

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

QIAGEN SCIENCES, LLC,
Petitioner,

v.

TECAN GENOMICS, INC.,
Patent Owner

Case No. IPR2025-00026
U.S. Patent No. 11,098,357

PATENT OWNER'S SUR-REPLY

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I. INTRODUCTION

Petitioner's Reply does not remedy the deficiencies in the arguments made in its Petition. Petitioner has failed to establish that Porreca discloses all elements of the challenged claims as arranged in the claims. Rather, Petitioner improperly picks and chooses disparate elements from various embodiments of the reference to piece together the method of the challenged claims. This is insufficient to show that Porreca anticipates the challenged claims.

Petitioner's obviousness arguments also fail. Petitioner has not, and indeed cannot, point to any disclosure in Schmitt where both the SMI tags and the target sequence were used in combination to identify duplicates. Petitioner fails to acknowledge that every instance where Schmitt describes the analysis of its sequence reads, it uses the SMI tags alone to sort the reads into families. Petitioner resorts to improperly using its expert to fill in the gaps in the prior art, which cannot support a finding of obviousness.

II. CLAIM CONSTRUCTION

The only term in dispute is "identifying sequence reads with identical identifier and target sequences as duplicates," and the only aspect of that term on which the parties disagree is whether the target sequence and the identifier can be used in separate steps of the method. As explained in Tecan's Response and further

below, the intrinsic record confirms that these data points must be used *in combination* to identify duplicates.

Term (Claims)	Tecan’s Proposed Construction	QIAGEN’s Proposed Construction
“identifying sequence reads with identical identifier and target sequences as duplicates” (’357 patent, claim 1)	“identifying sequence reads as duplicates through a step that uses both the identifier and at least a portion of the target sequence”	“identifying sequence reads with identical identifier and at least a portion of the target sequences as duplicates”

The claims of the ’357 patent are all method claims that set forth the steps of the method. To meet the claims, each step must be “carried out or performed” as claimed. *See Kaneka Corp. v. Xiamen Kingdomway Grp. Co.*, 790 F.3d 1298, 1305-06 (Fed. Cir. 2015) (holding that the method claims “affirmatively recite the step of ‘oxidizing,’ [and] ‘oxidizing’ cannot be interpreted as doing nothing, or to simply allow oxidation to occur on its own”). Thus, the ordinary meaning of the “identifying” step requires that both the identifier and at least a portion of the target sequence are used as part of the step that identifies duplicates.

The dispute here is whether the identifying step of the claims (1) allows for performing a series of steps that eventually lead to the identification of duplicates, without regard as to how the identifier and target sequences are used, as Petitioner contends, or (2) instead requires using the identifier and target sequences in combination in the step that identifies duplicates, as Tecan contends. This is not a

question of the order of steps, but a question of what is required within the identification step. Here, the prosecution history, which Petitioner largely ignores, confirms that Tecan's construction aligns with the inventors' and examiner's understanding of the claims.

There is no ambiguity in Applicants' representations that the identification of duplicates requires that both the target sequence and the identifier be used together. As explained in Tecan's Response (Paper 19, 19-20), Applicants repeatedly stressed the importance of the claimed identification step:

- “Samuels *et al.* do not teach (1) *the active step of* ‘identifying a duplicate sequencing read as the sequencing read comprising the same identifier site and nucleic acid fragment as another sequencing read in the population of sequencing reads.’” EX2021.0797-98 (emphasis added).
- “However, the instant invention relies on the indexing site for batch identification of samples, and the *sequence of the identifier site and the sequence of the fragment that is amplified are used in combination to discern duplication.*” EX2021.0799 (emphasis added).
- “This is obviated in the claimed methods by using the identifier and fragment sequence to identify duplicate reads. Moreover, because *the fragment sequence is used in conjunction with the identifier to find*

duplicates, the identifier can be less complex than the ‘barcode’ in McCloskey.” EX1013.0070 (emphasis added).

The only reasonable reading of the prosecution history is that Applicants amended the claims to require that the identifying duplicates step requires the use of these two pieces of information together. There is no ambiguity that would allow for using the target sequence and identifier in separate steps of the method. Applicants amended the related claim language to overcome a prior art rejection, which must be considered when construing the claims. Paper 19, 18-20; *Spectrum Int’l, Inc. v. Sterilite Corp.*, 164 F.3d 1372, 1378 (Fed. Cir. 1998) (“explicit statements made by a patent applicant during prosecution to distinguish a claimed invention over prior art may serve to narrow the scope of a claim”).

As the Federal Circuit has repeatedly emphasized, the “prosecution history ‘is often of critical significance in determining the meaning of the claims’ because it ‘contains ... any express representations made by the applicant regarding the scope of the claims.’” *Genentech, Inc. v. Iancu*, 809 F. App’x 781, 783 (Fed. Cir. 2020) (citations omitted). The prosecution history is of critical significance here because it unambiguously demonstrates how Applicants and the examiner viewed the identifying step.

Petitioner relies on Example 1 (Paper 23, 3-4), but the prosecution history makes clear that Tecan narrowed the claims to exclude Example 1 from the scope of

the claims. EX2021.0797-799; EX1013.0070. There is no requirement that the claims cover every embodiment discussed in the specification. *See Baran v. Med. Device Techs., Inc.*, 616 F.3d 1309, 1316 (Fed. Cir. 2010) (“It is not necessary that each claim read on every embodiment.”); *see also SIMO Holdings Inc. v. Hong Kong uCloudlink Network Tech. Ltd.*, 983 F.3d 1367, 1378-79 (Fed. Cir. 2021) (emphasizing its “repeated[] ... caution” that “we should not infer that any particular embodiment is included in a claim” when there exists “*probative evidence to the contrary*” (citations omitted)). Indeed, the Federal Circuit has consistently found that applicants have narrowed claims so as to cover only certain embodiments in light of prior art raised during prosecution. *See, e.g., Spectrum*, 164 F.3d at 1378.

Here, the specification describes different methods of identifying duplicates. EX1002.0018 (14:21-31), 19 (15:23-35). Examples 1 and 5 illustrate these different methods. Example 1 describes using portions of the sequence reads to determine the genomic coordinates of the sequence (not to identify duplicates). EX1004.0020 (17:39-46). The starting coordinates, not the target sequence, are then used in the step of identifying duplicate reads. EX1004.0020 (17:42-43) (“***duplicate reads were identified by their genomic start positions.***” (emphasis added)), 11 (Fig. 5). Example 1, therefore, does not describe a duplicate identification step that uses the sequence and the identifier in conjunction. *See* EX2107.¶102 (“a POSA would understand the claim language, specification, and prosecution history of the ’357

patent to require that duplicate sequence reads are identified using a step wherein the combination of both the identifier site and a portion of the target sequence were used”).

The prosecution history and the language of the claims, however, reflect the method described in Example 5. There, a sequence that includes both the identifier and a portion of the sequence is used to identify the duplicates. EX1002.0021 (20:58-62) (“The first 50 bases of the target sequence read are compared to each other. Any read that has identical sequence to any other read is identified as a duplicate”). There is no question that, in the method described in Example 5, both pieces of information are used “in conjunction” for the step of identifying duplicates. The rest of the specification either does not contradict Tecan’s proposed construction or confirms it, including the method described in Example 5.

Further, Dr. Bustamante’s testimony aligns with Tecan’s proposed construction. EX2107.¶¶95-97. He explains that “[b]ased on the structure of the adaptor used in Example 5, the ‘target sequence read’ includes **both** the claimed identifier sequence and a portion of the target sequence.” EX2107.¶96. He further notes that the identifier sequence is not removed until after duplicate identification, confirming that the identifier sequence is used “in conjunction” with a portion of the target sequence to identify duplicate reads. EX2107.¶97. Thus, Example 5 describes

a method where the identifier and a portion of the target sequence are used in combination to identify duplicates.

Petitioner contends that the claims allow for the separate use of the target sequence and the identifier as part of a multi-step process. Paper 23, 2-4. This interpretation reads out the aspect of the invention that Applicants stressed during prosecution—that the target sequence and the identifier be used *in combination*. While, in theory, the claimed identification step can include multiple steps, the claims still require that the target sequence and the identifier be used together as part of the identification step. There is no reference cited in the Petition that requires the Board to determine whether a multi-step process would meet the claims—as discussed further below, neither Porreca nor Schmitt discloses the claimed duplicate identification method that uses the target sequence and identifier in combination.

III. GROUND I: PORRECA DOES NOT ANTICIPATE CLAIM 1

A. Porreca Fails to Disclose an Embodiment with Both Limitations 1.a and 1.c

Petitioner's Reply fails to establish that a POSA would understand the adaptor used in Figure 4C—the only portion of Porreca that Petitioner points to for disclosure of limitation 1.a—to include the claimed indexing site. *See* Paper 23, 5-11. Instead, Petitioner selectively picks and chooses elements from different sections of Porreca to arrive at the challenged claims. *See id.* To anticipate a claim,

a prior art reference cannot simply “include[] multiple, distinct teachings that the artisan might somehow combine to achieve the claimed invention,” it “must disclose ... all elements of the claim ... arranged as in the claim.” *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369, 1371 (Fed. Cir. 2008).

Petitioner attempts to supplement Figure 4C by pointing to disparate disclosures in the reference, Paper 23, 5-11, but this does not remedy the deficiencies in Petitioner’s anticipation argument. Petitioner has not sufficiently explained how a POSA would have understood Porreca’s ligation method to include the specific elements identified in the challenged claims. None of the disclosures to which Petitioner points connect the ligation method of Figure 4C to an adaptor that contains the claimed identifier site.

Petitioner relies on *Kennametal, Inc. v. Ingersoll Cutting Tool Co.*, 780 F.3d 1376 (Fed. Cir. 2015), to argue that a POSA “would at once envisage the claimed arrangement or combination” of “an adaptor having both a barcode and a random differentiator tag.” Paper 23, 5, 9. However, *Kennametal* does not support Petitioner’s conclusion. In *Kennametal*, the challenged patent claimed a cutting tool that included a substrate comprising a ruthenium containing binder and a coating on the substrate that was applied by physical vapor deposition (PVD). 780 F.3d at 1379. The Federal Circuit held that, in *Kennametal*, while the prior art “never disclosed the specific combination of ruthenium and PVD, [] *it taught that any of the five*

binding agents could be used with any of the three coating techniques.” Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co., 851 F.3d 1270, 1274 (Fed. Cir. 2017) (emphasis added). In *Kennametal*, the number and scope of possible variations disclosed in the cited prior art was narrow enough for a POSA to “immediately envisage” the claimed combination and the reference expressly taught that the embodiments were interchangeable.

In contrast, Porreca does not expressly teach interchangeability or that all of the large number of disclosed adaptor elements can be used with all of the disclosed preparative methods. The library preparation methods described in Porreca operate in fundamentally different ways. EX2107.¶¶104-105. For example, as explained in Tecan’s Response, and as Petitioner seemingly admits, the MIP library preparation process is necessarily performed in a different order with different steps than a ligation method. Paper 19, 25-28; Paper 23, 7-8. In light of these differences, there is no support for a conclusion that a POSA would have immediately understood the method of challenged claims from the disclosure of Porreca. Petitioner’s attempts to fill in the gaps of Porreca are exactly what the Federal Circuit has repeatedly rejected. *Galderma Lab’ys, L.P. v. Teva Pharms. USA, Inc.*, 799 F. App’x 838, 844 (Fed. Cir. 2020) (“not permitted to fill in missing limitations simply because a skilled artisan would immediately envision them” (cleaned up)).

Porreca only teaches using an indexing site with the MIP preparative method, which does not align with the method of the challenged claims. Petitioner's Reply attempts to expand the interpretation of certain paragraphs to cure the deficiencies in Porreca's disclosure, but as explained further below, these should be rejected.

1. Petitioner's Reliance on Paragraph 31 of Porreca is Misplaced

Petitioner's reliance on paragraph 31 of Porreca to establish that "tagging" can be used with all preparative methods is misplaced. *See* Paper 23, 6-7. Petitioner has not established that the "tagging" techniques discussed in paragraph 31 include the indexing site required by the claims. As Dr. Bustamante explained, "tagging" in paragraph 31 is molecular tagging, not the sample-index "indexing site" of limitation 1.a. Dr. Bustamante testified: "[s]o I would read Paragraph 31 to be referring to 'tagging' in the sense of molecular tags. Whereas [in ¶102] we're referring to 'tagging' using subject specific tags." EX1034.0060:21-61:15. He further explained: "[g]iven that this is in the library prep method, it's more likely to be discussing the preparative methods and how they use 'tagging,' which do differ [in] meaning, molecular random barcodes versus sample barcodes." EX1034.0066:14-67:11. Dr. Bustamante concluded: "if we're talking about preparative methods, 'tagging' is largely referring to molecular barcodes that are randomers versus when we're talking about 'tags,' in the context of patient tags." EX1034.0068:10-69:10.

Therefore, paragraph 31 cannot be broadly interpreted to cure the deficiencies in the disclosure, discussed in Tecan's Response and in more detail below.

2. Paragraph 149 Relates to "a MIP Library Preparation Process"

Petitioner contends that paragraph 149 broadly discloses the use of adaptors, but Paragraph 149 explicitly describes elements that are "part of a MIP library preparation process." There is no ambiguity that the disclosure of that paragraph is directed specifically to the MIP embodiment.

Petitioner points to the "and/or" sentence in paragraph 149 ("PCR priming sites...and/or sequencing priming sites") to argue that the paragraph is not limited to the MIP process. Paper 23, 7-8. Specifically, paragraph 149 states: "Adapters often contain PCR primer sites (for amplification or emulsion PCR) and/or sequencing primer sites." EX1006.0033, [149]. Petitioner argues that by using "and/or," this sentence teaches that the adaptors described in this paragraph are not limited to MIPs, but this argument fails. Paper 23, 8. Petitioner attempts to misconstrue Dr. Bustamante's testimony to invent ambiguity. Petitioner claims that Dr. Bustamante "could not explain" how the "and" embodiment relates to the MIP process. Paper 23, 8. However, Dr. Bustamante testified that such adaptors (with both PCR and sequencing primer sites) would be used for additional amplification. Specifically, he testified: "So following the logic, it [would] be PCR primer sites for amplification and sequencing primer sites or, if so chosen, for emulsion PCR and

sequencing primer sites So it would require an experimental setup where you want to use those PCR primer sites for additional amplification, emulsion PCR and sequencing.” EX1034.0095:4-97:4. This testimony is unrebutted. Thus, contrary to Petitioner’s assertion, the “and” embodiment of paragraph 149 does not demonstrate that the disclosure applies beyond the MIP process. Rather, it describes an adaptor that would be ligated to amplicons resulting from the MIP process for additional amplification.

Petitioner further points to Porreca’s reference to McCloskey to broaden the disclosure, but this similarly fails. Paper 23, 8. After teaching that adaptors can include “barcodes ... to uniquely identify individual samples (e.g. patient samples) that may be mixed together,” paragraph 149 cites to McCloskey. Based on this citation, Petitioner asks the Board to conclude that a POSA would have understood that paragraph 149 is broadly applicable to adaptors used with any preparative process, not just MIPs. Paper 23, 8. When read in context with the rest of the paragraph, however, McCloskey is cited for the general concept of patient-specific barcodes used for multiplexing. There is no implication that the specific library preparation methods of McCloskey are being incorporated into paragraph 149 to expand the disclosure beyond MIPs.

Moreover, Dr. Bustamante explained that, while a POSA might be able to use the individual elements of paragraph 149 in ways not described in Porreca,

paragraph 149 *as written* is referencing the MIP library process for the patient-specific barcodes. Specifically, he testified: “[I]f I understand your question correctly, you’re asking me whether Paragraph 149 refers to the MIP library preparation process, which I’ve stated it does. And I also believe you’ve asked me would somebody reading this skilled in the art understand that what is written here could also apply to other methods. And I would have to say that somebody could read this and understand it would apply to other methods. ***But, as stated in 149, as written in the patent, it is referencing the MIP library process.***” EX1034.0085:20-86:10 (emphasis added).

Petitioner bears the burden of showing where in the reference the claimed methods are disclosed. Petitioner has failed to show how a POSA would have understood paragraph 149 to disclose the use of an indexing site with Porreca’s ligation method.

3. Paragraph 102’s Disclosure of Patient-Specific Tags is Limited to the MIP Preparative Method

Petitioner’s arguments that paragraph 102 is not limited to MIPs ignores the context of that paragraph and testimony from Dr. Bustamante. Paper 23, 9-10. Read in context, paragraph 102 describes variations of using MIPs to analyze a sample using multiple probes and multiple patient samples:

It should be appreciated that different embodiments of the invention may involve conducting two or more *target*

capture reactions and/or two or more patient sample analyses in parallel in a single multiplex reaction. For example, in some embodiments a plurality of capture reactions (e.g., *using different capture probes* for different target loci) may be performed in a single multiplex reaction on a single patient sample. In some embodiments, a plurality of *captured nucleic acids* from each one of a plurality of patient samples may be combined in a single multiplex analysis reaction. In some embodiments, samples from different subjects are tagged with subject-specific (e.g., patient-specific) tags (e.g., unique sequence tags) so that the information from each product can be assigned to an identified subject. In some embodiments, each of the *different capture probes* used for each patient sample have a common patient-specific tag. In some embodiments, *the capture probes* do not have patient-specific tags, but the captured products from each subject may be amplified using one or a pair of amplification primers that are labeled with a patient-specific tag.

EX1006.0028, [0102] (emphases added).

Throughout this description, paragraph 102 consistently references the target capture method being described. As Dr. Bustamante explained, and Petitioner does not rebut, a POSA would read paragraph 102's reference to "capture" reactions and "captured nucleic acids" to mean nucleic acids captured through use of a MIP. EX2107.¶121. The repeated references to "captured nucleic acids," "capture reactions," and "capture probes" throughout this passage make clear that the MIP embodiment is being discussed. The use of "in some embodiments" at the beginning of each sentence does not transform these into separate, non-MIP embodiments

when the entire context points to MIPs. Thus, paragraph 102, like paragraph 149, is describing aspects of using MIPs.

B. Porreca Does Not Disclose the Claimed Method of Identifying Duplicates

Petitioner's anticipation argument also fails because Porreca does not sufficiently disclose how duplicates are identified. Petitioner relies on Porreca's disclosure of a "collapsing" step, but there is no information in Porreca that describes how that step is performed.

Petitioner argues that Porreca satisfies the "identifying" limitation based on the disclosure of Figure 5. Paper 23, 11-12. Figure 5, however, shows a collapsing step, and the specification describes that "[s]equencing reads of target and differentiator tags sequences are collapsed to make diploid genotype calls." EX1006.0033, [0148]. Porreca does not provide any disclosure for how this collapsing is done. Figure 5 only depicts sequences that have an identifier site and portrays a single nucleotide in the sequence. There is no information about whether the process depicted in Figure 5 involves the use of both identifier and target sequence in combination, as required in the challenged claims. There is no method disclosed for comparing the sequences to determine if they are duplicates in the first instance.

Petitioner relies on Dr. Metzker's testimony that Porreca is "looking at both the target sequence and the differentiator tags at the same time," but there is no support for this conclusion. Paper 23, 13. Dr. Metzker's testimony is precisely the type of expert testimony that the Director has cautioned against. *Interactive Commc'ns Int'l, Inc., v. Blackhawk Network Inc.*, IPR2024-00465, Paper 40, at 3 (PTAB Oct. 9, 2025). Dr. Metzker is filling the gaps in Porreca's disclosure with his own, self-serving interpretation. Petitioner's reliance on *Sage Products, LLC v. Stewart* to prop up this testimony is unavailing. Paper 23, 13. There, the expert was interpreting the disclosure and explaining what the referenced disclosed. *Sage Prods., LLC v. Stewart*, 133 F.4th 1376, 1384-85 (Fed. Cir. 2025). Here, however, Dr. Metzker's testimony is manufacturing a critical claim limitation where the reference lacks any disclosure. Porreca does not disclose how duplicates are identified, and therefore, Petitioner cannot meet its burden of showing that Porreca anticipates the challenged claims.

IV. PORRECA FAILS TO DISCLOSE DEPENDENT CLAIMS 2-3 AND 5-10

As explained above, Petitioner fails to show that Porreca anticipates claim 1 because the prior art lacks disclosure of required elements of the claims. Therefore, the Petition similarly fails to show anticipation of any of the dependent claims.

V. GROUND 2: PETITIONER HAS FAILED TO ESTABLISH THAT CLAIM 1 IS OBVIOUS

A. Schmitt Fails to Disclose the Identifying Limitation

Petitioner claims that paragraph 99 of Schmitt “by itself is sufficient to demonstrate disclosure of limitation 1.g.” Paper 23, 15. But paragraph 99 contains the same disclosures as paragraphs 85 and 98 regarding Schmitt’s use of SMI sequences—that “members of the same PCR ‘family’ are [] grouped together by virtue of having a common (i.e., the same) SMI tag sequence.” *Compare* EX1007.0034, [0099] *with* EX1007.0030, [0085] (“PCR duplicates may be unambiguously identified by virtue of having a common (i.e., the same or identical) SMI sequence.”) and EX1007.0034, [0098] (“Every duplicate that arises from a single strand of DNA will have the same SMI.”).¹

¹ Petitioner’s reliance on *Tile* to argue that Tecan waived any response to the subject matter discussed in paragraph 99 is misplaced. Paper 23, 15. *Tile* stands for the unremarkable proposition that the Board needs not consider claim limitations that Patent Owner does not dispute. *Tile, Inc. v. Linquet Techs., Inc.*, IPR2021-00927, Paper 53 at 19 (PTAB Nov. 16, 2022). Here, Tecan’s Response clearly disputed Petitioner’s allegations regarding limitation 1.g and indeed specifically disputed the subject matter disclosed in paragraph 99, citing the other paragraphs where overlapping disclosures appear. Paper 19, 30-31.

Petitioner now points to the second sentence of paragraph 99, which reads: “[t]he sequences of uniquely tagged PCR duplicates are *subsequently* compared in order to create a PCR consensus sequence.” Paper 23, 14, 15-16 (quoting EX1007.0034-35, [0099]) (emphasis changed). This sentence, however, further underscores that Schmitt identifies duplicates with the SMI tags alone *before* the target sequence is used to create a consensus sequence. As Schmitt states, the creation of the consensus sequence involves the comparison of “PCR duplicates”—sequences that have already been identified as duplicates without reference to the target sequences. As Tecan detailed in its Response, Schmitt is clear that the “PCR duplicates” are identified by only consulting the SMI. Paper 19, 30-31; EX1007.0030, [0085].

Notably, this is the first time Petitioner has asserted that the claimed generation of a consensus sequence meets the identification of duplicates limitation. The Petition merely asserts that “*in order to generate a consensus read*, the target sequences must be identical,” without any explanation of how making a consensus sequence *after* the duplicates are identified would satisfy limitation 1.g. Paper 2, 45 (emphasis added). This argument is insufficient to carry Petitioner’s burden of establishing that limitation 1.g is disclosed in the prior art.

Petitioner further incorrectly asserts that Schmitt’s reference to “shear points” in paragraph 85 shows that both the SMI and target sequence are used in identifying

duplicates. Paper 23, 16. This argument fundamentally misrepresents Schmitt's disclosure. In paragraph 85, Schmitt explains "the SMI adaptor molecules may be used in methods for unambiguous identification of PCR duplicates." EX1007.0029, [0085]. The paragraph then describes prior art methods that used shear points for identifying duplicates and the problems with that method. EX1007.0029-30, [0085] ("*[M]any sequencing studies* include a step to filter out PCR duplicates by using the shear points at the ends of DNA molecules However sequence reads with identical shear points can also reflect distinct molecules because *there are a limited number of possible shear points at any given genomic location.*" (citing a 2010 journal article) (emphasis added)). The inventors then explain that the disclosed SMI tags are used instead of shear points to overcome the flaws of using shear points for duplicate identification: "[the use of SMI tags] would thereby minimize the loss of data by overcoming the intrinsic limitations of using shear points to identify PCR duplicates." EX1007.0030 [0085]. Accordingly, contrary to Petitioner's representations, nothing in paragraph 85 discloses using shear points in combination with the SMI in order to identify duplicates.

Petitioner also newly relies on Dr. Metzker's testimony that Figure 3 of Schmitt shows "that the reads are being sorted and characterized both by the SMI and the target sequence." Paper 23, 18. Figure 3, however, does not show what Petitioner contends. The only description of Figure 3 states that Figures 3a-3c

“show[] sequence reads (brown) sharing *a unique set of SMI tags* are grouped into paired families with members having strand identifiers in either the $\alpha\beta$ or $\beta\alpha$ orientation.” EX1007.0007 [0014] (emphasis added). In other words, Schmitt simply explains that reads are grouped solely by their unique SMIs. Dr. Metzker’s testimony that Figure 3 shows that the target sequence is somehow being used in this process is, therefore, at odds with Schmitt’s actual disclosure and should be rejected. *See, e.g., Xerox Corp., et al. v. Bytemark, Inc.*, IPR2022-00624, Paper 9, at 16 (PTAB Aug. 24, 2022) (noting that conclusory expert testimony is “particularly problematic in cases where, like here, expert testimony is offered not simply to provide a motivation to combine prior-art teachings, but rather to supply a limitation missing from the prior art”); *Tinnus Enters., LLC v. Telebrands, Corp.*, 733 F. App’x 1011, 1022 (Fed. Cir. 2018) (“[W]e must disregard the testimony of an expert that is plainly inconsistent with the record”).

B. Petitioner’s Motivation to Combine Schmitt and McCloskey Is Also Deficient

As Tecan detailed its Response, Petitioner relies on hindsight reasoning and ignores the differences between Schmitt and McCloskey in arguing that a POSA would have been motivated to modify the method of Schmitt based on the teachings of McCloskey to arrive at the challenged claims. Paper 19, 32-34. In particular, Petitioner ignores the fact that Schmitt’s inventive method relies on using adaptors

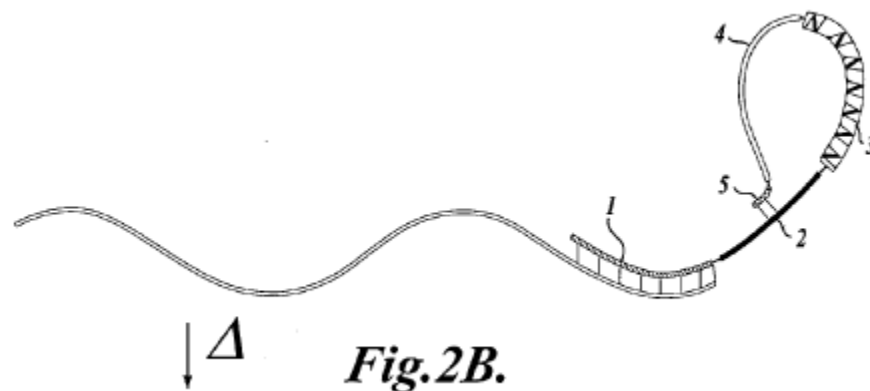
with double-stranded target nucleic acid molecules in contrast to traditional single-stranded methods:

The accuracy of current approaches to next-generation sequencing is limited due to their ***dependence on interrogating single-stranded DNA***. This dependence makes potential sources of error such as PCR amplification errors and DNA damage ***fundamentally limiting***. However, the complementary strands of a double-stranded DNA molecule (or “DNA duplex”) contain redundant sequencing information (i.e., one molecule reciprocally encoding the sequence information of its partner) which can be utilized to eliminate such artifacts. ***Limitations related to sequencing single-stranded DNA (e.g., sequencing errors) may therefore be overcome using the methods described herein.*** This is accomplished by individually tagging and sequencing each of the two strands of a double-stranded (or duplex) target nucleic acid molecule and comparing the individual tagged amplicons derived from one half of a double-stranded complex with those of the other half of the same molecule. Duplex Consensus Sequencing (DCS), significantly lowers the error rate of sequencing....

As described above, one approach that has previously been reported for DNA sequencing involves incorporation of a random tag sequence into a PCR primer [36]. This approach results in an improvement in accuracy relative to standard Illumina sequencing, ***but is fundamentally limited in that it is based upon amplification and sequencing of single-stranded DNA*** and thus cannot overcome limitations in sensitivity owing to single-stranded DNA damage events.

EX1007.0027-28, [0080, 0081] (emphasis added). But McCloskey is an example of these traditional approaches that are “fundamentally limited.” For example,

McCloskey describes and shows appending an adaptor to a single-stranded target DNA molecule: “FIGS. 2A-2D shows the steps in a representative method of the invention for authenticating a DNA amplification product [FIG. 2]B: the bar-coded oligonucleotide shown in FIG. 1 is annealed to one strand of the target DNA molecule.” EX1005.0006, [0014].



EX1005.0003 (Fig. 2B). Indeed, as Petitioner states, Schmitt references a journal article by the first-named inventor of McCloskey that contains “overlapping disclosures” as McCloskey (Paper 23, 19) as an example of these “fundamentally limited” techniques. EX1007.0004, [0006] (“Although several groups have attempted to increase sensitivity of sequencing, several limitations remain. For example techniques whereby DNA fragments to be sequenced are each uniquely tagged [34, 35] prior to amplification [36-41] have been reported.”); EX1007.0050 (identifying reference [35] as “McCloskey ML, Stöger R, Hansen RS, Laird CD.

Encoding PCR products with batch-stamps and barcodes. *Biochem Genet.* 2007;45:761-7.”).

Accordingly, Petitioner has failed to show why a POSA reading Schmitt would have been motivated to look at the “fundamentally limited” single-stranded target molecule methods such as McCloskey in order to improve the method. *See, e.g., Merck Sharp & Dohme B.V. v. Warner Chilcott Co., LLC*, 711 F. App’x 633, 637 (Fed. Cir. 2017) (reversing district court’s obviousness ruling of a claim requiring a single-compartment that includes a progestogenic steroidal compound and an estrogenic steroidal compound and finding no motivation to modify the prior art reference because it “criticizes the use of one compartment to deliver both compounds”). The Petition overlooks the specific disclosures of Schmitt, further highlighting the hindsight nature of Petitioner’s arguments.

C. The Combination of Schmitt and McCloskey Fails to Render Obvious Dependent Claims 2-3 and 5-10

As explained above, the Petition fails to show that the prior art renders claim 1 obvious, and therefore, the Petition similarly cannot establish that any of the dependent claims are obvious.

VI. GROUNDS 3-6: PETITIONER HAS NOT SHOWN THAT ANY CHALLENGED CLAIM IS OBVIOUS

In Grounds 3-6, Petitioner relies on the disclosures of Porreca or the combination of Schmitt and McCloskey for the elements of claim 1. None of

Petitioner's additional references cure the deficiencies of Porreca or the combination of Schmitt and McCloskey with respect to claim 1. Therefore, Petitioner has failed to show that any dependent claims are rendered obvious.

VII. TECAN'S DISCLAIMER OF CLAIMS IN ANOTHER PATENT IS IRRELEVANT

Petitioner improperly attempts to cast a shadow over the challenged patent by reference to Tecan's decision to disclaim other patents in the same family. The Federal Circuit has affirmed that a disclaimer of patent claims is irrelevant to a patent holder's ability to defend previously issued patent claims. *Softview LLC v. Apple Inc.*, 108 F.4th 1366, 1373-75 (Fed. Cir. 2024). The Acting Director's September 16 guidance does not change that law. There was no substantive assessment or ruling by the Board or another tribunal regarding the disclaimed claims that could possibly be persuasive to the Board on the merits of the current dispute. There is no "prior findings of fact and conclusions of law" for this Panel to consider. Further, there is no legal basis for the Board to make an adverse inference against the challenged claims based on Tecan's decision to streamline the dispute between the parties to a single patent in this family. Petitioner's arguments are merely an attempt to muddy the current dispute with irrelevant atmospherics.

VIII. CONCLUSION

For the reasons set forth in Tecan's Response and further discussed here, the Board should find that Petitioner has failed to show that any challenged claim is unpatentable.

Dated: December 19, 2025

Respectfully submitted,

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CERTIFICATE OF WORD COUNT

The undersigned hereby certifies that the foregoing **Patent Owner's Sur-Reply** complies with the type-volume limitation of 37 C.F.R. §§ 42.24(a)(1)(i) and 42.24(b)(1). The Sur-Reply contains 5,369 words, excluding the parts exempted by 37 C.F.R. § 42.24(a)(1), as measured by the word-processing system used to prepare the Sur-Reply.

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that, on December 19, 2025, a copy of the foregoing **Patent Owner's Sur-Reply** and all supporting documents were served on the counsel of record for Petitioner by filing the same through the P-TACTS System as well as delivering a copy via electronic mail to the following addresses:

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