B. Ground 6 Of The Petition Relies On Undisputed Prior Art Material For Claim 1	6
1. [Preamble] A method of unambiguously detecting any unique combination of presence or absence of at least five polynucleotide analytes in a plurality of droplets, the method comprising:.....	6
2. (a) providing a sample comprising, or potentially comprising, at least one of said at least five polynucleotide analytes;.....	7
3. (b) forming a mixture of said sample and at least five hybridization probes,.....	8
4. wherein each of said at least five hybridization probes further comprises at least one fluorophore and at most four fluorophores;	9
5. (c) partitioning said mixture into said plurality of droplets;.....	10
6. (d) exciting said at least one fluorophore to generate one or more signals if one or more of said at least five polynucleotide analytes is present in said plurality of droplets, wherein said one or more signals comprise at least one signal generated by excitement of said at least one fluorophore;.....	12
7. (e) measuring said one or more signals to generate a cumulative intensity measurement,.....	13

8.	wherein said cumulative intensity measurement corresponds to the presence of a unique combination of presence or absence of said at least five polynucleotide analytes in said sample; and.....	14
9.	(f) determining whether each of said least five polynucleotide analytes is present, in any unique combination of presence or absence, based on said cumulative intensity measurement, wherein the method does not require any step of immobilization of said at least five polynucleotide analytes or mass spectrometry.....	14
V.	CONCLUSION.....	15

TABLE OF AUTHORITIES

	Page(s)
Cases	
<i>Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.</i> , 800 F.3d 1375 (Fed. Cir. 2015)	4
<i>Merial Ltd. v. Virbac</i> , IPR2014-01279, Paper 18 (P.T.A.B. Apr. 15, 2015)	3
<i>SAS Inst. Inc. v. Iancu</i> , 138 S. Ct. 1348 (2018)	6
Rules	
37 C.F.R. § 42.71(c)	3
37 C.F.R. § 42.71(d)	4

I. INTRODUCTION

Petitioner Bio-Rad Laboratories, Inc. (“Petitioner”) respectfully requests rehearing of the Board’s Decision Denying Institution of *Inter Partes* Review of U.S. Patent No. 10,770,170 (the “170 patent”). *See* Paper 10 (“Decision”).

Rehearing is needed because the Board did not meaningfully consider Grounds 6-10 of the Petition. Indeed, the Board’s consideration of these five grounds encompassed just seven lines of text. *Id.* at 24. The sum-total of the Board’s analysis was to note that Grounds 6-10 relied partly on the Saxonov reference, and then summarily dismiss them without further consideration based on its finding that certain material from Saxonov that was cited in Ground 1 was not prior art. *Id.* In other words, the Board assumed—without any analysis—that because institution could be denied for Ground 1 because certain portions of Saxonov were not prior art, institution could be denied for Grounds 6-10 for the same reason.

This, however, was erroneous. The Board did not appreciate that Grounds 1-5 and Grounds 6-10 are based on distinct theories and evidence. While Grounds 1-5 are based primarily on single reference obviousness in view of Saxonov, Grounds 6-10 are based on the **combination** of Saxonov with another reference—Larson. *See* Petition at 24. These grounds are critically different because, with Grounds 6-10, the invalidity analysis for the key claim elements relies upon **Larson**, not Saxonov.

See id. at 58-66; *see also infra* Section IV.B. And it is undisputed that the entirety of Larson is prior art.

Nevertheless, with respect to Grounds 6-10, the Board apparently concluded that because the invalidity analysis included a small number of citations to material from Saxonov that was disputed to be prior art, it could summarily dismiss these grounds entirely with no analysis. Decision at 24. No law, however, supports this approach of throwing the baby out with the bath water because a proposed invalidity ground includes a few citations to material that might not be prior art.

Even a minimal analysis would have revealed that Grounds 6-10—based on both Saxonov and Larson—cannot simply be lumped together with Grounds 1-5. Because Grounds 6-10 rely on Larson for the key claim elements, the Board’s finding that Grounds 1-5 were fatally infected by non-prior art material from Saxonov cannot be summarily ported to Grounds 6-10. In fact, Grounds 6-10 are fully supported by prior art disclosure that the Board did not consider. The Board should now correct this error and grant rehearing.

II. BRIEF SUMMARY OF THE BOARD’S ERROR

In its evaluation of the Petition, the Board failed to consider whether each individual ground, based on the evidence contained in that ground, provides sufficient evidence for institution. Instead, the Board only analyzed the evidence

put forward in Ground 1 that relies on Saxonov to decide that Petitioner did not meet its burden to show that Saxonov qualifies as prior art because material was not carried forward from the '013 provisional. The Board then assumed without analysis that it could deny Grounds 6-10 on this basis merely because these grounds happened to include a few references to disputed material—some of which are mere “*see also*” citations and none of which are needed to fully support Grounds 6-10. Indeed, the decision on Grounds 6-10 encompassed only seven lines of text.

Grounds 6-10, however, present a different combination of art based on a different rationale, for which there can be no question there was full support in prior art material. By summarily concluding that this was not the case simply because Grounds 6-10 included a few citations to material that had a disputed prior art status, the Board wholly ignored the substance of these grounds, failed to conduct a fair review, and abused its discretion.

III. STANDARD OF REVIEW

The Board reviews a non-institution decision for an abuse of discretion. 37 C.F.R. § 42.71(c). Misapprehending or overlooking a significant fact or argument is an abuse of discretion. *See Merial Ltd. v. Virbac*, IPR2014-01279, Paper 18 at 7, 8, 14 (P.T.A.B. Apr. 15, 2015). To identify an abuse of discretion on this basis in a request for rehearing, the “request must specifically identify all matters the party

believes the Board misapprehended or overlooked, and the place where each matter was previously addressed.” 37 C.F.R. § 42.71(d).

IV. ARGUMENT

In its decision, the Board abused its discretion by overlooking a significant argument. In fact, the Board effectively overlooked entire grounds, specifically Grounds 6-10 that rely on the combination of Saxonov and Larson. The Board did not recognize that Grounds 6-10 represent a different invalidity theory compared to Grounds 1-5, wherein the analysis for key elements relied upon Larson, which is undisputedly prior art. To the extent Grounds 6-10 cited Saxonov, the Board did not recognize that Grounds 6-10 were more than sufficiently supported by material from Saxonov that is indisputably carried forward from the '013 provisional and is thus prior art to the '170 patent. Indeed, the Board did no analysis whatsoever to this effect.

For Grounds 6-10 the Board thus failed to apply the standard set forth in *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1377, 1381–82 (Fed. Cir. 2015) that teaches a reference is prior art if (1) the provisional provides sufficient support for at least one claim of the reference patent; and (2) the provisional provides sufficient support for the subject matter relied upon for prior art purposes in the reference patent.

A. Denying Institution Of Grounds 6-10 Based On Saxonov's Status As Non-Prior Art Requires Careful Analysis Because It Is Undisputed That Almost All Of Saxonov Is Prior Art

As noted above, the Board declined to institute review of Grounds 6-10 based on its conclusion that Ground 1 relied upon certain limited portions of Saxonov that are not prior art. *See* Decision at 24. Before delving into the specifics of why it was erroneous for the Board to draw such a conclusion with respect to Grounds 6-10, it is worth noting that any decision to deny institution based on whether Saxonov is prior art should be taken with great care because it is undisputed that virtually *all* of Saxonov is prior art.

Indeed, there is no question that Saxonov is overwhelmingly prior art, with the only possible exceptions being Figures 9-10 and paragraphs 17-18, 37, and 76-79. Everything else in Saxonov is carried forward and is undisputed prior art. *See Id.* at 17-24; *see also* Paper 6 at 33-42. This is confirmed by Patent Owner's *own* comparison of the '013 provisional and Saxonov. *See* EX2007.

Despite the foregoing, the Board conducted no meaningful analysis of Grounds 6-10 or how they differ from Ground 1, let alone an inquiry into what material from Saxonov relied upon in Grounds 6-10 of the Petition is prior art.

B. Ground 6 Of The Petition Relies On Undisputed Prior Art Material For Claim 1

Material that is undisputed prior art supports Grounds 6's showing in the Petition that claim 1 of the '170 patent is invalid. This ground is distinct from Ground 1 and relies on Larson to address multiple elements of claim 1. Because the grounds are different, there can be no question that Ground 6 cannot be deemed defective based on alleged reliance on non-prior art material—especially with no analysis performed by the Board to make such a finding.

A detailed explanation showing how Ground 6 is fully supported by undisputed prior art material is provided below on an element-by-element basis with respect to Ground 6's treatment of claim 1. While the arguments in the Petition for other claims and for Grounds 7-10 are similarly supported by prior art, for the purposes of this rehearing request, Petitioner addresses only on claim 1 because a decision to institute with respect to this claim suffices to justify institution of the Petition as a whole. *See SAS Inst. Inc. v. Iancu*, 138 S. Ct. 1348, 1354-1358 (2018).

- 1. [Preamble] A method of unambiguously detecting any unique combination of presence or absence of at least five polynucleotide analytes in a plurality of droplets, the method comprising:**

The preamble of claim 1 in Ground 6 relies upon the evidence set forth in Ground 1, which does not cite any material that Patent Owner contends is not carried

over. *See* Paper 6 at 38; *see also* Petition at 27. Accordingly, nothing in Petitioner’s treatment of the preamble would justify the Board’s conclusion that Ground 6 should not be instituted.

2. (a) providing a sample comprising, or potentially comprising, at least one of said at least five polynucleotide analytes;

This claim element pertains to the trivial concept of providing a sample that “potentially” comprises five or more polynucleotide analytes in a given sample. The element requires no more than this routine concept.

To show this is rendered obvious, Ground 6 relies on Larson and differs from Ground 1 considered by the Board. *See* Petition at 60-62. The Petition discusses in great detail how Larson discloses numerous assays that meet this element, disclosing even assays that detect 9 targets in a sample using two colors. *See id.* Thus, this aspect of Ground 6 is fully supported by prior art disclosure. Just as with the preamble, nothing in Petitioner’s treatment of this element would justify the Board’s conclusion that Ground 6 should not be instituted.

Unlike Ground 6, it is true that Ground 1 of the Petition has two citations to paragraph 77 and one citation to paragraph 17 of Saxonov, which is material the Board has found is not prior art in Saxonov. The use of this material in Ground 1 but not Ground 6, however, illustrates how the two grounds differ. Paragraphs 17

and 77 of Saxonov relate “multiplexed detection of polynucleotides,” *id.* at 28, and “the analysis of more than two targets in the same channel,” including “three or more distinct targets.” *Id.* at 29. Such disclosure is *immaterial* to Ground 6. Indeed, as discussed above, Ground 6 treats this element differently, relying instead upon Larson’s disclosure of these concepts in the form of, for example, its exemplary nine target assay performed in two colors. *See id.* at 60-62.

3. (b) forming a mixture of said sample and at least five hybridization probes,

This limitation is nothing more than a well-known and routine step that is needed to perform *any* method of PCR multiplexing that adds nothing inventive to the claims. *See, e.g., id.* at 2-6. Patent Owner does not dispute that this limitation is met in its Preliminary Response, *see* Paper 6 at 42-53, and Patent Owner’s own expert admits that multiplex PCR techniques that rely on TaqMan probes that are associated with and bind to specific targets were known in the art. EX2001 ¶ 30.

Consistent with this limitation being a well-known element of any PCR multiplexing technique, Saxonov is replete with disclosure of this limitation that is undisputedly prior art. For example, the Petition cites paragraph 26—part of the “SYSTEM OVERVIEW” section of Saxonov—which states “preparation of the sample may include combining the sample with reagents for amplification and for reporting whether or not amplification occurred.” Petition at 32 (quoting EX1004 ¶

26). The Petition further states citing Saxonov paragraphs 50, 63-67 and Figure 5 that “at least one probe is needed for each analyte, as taught by Saxonov and as commonsense dictates.” *Id.* This undoubtedly fully discloses the claimed limitation and is undisputed prior art.

While the Petition includes citation to paragraph 77 and Figure 9, this cannot as a matter of law or logic negate that Saxonov has a full prior art disclosure of this element. Indeed, paragraph 77 and Figure 9 are cited merely as a visual representation of the already described disclosure, included to aid the Board rather than to add new material, and is cited alongside indisputably prior art paragraph 49 that discloses “corresponding probes” specific for each target. *Id.* at 33. Thus, for Ground 6, this limitation is fully supported by material that is indisputably prior art.

4. wherein each of said at least five hybridization probes further comprises at least one fluorophore and at most four fluorophores;

Just like claim element “(a)...” discussed above in Section IV.B.2, Ground 6 relies on evidence that differs from that in Ground 1. Ground 6 specifically states that it would have “been obvious in view of Larson to use hybridization probes [labeled] with at most four fluorophores to detect at least five targets.” *Id.* at 62. The petition then describes, *without reference to any material of Saxonov*, how Larson renders obvious this limitation of the claimed invention. *See id.* at 62-64.

While the Petition does incorporate material by reference from Ground 1, *see id.* at 63-64, it does so to support the narrow proposition that a skilled artisan would have appreciated the ability to use up to four fluorophores in an assay. The '170 patent itself admits this. *See* EX1001 at 35:19-24 (known instruments “enable the detection of fluorescent signals in four colors.”); *see also* Petition at 34-35. It cannot reasonably be disputed that this is prior art to the '170 patent.

5. (c) partitioning said mixture into said plurality of droplets;

As to this limitation, Ground 6 relies on the same disclosure as in Ground 1. Similar to limitation “(b)...” discussed above in Section IV.B.3, this step is nothing more than a routine step of PCR methods such as Saxonov. *See, e.g.*, Petition at 5 (“In dPCR, the PCR solution including sample is partitioned into small droplets, where separate PCR reactions occur.”).

Unsurprisingly, Saxonov has many instances of prior art disclosure showing that its methods perform this limitation. The Petition shows, for instance, that Saxonov teaches exemplary methods in which the sample is separated into partitions, including through the cited Figure 1 and paragraph 28 which states “the partitions may be droplets disposed in a continuous phase.” *Id.* at 36. The Petition cites yet another example of Saxonov’s disclosure that the mixture containing the sample and the probes is partitioned into droplets, “including ‘with a fluid dispenser, such as a

pipette, with a droplet generator, by agitation of the sample (e.g., shaking, stirring, sonication, etc.), and/or the like.” *Id.* at 36 (quoting EX1004 ¶ 29). This disclosure is all *indisputably carried forward and prior art*.

To this disclosure, the Petition appends, as a *mere “see also” citation*, a citation to paragraph 78 of Saxonov. *Id.* It cannot reasonably be said that such a “see also” negates the prior art disclosure in Saxonov relied upon for this claim element. Indeed, the very definition of a “see also” citation is that it “is commonly used to cite an authority supporting a proposition *when authorities that state or directly support the proposition already have been cited or discussed*,” makes clear that the undisputed prior art material that is primarily cited is what is relied upon in the petition. *See* The Bluebook: A Uniform System of Citation (Columbia L. Rev. Ass’n et al. eds., 21st ed. 2020), Rule 1.2 (a). It is erroneous to dispense with an entire ground on the basis that a reference is not prior art due to a citation that is merely exemplary and for which the proposition supported is wholly supported by prior art material.

6. **(d) exciting said at least one fluorophore to generate one or more signals if one or more of said at least five polynucleotide analytes is present in said plurality of droplets, wherein said one or more signals comprise at least one signal generated by excitement of said at least one fluorophore;**

For this limitation, Ground 6 relies on the same disclosure as in Ground 1. Similar to limitations “(b)...” and “(c)...” discussed above in Sections IV.B.3 and IV.B.5, this limitation recites a requirement for any method that relies on fluorophores to detect signals. *See* Petition at 3-4.

The Petition cites extensive prior art support from Saxonov proving that it discloses this element. For example, the Petition cites Figure 5, which depicts a measurement of signals from droplets that are the result of detection of a FAM fluorophore and accompanying paragraphs 63-67. *Id.* at 37-38. This example alone fully supports Saxonov’s disclosure of this limitation. The Petition, however, then further cites Figure 3 and accompanying paragraph 52, which show and describe exemplary probes comprising fluorophores that bind to targets and emit increased fluorescence upon cleavage from their targets and excitation. *Id.*

In conjunction with this disclosure, the Petition makes a “*see also*” citation to paragraph 37. *Id.* For the same reasons as discussed above in Section IV.B.5, this mere “*see also*” citation does not undo the fact that Saxonov includes a prior art

disclosure of this element. Thus, this limitation is fully supported by material that is indisputably prior art for Ground 6.

7. (e) measuring said one or more signals to generate a cumulative intensity measurement,

For this limitation, Ground 6 relies on the same disclosure as in Ground 1. The Ground relies on numerous examples of this measurement disclosed by Saxonov that are undisputed prior art, including Figures 4 and 5 and paragraphs 12-13, 20, 41, 53, and 67. Petition at 38-39. This disclosure fully supports this element of the Petition.

The Petition additionally cites paragraphs 76-78 and Figure 10, but does so in conjunction with indisputably prior art material to support the same proposition. *Id.* at 39. Indeed, the concurrently cited portions of Saxonov—paragraphs 12, 20, 53, and Figures 4-5—fully support the Petition’s statement that “A POSA would have understood that the measured signals include both different colors and intensities.” *See id.* (for example, paragraph 20 of Saxonov describes extending assays to detect more targets by analyzing more than one target in a channel (the utilization of differing intensities), and/or by differentiating targets by the channel(s) in which they are analyzed (the color(s) detected)). Thus, it is undoubtedly true that this limitation of Ground 6 is fully supported by material that is indisputably prior art.

- 8. wherein said cumulative intensity measurement corresponds to the presence of a unique combination of presence or absence of said at least five polynucleotide analytes in said sample; and**

For this limitation, Ground 6 differs from Ground 1 and relies on Larson, similar to claim elements “(a)...” and “wherein each of said at least five hybridization...” discussed above in Sections IV.B.2 and IV.B.4. In fact, the Petition states that Larson itself discloses the identification of the presence or absence of nine different targets using just two colors. Petition at 65. The portion of the Petition that is incorporated by reference in this Ground regarding a POSA’s motivation and reasonable expectation in success in detecting five analytes likewise does not depend on any material that is disputed as to whether it is carried forward. *See id.* at 65, 31-32; *see also id.* at 42. Thus, for this limitation in Ground 6 the Petition is fully supported by material that is indisputably prior art.

- 9. (f) determining whether each of said least five polynucleotide analytes is present, in any unique combination of presence or absence, based on said cumulative intensity measurement, wherein the method does not require any step of immobilization of said at least five polynucleotide analytes or mass spectrometry.**

This portion of claim 1 is addressed in two subsections in the petition, however, Patent Owner does not contend that any material cited in the Petition is not carried over. *See* Paper 6 at 40-41; *see also* Petition at 42-44. Thus, nothing in

Petitioner’s treatment of these limitations would justify the Board’s conclusion that Ground 6 should not be instituted.

V. CONCLUSION

The Board failed to separately evaluate the distinct Grounds that rely only on Saxonov and those that rely on the combination of Saxonov and Larson to show how the claims of the ’170 patent are invalid. Instead of meaningfully evaluating all grounds, the Board only addressed the grounds that depend primarily on Saxonov.

The extent of the Board’s evaluation of any grounds that rely on the combination of Saxonov and Larson was a single paragraph that summarily decided—with no analysis—that because each “of the remaining grounds asserted in the Petition relies on Saxonov to reach a number of limitations of independent claim 1 and the challenged dependent claims” institution should be denied. Decision at 24. The Board engaged in no evaluation of whether such “Remaining Grounds” relied on disputed material or not. *See id.* If the Board had done such an analysis it would have revealed, as is shown above, that the grounds are fully supported by prior art material. These cast aside “Remaining Grounds” are meritorious and the Board should institute review.

Dated: February 28, 2025

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of **PETITIONER'S REQUEST FOR REHEARING OF THE BOARD'S NON-INSTITUTION DECISION UNDER 37 C.F.R. § 42.71(d)** as being served on February 28, 2025, via email pursuant to 37 C.F.R. § 42.6(e) to counsel for Patent Owner at the address below:

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