

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

QIAGEN SCIENCES, LLC,
Petitioner,

v.

TECAN GENOMICS, INC.,
Patent Owner.

IPR2025-00026
Patent 11,098,357 B2

Record of Oral Hearing
Held: February 11, 2026

Before GEORGIANNA W. BRADEN, ZHENYU YANG, and
TIMOTHY G. MAJORS, *Administrative Patent Judges*.

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P R O C E E D I N G S

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JUDGE BRADEN: Good afternoon. We are convened here for oral arguments in IPR2025-00026, which challenges claims in U.S. Patent Number 11,098,357. I'm Judge Braden. Appearing from the USPTO Southwest Regional Outreach Office, also appearing by video, is my colleague, Judge Majors. And in person with you at the USPTO Headquarters in Alexandria, Virginia is Judge Yang. We're going to take a moment to go through some housekeeping issues, such as the fact that recording of any PTAB hearing is prohibited. The Court Reporter will provide a transcript of the hearing that will become a part of the record in this proceeding at a later date.

To ensure that the transcript of this hearing is clear, we ask that you please speak directly into the microphone when talking, and to identify specific slide numbers, numbering in the figures, and any other pertinent identifying information when referring to your demonstratives. Please note that this proceeding is public and that there may be those listening in on the public line. If the parties wish to discuss any confidential information, please notify the panel before doing so, so we can go off the public line.

In the hearing order for this proceeding, which is paper 33, each party was given 60 minutes total time to argue their case. Petitioner will open the argument and may reserve rebuttal time, which may not exceed more than half of Petitioner's total argument time. Patent Owner will then respond to Petitioner's arguments and may reserve surrebuttal time, also not to exceed more than half of Patent Owner's total argument time. I'll remind the parties that the Petitioner has the ultimate burden of establishing

1 unpatentability by preponderance of the evidence.

2 Please remember that your arguments should be limited to only
3 those arguments previously presented in your briefs. Please make it clear
4 which challenges and which claims you're addressing at all times. We ask
5 the parties to please hold any objections regarding a party's arguments until
6 it is your turn at the podium to note such objections.

7 Let's go ahead and get started with appearances for both parties for
8 those who will be arguing today. If there's anyone else attending in person
9 or remotely with you but will not be arguing, please identify them, as well.
10 For example, please state if your client is attending. Following the hearing,
11 please confirm with the Court Reporter to ensure that there's no questions
12 regarding spellings of names or terms. We're going to go ahead and start
13 with appearances for Petitioner.

14 MR. TRAUPMAN: Good afternoon, Your Honor. This is Matt
15 Traupman from Quinn Emanuel and I will be presenting the arguments by
16 myself, but for introductory purposes, to my left is my colleague, Landon
17 Smith. Behind me is my colleague, David Bilsker, and to his right is our
18 client, Urek (PHONETIC) Snyder.

19 JUDGE BRADEN: Very good. Thank you very much. And now
20 for Patent Owner?

21 MS. CIPRIANO: Good afternoon. I am Linnea Cipriano and I
22 will be arguing for Patent Owner, Tecan Genomics. With me at counsel
23 table is TJ Beavers. Also with me is Scott Weingaertner and John Padro
24 from Goodwin, and Andrea Schultz (PHONETIC) from Tecan Genomics.

25 JUDGE BRADEN: Very good. Thank you. Judge Yang will
26 maintain a clock, which you see on the bench, and she will endeavor to give

1 you maybe a five-minute warning during your opening argument to give an
2 appropriate warning near the end of the reserved rebuttal time. But as you
3 can see in the hearing room, there is a timer above her head that's going to
4 be set with each party's allotted amount of time. The light on the clock
5 changes to yellow when you near the end of your time, whether it's opening
6 or rebuttal. When the light has turned red or you see the number wind down
7 to zero, that means you have run out of time and you should conclude your
8 argument. Petitioner, do you wish to reserve any rebuttal time?

9 MR. TRAUPMAN: Yes. I'd like to reserve 15 minutes, please.

10 JUDGE BRADEN: Very good. Are there any questions or issues
11 that the parties would like to raise before we begin, starting with Petitioner?

12 MR. TRAUPMAN: Not from Petitioner.

13 JUDGE BRADEN: Patent Owner?

14 MS. CIPRIANO: None, Your Honor.

15 JUDGE BRADEN: Very good. Petitioner, you may begin your
16 argument when ready.

17 MR. TRAUPMAN: So, just to clarify, it's going to be 45 minutes
18 for the primary argument and 15 minutes on rebuttal, right? Don't think you
19 need to listen to me for 15 extra minutes.

20 JUDGE BRADEN: Very good. Thank you.

21 MR. TRAUPMAN: All right. Thank you. Matt Traupman on
22 behalf of the Petitioner. We're here, of course, to talk about the '357 patent,
23 which the parties have referred to as the UMI patent, so I might use that
24 terminology as I progress through my presentation here today.

25 So, going on to Slide 2, there actually really aren't that many
26 disputes for Your Honors to decide in this proceeding. There's a claim

1 construction dispute regarding the identifying limitation, and then Ground 1
2 which is an anticipation argument based on the Porreca reference. There's a
3 question about whether or not we are relying on disparate embodiments for
4 the indexing site limitation. That's point number one. Point number two is a
5 dispute about the -- whether or not Porreca discloses the identifying
6 limitation. And then moving on to Ground 2, which is a 103 combination
7 between the Schmitt and the McCloskey references. Again, there's a dispute
8 about the -- whether or not Schmitt discloses the identifying limitation and
9 the second dispute regarding motivation to combine the two references that
10 we've cited in Ground 2.

11 And before I get into the details, my high level argument is to
12 invite Your Honors to very much pay attention to how little expert testimony
13 that Patent Owner has presented on the vast majority of these issues, even
14 -- there's some issues for which they don't have any expert testimony at all,
15 and even for the issues in which they do present expert testimony, the expert
16 only addresses a subset of our arguments. And in our view, that's very
17 telling and that's going to be a point that I repeatedly come back to as I go on
18 with my presentation here today.

19 So, just to briefly go to -- and I'm now on Slide 5. Claim 1, which
20 is the only independent claim of the '357 patent, and the only claim upon
21 which I expect to be talking about today. There's many challenged
22 dependent claims, but Patent Owner has not raised any dispute with respect
23 to the dependent claims. The arguments are going to rise and fall solely on
24 Claim 1 here today, Your Honors. And so, Claim 1 is, as it states, a method
25 of identifying its sequencing reads. Basically, it requires an adapter to be
26 ligated onto a target DNA, and that adapter needs to have two different

1 sequences of DNA that are used for identification. A so-called identifier
2 that's one to eight nucleotides in an indexing site. And then the steps of the
3 method require amplifying that DNA, sequencing it, and then following
4 sequencing, identifying duplicate sequencing reads.

5 It definitely -- let me just read it. It's the identifying step.

6 Identifying sequence reads with identical identifier and target sequences as
7 to duplicates. So in other words, both the identifier and the target sequence
8 needs to be used in that step. And I've already mentioned the prior art, but
9 just to briefly orient Your Honors, we have, again, our Ground 1 is based on
10 anticipation by Porreca. That's Exhibit 1006, and I should note, on Slide 7
11 of my presentation, it just highlights some of the key parts of Porreca, which
12 is Figure 5. I'm going to get to it more in my presentation as I go through it.

13 Going on to Ground 2, Schmitt, which is Exhibit 1007 that's shown
14 here on Slide 8. Again, some key disclosures on paragraph 99 and Figure 3.
15 Again, we'll be discussing those in more detail. And the last piece of prior
16 art to orient Your Honors with is the McCloskey reference, as being shown
17 here on Slide 9, and that's Exhibit 1005. And all of them -- all of these
18 references -- disclose at least one unique identifier, and in some instances,
19 both the indexing site and the identifier site, as we'll go through in more
20 detail.

21 So, now switching on to Slide 11, I'm going to address the claim
22 construction issue.

23 JUDGE BRADEN: Actually, Counselor, I'd like us to address the
24 indexing and adapter, and the amplification issue first, please, for Porreca.

25 MR. TRAUPMAN: Yeah. So, I'd be happy to jump ahead, Your
26 Honor.

1 JUDGE BRADEN: Thank you.

2 MR. TRAUPMAN: So, this is Ground 1. I believe the -- you
3 mention the amplifying sequencing issue. I don't believe there's any disputes
4 there, Your Honor. My understanding is the only dispute is -- the only
5 dispute is whether or not we are relying on disparate embodiments of
6 Porreca for the identifier -- the claimed identifier -- which is in -- getting to
7 go back -- sorry I keep jumping around on you, Your Honor, but to go back
8 to Claim 1 of the Patent. Again, it's highlighted here on Slide 5 -- the
9 indexing site. That's the dispute, other than the identifying limitation on
10 Porreca as to whether or not we're relying on disparate embodiments. I
11 understand that's what Your Honor would like to address, so I'm going to
12 address that. Assuming that my understanding is correct, that's what I'm
13 going to go to now.

14 JUDGE BRADEN: That'll be a good start.

15 MR. TRAUPMAN: Okay. So, I'm now on Slide 28, which -- so,
16 again, this is, again, just to orient ourselves as I go through and explain why.
17 We are not relying on disparate embodiments from Porreca. In fact, we're
18 following the expressed teachings of Porreca, which is that -- to bring it
19 down to a short summary -- Porreca expressly teaches that any of its
20 preparative methods can be used with the disclosures that come throughout
21 the patent.

22 So, we're showing here on Slide 28, this is paragraph 27 of
23 Porreca, this is in the summary of the invention, it's talking about that -- the
24 fact that as you go through to prepare this DNA for sequencing, there are
25 different preparative methods. There's circularization, there's an
26 amplification, and there's hybridization. And that's similarly reflected as I

1 move on to Slide 29, Figure 4 of Porreca, Figure 8, Figures 4A, 4B, and 4C.
2 4A is circularization. Also sometimes called a MIP, M-I-P, from molecular
3 inversion probe. And what happens there, as you can see in Figure 4A,
4 there's two targeting arms that are specific to the target DNA that you want
5 to attach to. You ligate those targeting arms onto that target DNA, and as
6 -- hopefully you can imagine just looking at 4A -- it becomes circularized.
7 You have now circularized that target and are able to amplify it. And
8 relevant to this discussion, I'll note, as shown in Figure 4A, the MIP or
9 circularization probe has two PCR primers, which are noted there -- PCR
10 primer 1 and PCR primer 2, as well as the N N N. There's four Ns, but
11 they're representative -- those are the random nucleotides of the identifier
12 that you see in Figure 4A. That, again, is the circularization or MIP
13 technique that's described in the patent.

14 Next is Figure 4B, which is a hybridization technique that we just
15 looked at, described in paragraph 27, among other places. And there, you
16 can see it's a -- there's a probe -- hybridization probe -- that it basically has a
17 tail that hangs off the target DNA, but again, you see the N N Ns, because a
18 key part of the Porreca teachings is how do we get this random identifier,
19 this tag, as they call it, onto the target DNA. And so, it's done through
20 hybridization, as shown in Figure 4B, and then of course, 4C is the
21 amplification method, which involves ligation, as noted there in Figure 4C.
22 You take an adapter. It's just being shown here as random nucleotides, but
23 of course, you can have more than just that for the adapter, as I will show in
24 a second. And those are the three preparative methods of Porreca.

25 JUDGE BRADEN: I don't want to put words in Patent Owner's
26 mouth. I will allow them to do that when it gets their turn at the podium, but

1 as I understand their argument, they're saying that you cannot use this MIP
2 of 4A because the amplification occurs before the ligation, and they note
3 several of the examples in Porreca where you actually have the PCR
4 protocol beforehand. You use that to, you know, create your amplicon
5 population. You then purify the amplicon population.

6 And right now, I'm specifically looking at example two, which
7 goes through and actually gives you a method for doing this. And then once
8 you've created this amplicon population that you shred into the fragments,
9 you then ligate the adapters into -- you ligate the adapters that are required
10 for amplification by the sequencing platform. So, it's not in the same order
11 as the claims. And so, my understanding is that they're saying you could not
12 use this and combine it with the others, 4B and 4C, and therefore, you don't
13 have -- the petition is incorrect and that you don't actually have your
14 identifier and the indexer that you would need to meet the claim limitations.
15 What am I misunderstanding?

16 MR. TRAUPMAN: I think you largely describe the MIP process
17 correctly, Your Honor, but what I think you're maybe misstating -- maybe
18 that's an overstatement -- but I think what you're missing is we're relying on
19 Figure 4C. That's what our petition is based upon and why 4C, the ligation
20 preparative method or the amplification preparative method is anticipatory.
21 What it really comes down to, and I'm going to get to this in a second, is
22 they try to say that paragraph 149 -- and I'm going to get there in a second,
23 but I'm happy to -- and I'll address it.

24 They're saying paragraph 149 is the only disclosure of the -- both
25 of the identifier and the indexing site, and that's solely limited to the MIP
26 embodiment, and therefore, our reliance on paragraph 149 is improper

1 because we're otherwise relying on figure -- on the 4C, the
2 amplification/ligation embodiment. That's my understanding of their
3 arguments, Your Honor. And I'm going to show you why they're misreading
4 paragraph 149 and why a person skilled in the art would understand that
5 that's -- it's not limited to just MIPs, and that's our counter-argument to that
6 point. So, I hope that answers Your Honor's --

7 JUDGE BRADEN: It does. Thank you.

8 MR. TRAUPMAN: -- question. So, but I mean, here, again, we're
9 not just focusing on one paragraph of Porreca, and you have to read this
10 prior art reference as a whole, okay? And so after, you know, we just looked
11 at paragraph 27 where they introduced the three preparative processes, and
12 then paragraphs 28, 29, and 30 are each individually a paragraph describing
13 in more detail each of the three preparative processes. And then as to the
14 very next paragraph -- again, this is in the summary of the invention
15 -- they're telling the world it should be appreciated that any of the
16 circularization amplification and/or hybridization based methods described
17 herein may be used in connection with one or more of the -- and we
18 highlight most relevant -- tagging methodologies described herein. So, in
19 other words, they're teaching you, yes, we might exemplify a particular
20 strategy with MIPs, but I'm telling you here, all of the preparative processes
21 can be used with the different techniques that are described as we go
22 throughout the disclosure in the patent.

23 And so then, again, moving on. Kind of -- I'm going to end and
24 -- I want to telegraph where I'm going -- I'm going to end with a discussion
25 of paragraphs 149 and 150, which we think is where the rubber really hits
26 the road, but just to give a little bit more orientation to Your Honors, is that

1 we separately rely on paragraph 102, which I will also note is important
2 context. It starts with paragraph 101, which obviously is the immediately
3 preceding paragraph.

4 I'm on Slide 31, for the record, showing paragraphs 101 and 102 of
5 Porreca. And it talks about here in paragraph 101, in some embodiments,
6 one or more of the techniques described herein may be combined in a single
7 assay protocol for evaluating multiple patient samples in parallel. In other
8 words, it's multiplexed, and I don't think there's any dispute in the record that
9 when you multiplex -- when you have patient samples from multiple
10 different patients being done in one assay, as described in paragraph 101 and
11 102, you're going to need that identifier site, in addition to the indexing site.
12 You need the two.

13 So, in other words, the identifier site identifies the patient sample
14 and the indexing site is it -- allows for the identification of duplicates.
15 That's what we're talking about here, and so, Porreca is talking about, yeah,
16 you might want to use -- in addition to that N N N that's in all the Figure 4
17 embodiments, you're going to use multiple patient samples. Well, you need
18 a -- and this gets down into 102 -- you need to have a separate identifier to
19 show which patient sample it came from. And so then moving on to
20 paragraph 102, it should be appreciated that aspects of the invention may be
21 useful for high throughput, cost effective, yet reliable genotyping of multiple
22 patient samples, e.g. in parallel, for example, multiplex reactions.

23 So, again, that's just kind of, again, reiterating what is introduced
24 in paragraph 101. And these are the -- this is the first sentence of paragraph
25 102. Paragraph 102 is a lengthy paragraph. It spans roughly half a column
26 of the Porreca publication. It's not really suitable for putting up in a slide,

1 but this is the first sentence of paragraph 102, and I think it's very important
2 because what we hear from the Patent Owner is, oh, 102 is just all about the
3 MIP embodiment. No, it's not.

4 This paragraph is beginning -- again, consistent with what we saw
5 on paragraph 31 and also 101, this is general techniques. You can use these
6 different preparative methods for, for instance, multiplexing, and if you
7 multiplex -- and this is now down farther into paragraph 102 -- it's some
8 embodiments -- so, in other words, some embodiments -- not all, but some
9 embodiments -- samples from different subjects are tagged with subject-
10 specific tags so that information from each product can be assigned to an
11 identified subject.

12 Again, that's a natural consequence of running multiple patient
13 samples on the same assay. And again, there's nothing about this sentence
14 that is specific to MIPs, and yes, if you read the rest of paragraph 102, there
15 are references to inversion probes and how you could do things with
16 inversion probes, but they universally start with the same introductory clause
17 in some embodiments. And so, yes, there are some embodiments in
18 paragraph 102 that are talked about -- that are specific to MIPs, and there are
19 other things that are talked about in 102 that aren't specific to MIPs.

20 And here, relevant for our discussion here, is that patient-specific
21 tags is not specific to MIPs. There's nothing about this sentence that is
22 specific to MIPs. It is just some embodiments. And flowing again from the
23 introduction in 101 and the first sentence of 102 that you can run multiplex
24 analyses in this invention. It's not limited to the MIPs. Again, paragraph 31,
25 all the different preparative methods can be used.

26 And now, I think where the rubber really hits the road, and I'm on

1 Slide 32, is paragraph 149. And this states that -- this is the disclosure here
2 -- barcodes may be included, for example, to uniquely identify individual
3 samples, e.g. patient samples, that may be mixed together. That's, again,
4 referring to the same concept that we saw on paragraph 102 of Porreca
5 where -- again, if you're multiplexing, you're taking multiple patients on a
6 single assay, you need some way to identify it. And it cites here the
7 McCloskey publication, which of course, is part of what is in our Ground 2.
8 And it discloses, again, embodiments -- again, with both the identifier site
9 and the indexing site in a single embodiment. And so, that's further
10 disclosure in Porreca.

11 Now, looking at the totality of paragraph 149, Patent Owner seizes
12 upon the topic sentence. The first sentence of paragraph 149. It says, the
13 skilled artisan will appreciate that as part of the MIP library preparation
14 process, adapters may be ligated onto the ends of molecules of interest, and
15 their argument is, ah ha, it's MIPs, it's only MIPs, and this whole paragraph
16 only applies to MIPs, and we disagree with that. And our expert, Dr.
17 Metzker, explained why we disagree with it. And it really starts -- well,
18 there's a couple of points here, but it's going to start with the next sentence,
19 but also, it's going to be relevant to McCloskey.

20 So, the citation of McCloskey, as I noted, and now I'm on
21 paragraph 33, McCloskey doesn't disclose any MIP embodiment.
22 McCloskey doesn't disclose a barcode used in a MIP. McCloskey discloses
23 a barcode used for the other two preparative methods -- the hybridization
24 method and the ligation method, and there, they show the identifier cite, but
25 there's no MIP embodiment in McCloskey, and that's undisputed, and as I'm
26 showing here on Slide 34, is Dr. Bustamante admits that McCloskey hasn't

1 disclosed a MIP embodiment.

2 And then the other really important piece -- and this gets back to
3 your question, Judge Braden, earlier about how that MIPs process works.
4 Because then it goes on, you know -- the second sentence of paragraph 149
5 goes on to explain adapters can often contain PCR primer sites and/or -- and
6 that's -- we obviously highlight the and/or, because that's going to do -- it's
7 going to really signal a lot here -- and/or sequencing primer sites. So, in
8 other words, just reading the natural meaning of and, and or, that means an
9 adapter can have a PCR priming site, it can have a sequencing priming site,
10 or it can have both. That's what and/or means in paragraph 149.

11 JUDGE BRADEN: So, Counselor, if we were to find that this
12 paragraph, 149, was only directed to MIP library preparation and its related
13 process, then does your challenge fail? Are the claim limitations not met,
14 given the 102 challenge?

15 MR. TRAUPMAN: Well, I respectfully disagree with the premise
16 of your question, but putting -- accepting the premise of your question, and
17 I'm about to explain why 149 clearly is not limited to the MIP process, but if
18 you do, I think I just showed you why 102 also discloses adding the
19 indexing site. And again, I don't think there's any language there that is
20 limiting it to MIP preparative process.

21 So, the answer to your question is no, but also, I -- you know, I
22 think that really the nub of this is why 149 isn't really limited to MIPs, and
23 it's really -- I'm about to explain why that's the case, as I go through this.
24 And again, it's because - and it gets back to, Judge Braden, your explanation,
25 which if I'm recalling it correctly, I think accurately described the MIP
26 process and the point is in a MIP process, you are never going to have an

1 adapter that has both a PCR priming site and a sequencing site because it's
2 not -- that's not how the workflow goes. And how do we know that? It
3 comes straight from both, Petitioner and their expert, and so this is Dr.
4 Bustamante's declaration.

5 I'm on Slide 36 or paragraph 75 of his declaration. And this is the
6 MIP process, and as you see, you go from panels A, B, C, so that's the
7 circularization process. Now, just to remind you, reminding back to Figure
8 4A, that gray part of the circle in the MIP has PCR priming sites on it.
9 That's not the adapter that we're talking about. And you follow through to
10 step D, you've created a circle, then you break it away and make it linear in
11 step E, and then you amplify. No adapter has been added at this point. The
12 PCR priming sites come from the probe itself -- the molecular inversion
13 probe. There's no adapter, and you've amplified it. The result is F. You've
14 amplified that product and no adapter, okay?

15 And so now, you may want to add an adapter for sequencing, but
16 that's going to have the sequencing -- you know, going back to the "or" part
17 of 129, that's going to have a sequencing priming site, but there's no reason
18 why you're going to have a PCR priming site because the PCR site, as we
19 saw in Figure 4A of Porreca is on the molecular version probe.

20 And so, a person of skill in the art who sees the "and" and the "or"
21 in paragraph 149, that says an adapter can have both of these things, both the
22 PCR priming site and a sequencing site, is going to know that's not talking
23 about MIPs because that's not how the MIPs workflow goes. And I didn't
24 get it in slides, but it's pretty clear in Dr. Bustamante's declaration, paragraph
25 122, he says, a POSA would've understood that the methods Porreca
26 described using barcodes indexing sites with padlock probes or MIPs do not

1 include a step where the adapter with the indexing site is ligated to the
2 nucleic acid fragment or a step where the adapter ligated fragments are
3 amplified. That's right. The amplification happens because the PCR site is
4 on the MIP, but again, that's inconsistent with the "and" part of the "and/or"
5 of paragraph 149.

6 And Dr. Bustamante goes on at the end of paragraph 142, the only
7 description of ligating an adapter prior to amplification is in relation to blunt
8 ended ligation. And the only description of an adapter having an indexing
9 site is in relation to MIPs. Now, we obviously disagree with that, but he's
10 admitting that the only talking about -- the only description of ligating an
11 adapter prior to amplification, i.e. one that needs a PCR priming site, is 4C,
12 which is what we're relying on. And --

13 JUDGE BRADEN: So, let me make sure I understand. You're
14 stating that the sentence in paragraph 149 of Porreca that says, adapters often
15 contain PCR primer sites for implication or emulsion of PCR and/or
16 sequencing primer sites, that indicates that it has to be for more than just
17 MIP library preparation process?

18 MR. TRAUPMAN: Yes, Your Honor. And specifically, the use
19 of the word "and" in that sentence is the reason why, but yes.

20 JUDGE BRADEN: Right. Thank you.

21 MR. TRAUPMAN: And again, we're citing here -- this is Dr.
22 Metzker here on Slide 37. MIPs don't typically contain an additional PCR
23 priming site because again, the PCR primer is in the inversion probe itself.
24 And, you know, we ask Dr. Bustamante -- notwithstanding his declaration,
25 which was pretty clear that you don't amplify with -- you don't use the
26 adapters in a MIP preparative process to amplify, why would you have the

1 "and" part, and he basically said, for additional amplification or emulsion of
2 PCR and sequencing. Well, he's just reading what 149 says and saying
3 "additional", but he doesn't actually provide any explanation why that would
4 actually happen in real life or why a person of skill in the art would
5 understand that, and as a matter of fact, he said the opposite in his
6 declaration, which he submitted before he was confronted with this point in
7 his deposition. He said, MIPs don't -- you don't amplify with the adapter in
8 MIPs. And by the way, it wasn't just Dr. Bustamante who said that on
9 paragraph 25 of the Patent Owner reply.

10 Patent Owner says, unlike the blunt end ligation process of Figure
11 4C, a POSA would've understood that in the MIP process, the adapter is
12 never ligated to the nucleic acid fragment/molecule of interest in the sample,
13 and no adapter ligated fragments are amplified. It's pretty clear what they
14 said and it's pretty clear that that's inconsistent with the "and" embodiment in
15 paragraph 149. And again, this is largely admitted to by Dr. Bustamante.

16 We're showing here pages 85 and 86 of his deposition. This is
17 Slide 39. His deposition is Exhibit 1034. He, when presented with 149, he
18 admitted, I would have to say that anybody could read this and understand
19 that it would apply to other methods. We agree, and that's also what the
20 patent says in paragraph 31, that I've also already shown.

21 So, a person of skill in the art can read paragraph 149 and know it's
22 not limited to MIPs. Dr. Bustamante admitted it and that fits very well
23 within the case law that we cited -- the Kennametal case -- where it says if a
24 person of skill in the art reading the reference would at once envisage the
25 claimed arrangement or combination, it could be anticipatory. And that's
26 exactly what Dr. Bustamante admitted is happening here in paragraph 149.

1 And we don't have to go far in the patent to understand that, in fact, it's
2 disclosing how you can have adapters in the "and" configuration -- the PCR
3 and the sequencing site. And guess what? It's not for MIPs.

4 So, you go to the very next paragraph -- paragraph 149 -- and
5 again, a person of skill in the art is going to be reading this patent and they're
6 going to understand what they're talking about. So, you go to the very next
7 paragraph after talking -- the disclosure 149 talks about adapters and how
8 adapters can have the indexing site in it. They talk about, now, here's how
9 you incorporate the random differentiator tag. That's the other identifier
10 here, and it can be done through various methods known in the art. One of
11 which, for example, is incorporation by ligation. That's Figure 4C. It very
12 clearly describes ligation.

13 And you go farther on in paragraph 150, and I don't think there's
14 any argument from Patent Owner that 150 is not talking about MIPs.
15 Another method is to incorporate the differentiator tag sequence into a PCR
16 primer, such that the primer structures arranged with the common adapter
17 sequence, followed by a random differentiator sequence, followed by the
18 PCR priming sequence. So, the common -- I'm going to get to the common
19 adapter sequence in a second, because if you go to the next sentence, which I
20 believe I have highlighted on the next -- yeah, next slide.

21 A differentiator tag sequence and adapter sequence -- that's the
22 common adapter sequence that's referenced in the immediately preceding
23 sentence -- may contain a sequencing primer incorporated as tags. So, here
24 in these two sentences of 150, through ligation, Figure 4C, you're disclosing
25 the very "and" embodiment -- the use of "and" -- from 149. It has a
26 sequencing primer and a PCR primer, and it has the differentiator tag. And

1 of course, 149 says you could also have the indexing site.

2 So, it's clear. You really have to read one more paragraph past 149
3 to see an example in the patent of adapter with a PCR primer site and a
4 sequencing site, and it has nothing to do with MIPs. So, in total, we think
5 this, again, comes back to what we came to, which is the teaching in
6 Porreca. Any of the preparative methods can be used with any of the
7 techniques taught throughout the patent, and that's clearly what we're seeing
8 here as you actually read what Porreca is teaching, and so that's why we
9 think the limitation requiring both, the indexing site and the identifier site, is
10 disclosed by Porreca. So, I don't know if you have any other issues you'd
11 like me to go to. Otherwise, I can -- my time left, I can -- I think I'm going
12 to go to -- I'll finish discussing the identifying limitation of Porreca, if that is
13 okay with Your Honors.

14 So, here we have the identifying limitation and this -- so, that issue
15 that we've just been talking about with Porreca, that's like really the one
16 issue where they actually do have expert testimony on, Your Honors. This is
17 one where they don't have any expert testimony. Dr. Bustamante didn't
18 opine about Porreca's disclosure about the identifying limitation at all.
19 They're relying exclusively on attorney argument and they don't even
20 address, as I'm going to show, the -- we think the key, you know -- a key
21 disclosure in Porreca.

22 So, here's Figure 5 of Porreca. I'm on Slide 46. It talks about how
23 you collapse the -- so, just to actually take a step back and go through all of
24 Figure 5. So, you start with four different samples, then you amplify them,
25 then you sequence them. And as is clearly shown, you are sequencing both
26 the target interest and to be clear, it's only showing where there's divergence,

1 in this case, in a single place between an A and a T, but you're sequencing as
2 the straight lines indicate the entire target sequence, and then the unique
3 identifier. And then it talks about collapsing the differentiator tag sequences
4 down, so you go from approximately 10 to four as you move from the
5 middle column to the right column in Porreca. That's all done in a single
6 step, so I didn't -- and I'm probably not going to, given my time constraints
7 have time to address the claim construction issue. We think we win under
8 either construction, whether or not the claims require a single step or not.
9 And here's paragraph 298. It very clearly discloses, "For any
10 target: differentiator tag combination." In other words, both, the identifier
11 and the target sequence observed more than once. All such reads are
12 collapsed into a single read before base calls are determined. So in other
13 words, collapsing into a single read, that's identifying duplicates and that's
14 exactly what Figure 5 shows on Slide 47, showing paragraph 298.

15 And again, moving on to Slide 48, our expert, Dr. Metzker,
16 explained exactly what "collapsing" means. This is from paragraph 88 of
17 his declaration. And just to drive home this point on the identifying
18 limitation, we cited it, paragraph 298 in our petition. The institution
19 decision relied upon it in finding that this proceeding warranted being
20 instituted. Tecan's Patent Owner response doesn't even mention paragraph
21 298 at all. Again, they don't have any testimony from Dr. Bustamante. Just
22 some attorney argument. No mention of paragraph 298. We cited again in
23 our reply to really point home that 298 is important. Surreply -- nothing.
24 Now, I don't know if they're going to address 298 for the first time here in
25 the oral argument, but their papers don't have any argument whatsoever on
26 paragraph 298 of Porreco. Unless there's any questions, I'm going to use my

1 last 11 minutes to talk about Ground 2, which is the combination of Schmitt
2 and McCloskey.

3 And so the first issue is again, whether or not Schmitt discloses the
4 identifying limitation. And here again, what we see here is they do have
5 expert testimony, but their expert testimony -- their expert just completely
6 ignored, one -- and we'd say one very important paragraph of Schmitt -- that
7 again, was relied on in the petition and cited in the institution decision, and
8 yet, their expert never opined upon, and as noted in our motion to strike,
9 they only address for the first time in the surreply.

10 So, that key paragraph is here on Slide 54, it's paragraph 99 of
11 Schmitt. And again, it's talking about how you have members of the same
12 PCR family are grouped together by virtue of having common SMI tags, so
13 that's the identifier. So, the sequences of uniquely tagged PCR duplicates
14 are subsequently compared in order to create a PCR consensus sequence.
15 So, in other words, the sequences of the target DNA are compared to create
16 a consensus sequence. Only positions that yield the same DNA sequence in
17 a specified proportion of the PCR duplicates in a family, such as 90 percent
18 in one embodiment, are used to create the consensus. So, in other words,
19 again, you're creating -- you're identifying duplicates and creating a
20 consensus read, both based on both, the SMI and the target of interest. The
21 target DNA. And again, here's Dr. Metzker explaining what it means to
22 generate a consensus read. This is Slide 55, citing paragraph 128 of Dr.
23 Metzker's declaration, submitted with our petition.

24 And again -- this is Slide 56 -- the institution decision very clearly
25 is relying on paragraph 99, saying that it, again -- you're relying on the
26 consensus sequence disclosure in paragraph 99 to decide that this proceeding

1 warrants institution. And so, again, they -- Patent Owner argues for the first
2 time in the surreply that, oh, well we addressed paragraphs 85 and 98, which
3 are two different paragraphs that admittedly were cited in our petition, but
4 they're duplicative of paragraph 99, and so that's why we didn't cite
5 paragraph 99. That's why we didn't have Dr. Bustamante addressed on
6 paragraph 99. But there's no disclosure in paragraph 85 or 98 of Porreca that
7 disclosed generating consensus read. That's only in paragraph 99 and it's left
8 wholly unaddressed by Patent Owner.

9 JUDGE BRADEN: Just to clarify, that's paragraph 98 and 99 of
10 Schmitt?

11 MR. TRAUPMAN: Yes. That's just to be -- to clarify that, Your
12 Honor. Paragraphs 85 and 98 of Schmitt were also cited, in addition to
13 paragraph 99. I apologize if I misspoke. Again, we cited all three
14 paragraphs in our petition and what you see in Patent Owner's response and
15 Dr. Bustamante's declaration -- I think I have a slide that I can show -- they
16 only address 85 and 98. And then in our reply, we said, what about 99, and
17 for the first time, in the surreply, they try to take on 99 and to say, well, it's
18 all the same as 85 and 98, and therefore, we didn't really need to address it.
19 And my point here that I'm trying to show here on the slide is, here's 85
20 -- I'm on Slide 58 of Schmitt. Let me start over because that's going to
21 muddle the record.

22 I'm on Slide 58 of our presentation showing paragraph 85 of
23 Schmitt. There's nothing about generating a consensus read here. Same
24 thing now on Slide 59, showing paragraph 98 of Schmitt. Nothing about
25 consensus reads here. And here's the point I was trying to make. I knew I
26 had a slide. Here on Slide 60, Dr. Bustamante's declaration, he says, we

1 only rely on 85 and 98. Well, clearly, I showed you we don't and the
2 institution decision recognized that we don't. And he's admitting here in his
3 deposition that's all he opined upon for paragraphs 85 and 98 of Schmitt.
4 And of course, it's -- I think 99 is very persuasive, but we also, as cited in the
5 institution decision at Figure 3. And Figure 3 shows the use of both, the
6 identifier sites -- that's the alpha and beta in gray shading on -- I don't know
7 if you guys can see it -- in the -- on the slide, but on each end of the
8 molecule, they have the identifier. And what Schmitt does is they have a
9 -- it's double-stranded, so they have a top strand and a bottom strand. So, if
10 you notice the alpha in the bottom, the complementary stance is on the right
11 because of the different directionality of that bottom strand of the DNA. But
12 you have Figures A through B, and they show basically how, for instance, in
13 A, the third sequence of the top strand has a mutant in it, but they're able to
14 show through the cogeneration of the consensus, yeah, that's just an error.
15 We're not going to count that and we can collapse that down into the
16 consensus read shown in Figure 4D. And similar methodologies used in
17 Figures 3B and 3C, all collapsing down to the consensus shown in Figure
18 3D.

19 Now, I noticed on the slides that Patent Owner is going to present,
20 they chop it off after Figure C -- after, you know, 3A, B, and C, and they
21 don't show you D. Well, that's an important part of the whole point because
22 again, as we cited in paragraph 99, it's the generation of the consensus read
23 that shows you how you're identifying the duplicates. And again, just noting
24 here what the institution decision says about Figures 3 and they also rely on
25 Figure 4. I don't have time to address that.

26 And now, moving on to the other point in Ground 2 in the last five

1 minutes that I have, is the motivation to combine. And here on Slide 65,
2 we're showing paragraph 6 of Schmitt, and Schmitt is citing -- it has a
3 reference 35. It's citing a McCloskey paper. I believe it's referred to in our
4 petition as McCloskey 2007. And so, it -- and it's clearly referring about
5 uniquely tagging. It's just citing McCloskey for the concept that you can
6 uniquely tag different samples prior to amplification, so that's the same topic
7 subject matter that we're talking about here. And again, it's citing
8 McCloskey 2007 and then our -- but our reference is -- and I'm going to
9 explain why we cite the McCloskey patent. It's the same patent that was
10 cited in Porreca, overlapping authors, overlapping subject matter, but
11 important -- McCloskey has important -- McCloskey patent -- that is, for the
12 record, Exhibit 1005, as opposed to McCloskey 2007, which is Exhibit
13 1015. McCloskey the patent, Exhibit 1005, has important additional
14 disclosures beyond what's in McCloskey 2007.

15 And I'm going to -- so again, so this is -- start with the similarities.
16 They had this hairpin embodiment. It's in both, the McCloskey patent,
17 which is on the left of Slide 67, and McCloskey publication, which is on the
18 right of Slide 67. And again, on Slide 68, more similarities. Again, using
19 this hairpin embodiment. But what's significant, and really, this is again,
20 something that was addressed for the first time in the surreply. Again, on
21 motivation to combine. No expert testimony whatsoever from the Patent
22 Owner. It's all lawyer argument. All attorney argument that we're
23 addressing here. And also, really identifying alleged fundamental
24 incompatibilities between McCloskey and Schmitt for the first time in the
25 surreply, which again, we think is untimely, it's the subject of a motion to
26 strike, but they're also just profoundly wrong on the merits of that argument.

1 And what's significant, our petition relied on a -- the double-stranded adapter
2 of the McCloskey patent.

3 That's shown here on the left of Slide 69. This is a screenshot from
4 Metzker's declaration at paragraph 115, but he's screenshotting the
5 McCloskey patent and that's what we rely on for our motivation -- for our
6 combination in our petition, and it's wholly unaddressed, even in the
7 surreply by the Patent Owner. So, and again, that's the key -- one of the key
8 distinctions between the McCloskey patent and the McCloskey publication.
9 The McCloskey patent has this specific double-stranded adapter with both,
10 an identifier site and an indexing site.

11 That point is undisputed, and that is why a person of skill in the art
12 would've been motivated to combine McCloskey and Schmitt. And again
13 -- this is Dr. Metzker -- again, he's the only expert who's opined on this
14 motivation to combine expert, explaining why a person of skill in the art
15 would've been aware of the McCloskey patent publication. It's particular
16 because Schmitt is citing to the McCloskey paper. A natural thing for a
17 person of skill in the art is going to do is going to be, okay, this patent is
18 telling me that other references are relevant and helpful. I'm going to go
19 look at the other publications from the same authors on the same subject
20 matter, and of course, in addition to the legal presumption that a person of
21 skill in the art knows about all the prior art. They're going to know about the
22 McCloskey patent application and they're going to be motivated to look at
23 those teachings and apply them to Schmitt.

24 Why? Because Schmitt specifically identifies that the work of the
25 McCloskey group is relevant. And again, the institution decision explicitly
26 cited this citation here as being persuasive, and again, it's something that was

1 wholly ignored in the Patent Owner response, and something that Dr.
2 Bustamante didn't opine upon whatsoever, and we finally hear some
3 arguments about it in the surreply. But again, ignoring the actual
4 embodiments of the McCloskey patent publication that we're relying on. So,
5 unless Your Honors have any questions for me, I reserve my time.

6 JUDGE BRADEN: Very good. Thank you very much, Counselor.
7 Patent Owner's Counsel, you may begin your arguments when ready.
8 Although, I would appreciate if you would address things in a similar order,
9 if you wouldn't mind --

10 MS. CIPRIANO: Yes, Your Honor.

11 JUDGE BRADEN: -- starting with the MIPs and then if you
12 wanted to discuss claim construction, that would be fine.

13 JUDGE YANG: Before you start, have you decided or did I miss
14 how much time you want to reserve for --

15 MS. CIPRIANO: I'd like to reserve 15 minutes, please.

16 JUDGE YANG: Okay.

17 MS. CIPRIANO: As you've just heard, there are three main issues
18 in dispute in this proceeding, and I understand that I'm going to skip over a
19 claim construction in large part at the beginning, but I'd just like to introduce
20 the positions as a whole as we start out. So, the first issue is claim
21 construction and it's Tecan's position that the prosecution history of the '357
22 patent makes clear that the challenged claims require the identifier and the
23 target sequence to be used in combination in the step that identifies
24 duplicates.

25 The second issue before the Board is whether Porreca anticipates
26 the challenged claims. Now, Porreca is a patent application focused on

1 reducing bias and increasing reproducibility in the analysis of genetic loci.
2 Now, Porreca's specification touches on a number of varied techniques, as
3 Petitioner points out, but at its core, the substantive disclosures of Porreca all
4 relate to molecular inversion probes that we've referred to as MIPs. Now,
5 the MIPs methods in Porreca are fundamentally at odds with the
6 requirements of the challenged claims, and Petitioner has not put forth an
7 argument that a MIP embodiment would anticipate the challenged claims.
8 Instead, Petitioner points to elements from discreet embodiments throughout
9 Porreca, which is improper under Federal Circuit law.

10 Now, finally, Porreca fails to disclose sufficient detail regarding its
11 methods for identifying duplicates to anticipate the claims, and therefore,
12 finding that Porreca anticipates the challenged claims would be legal error.
13 And finally, the parties dispute whether the combination of Schmitt and
14 McCloskey would render the challenged claims obvious. The answer is
15 similarly no. Petitioner relies --

16 JUDGE BRADEN: So Counsel, what is your comment then about
17 -- I believe it was -- was it paragraph 149 where you had the and/or
18 argument from Petitioner? Where you can use any of these together and that
19 it's not just limited to the MIP process?

20 MS. CIPRIANO: So, let's -- I'm going to put that language on the
21 screen. I skipped ahead to Slide 20, and just for reference, the paragraph is
22 on the left-hand side of Slide 20. Now, Petitioner relies on paragraph -- the
23 two places for the disclosure of the indexing site is paragraph 149 and
24 paragraph 102. And Petitioner's argument that paragraph 149 should be read
25 beyond the MIP embodiment simply doesn't -- even if it's read beyond the
26 MIP embodiment, there's still insufficient disclosure to lead -- for that

1 disclosure to lead someone to the amplification based technology, and then
2 also, put all the other pieces together to lead to the challenged claims.

3 The fact that there is ambiguity or confusion about how these
4 pieces should work together, it's not Patent Owner's burden to say how a
5 person of ordinary skill in the art would understand this in the concept of
6 Porreca. Here, the record is murky, at best, of whether -- how a person of
7 ordinary skill in the art would've understood why --

8 JUDGE BRADEN: I'm not sure I agree with you, Counsel. If you
9 look at paragraph 150, it says the actual incorporation of the random
10 differentiator tag sequences can be performed through various methods
11 known in the art. Explain to me how that's ambiguous.

12 MS. CIPRIANO: So, I don't disagree that the random
13 differentiator tags can be incorporated in those ways, and if we go back to
14 Figure 4 -- and I'm going to direct you to Slide 11. So, if we look at the
15 description -- so, a lot of the party's discussion has been around Figure 4.
16 And if we look at the patent's description -- Porreca's description of Figure 4
17 -- and that's at Column 3, starting at line 30 -- that explains that Figure 4
18 -- just so I don't misquote -- Figure 4 depicts a schematic of two -- this is the
19 wrong patent. Apologies. I'm sorry. I have the wrong citation for you, but I
20 will get the right citations.

21 The explanation of Figure 4 is -- these are methods for combining
22 differentiator tags with target sequences. Porreca does not represent Figure
23 4, as representing the three preparation methods it discloses. Now, the
24 parties have used this as a shorthand for those, and the figures are consistent
25 with the three preparation methods, but Porreca itself does not say that
26 Figure 4C is the amplification-based preparation method. It is possible, as

1 we've seen in the examples of Porreca, that adapters are ligated to the
2 nucleic acid fragments in the MIP preparation process. So, to say that a
3 statement as broad as adapters can be attached with any known method does
4 not point a person of ordinary skill in the art to use an amplification-based
5 method with all of the requirements of the challenged claims based on the
6 disclosures in Porreca.

7 Now, if we look at -- I'd like to take a step back and really focus on
8 the law that's applicable to this case, and then I want to -- kind of in that
9 framework of the law, we'll talk about the various embodiments the
10 Petitioner is pointing to. So, the Federal Circuit has provided guidance
11 regarding how to succeed and showing anticipation by pointing to different
12 parts of a reference and different embodiments within a reference. And as
13 an initial point, the Federal Circuit has confirmed in the Net Money case
14 that's cited on Slide 12. For anticipation is not sufficient for reference to
15 provide discreet disclosures that could be combined to arrive at the
16 challenged claims. That would be an obviousness analysis, and with that
17 would require an explanation of a motivation to combine and a reasonable
18 expectation of success, and those arguments. But that would not be an
19 anticipation.

20 And in contrast, as the Federal Circuit confirmed in the Otonomy
21 case, anticipation requires specific guidance leading a person of ordinary
22 skill in the art to an embodiment with all elements of the challenged claims,
23 as arranged in the claims. So, Petitioner relies heavily on the Federal
24 Circuit's Kennametal case, which explained that a reference can anticipate if
25 a person of ordinary skill in the art would at once envisage the claimed
26 arrangement or combination. That is the skilled person must be able to read

1 the reference and see the claimed combination without any mental
2 gymnastics and without applying any creativity or modification. The skilled
3 person would understand the embodiment to be disclosed in full in the
4 manner claimed. So, to understand what the Federal Circuit was looking at
5 in the Kennametal case, it's important to understand the facts of that case,
6 and I've put excerpts on Slide 14.

7 So, the question in Kennametal was whether a claim directed to the
8 combination of ruthenium and a PVD coating was anticipated. In a prior art
9 cited in that case, the specification disclosed only three coating methods and
10 the prior art included a claim that explicitly listed ruthenium as one of five
11 metals. In addition, the prior art explicitly referred -- the claim explicitly
12 referred to coatings. Slide 5 is at the top -- Claim 5 at issue in the
13 Kennametal case is at the top of Slide 14, and explicitly refers to a coating
14 -- coated cutting insert.

15 So, the Federal Circuit held that a person of ordinary skill in the art
16 would be able to immediately envision the claimed combination in this
17 limited set of options. Now, the disclosure of Porreca, however, does not
18 include such a straightforward disclosure of the challenged claims.

19 JUDGE BRADEN: So, Counsel, I'm going to point you to
20 paragraph 31 of Porreca. So, let's talk about that and the fact that it gives me
21 three -- very similar to Kennametal. It gives circularization, amplification,
22 and/or hybridization-based methods. And then it gives you the fact that you
23 can do any of these in connection with staggering, tagging, size detection,
24 and/or sensitivity enhancement algorithms described herein. And given the
25 level of skill in the art, why would this not be similar to Kennametal? Why
26 would this not be telling somebody of skill in the art, you could use tagging

1 with any of these three methods?

2 MS. CIPRIANO: So, paragraph 31 certainly does disclose the
3 three methods. The issue here is that Porreca does not disclose anything
4 about the amplification-based method that it's talking about, besides listing it
5 as an option for a preparation method. The entirety of the substantive
6 discussion of Porreca is revolving around MIPs. It is possible that a person
7 of ordinary skill in the art might have been able to use creativity to create
8 adapters for an amplification-based method, based on the disclosures of
9 Porreca, but that's not the legal framework we're in today. A person of
10 ordinary skill in the art would not be able to create the claimed method from
11 these scant references to amplification preparation methods. As we've seen
12 in the prior art, there are many ways to do the amplification methods, and
13 the challenged claims is just one that Porreca does not point to.

14 So, I'd like to focus on Petitioner's -- what they actually -- how
15 they constructed their argument in -- from the petition. So, Petitioner relied
16 on Figure 4C and the description of ways to attach the differentiator tags
17 throughout the -- as we've heard -- for the ligation element of the claims.
18 And I put the claim as the parties have identified them on Slide 15.
19 Petitioner relied on a MIP embodiment for the disclosure of the indexing site
20 and the primer binding site, and I'll get to that -- those disclosures in a
21 moment. Petitioner relied on the general disclosures for the elements of
22 amplification and sequencing that were known in the art, and then relied on
23 a data analysis disclosure for the identification of duplicates.

24 Now, Petitioner was unable to provide a tidy argument here based
25 on straightforward disclosure because the discussion of Porreca is not
26 directed to methods that actually align with the challenged claims. So, if we

1 look at the claims -- importantly, Claim 1 requires that an adapter containing
2 an identifier site and an indexing site, so that's limitations 1A, 1B, and 1C.
3 So, ligating the adapter -- the adapter has the identifier and the adapter has
4 the indexing site. And then the claim further requires that the adapter ligated
5 fragments are amplified, and that's 1E. So, this indicates that the adapters
6 are ligated prior to the amplification step that's contemplated in the claimed
7 methods.

8 So, Petitioner relies on what it calls the amplification-based
9 embodiment that we've been discussing, and it alleges that, as I said, that
10 Figure 4C -- I guess we can agree that the 4C is consistent with something
11 that would happen in an amplification-based embodiment, but Porreca
12 doesn't describe 4C in that manner. So, as Tecan's expert, or Tecan's papers
13 explain, there is no disclosure in Porreca that describes the ligation of an
14 adapter with both, the identifier site and an indexing site to the molecule of
15 interest. There's similarly no discussion of how the amplification-based
16 embodiment works at all. There's no information about how to construct an
17 adapter for an amplification-based embodiment, no information regarding
18 how an embodiment would progress, or how that -- those elements would be
19 used to identify duplicates. And these general disclosures are not enough to
20 anticipate the challenged claims.

21 Now, most of these disclosures, as we've discussed in -- on which
22 Petitioner relies are describing the MIP embodiments of Porreca, and I'd like
23 to just take a moment and highlight -- and I think, Judge Braden, your
24 question originally was directed to this. I'd like to talk to how a MIP
25 embodiment works and make sure that we're on the same page there. So, on
26 Slide 17, I've depicted what the MIP embodiment looks like. So, at the top

1 of slide -- at the figure on the right of Slide 14, I've shown a broken oval and
2 this diagram is in Patent Owner's papers, as well. I've shown a broken oval,
3 meant to depict the probe that is shown in -- that is illustrated in Figure 4A,
4 with the green hash marks representing the targeting arms in the construct.
5 And the MIP constructs would be introduced to a sample of nucleic acid
6 fragments and the targeted arms bind to the complementary sequence in the
7 sample. When bound, there would be an extension reaction to complete the
8 circle and circularize the probe. And then that circularized material is
9 amplified and made linear for further processing. And it's important to note
10 that when using a MIP, the contemplated differentiator tag is included in the
11 probe, as indicated -- we're assuming as indicated in Figure 4A. And it's not
12 ligated to a nucleic acid fragment before amplification in the figure that I've
13 shown on the right.

14 So, Petitioner makes a claim that it would make little sense to
15 ligate adapters at the end of a -- of a MIP process, but this is precisely what
16 Porreca discloses in its examples, and I've put a few examples on Slide 18. I
17 will note that all of the examples -- all of the examples that provide methods
18 in Porreca -- are related to MIP processes.

19 Now, on Slide 18, we have example one, example two, and
20 example six. And in each of these examples, the same series of events
21 occurs, and I've highlighted them to illustrate the order of events. So, the
22 examples use a capture probe, which a capture -- the only capture probe that
23 is disclosed in Porreca is the MIP capture probe. And I've highlighted it in
24 green with the interpretation that the probe includes the differentiator tag
25 depicted in Figure 4A. Although it doesn't explicitly say that, certainly, we
26 would not agree -- would not disagree that that is a reasonable interpretation.

1 So, in the method, after the probe does its job, the circular material is
2 amplified, and I have that highlighted in orange. And only when the sample
3 is being prepared for sequencing are adapters ligated for amplification for
4 sequencing.

5 Now, if we compare these examples with the challenged claims, it
6 becomes clear that the MIP embodiment cannot anticipate the challenged
7 claims. On Slide 19, I've put Claim 1 of the '357 patent next to example one
8 of Porreca, and I've highlighted the elements as we see them. As we
9 discussed, the claims require ligation, which I've highlighted in blue here.
10 It's at the beginning of the process in the example -- the MIP example in
11 Porreca -- it's at the end of the process.

12 There's ligation of adapter, the adapter contains the identifier site
13 and the indexing site, and in the contemplated example in Porreca, these are
14 attached at two different places, according to Petitioner. If we understand
15 that the index site is ligated, the only ligation that's disclosed in the MIP
16 process is at the end of the method. And then finally, the amplifying, where
17 it's at the end of our -- the mini part that we're talking about here
18 -- amplifying in the claims happens after ligation of these adapters where
19 amplification in the Porreca examples happens in between.

20 Now, if we go to -- if we really focus on paragraphs 149 and 102,
21 let's talk about how a person of ordinary skill in the art would really
22 understand these to be related to the MIP process. Even if aspects of them
23 can be expanded beyond the MIPs, there is no teaching in these paragraphs
24 to point a person of ordinary skill in the art to the amplification-based, as
25 Petitioner suggests. So, Petitioner attempts to point to these, and I've put the
26 -- I guess, reoriented the Board. I'm on Slide 20 with excerpts of paragraph

1 149 and paragraph 102.

2 So, the petition relies on paragraph 149 for the disclosure of
3 barcodes and/or -- Porreca calls them barcodes. In the patent, they're
4 referred to as indexing sites. And while Petitioner attempts to contort this
5 paragraph, there are -- you cannot deny that the very first sentence of the
6 paragraph explicitly states that this is as -- this is referring to, as part of a
7 MIP library preparation process. And interpretation that this paragraph deals
8 with something else is in direct contrast to what it actually says. And here, I
9 talked a little bit about the and/or confusion, but they are -- we don't agree
10 that that would point a person of ordinary skill in any direction besides
11 they're expanding the possibility of different ways to use the MIP
12 technology. Now, Petitioner, you heard --

13 JUDGE BRADEN: So, Counselor, even if -- let's say that you're
14 correct -- that 149 has to be read to where it only applies to MIP.
15 Disregarding what Petitioner is arguing, I'm not saying right now whether
16 they're right or wrong. How do we get away from paragraph 31 and other
17 paragraphs that say, look, we've got multiple methods of preparation here
18 and all of what we have in here can apply to these three different methods of
19 preparation and tagging is one of those things that could apply to all of these.
20 How do we get away from that and how is this not really more of a non-
21 enablement argument?

22 MS. CIPRIANO: So, I think the issue that we have with paragraph
23 31 is that it's too broad to point a person of ordinary skill in the art to the
24 specific claimed limitations. As I said before, amplification-based
25 preparation methods, they're -- you don't have to have the elements that we
26 -- that are claimed. You don't have to have all of the things. You don't have

1 to have it in the order that are in the claimed methods. Porreca doesn't say,
2 use an adapter with both of these -- with two of the very extension lifts of
3 pieces that could be part of the adapter in an amplification method for the
4 identifying the duplicates.

5 Porreca says generally throughout the reference, you can use these
6 anywhere, and it's our position that legally, that is not an anticipation
7 argument. That may -- should have been an obviousness argument, but
8 that's not before the Board right now. A person of ordinary skill in the art
9 could not immediately envisage a claim with these specific limitations from
10 the disclosures in Porreca. And I say that because -- I want to highlight that
11 Porreca -- the substance of Porreca is about a MIP, and that's evident in the
12 paragraph 102 that Petitioner points to. This paragraph doesn't actually -- I
13 don't think -- doesn't actually use the word or reference the abbreviation
14 MIP, but it talks consistently about target capture, reactions target capture,
15 capture to nucleic acid, and capture probes. The only capture probes
16 disclosed in Porreca are MIPs. So, the substance of paragraph 102 is talking
17 about how to use the MIP technology the way that it's described.

18 So, the prevalence of the MIP embodiments and the paragraph's
19 references to the MIPs is unsurprising here. If you look, all the substantive
20 discussions relate to MIPs, all of the examples relate to MIPs, and all the
21 claims in the Porreca reference are directed to MIP methods.

22 JUDGE BRADEN: Very good, Counsel. I do believe that we
23 probably understand your position on this, so if you want to wrap this one up
24 and then perhaps move either onto Schmitt and/or claim construction.

25 MS. CIPRIANO: Sure. Do you have a preference, Your Honor?

26 JUDGE BRADEN: You do whatever you prefer.

1 MS. CIPRIANO: Okay. Let me talk about claim construction,
2 because I think it is very relevant to the Patent Owner's arguments on
3 Schmitt, and I'll do that with some brevity. So, to reorient the Board on the
4 dispute and claim construction here, I've put some language on Slide 3. And
5 so, the parties agree that at least a portion of the target sequence must be
6 used in the identifying duplicates limitation, and the only dispute between
7 the parties is whether the identifier and the target sequence must be used
8 together in a step to identify duplicates. And I think I heard Petitioner's
9 Counsel note that they do agree that both of these pieces have to be used to
10 identify duplicates. The dispute seems to be narrowed to this definition of
11 step.

12 Now -- and I'm sure I'll be corrected if I'm misunderstanding -- but
13 really here, the important part of the intrinsic record that Patent Owner
14 believes is critical is the prosecution history. And as the Federal Circuit
15 -- very briefly, the Federal Circuit has instructed that the prosecution history
16 is usually the best source of understanding the claims. It contains expressed
17 representations from the applicant and it is particularly important where the
18 applicant limited the invention, making the claims go narrower than it
19 otherwise would be, and that's precisely the case here.

20 The patent specification, as initially filed, broadly describes the use
21 of unique molecular identifiers to identify duplicates in a sample. And the
22 claims, as originally filed, reflected that breadth. But during prosecution, the
23 examiner rejected the claims based on prior art that overlapped with that
24 broad subject matter, and the applicants narrowed the claims to avoid the
25 prior art. So, specifically, in response to the examiner's rejection
26 -- obviousness rejection -- based on a reference called Samuels and a

1 McCloskey reference, the applicants made the claim amendments that I've
2 put on Slide 5. And applicants amended the claims, modifying the duplicate
3 identification limitation, to make it an express identification step, but
4 importantly, also included a number of statements about the prior art,
5 distinguishing the claims.

6 So, when discussing Samuels, applicant stated that Samuels did not
7 teach the active step of identifying duplicates as claimed. Applicant went on
8 to distinguish McCloskey, stating that the claimed invention uses the
9 identifier and the target sequence in combination to identify duplicates. So,
10 Applicant made note that this was -- it was the combination of these that
11 provided an improvement over McCloskey. So, the examiner later allowed
12 the claims -- these claims to issue in the '399 patent. The prosecution
13 continued, when the continuation application that led to the '357 patent was
14 filed. When the examiner continued to raise the same prior art against the
15 pending claims and issued another 103 rejection --

16 JUDGE BRADEN: So, Counselor, is there something in the
17 relevant prosecution that says that there is a temporal limitation that says
18 that these must be used either simultaneously or right after one another, that
19 a step isn't something that has to be done simultaneously? Is there some sort
20 of indication that makes this a step?

21 MS. CIPRIANO: I think the important language that's used in the
22 prosecution history is that they are used in combination. Now, Tecan is not
23 making an argument that they need -- that it needs to be --

24 JUDGE BRADEN: So, combination means temporally next to
25 each other, temporally at the same time, simultaneous? Is something done in
26 combination if I was saying, hey, I'm sequencing this and I'm sequencing

1 this part before lunch and then I'm sequencing this part after lunch. Is that
2 the same step, if I'm still doing sequencing? How does that work?

3 MS. CIPRIANO: I think it's Tecan's position that the -- using
4 these two pieces of information in combination means that they are both
5 considered when analyzing the duplicates. That it is -- they're both used for
6 the purpose of the identifying duplicates step, and I think that's the -- looking
7 at the prosecution history in the Samuels reference, it's particularly the
8 distinguishing of that is particularly relevant where in Samuels -- Samuels
9 looked at the identifiers, and then looked to the sequence to look for
10 mutations, as discussed in the prosecution, and that wasn't enough. That
11 wasn't -- the applicants explained that that was not sufficient to meet the
12 challenged claims. The challenged claims were different than Samuels. So,
13 I think really that --

14 JUDGE BRADEN: I believe that was because Samuels was
15 specifically looking for those mutations, that it wasn't a duplicate read.
16 Nothing that this was a temporally relative step. What am I missing?

17 MS. CIPRIANO: No, I agree, but there, the identifier and the
18 target sequence were used for different purposes. The target sequence in
19 Samuels was used to identify the mutations and the identifier site was used
20 to group the reads in Samuels. And that's exactly the prior art that the
21 applicant was distinguishing over, and I think that that's really telling in the
22 differentiation of the challenged claims.

23 So, let me now turn to the Schmitt and McCloskey ground. Unless
24 you have more questions about claim construction, I'll move on. Okay. So,
25 skipping ahead to Slide 22, just to reorient. So, Ground 2, Petitioner has
26 similarly failed to establish that the combination of Schmitt and McCloskey

1 render the challenged claims obvious, and I've put an annotated version of
2 Figure 3 on Slide 23.

3 And now, the petition relies solely on Schmitt for the disclosure of
4 the identifying duplicates limitation, but as I was just discussing, Schmitt is
5 just like the references and particularly, Samuels that applicants overcame
6 during prosecution. It discloses identifying duplicates or families using only
7 the SMI tag, which we've interpreted as the identifier. And as shown in
8 Figure 3 of Schmitt, the reads are grouped into families by comparing their
9 SMI tags, and Schmitt then does further analysis to identify the mutations.
10 And this is reinforced by the language that Schmitt uses to describe its
11 process. In every instance, Schmitt explains that duplicates are identified
12 using SMI sequences alone, without any reference to analysis of the target
13 sequence.

14 Now, Petitioner relies on various description that Schmitt provides
15 regarding identifying duplicates, and I've put those paragraphs on Slide 24,
16 but the takeaway, they all disclose the same method of grouping reads by
17 SMI sequences. So, paragraph 85, the PCR duplicates may be
18 unambiguously identified by virtue of having a common SMI sequence.
19 Paragraph 98, every duplicate that arises from a single strand of DNA will
20 have the same SMI sequence. And contrary to Petitioner's representation,
21 paragraph 99 represents the same concept. Members of the same PCR
22 family are then grouped together by virtue of having a common SMI tag
23 sequence, and there's simply no mention of using the SMI tag in
24 combination with the target sequence in this identifying duplicates step.

25 Now, Petitioner relies heavily on Schmitt's reference to the
26 creation of a consensus sequence in paragraph 99, and there are a few issues

1 with that analysis. First, Petitioner never explains how Schmitt's consensus
2 sequence meets the identification limitation -- the identification of duplicates
3 limitation. It's very cursory. It just says that, of course, a consensus
4 sequence must do this.

5 And second, there does not need seem to be any dispute that the
6 consensus sequence generation occurs separately from the process of
7 grouping reads into families, and that's really the distinguishing fact from the
8 challenged claims, and I think gets to the heart of, Judge Braden, your
9 questions. During prosecution, the applicants distinguished over references
10 that used a tag and then looked at the sequence for different purposes. Here,
11 Schmitt is doing the exact same thing. They're looking at the tag to sort the
12 reads and group them into families, and then they're going through a process
13 of doing a consensus sequence so they can identify the mutations in the
14 sequence. So, Petitioner relies on Dr. Metzker's --

15 JUDGE BRADEN: So, Counsel, I have a question. It's on
16 paragraph 85 --

17 MS. CIPRIANO: Um-hum.

18 JUDGE BRADEN: -- of Schmitt, where it discusses an increasing
19 sequence depth to look at the distinct molecules. So, it appears as though
20 they're using the SMI tags to originally sort, and then they're looking at
21 specific amounts of the target sequence to continue their sorting to find a
22 consensus sequence. Am I misreading that?

23 MS. CIPRIANO: Let me just -- give me one moment. Let me
24 orient myself with this.

25 JUDGE BRADEN: It's calling it shear points. It's talking about --

26 MS. CIPRIANO: Um-hum.

1 JUDGE BRADEN: -- the order to restrict the sequence analysis to
2 uniquely sequence DNA fragments. Many sequencing studies include a step
3 to filter out PCR duplicates by using these shear points.

4 MS. CIPRIANO: Yeah. So, shear points are another -- shear
5 points can be used to compare sequences that -- my understanding of the use
6 of shear points is that the fragments are exposed to predictable break, and
7 they are able to use those shear points to compare different sequences based
8 on the predictability of the breaks. Here, that's using -- not the target
9 sequence, but the location of the break to identify duplicates as a separate
10 kind of identifier site type of information. Does that answer your question?

11 JUDGE BRADEN: I believe I understand your --

12 MS. CIPRIANO: Okay.

13 JUDGE BRADEN: -- position.

14 MS. CIPRIANO: Okay.

15 JUDGE BRADEN: Thank you.

16 MS. CIPRIANO: I wanted to take a moment to talk about Dr.
17 Metzker's testimony related to Figure 3 of Schmitt, and I've put the
18 testimony on Slide 25 -- some of the testimony on Slide 25 and compared it
19 to Schmitt's disclosure regarding an explanation -- description of Figure 3.
20 And so, Petitioner is really relying on Dr. Metzker's testimony to fill in the
21 gaps of what Figure 3 actually does. Dr. Metzker asserts that Schmitt
22 discloses the use of both, the target sequence, and the SMI tag in Figure 3.
23 And Dr. Metzker relies only on -- in this paragraph -- cites to paragraph 85
24 and 98, but as we saw, those same paragraphs have no disclosure of using
25 the target sequence in combination with the SMI tag. Those -- paragraphs
26 85 and 98 are unambiguous in saying that they group reads by the SMI tag

1 alone. So, Dr. Metzker's testimony on this point should be disregarded.

2 As the Board held in the Xerox case, expert testimony cannot be
3 used to fill in the gaps, to supply missing limitations, and Dr. Metzker's
4 testimony is doing just that. And alternatively, the Federal Circuit has held
5 that expert testimony should be disregarded, where it's plainly inconsistent
6 with the record. And certainly, we contend that Dr. Metzker's testimony
7 here is at odds with what the reference actually says, and that those
8 paragraphs talk about using duplicate -- identifying duplicates using SMI
9 tags alone.

10 So, I think I will turn back a moment to talk about this limitation in
11 the Porreca reference, since I have a little bit of time. And I put Figure 5 on
12 Slide 21. So, setting aside Porreca's MIPs methods, we don't believe that
13 Porreca's disclosures of the MIP methods would lead a person of ordinary
14 skill in the art to the challenged claims. Porreca's disclosure of the
15 identifying duplicates limitation is extremely thin.

16 So, Petitioner relies on Figure 5 in paragraph 298, but under the
17 proper construction of the claims that I just discussed, Porreca does not
18 provide sufficient information to understand how this collapsing of
19 differentiator tag sequences actually occurs. Figure 5 itself does not even
20 mention using the target sequence at all, indicating that the differentiator tag
21 sequences are what is collapsed. And if you look at the figure itself, there is
22 no difference that it's -- if you look at all of the sequencing reads with 1011,
23 also have the T. That's disclosed. The only part of the sequence that's
24 disclosed. All of the fragments that have 0010 also only have a T. All the
25 ones with 0001 as a differentiator tag only have an A, so there would be no
26 difference in the example between sorting by differentiator tags or sorting by

1 sequence. It's impossible to understand how Porreca would use both of
2 these pieces of information from the disclosure on Figure 5.

3 Now, Petitioner points to paragraph 298, but that is similarly -- it's
4 just statements of what happens, and it's our position that those -- that is
5 insufficient disclosure to meet the challenged claims. So, unless you have
6 further questions, I think I'm going to reserve the rest of my time for rebuttal
7 and I'll sit down.

8 JUDGE BRADEN: Thank you very much, Counsel. We
9 appreciate it. Petitioner, you may begin with your rebuttal when you are
10 ready. Although, I would like to hear from you specifically where in
11 Schmitt and McCloskey it shows the target sequence.

12 MR. TRAUPMAN: So, to pick up where we -- your question,
13 Judge Braden, I think you were asking about Ground 2, the disclosure with
14 respect to the identifying limitation. And it's paragraph -- the answer -- short
15 answer to your question is paragraph 99 of Schmitt, which I've shown here
16 on Slide 54, and what we saw from Patent Owner's presentation was a
17 portion of paragraph 99, but not all of it. So, I think you need to read the
18 entirety of the paragraph, and I do want to, if I have time, hopefully address
19 some of the claim construction issues, because I do disagree with some of
20 the characterizations about the methodology disclosed in the patent, as well
21 as the -- what was discussed in the prosecution history, but focusing here on
22 Schmitt to answer your question, Judge Braden.

23 So, paragraph 99. Following tagging with a double-stranded SMI
24 and PCR amplification -- so again, the SMI is the identifier -- a family of
25 molecules is obtained that arose from a single DNA molecule. That's
26 exactly what's being shown and the figures of Schmitt, as well, which again,

1 here's Figures 3A through 3D of Schmitt. Sorry, Your Honor, to be
2 bouncing around. Get back to paragraph 99. Okay. A family of molecules
3 is obtained that arose from a single DNA molecule. Members of the same
4 PCR family are then grouped by having a common SMI tag. So, that's step
5 one. They're grouping based on the SMI, but then --

6 JUDGE BRADEN: So, is the SMI the identifier --

7 MR. TRAUPMAN: Yes, yes.

8 JUDGE BRADEN: -- or is it the target sequence -- okay, it's the
9 identifier.

10 MR. TRAUPMAN: Yes, yes, Your Honor. It's the identifier.
11 Sequences of uniquely tagged PCR duplicates are subsequently compared in
12 order to create a PCR consensus sequence. That's the sequences of the target
13 DNA in that next sentence there, Your Honor. So, first, you look at the
14 SMI, then the very next sentence, you're looking at the target sequence. So,
15 to answer your question, it's right here in paragraph 99, which to repeat, was
16 completely ignored by Dr. Bustamante and in the Patent Owner response.
17 And it lines up, as I'm going to hopefully have time to show you, very
18 closely with how the patent does it, which is, again, a two-step example.
19 One of the patent, in particular, a two-step technique or a this and then that
20 technique. I don't even want to call it two different steps.

21 First, you look at the SMI, then you look at the target sequence.
22 Example one is first, you look at the target sequence, then you look at the
23 identifier. I don't think the order of what you look at matters based on the
24 claim. And again, this paragraph 99 lines up very closely with example one
25 of the patent, and so here, you're generating this consensus read, first by
26 grouping the same PCR family from the SMI tag, then looking at the

1 sequences of that PCR family. That's the target DNA, so I hope that answers
2 your question because in the interest of time, I'd like to --

3 JUDGE BRADEN: It did. Thank you very much.

4 MR. TRAUPMAN: -- move on to some other issues. So, just to
5 -- so Judge Braden, you asked about the prosecution history and I just want
6 to reiterate, from Petitioner's perspective, we very much agree with your
7 characterization of the prosecution history. It has nothing to do with this
8 single step or used in combination. The base level with Samuels wasn't
9 identifying duplicates at all. It was identifying PCR errors. That's not
10 -- that's what the Patent Owner argued and that's what they're partly
11 distinguishing. It had nothing to do with what they're now trying to read
12 into this claim construction, and McCloskey, according to the Patent Owner,
13 didn't look at the target sequence at all. They just wholly looked solely on
14 the identifier. Those were the --

15 JUDGE BRADEN: So, how do you address their argument that in
16 prosecution history, the applicant argued that it was the active step that
17 Samuel was taking?

18 MR. TRAUPMAN: Well, I believe what they argued is that the
19 -- it's the active step that's in -- Samuels does not disclose the active step. I
20 think that's what I'm closely paraphrasing that was in the prosecution history.
21 So, what they're -- and it's the active step of identifying duplicates, as
22 opposed to PCR errors. It's not an active step where both are together.
23 Again, to your point, some of the questions you were asking, Judge Braden,
24 it has nothing -- there's no temporal -- like how close to -- how immediately
25 after you're looking at say, the identifier, you have to look at the target
26 sequence or vice versa. It's just you have to -- the step of identifying

1 duplicates needs to rely on both, the identifier and the target sequence.
2 That's what the claim requires, that's what's reflected in the patent, and
3 there's nothing in the file history that distinguishes that, because again, their
4 point of distinguishing Samuels was that Samuels wasn't about duplicate
5 identification at all. It was identifying PCR errors, which is just they argue
6 to the patent office different than identifying duplicates.

7 So, briefly, I'd like to just briefly look at example one of the patent,
8 Your Honor, because it -- it depends, again, what it means to be a step, but it
9 shows this "two-step process" that is, by its very terms, identifying
10 duplicates. That's shown here. That's shown here in example one. And by
11 the way, there's nothing in the file history that points out that example one
12 wouldn't be covered by the claims. There's no testimony from Dr.
13 Bustamante at all on example one, so there's nothing, you know -- there's
14 nothing from Patent Owners on this point.

15 So, to quickly go through example one, Your Honor, I'm here on
16 Slide 13. I'm showing column 17, lines 30 to 37, is you take this fragmented
17 DNA, add an adapter, the adapter has got both, the identifier site and the
18 indexing site and sequencing, and you get, as shown up on the top, three
19 different reads. The important read is the second read. That's got the
20 identifier in it. It's eight bases of the indexing and six. If we go back to the
21 prior slide, it talks about how the identifier site has six random bases. So,
22 index is eight, identifier is six. That obviously adds up to 14. And notice it
23 says here, it's set aside. So, we've got that read with the identifiers in it.
24 We're setting it aside.

25 Then we go to -- and this is now Slide 14, column 17, lines 39 to
26 52. Then we go to our pipeline analysis. We use a bow tie aligner and find

1 the genomics start positions of the target DNA, and so that's -- in other
2 words, where does the genomic DNA, because of course, example one is
3 talking about seeing the genomic DNA -- where does that start, as opposed
4 -- compared to the adapter sequences, the stuff that you add in the prep
5 process -- where's the start position? And we line them up with the bow tie
6 aligner, okay, and then the next step -- I'm just highlighting a different -- on
7 Slide 15, a different portion of the same part of example one -- this point,
8 sequencing reads that started the same genomic start position were checked
9 against the random base file to see if they have the same or different set of
10 random bases that were ligated to them.

11 So, in other words, it's this two-step process. Again, call it
12 whatever you want to call it. Two -- you know, this and then that process,
13 right? First, you looked at the target DNA, then you looked at the identifier,
14 and again, on Slide 16, just moving down the same paragraph were two
15 sequences with the same start of genomic coordinate, had the same set of
16 random bases. They were considered to have come from the same initial
17 ligation event, and then it references farther on, on Slide 17. This is all
18 example one. I'm down farther in column 17, lines 59 to 63. Talked about
19 59, identifying true duplicates, and if you look then at Figure 5, it's
20 distinguishing between true and apparent duplicates based on the start
21 coordinates -- start and end coordinates of the genomic DNA.

22 So, again, it's not this one single "step" where everything is looked
23 at together. First, they looked at genomic DNA, then they looked at the
24 identifier in example one, and just like example five, which Patent Owner
25 claims is covered by the patent, it's -- they're both called identification of
26 duplicate sequencing reads. One is an MRNA and one is with the ovation

1 target enrichment library, which we've heard practices the claims.

2 So, again, we don't think there's any support in the intrinsic record
3 to kind of draw these distinctions that Patent Owner is doing. So, unless you
4 have any questions on the identifying limitation, I'd like to take my last five
5 minutes to come back to Porreca and the alleged mixing and matching of
6 embodiments. And so, I just want to clarify some positions. We saw Slides
7 -- I have written down Slides 18, 19, and 20 of Patent Owner's presentation,
8 talking about MIP embodiments of Porreca. I want to be very clear. We're
9 not alleging that those examples -- examples, I believe, it's one, two, and six,
10 if memory serves me right that was shown by Patent Owner -- we're not
11 alleging they practice the claims.

12 We're not alleging that those examples are anticipatory and those
13 examples, again, highlighted the point that I was making in my opening
14 presentation, which is if you're going to have an adapter that has both, a
15 sequencing primer and a PCR primer, again, straight out of paragraph 149,
16 it's not going to be a MIP embodiment because as Patent Owner's Counsel
17 showed you, the amplification happens -- the PCR amplification happens
18 before you add the adapters in the MIP process. And so, if the "and" in
19 paragraph 149 means anything, it's being used for something other than the
20 MIP preparative process. So, again, we're not relying on the -- we're not
21 saying, again, any of those examples are anticipatory, and I also want to, I
22 guess -- I think I heard some -- I'm not quite sure if it rise to the level of
23 disagreement, but saying -- trying to say some alleged allegations that there's
24 ambiguity that Figure 4C corresponds to the amplification process. And it's
25 kind of the first time I'm hearing about this, but I just want to call Your
26 Honor's attention. I'm sorry I don't have this on a slide.

1 Paragraph 29. Again, as I showed you on my presentation, 27 of
2 Porreca -- paragraph 27 of Porreca -- introduce the three preparative
3 methods, then 28 talks about circularization, 29 talks about amplification.
4 I'm just reading from paragraph 29. An amplification-based EG PCR or
5 LCR-based preparative methods, genomic loci target nucleic acids are
6 isolated directly by means of preliminary chain reaction or ligase chain
7 reaction, or other amplification methods that selectively amplifies each locus
8 using one or more oligo nucleotide primers.

9 Okay, so PCR, you can use -- you use PCR to amplify the
10 amplification method. Now, another important piece, the end of paragraph
11 29, and this ties directly into paragraphs 101 and 102 that we looked at,
12 amplification-based methods include amplification of a single target nucleic
13 acid and multiplex amplification, which, and then parenthetical,
14 amplification of multiple target nucleic acids in parallel. So, they're
15 expressly telling you that the amplification-based preparative method can be
16 used for multiplex.

17 And again, to go back to paragraph 102 of Porreca -- let me see if I
18 can find it. Wasting my time here, sorry. Here it is, 102. Should be
19 appreciate that aspects of the invention may be useful for high throughput,
20 cost effective, yet reliable genotyping of multiple patient samples, e.g. in
21 parallel, for example, in multiplex reactions. So, again, they talked about
22 amplification-based preparative method being used for multiplex. Then in
23 31, as Your Honor, noted, it talks about any of the methodologies can be
24 used with any of the preparative methods, and here, they've saying, patient-
25 specific tags are really good for multiplex, and again, amplification can be
26 used for multiplex, and yes, if you read the other sentences -- I don't have

1 their Slide 18 able to put up for you -- there are other sentences in paragraph
2 102 that talk about in some embodiments, and they talk about the inversion
3 probe. Yes, there are inversion probe embodiments in Porreca, but that does
4 not change the teaching of Porreca.

5 That -- the amplification-based methodology, which doesn't
6 involve MIPs, can be used for multiplex, and when this paragraph 102 then
7 says, in some embodiments, samples from different subjects are tagged with
8 subject-specific tags, a person of skill in the art is going to immediately
9 understand that'll cause the amplification. Why? Because paragraph 29 of
10 Porreca tells them it does. And likewise, we've heard -- I think Counsel said
11 the entire discussion of Porreca is around MIPs, but that's also just not true
12 because 150 does -- isn't about MIPs. 150 is about incorporation of various
13 methods, including by ligation. No one is arguing that ligation is a MIP -- is
14 how you incorporate the random sequence by -- through MIPs. It's through
15 the ligation.

16 And then 150, up until the very end of that paragraph, it's talking
17 about non-MIP embodiments, and it's talking about how you can put a PCR
18 priming site on an adapter. Well, with the PCR priming site, it's the
19 amplification-based method. And again, how do you know it's that?
20 Because paragraph 29 that I just read to you tells you that. And again, you
21 just need to read this as a person of skill in the art would, which is that all of
22 these preparative methods are applicable to what's disclosed in the rest of
23 Porreca. So, unless Your Honors have any further questions, I'll --

24 MS. CIPRIANO: Okay. So, I certainly won't take my full 20
25 minutes here. I'd like to -- and I'm not going to waste the time to put up the
26 slide, but I do have a slide that I'd like to talk about, and that's Slide 8 in

1 Patent Owner's presentation, talking about example 5 of the '357 patent. So,
2 you just heard Petitioner's Counsel talk about example one of the patent and
3 how that plays, but I'd really like to focus on example five, because we
4 believe that that is the critical embodiment and example of the '357 patent in
5 the claims.

6 So, example five of '357 patent describes an embodiment that
7 shows how an identifier and a target sequence can be used in combination to
8 identify duplicates, and that's really the important part. So, in example five,
9 a library was created using the adapters illustrated at the top of column 20 of
10 the '357 patent, and it's reproduced on the left side of Slide 8. And these
11 adapters contain an index site, a sequencing primer binding site, an identifier
12 site, and I've color-coded that, as indicated. And then the adapters were
13 added to the fragments in the library, and the library was sequenced.

14 So, after sequencing, example five describes two parts to its data
15 analysis. First, in the first part, it takes the first six bases of the index read
16 and uses that to separate the reads into sample type, so that's the indexing
17 portion of the data analysis. The second data analysis step that example five
18 talks about is the first 50 bases of the target sequence read were compared to
19 identify duplicates and duplicates were then removed from the data set.

20 And importantly, based on the structure of the adapters disclosed
21 in the figure disclosure at the top of column 20 of the '357 patent, that first
22 50 base pair read of the target sequence read, that is used for the duplicate
23 identification, would necessarily include both, the identifier site and the
24 target sequence. And therefore, the comparison described in example five is
25 precisely what Patent Owner was directing the examiner to as the claim
26 coverage of the claims at issue.

1 Now, Petitioners focus only on example one, but based on the
2 prosecution history that I discussed, the claims do not extend to example
3 one, and that's important because the target sequence in example one is not
4 used for duplicate identification. The target sequence in example one is used
5 for mapping the reads and creating a different data set here than the
6 -- actually, didn't use the target sequence. It uses the gene and position,
7 which is a set of coordinates of where that target sequence aligns to the
8 genel.

9 In that separate data set, those coordinates were then used with the
10 target sequence to identify duplicates, and it's -- this process -- it's Patent
11 Owner's position that this process is different than applicant's description of
12 the claims, because the target sequence and the identifier are never used
13 together when duplicates are identified. So, applicants narrowed their
14 invention during prosecution, made these statements, and we think that they
15 clearly focus on the embodiment of example five to the exclusion of
16 example one.

17 JUDGE BRADEN: Okay. So, I want to make sure I understand.
18 So, say that again, as far as when you use the target sequence and the
19 identifier sequence. Do you use them in the same run, or is it you do the 50
20 base pair, you know, first read and that's your identifier or your target
21 sequence, and then you do a second read that -- of that group that is then the
22 target sequence or the identifier. Do you do them together or separate?

23 MS. CIPRIANO: So, in example five, if we can just go around
24 that example, that -- the first 50 base pairs of that target sequence read would
25 include the sequence of both, the identifier site and a portion, depending on
26 the size -- I don't remember the size of the identifier site -- but a chunk of the

1 target sequence. We do not think it is imperative whether the data analysis
2 step compares the target sequence in the identifier, the identifier in the target
3 sequence. The important part is the example five explains that those two
4 pieces of information were used together when they compared that first 50
5 base pair chunk to identify the duplicates.

6 Now, in example five, a logical read is that they used that as one
7 strand of a sequence and compared those to identify the duplicates, but it's
8 not our position that if you only took the identifier and compared that, and
9 then only compared the target sequence and compared that, we still believe
10 that that would be an embodiment of the claims because both pieces of
11 information are used in the step to identify the duplicates.

12 JUDGE BRADEN: Thank you. I believe I understand your
13 position. Thank you.

14 MS. CIPRIANO: So, unless there are other points, I'll concede the
15 rest of my time. Thank you.

16 JUDGE BRADEN: Judge Yang, Judge Majors, any questions?

17 JUDGE YANG: Not from me. Thank you.

18 JUDGE BRADEN: All right, very good.

19 JUDGE MAJORS: Me neither. Thank you.

20 JUDGE BRADEN: Yes, Counselor?

21 MR. TRAUPMAN: Yes. So, Your Honor, just one point. I know
22 in the other proceeding involving the '357 patent, there was some additional
23 briefing ordered on the issue of the disclaimer by the Patent Owner. Is that
24 something that Your Honors would like --

25 JUDGE BRADEN: That's not necessary --

26 MR. TRAUPMAN: Okay.

1 JUDGE BRADEN: -- in this proceeding.

2 MR. TRAUPMAN: Okay, thank you.

3 JUDGE BRADEN: Thank you. We'd like to thank all the parties
4 appearing here today, and for answering all of our many questions. Your
5 answers have helped the panel. We will take this case under advisement and
6 issue a decision in due course. As a reminder, we ask that you please stay
7 here a bit longer to answer any questions from the Court Reporter regarding
8 spelling. That being said, we wish you all a very good day. Thank you, and
9 the hearing is now adjourned.

10 (Whereupon the above-entitled matter went off the record at 3:08
11 p.m.)

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