

RECORD OF ORAL HEARING
U.S. PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ILLUMINA, INC
Petitioner
v.
MOLECULAR LOOP BIOSCIENCES, INC
Patent Owner.

Case IPR2024-0149 (Patent 11,840,730)

Oral Hearing Held: January 29, 2026

Before ANNETE R. REIMERS, SUSAN L. C. MITCHELL, and
ZHENYU YANG, Administrative Patent Judges.

APPEARANCES:

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The above-entitled matter came on for hearing Thursday, January 29, 2026, commencing at 1:00 p.m. EST, at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia.

P-R-O-C-E-E-D-I-N-G-S

1:00 p.m.

THE BAILIFF: All rise.

JUDGE MITCHELL: Thank you. And good afternoon. You all may be seated. So we have a final hearing this afternoon in *inter partes* review 2024-01419. I am Judge Mitchell and with me by video conference are Judges Yang and Reimers.

I would like to get appearances for the parties on the record if I could, so beginning with Petitioner.

MR. BROUGHAN: Good afternoon. My name is Tom Broughan on behalf of Petitioner Illumina.

MS. FUKUDA: And I'm Ching-Lee Fukuda, also with Sidley, on behalf of Petitioner.

JUDGE MITCHELL: Great. Thank you and welcome.

MS. FUKUDA: Thank you.

JUDGE MITCHELL: And for Patent Owner?

MR. MATTY: Good afternoon, Your Honors. Brian Matty on behalf of Molecular Loop. And with me is my colleague, Michael Wueste. We also have with us Dr. Greg Porreca, who's one of the inventors on the patent we'll be talking today -- talking about today, as well as Pat Saunders and Tom Laurio (phonetic) from Molecular Loop.

JUDGE MITCHELL: Great. Thank you and welcome. Thanks for coming out in the --

MR. MATTY: I --

1 JUDGE MITCHELL: -- less than ideal weather.

2 MS. FUKUDA: -- I apologize, I should have introduced our
3 clients as well.

4 JUDGE MITCHELL: Yes, please.

5 MS. FUKUDA: So from Illumina, we have Roland
6 Schwillinski and Marcus Burch.

7 JUDGE MITCHELL: Great. Thank you and welcome.

8 So as set forth in our oral hearing order, each side has 60
9 minutes to present their case. So just a reminder, to assist us in
10 following along with your argument and for the clarity of the record,
11 make sure that if you are referring to an exhibit, you give me the
12 exhibit number and page number of the exhibit to which you are
13 referring, and if you're referring to demonstratives and you all have
14 them locally too in addition.

15 I know you have them on the screen, but make sure you refer to
16 the slide number. It's very helpful because I love, when we go back
17 over the trial transcript, to make sure I understand what you were
18 talking about.

19 So the petitioner will present its argument first because the
20 petitioner bears the burden of showing unpatentability of the
21 challenged claims.

22 So let me ask first, Petitioner, would you like to reserve any of
23 your time for rebuttal?

24 MR. BROUGHAN: Yes. Ten minutes.

1 JUDGE MITCHELL: Great. And Patent Owner, you will have
2 the last word. Would you like to reserve some time?

3 MR. MATTY: Yes, the same. Ten minutes, please.

4 JUDGE MITCHELL: Okay. Great.

5 So as soon as I get the clock set, Petitioner, when you are ready,
6 you can begin.

7 MR. BROUGHAN: We -- I know you can bring up the slides
8 on the screen. We have paper copies, if you would --

9 JUDGE MITCHELL: Oh, I would like one. Thank you.

10 MR. BROUGHAN: I assume I may approach?

11 JUDGE MITCHELL: I hate to be old school. Thank you.

12 MS. FUKUDA: Thank you.

13 MR. BROUGHAN: May I begin?

14 Good afternoon. My name is Tom Broughan. Today I will be
15 addressing the -- how the art maps on to the challenged claims, and
16 then I'll be turning it over to my co-counsel, Ms. Fukuda, who will
17 address Chee's priority dates and Molecular Loop's prior invention
18 claim.

19 If we go to slide 2 of Petitioner's demonstratives, which are
20 Exhibit 1070, there's seven grounds at issue in this proceeding. Three
21 of them are based on the Chee reference. Four are based on the
22 combination of McCloskey and Bignell. So we'll go to slide 3.

23 I'm going to start by addressing the grounds based on
24 McCloskey and Bignell, because there are fewer issues disputed

1 between the parties for that. Then I'll address the grounds based on
2 Chee before turning it over to Ms. Fukuda.

3 Now if you look at the first two bullet points under each of
4 these sets of grounds, Molecular Loop has raised a challenge to
5 whether the art discloses the collapsing step of Claim 1. And that is
6 their only challenge to whether the art discloses all the limitations of
7 Claim 1.

8 Go to Claim -- slide 4. Slide 4 is a reproduction of Claim 1,
9 and the collapsing element is highlighted at the bottom. You can see
10 that that element is the second half of the last element of a series of
11 steps. And again, this is the only element in Claim 1 that Molecular
12 Loop contends is not disclosed by the priority.

13 But to understand kind of the -- what the claim is about, let's
14 turn to slide 5, which shows an example of a process that is covered
15 by -- that could be covered by Claim 1. And parties have both pointed
16 to this as such an example, and I believe the Board likely is familiar
17 with it, but let me just go over it briefly.

18 On the left is an initial sample of nucleic acids, and in this
19 example, there are four nucleic acids. To each of those nucleic acids
20 are targets that are, -- that's in the initial sample, a tag is attached to
21 each one. As you can see in the box in red, each tag is unique. Those
22 nucleic acids in the initial sample are amplified to create an amplified
23 sample, which appears in the middle. Amplification is just a process
24 for making copies of the nucleic acids.

1 And if you look carefully at that middle column, you'll see that
2 more copies were made of some nucleic acids than others. This is a
3 common, well-known property of amplification processes, and it's
4 known as amplification bias or skewing. The process just makes
5 different numbers of copies of each nucleic acid there.

6 So to address that step, to address that, I guess, property of it,
7 there's a collapsing step which is shown in the orange box. And in
8 that collapsing step, what you see reads "collapsing differentiator tag
9 sequences", redundant sequence reads are removed to create the
10 collapsed sequence readings, which you can see on the far right. And
11 you'll -- I'll point out that the number of collapsed sequence reads,
12 there's four, it's the same number as there are in the initial sample of
13 nucleic acids.

14 So what is the purpose of this collapsing step? As I mentioned,
15 it's to remove redundant sequences, but let's turn and look at what
16 Molecular Loop has had to say about this limitation. If we go to slide
17 6. These are passages from Molecular Loop's Patent Owner
18 Response. And they have taken the position that the purpose of the
19 collapsing step is that it collapses -- or sorry, excuse me.

20 They've taken the position that the specification says that
21 collapsing corrects for skewing, which is an issue related to over or
22 under-amplification. That's the amplification bias problem I
23 mentioned a moment ago. They also say that the purpose of
24 collapsing is to remove redundant sequence reads prior to counting the

1 number of nucleic acids that are in the sample. Then the last quote
2 says more or less the same thing.

3 I'd like to turn to the ground based on McCloskey now, or
4 Bignell McCloskey, and just give a brief overview of the combination.
5 And I've gone to slide 9 of our demonstratives. Bignell is a patent that
6 describes next generation sequencing techniques. In particular, it
7 describes techniques for adding sample tags to nucleic acids before
8 running them on a sequencer to allow multiple samples to be
9 sequenced simultaneously and then be able to filter the reads out back
10 to the sample they belong to.

11 And you'll note the passage from Bignell on the screen. It
12 basically says this. It notes that the invention relates to methods for
13 indexing samples for sequencing involving the attachment of tags
14 specific to the source of each nucleic acid sample. Those are the
15 sample tags that I -- that I just mentioned.

16 At the bottom is a figure from Bignell, and it shows just an
17 example of a tag nucleic acid, and it notes that there's amplification
18 steps. Now Bignell discloses a number of amplification steps as part
19 of its method of preparing a library and sequencing. On the right of
20 the screen, we have McCloskey, and McCloskey is a reference that
21 describes a technique for using tags to address problems with
22 amplification bias.

23 And you'll note that McCloskey says as -- in the passage on the
24 screen that, "Nucleic acid molecules are labeled with distinct sequence
25 tags prior to PCR amplification." McCloskey goes on to say that this

1 barcoding process -- the barcoding permits correcting for skewing that
2 can arise from PCR amplification. In the bottom passage, McCloskey
3 notes that this barcoding technique is a definitive solution to the
4 amplification bias problem, which is described as where multiple
5 amplified sequences are derived from a single original molecule.

6 So let's look at what McCloskey's tags actually look like. Go to
7 slide 10. At the top is figure 3 of McCloskey, and this is an image of
8 McCloskey's tag. And the tag has two components here. One is a
9 barcode, and the other is a batch stamp. The barcode is a unique
10 sequence that uniquely identifies a target nucleic acid in the
11 experiment. The batch stamp may be used to identify a particular
12 sample. So this is akin to what -- this is the same thing that Bignell
13 discloses, the ability to add a tag that identifies the nucleic acids in a
14 sample. McCloskey enhances that by adding this barcode that can
15 identify individual nucleic acids.

16 So with that in mind, I'd like to turn to the combination and
17 Molecular Loop's arguments against the combination. First, they
18 assert that McCloskey does not teach the collapsing step of Claim 1.
19 And if we go to slide 12, again, this is Patent Owner's own description
20 of the purpose of the collapsing step, and they have taken the position
21 that the collapse -- the purpose of this collapsing step is to correct for
22 skewing. That's an amplification bias problem.

23 During their expert's -- their expert, Dr. Puglisi, during his
24 deposition, we asked him whether McCloskey does that exact thing.
25 And we asked him to confirm whether McCloskey's barcodes are used

1 to correct for amplification bias. And he said, yes. That is stated as
2 one of the amplification -- applications in the specification. There,
3 he's talking about the McCloskey specification. And he goes on to
4 say that she's using the barcodes as a way to correct for amplification
5 bias. That, there's no doubt about. So we agree with Dr. Puglisi in
6 that respect, that there is no doubt McCloskey is using these barcodes
7 to correct for amplification bias and skewing.

8 Go to slide 13. All right. So what does Molecular Loop say
9 about the collapsing step in McCloskey? Well, they seem to admit
10 that McCloskey removes duplicates, but they say, well, McCloskey
11 doesn't collapse the duplicates into a single count. But that's not
12 accurate. The bottom of slide 13 are two passages from McCloskey.
13 The top one -- the top one in McCloskey is explaining that the
14 barcodes allow her to identify redundant sequences and that when
15 she's quantifying the number of molecules in the initial sample, that
16 she does so by counting only distinctly tagged sequences. So she's not
17 counting every time the sequence appears, but only the distinctly
18 tagged sequences.

19 And this is made more clear in a later passage of McCloskey
20 where she's describing a particular experiment. There, she noted that
21 there's a redundant sequence that was recovered during the
22 experiment, and she says that only one of these two sequences was
23 counted as a valid sequence. So when McCloskey finds two or more
24 sequences with the same barcode, only one is counted. So McCloskey

1 does show collapsing duplicate redundant sequences into a single
2 count.

3 Go to slide 14. Molecular Loop next argues that McCloskey is
4 different because McCloskey uses the tags to collapse and the claim
5 specifies collapsing target differentiator tag combinations observed
6 more than once. Well, what their argument overlooks is that in
7 McCloskey, the random barcode uniquely identifies one new target --
8 excuse me, one target nucleic acid. So a given tag is only part of one
9 combination of target differentiator tags. So when McCloskey is
10 using the tag to collapse, it necessarily is collapsing combinations that
11 appear more than once into a single count. So there is -- and to
12 illustrate this, our expert provided some diagrams showing how it
13 works.

14 If we go to slide 15, this is from -- this is from our expert,
15 Dr. Stacey Gabriel, her rebuttal expert report, her reply expert report.
16 And at the top is a figure that shows looking at the tag target
17 combinations. At the bottom is a figure that shows looking at the
18 tags. And as you can see at the top, when looking at the tag target
19 combinations to collapse, in the first box, the red box, there's a T
20 associated with the 1011 tag. There's three instances of that, and they
21 get collapsed into one instance in the collapse on the right.

22 At the bottom, when you look at the tag, you can see there's a
23 box with three -- a red box with three 101s in it. All those are
24 connected to that T molecule. So when it collapses -- when there's the
25 collapsing, that 1011 is collapsed into a single count. So in both of

1 these instances, whether you're looking at the tag or the tag and target,
2 the combinations that appear more than one time are collapsed into
3 one count.

4 JUDGE MITCHELL: So is your argument it's just a distinction
5 without a difference, right? Whether you're looking at the tag itself or
6 the tag with whatever is going to be essentially the same --

7 MR. BROUGHAN: It's --

8 JUDGE MITCHELL: -- nucleic acid or the same, you know,
9 base.

10 MR. BROUGHAN: Yes, it's -- I mean, we don't think there is a
11 difference, but distinction without difference is disclosed, yes.

12 When you're looking at the tag itself, you're necessarily
13 considering the combination, because that tag is always associated
14 with the same molecule. So it's the same.

15 JUDGE MITCHELL: Are there ever instances where it's not?
16 Where you have to distinguish where there's some kind of problem in
17 amplification and that's part of the bias too, where you wind up with a
18 different base attached to the tag?

19 MR. BROUGHAN: Not in McCloskey, no.

20 JUDGE MITCHELL: Okay.

21 MR. BROUGHAN: And to perhaps build on that point a little
22 bit more, if we go to slide 16, the idea that looking at the tag is in fact
23 the same thing I think comes through when we look at the structure of
24 the claims. On slide 16, we see the last step of Claim 1 and Claim 2,
25 which depends from Claim 1.

1 And Claim 2 further limits Claim 1 and the correcting step and
2 says that, "It comprises collapsing all-sequence reads comprising the
3 same differentiator tag into a single read," not comprising the same
4 differentiator tag target combination, but the same differentiator tag.
5 Because Claim 2 limits Claim 1, Claim 1 must encompass that step
6 that's included in Claim 2 and Claim 1 wouldn't -- would be satisfied
7 by a process that collapses using tag limit.

8 Okay, I'd like to move on to Molecular Loop's next argument,
9 which is about whether there's a motivation to combine McCloskey
10 and Bignell. In our -- in the papers we identified a number of reasons
11 why a skilled person would have made the combination. If you go to
12 our slide 18, one of the reasons, as Dr. Gabriel explained, is that
13 Bignell's method includes a number of amplification steps. And a
14 skilled person would have known that amplification processes
15 typically introduce bias or errors into the amplified sample.

16 McCloskey teaches that its method provides a way to correct
17 for errors and/or bias introduced by amplification. So Dr. Gabriel
18 explained that a skilled person looking at these would have
19 understood that McCloskey provided a solution to any amplification
20 bias in Bignell's processes. Now this amplification bias problem was
21 well known by this time.

22 If we go to our slide 19. At the top are quotes from two
23 exhibits. One is Exhibit 1025. The other is Exhibit 1018. And both
24 of these -- the top one is an article from 2005. And the middle one is
25 a patent application published in 2008. And both of these note

1 problems with amplification bias and where amplifying one target
2 molecule, it may be copied more times than another target. So they
3 both are observing the same amplification bias problem well before
4 the priority date of the '730 patent. We also asked their expert about
5 whether this problem was known, and their expert, Dr. Puglisi, as
6 shown at the bottom of our slide 19, stated that the idea of correcting
7 for skewing was known in the art. And he went on to say that that's
8 one of the reasons people introduced barcodes long before even
9 McCloskey's patent. So McCloskey's patent was -- has a 2007 date.
10 So he -- Dr. Puglisi is admitting that this problem with skewing was
11 known even before 2007.

12 Go to our slide 20. Molecular Loop has said that, well, a
13 skilled person wouldn't have made the combination of McCloskey and
14 Bignell, because Bignell has a passage that criticizes a prior art
15 approach to using unique tags. And that prior -- that passage that
16 Molecular Loop refers to is shown on the top of the screen. And it's
17 describing a prior art approach by someone named Brenner. And the
18 Brenner -- in the Brenner approach, tags are used to label each target
19 molecule in a sample, so that each one has a unique tag. And those
20 tags are -- can then be used to sort the sample onto beads for various
21 applications. Bignell notes that while the Brenner approach is ideal
22 for treating one sample such that each individual molecule in the
23 sample has a different tag, it does not permit attachment of the same
24 tag to every molecule in the sample.

1 Well, that criticism of Brenner does not apply to McCloskey.
2 On the bottom of the screen, we have figure 3 of McCloskey, which
3 we looked at a moment ago. And McCloskey's tag has two different
4 components. It has a random barcode that identifies a particular
5 molecule in the sample, but it also has a batch stamp that is used to
6 identify a sample. So in McCloskey's tags, McCloskey permits every
7 molecule in the sample to have a same tag, the same identifier added
8 to it, that's the batch stamp. But McCloskey has more. It also
9 includes the additional feature of having the random barcode that can
10 uniquely identify nucleic acid. And our expert pointed out that this is
11 why a schooled person would have wanted to combine the two,
12 because McCloskey provides the same sample tagging functionality,
13 but adds this additional functionality that can be used to address the
14 bias.

15 So Molecular Loop also argues that a skilled person wouldn't
16 have considered McCloskey because it describes a technique that was
17 used in Sanger sequencing. If we go to our slide, at 21, we don't think
18 their description is accurate. In fact, the named inventor of the '730
19 patent knew about McCloskey and was considering McCloskey when
20 he was drafting the patent application. Molecular Loop has produced
21 a number of emails from the inventor in this case. The email and
22 along with the initial draft application is shown on the screen. And
23 Dr. Porreca asked his counsel, how much overlap do you see in the
24 bias detecting barcode application? That's what became the '730
25 patent. With a patent reference called out in Note 1, and it puts in

1 parentheses, McCloskey. That's the same McCloskey reference that is
2 at issue here today.

3 And when you look down at Note 1, Dr. Porreca raised a
4 concern that there is some prior art associated with random barcodes,
5 but I'm not sure if it anticipates the applications we're interested in.
6 Again, it's citing to McCloskey. So a person of ordinary skill in the
7 art considering this problem that the inventor was considering would
8 have considered McCloskey. The fact that it describes Sanger
9 Sequencing is really not relevant to whether the art was relevant or a
10 skilled person would consider it, because here it was considered.

11 Go to our slide 22. Molecular Loop next argues that a skilled
12 person would not have made the combination because it would have
13 been too expensive. And first, they don't put in any evidence showing
14 how much it would have cost. But second, our expert looked at this
15 and said -- and explained that synthesizing random, unique oligo
16 barcodes would not have been a significant expense. And she points
17 out that McCloskey, in fact, described several techniques for doing so
18 that were within the skill of the art. It shows that it was not too
19 expensive. It wasn't so expensive that a skilled person wouldn't have
20 considered it. And at the bottom of the screen, you'll see that
21 Dr. Puglisi confirms that she is doing just that.

22 Okay. I -- I'm going to move on to Chee, unless there's any
23 questions about Bignell or McCloskey that I can answer. Chee
24 teaches a technique for detecting or correcting errors or bias during
25 sequencing. Chee uses what he calls constructs. And an example of

1 what a construct looks like is shown at the top of the screen. This is --
2 would also be shown in figure 1 of the Chee patent. And each
3 construct consists of a region of interest or ROI, which is just a target
4 nucleic acid. When you look at the text passages of Chee, you'll see
5 ROI or region of interest rather than target nucleic acid, but that's
6 what Chee is referring to. And the construct also includes a unique
7 identifier that's in Chee's language, which is just a barcode or a tag.
8 These unique identifiers, as Chee explains in the bottom passage on
9 slide 26, they are -- excuse me. Chee explains that unique identifiers
10 are associated with individual molecules in the start of the sample.
11 And he goes on to say that because of this any amplification products,
12 any -- and, you know, when he's looking at the amplified sample,
13 Chee can determine which molecules are copies of each other by
14 looking at that unique identifier.

15 So with that overview of Chee, I'll turn to the collapsing study.
16 Now, we map two different processes in Chee to this collapsing step.
17 Chee's process for correcting error and Chee's process for correcting
18 bias. I'll start with the one for bias and then move to the one for error.
19 Okay. Now, in our slide 28, we looked at this a moment ago, but
20 Chee is describing this problem with amplification bias and notes that
21 the unique identifiers, they allow the number of starting molecules can
22 be inferred. So Chee is saying that by using the unique identifiers,
23 you can infer the number of starting molecules in that initial sample.
24 On the bottom is another passage from Chee, where Chee is
25 describing amplification bias. And Chee notes that the quantification

1 of the molecules, that's like counting the number of molecules, can be
2 corrected to reflect this manner of bias.

3 So if you go to our slide 29, our expert looked at the same two
4 passages of Chee, as you can see in the first two highlighted parts.
5 And then she noted that what Chee is saying here is that -- Chee
6 means that where it reads multiple sequences with the same unique
7 identifier, it counts those as only one instance of the ROI, and that
8 counting multiple sequences is just one instance, that collapsed them
9 into a single count. So our -- you know, our expert has looked at this
10 and explained how this bias correcting process, Chee works, and how
11 it meets the claim.

12 Molecular Loop has argued that, well, a skilled person looking
13 at this wouldn't have known how to count. But Dr. Gabriel, again,
14 looked at this and explained that a person of ordinary skill in the art
15 would have known how to count distinct, unique identifiers based on
16 Chee's disclosure. This was something that was obtainable by a
17 person of skill in the art; it was known. It wouldn't have been difficult
18 for them to implement.

19 If we go to our slide 30. As I mentioned, the -- Chee's process
20 for correcting error also meets the collapsing step of Claim 1. But we
21 also map aspects of that process to the consensus base call of Claim 2.
22 So for efficiency, I'll just address those two together. And if you go to
23 our slide 31, this is the last step of Claim 1 of the '730 patent, along
24 with Claim 2. We looked at this a moment ago, but we didn't really
25 look at that term in green, the -- a consensus base call. And so Claim

1 2 specifies, as I said, (inaudible) comprises of collapsing all sequence
2 reads comprising the same differentiator tag into a single read before
3 determining a consensus base call.

4 So if you go to slide 32, this is a passage from Chee. And Chee
5 explains that using the unique identifiers, Chee can identify which
6 amplified molecules are copies of each other. And by being able to
7 look at multiple instances and multiple copies of the same molecule,
8 Chee explains that a consensus sequence can be determined using data
9 from multiple molecules, and this allows him to obtain a higher
10 accuracy rate. So consensus sequence, that's a little bit different
11 than -- that term is a little bit different than consensus base call. So
12 let's look at what a consensus sequence is. If you go to slide 33, a
13 consensus sequence was something that was known in the art. It's not
14 a term that's defined in the '730 patent. It's just something that would
15 have been within the knowledge of a skilled person. And on the
16 screen is a passage from the Bentley article, which is from 2006. And
17 at the top is a figure that shows how to create a consensus sequence.
18 And in explaining how this process works, Bentley explained that
19 multiple reads from the same sample can be aligned to derive a
20 consensus base call at each position. So to determine the consensus
21 sequence, Bentley explains that you have to make a consensus base
22 call at each position in that sequence.

23 So when Chee says that you create a consensus sequence using
24 multiple copies of the same molecule, Chee is describing a process
25 that makes a consensus base call for each base in that sequence. Now,

1 we don't think there's much dispute that this is how Chee works. If
2 you go to slide 34, this is a -- this is Molecular Loop's expert,
3 Dr. Puglisi. And we asked him about this passage of Chee. And he
4 agreed that where Chee describes creating a consensus sequence
5 derived from multiple colonial copies, that he's doing what Bentley
6 did. So that the process shown in Bentley is what's done by Chee and
7 it doesn't seem like there's a dispute between the parties in that.

8 So how does -- how do I map the -- that error correcting process
9 to the claims? Well, Dr. Gabriel explained that in this process, first,
10 Chee groups all the amplified products, all the copies together. And
11 she explained that this grouping collapses the identical constructs
12 because the bin that those groups are placed in represents a single
13 count of the nucleic acid in that original sample. She explained that
14 after they're grouped, that that's collapsing, she will use that group
15 to -- uses multiple means of the group constructs to generate a
16 consensus sequence. So first, Chee groups then collapses, then Chee
17 creates the consensus sequence, which makes its consensus base calls.
18 So as Dr. Gabriel explained, this is how Chee meets the collapsing
19 stuff and the consensus base call.

20 So if there's no questions here. I'm going to move to the
21 combination of Chee with Gahan.

22 JUDGE MITCHELL: Can I ask you one quick question?

23 MR. BROUGHAN: Yes.

24 JUDGE MITCHELL: So I guess -- and maybe this is kind of a
25 hard question to answer, but how well known in the art was consensus

1 sequencing at the time? I mean, I know, you know, we have one
2 reference that describes pretty detailed, but how do I know that that is
3 pretty much how everybody is going to determine it? And I know you
4 (inaudible).

5 MR. BROUGHAN: Their expert agrees that's how Chee does
6 it. But the consensus base calling is also discussed at a very high
7 level in the Shendure reference, which is Exhibit 1012.

8 JUDGE MITCHELL: Okay.

9 MR. BROUGHAN: I believe that's two exemplary cites, are
10 three -- page 3 and Pages 7 to 8. I'm not positive it describes
11 consensus sequencing, but it does describe the same consensus
12 process. But I think both experts here agree that it's a well known
13 concept.

14 JUDGE MITCHELL: Thank you.

15 MR. BROUGHAN: The final point is just with the
16 combination of Chee with Gahan. And here, Gahan is describing a
17 method for extracting nucleic acids from plasma, which is just blood.
18 And notes that nucleic acids extracted from plasma can be used in
19 diagnosing cancer -- in monitoring cancer and prenatal diagnosis and
20 other diseases. Our expert explained that a skilled person looking at
21 Chee would understand that you could get the nucleic acids from
22 blood. Molecular Loop has argued that a skilled person would not
23 have made the combination because there -- you need -- Gahan
24 reports that you need to have consistent -- you need to be consistent
25 with extraction techniques to ensure the reliability. But that kind of

1 warning, that you need to have consistent extraction techniques,
2 wouldn't have dissuaded the skilled person from making the
3 combination. In fact, Gahan itself notes that nucleic acids extracted
4 from blood had successfully been used in diagnosis and monitoring
5 activities, so a skilled person would have made that combination.

6 If there's no further questions, I will turn it over to Ms. Fukuda
7 to address the other issue.

8 MS. FUKUDA: Thank you. Good afternoon, Your Honors.
9 It's a nice surprise. Mr. Broughan left me more time than I had asked
10 for, so thank you. Okay. So I'd like to turn to the issues or the
11 disputes between the parties regarding the -- whether Chee is
12 considered prior art for this proceeding. And there are three primary
13 disputes. And we'll start first with that first issue, which is whether
14 Chee's provisional application discloses a biological sample in order
15 to be entitled to that priority date.

16 So Molecular Loop challenges that. And this is really the only
17 challenge. And you'll see that here in Claim 1 of the '730, it's really
18 about this limitation, a biological sample. Does the Chee provisional
19 disclose a biological sample? And the simple answer here is yes.
20 And we're looking at -- on slide 41, two passages. There are more,
21 but these two we highlight, Paragraph 60 and Paragraph 66.
22 Paragraph 60 expressly recites nucleic acids and biological samples,
23 using the same exact words. Paragraph 66 explains more. You will
24 hear a lot of argument from Molecular Loop when they get up here,
25 and they will argue that Chee is really about synthetic biology, right?

1 It is not about using human biological samples. But that's not what
2 Chee says. So in addition to actually calling it biological samples,
3 Paragraph 66 says, starting from the first sentence, "Although the
4 present invention is primarily described in the context of synthetic
5 biology and quantitative analysis, the constructs and methods can be
6 used more generally." Right. Those are the keywords. Chee says,
7 we're not limited to synthetic biology here. This can be used more
8 generally. You will not hear Molecular Loop focus on those words.
9 They do quote the same paragraph, but they will not point to the fact
10 that the disclosures, this goes beyond synthetic biology. And in fact,
11 if you go further in the paragraph, it specifically talks about diagnostic
12 use and clinical use. And there's really no debate between the parties
13 about what those two terms mean and the fact that they refer to human
14 use.

15 So on slide 42, we have a couple of quotes from Molecular
16 Loop's expert, Dr. Puglisi. And he was asked about the term clinical.
17 Does clinical refer to patient care? And his answer is, clinical
18 involves human patients and diseases. He was also asked about his
19 understanding of diagnosis. And in that bottom box, he says, "The
20 meaning here is targeted towards human patients, yes." So their
21 experts agree that the words clinical use and human use refer -- rather,
22 and diagnosis means human use.

23 So with that, I'll move on to the second dispute here. And now
24 we shift focus to Molecular Loop's proof, which is: Has Molecular
25 Loop shown that prior conception of Claims 1 to 3 and 9 took place in

1 the March 6, 2009, draft application? And here, we're going to focus
2 in on this one limitation in Claim 1, and that is -- '730 patent Claim 1
3 says, "It's a method for correcting for errors or bias," and that shows
4 up twice in the claim. So what this claim says is, this claim is broad
5 enough to cover a method that corrects for errors using this process.
6 It's also broad enough to cover a method for correcting bias using this
7 process. So the priority date -- the priority application must disclose
8 both correcting for errors and correcting for bias.

9 And the experts on both sides were asked whether errors and
10 bias are in fact different things. And here's Illumina's expert's
11 response. She says, "Errors and bias refer to different problems. An
12 error is something distinct from bias." And she further explains, in
13 Paragraph 40 here on slide 45, "Errors can occur when nucleotides are
14 incorrectly incorporated when making a copy of DNA or it can occur
15 when it's subsequently misread by the sequencing machine," right?
16 So those are errors. On the other hand, in contrast, bias generally
17 refers to an uneven amplification of target molecule. So errors are
18 changes in the sequence. Bias refers to an accounting issue, multiple
19 copies, how many copies, uneven copies being made. So therefore,
20 concluding -- the conclusion is bias is distinct from error.

21 Molecular Loop's own expert, Dr. Puglisi gives similar
22 testimony here during his deposition, and this time specifically with
23 respect to Claim 1 of the '730 patent, which was in front of him.

24 And he was asked, "Is there a difference between bias and
25 error?"

1 And his answer was, "Well, they say error or bias." And he
2 further explains here, pretty clearly he says, "An error is something
3 that involves changes in the sequence that happens during the
4 process." So changes in the sequence. On the other hand, he says,
5 "Bias is not changing the sequence, but you're changing the relative
6 population of the sequences." Right? So he -- those two things are
7 distinct from each other, even according to Molecular Loop's own
8 expert. And this is within the context of the '730 patent and Claim 1.
9 So he concludes, so they are different things. The claim is stating --
10 or what the claim is stating is that they are different than one another.

11 So having established that errors and bias are distinct, let's look
12 at what Molecular Loop's March 2009 application describes. And we
13 have an excerpt on slide 47, if you look at the bottom. The title of that
14 application says it's Methods for Reducing Bias, right? And then
15 when you get to the summary of the invention, it says, "The invention
16 is reducing the effects of the bias." And then later in that paragraph it
17 talks about the correction of biases. No mention of errors, no
18 disclosure of correcting for errors.

19 And moving to slide 49, when we look at what Molecular Loop
20 points to in its patent owner response for these two places in Claim 1,
21 where correcting for errors or bias shows up, you'll see that Molecular
22 Loop only points to the reduction of bias, right? So here's the first --
23 the preamble of Claim 1 and slide 50 is later on in Claim 1. And
24 every instance that they rely on shows correction of bias, but no
25 disclosure of correction for errors.

1 JUDGE MITCHELL: But when -- wouldn't their process -- I
2 mean, I think this is more inherently because that's brought with a lot
3 of -- you know, a number around that legally. But wouldn't you be
4 able to do a consensus read by correcting for bias? You're going to
5 have these different, you know, pots of the same sequence. And it
6 seems like that would just be a natural flow that you're going to
7 sequence it and you've got a bunch of, you know, the same sequence
8 because you've separated out your unique tags with the nucleic acid of
9 interest. So wouldn't it -- wouldn't that just naturally flow from that,
10 bias correction?

11 MS. FUKUDA: It does not naturally flow. There has to be a
12 step of actually deciding what is the correct consent -- correct
13 sequence. And there is no disclosure of that in the March 2009
14 application. So all that describes, is that you use these distinct tags,
15 and then you take everything that shows up with that same tag, and
16 you just collapse it into one. Now, if there is an error in those
17 multiple copies with the same tag, there is no disclosure in that
18 application of what -- how you -- what you do to correct that error.
19 All it says is just take the same -- take all the sequences with the same
20 tag and just count it once.

21 JUDGE MITCHELL: Would that have been known in the art
22 at the time though, how to do a consensus sequence read?

23 MS. FUKUDA: How to do a consensus base call was known in
24 the art, as Mr. Broughan just answered. However, if you look at the
25 March 2009 application, there's no disclosure of making a consensus

1 base call. So because that application is all about addressing the
2 impact of bias, it's to make sure that you're not counting too many
3 copies that happen during amplification. So it's not dealing with this
4 problem of errors and how to make a consensus base call.

5 JUDGE MITCHELL: Okay. Thank you.

6 MS. FUKUDA: Now, there, you know -- I -- I'll -- slide 52, I'll
7 just touch upon briefly. In the back and forth briefing, Molecular
8 Loop does bring up the fact that at some point, systematic errors have
9 come up, right? And they're trying to argue that, well, there's this
10 overlap between errors and bias. But, I -- I'll just say two things about
11 that. One is, that was not in the March 2009 application. It was first
12 added to a draft of the application on May 14th, 2009, which is after
13 Chee's priority date. So that's one issue with that.

14 Second is, even when systematic errors were added, it's pretty
15 clear, based on the description here in their own application, that
16 they're just talking about bias, right? It says -- you'll see, it talks about
17 systematic errors being over or under-representation. It says, "such
18 bias," right? So that is bias. And at the conclusion it says,
19 "Accordingly, new approaches are needed for overcoming bias." So
20 this is not an error correction here. They're just talking about bias.
21 And the fact that they use the word error, that came too late in the
22 process to count for their disclosure.

23 When we had the chance to take Dr. Porreca's deposition, on
24 slide 52, we asked him, you know, these concepts existed. And we
25 said, "What is your invention," right? "Can you tell me the difference,

1 if any, between bias and error?" And he could not -- he would not and
2 could not answer those questions. He said he's not prepared to discuss
3 specific terms in the patent.

4 And when we asked him, "Is bias the same as systematic
5 error?"

6 He also says, "I don't know."

7 On slide 53, more of the same. Focusing on Claim 1.

8 "Does claim one recite an invention that corrects for bias?"

9 Answer: "It recites what it recites."

10 And when pushed, he says, "I cannot give you an answer about
11 specific words like error or bias."

12 And so I asked this counterpart, "Does Claim 1 recite an
13 invention that corrects for errors?"

14 And he says, "Same answer."

15 "Is there any difference between error and bias?"

16 Again, refused to answer.

17 Dr. Porreca is the inventor of the '730 patent. If he invented
18 correction of both -- for both -- a method that corrects both bias and
19 errors, he would've known. But the fact that he is sitting there in his
20 deposition, he's unable to answer these questions is telling.

21 JUDGE YANG: Counsel, I have a question for you.

22 MS. FUKUDA: Yes.

23 JUDGE YANG: It's a little -- I guess it's similar to what Judge
24 Mitchell asked before. I just want to clarify one thing. So you said in

1 the March provisional application, they actually did teach collapsing
2 the multiple sequences into a single sequence.

3 Did I understand that part correctly?

4 MS. FUKUDA: Yes.

5 JUDGE YANG: Okay. So that single sequence, is it the
6 consensus sequence or no?

7 MS. FUKUDA: We don't know, right? So when you make a
8 consensus base call, you do look at the multiple reads, and then you
9 decide -- you know, for example, I think Mr. Broughan talked about
10 Bentley, right? Then you decide, you make a consensus base call and
11 you decide which base is the most accurate one. Yes, that part was
12 known in the art. But in the disclosure, in the March 2009
13 application, all we -- all they're concerned with there is to make sure
14 you don't get multiple copies. So it just says collapse everything with
15 the same tag into one, but it doesn't tell you which one it should be,
16 right? So because of that lack of disclosure, we don't know whether
17 that error is corrected or not. If you choose one that happens to be the
18 one that has an error in it, then no, it doesn't correct that error, right?
19 If you choose one that doesn't have the error, then that's great. But the
20 problem with the disclosure in that March 2009 application is, it
21 doesn't tell you which of those duplicate copies should be that one
22 read.

23 JUDGE YANG: Okay. Thank you.

24 MS. FUKUDA: All right. So I'll briefly address the last issue,
25 is whether Molecular Loop has shown reasonable diligence during the

1 critical period. And just to take a look at the overview, so we have the
2 March 6, 2009 application, which was sent by Dr. Porreca to his
3 attorneys on that date. And then we have, you'll see here, they
4 produced an email that's dated April 23rd of 2009, that's still before
5 Chee. And there, the prosecuting lawyers wrote back to Dr. Porreca
6 and they said, "You have" -- "I think that you have sent us all of the
7 important information that we need. Dan or I will send you updated
8 drafts today and they should not need any significant technical input
9 at this stage." So between March 6th and April 23rd, the lawyers have
10 had everything that they needed on the -- technically, and they had an
11 updated draft, and they don't think any additional technical input is
12 needed. All of that was before the critical period. And yet, they didn't
13 file until May 18th. So that's one problem.

14 If we look at the critical period here, it's a particularly short
15 amount. It's 20 days. It spans April 29th to May 18th. And we have
16 logged here, on a daily basis, based on the documents that they
17 produced, what activities had taken place. And in red are areas where
18 we do not see evidence of prosecuting -- basically pushing the
19 application forward to diligent filing. And the law requires
20 reasonably continuous diligence during this time period, right? Not
21 just diligence, but reasonably continuous diligence. So you do --
22 when you have a short critical period of less than three weeks, days do
23 matter.

24 Now, I know Molecular Loop cites a number of cases where
25 some leeway is given for gaps, and some of those gaps could be

1 weeks. There's the *Perfect Surgical* case, for example. However, in
2 those cases, the distinction is that those critical periods are months and
3 months. When you have months and months of critical period, and
4 there are a couple of weeks in between, it doesn't have the same
5 impact on diligence as when you have only weeks at issue here in
6 critical period. Here, we are more akin to the *In re Mulder* case,
7 which I'll bring up in a bit, where we're talking about a critical period
8 in terms of days and not months. So now there are -- there will be
9 some dispute from Molecular Loop about whether, in fact, there was
10 sufficient activity. We have identified 12 days. You know, whether
11 it's 12 days or 11 days, you know, it can be debated. However, that's
12 still more than half of the critical period. They have not met their
13 burden at this showing. In fact, if you look at slide 56 there's an entry
14 here on May 11th where Dr. Porreca sends an email and says, "Uri's
15 Application," that refers to the Application at issue here, Uri's
16 Application probably doesn't need further revision," right?

17 So what do we have so far? We have evidence showing that
18 almost all the work on the -- that Application had been done by
19 April 23rd. At that point, they're just making tweaks. And then we
20 have Dr. Porreca saying that that Application probably doesn't need
21 further revision on May 11th, and yet it wasn't filed until a week later.
22 That is not reasonably continuous diligence under the law.

23 So here's the quote from *In re Mulder*, and *Perfect Surgical*
24 actually discusses *In re Mulder*, so in fact, in *Perfect Surgical*, which
25 Molecular Loop relies on, they said, "The board cites *In re Mulder* for

1 the proposition that even a short period of unexplained inactivity may
2 be sufficient to defeat a claim of diligence." And in *In re Mulder* that
3 critical period was only two days. So those two days mattered.

4 And, of course, Molecular Loop will say, well, the distinction
5 there is that the patent owner there did not provide any evidence for
6 those two days, right? And we are -- yes, I'm not saying that we are
7 exactly the situation of *In re Mulder*, however, because our critical
8 period is only 20 days, we are closer to the facts of *In re Mulder* than
9 we are to any of the cases relied on than by -- than Molecular Loop.
10 The Molecular Loop cases give more leeway, but they have a lot more
11 time span to work with.

12 JUDGE MITCHELL: So have -- has Patent Owner offered,
13 you know, explanations as to why, you know, there were some gaps in
14 there as they were drafting and getting the Application on file?

15 MS. FUKUDA: Yes. Patent Owner has produced some email
16 correspondence which we had also culled through to create our chart.
17 So I'll go back to slide 56 here, right? So we have put that into a chart
18 form. Patent Owner also provided a declaration from one of their
19 prosecuting attorneys, Dr. Waller, however, the record that they did
20 produce shows that it was not Dr. Waller who did the bulk of the
21 prosecution on that Application, it was actually Dr. Young who did
22 the work. He was primarily drafting it.

23 So I'll show you on slide 58, we did -- they only submitted a
24 Declaration from Dr. Waller, none from Dr. Young, and so Dr. Waller
25 was the only person we had access to depose.

1 And we asked him: "Do you recall reviewing the draft
2 Application that Dr. Young sent to Dr. Porreca?"

3 And his answer was: "I don't recall doing that, no."

4 And we also asked him: "Do you recall drafting any portion of
5 what became the 358 Provisional Application?"

6 And his answer was: "No."

7 We asked him many, many more questions. Dr. Waller does
8 not have independent recollection of what happened back then. So his
9 Declaration, to the extent that he tries to add onto this diligence or the
10 reasonably continued diligence, we think it should be entitled to no
11 weight because he just doesn't have that recollection. He can look at
12 emails and basically rely on what the produced emails tell you.

13 And that's exactly what we did in slides 55 and 56. And when
14 we look at the email record, it shows that there is no reasonably
15 continuous diligence here, because almost all of the work was done
16 before the critical period, and then they made some tweaks during the
17 critical period. But there is no reason it should've taken three weeks
18 for them to file. They could've gotten that done all before the critical
19 period. And when we're dealing with the 20 days, it really does
20 matter. Every few days matter. You -- they were not reasonably
21 diligent under these circumstances.

22 JUDGE MITCHELL: So what would you -- what would you
23 say would be reasonable diligence? I mean, that you're seeing activity
24 every day to get this on file?

1 MS. FUKUDA: Yeah. Well, so in the facts of this
2 circumstance, if all the technology and input and drafts had been done
3 by April 23rd, and we're talking about making a few tweaks to their
4 charts and -- it looks like it could've been done over the course of at
5 least one, two, three, four, five, at least five or six days. It would not
6 have taken more than five or six days to wrap up those tweaks,
7 finalize the examples and their figures and so forth, and get that filed.
8 And if they did that, that would've been reasonable continuous --
9 reasonably continuous diligence, but that's not what they did. There
10 are big gaps for a 20-day period of lack of any written evidence
11 showing work was being done.

12 Now, they can say, well, you can assume that work was being
13 done in between, right? And oftentimes parties will produce invoices,
14 billing entries, things like that to show that the attorneys are actually
15 working on it, but here, they did not produce those invoices nor any
16 billing log. They relied on just these discrete emails, and the discrete
17 emails tell us that the bulk of the work was already done by
18 April 23rd. So we think there's a failure of proof on Patent Owner's
19 part to show that they were reasonably diligent under these
20 circumstances.

21 JUDGE MITCHELL: Okay. Thank you.

22 MS. FUKUDA: And with that, I will wrap up. Unless there
23 are further questions?

24 JUDGE MITCHELL: No.

25 MS. FUKUDA: Thank you, Your Honors.

1 JUDGE MITCHELL: I don't think there's anything.

2 When you're ready.

3 MR. WUESTE: Thank you, Your Honors. Good afternoon.

4 I'm Michael Wueste on behalf of Patent Owner, Molecular Loop, may
5 it please the board. I'm going to be addressing Petitioner's grounds 4
6 through 7, based primarily upon the obviousness or proposed obvious
7 combination of McCloskey and Bignell. My colleague, Mr. Matty,
8 will be addressing Petitioner's grounds based primarily on Chee.

9 And so to begin, I want to level set a little bit and return to
10 something that Petitioner's counsel mentioned early on in their
11 presentation. And it's a thing that I think infects the entirety of their
12 analysis and that is their mischaracterization of the problem that the
13 '730 patent was trying to solve. And what they say -- what they say
14 and what I heard Petitioner's counsel say, was that the '730 patent was
15 trying to solve the issue of skew and amplification bias. Now, that's
16 not incorrect, but it's also not complete, right?

17 What the inventors of the '730 patent recognized, in the context
18 of the time they were coming up with their invention, was that skew
19 and amplification bias, which were known problems in sequencing
20 technology prior to that, had downstream effects on analyses after,
21 right? And that's the issue that arose in the context of NGS, or next
22 generation sequencing. And NGS sequencing, as everybody here
23 admits, produce sequence runs on multitude -- magnitude more than
24 prior sequencing techniques. You're dealing with millions of
25 sequencing reads versus hundreds, right? And so the effects of

1 amplification bias and skew can have later on, follow-on effects on
2 downstream analyses like consensus base calls and genotyping calls.
3 And that's an issue. And so what the inventors of the '730 patent came
4 up with was a novel solution that addressed not just skew and
5 amplification bias, but also produced more accurate consensus base
6 calls and genotyping calls downstream. And that's throughout the
7 '730 patent.

8 Petitioner pulled out a couple of quotations from our Patent
9 Owner's Response, and I want to note that our Patent Owner
10 Response, even on Pages 1 and 2, makes clear that that's the entirety
11 of the problem that the '730 patent was trying to solve. If you look at
12 the end of the first full paragraph on Page 1 of the POR, we state,
13 "These errors," and we're talking about amplification bias and skew,
14 "these errors could lead to incorrect assumptions during the analysis
15 of sequence reads, such as longly -- wrongly designating an
16 individual's being homozygous for a particular allele of a gene instead
17 of heterozygous."

18 And so if you look at the next page, on Page 2, the bottom of
19 the first -- that paragraph, "For example, using the '730 patent
20 invention, the inventors were able to accurately track amplicons back
21 to the correct original target nucleic acid molecule before determining
22 the number of times that certain sequences appeared in the sample,
23 enhancing genotyping accuracy." When you consider what the '730
24 patent was trying to solve, the entirety of the problem, the '730

1 patent's disclosure and claimed invention addresses both of those
2 issues.

3 So the '730 patent, EX1001, and we're at slide 4 of Molecular
4 Loop's presentation, states, this is at Column 72, Line 67, "For any
5 target differentiator tag combination observed more than once, all
6 such reads are collapsed into a single read before consensus base calls
7 are determined. This will cancel the effect of bias on consensus base
8 call accuracy." That's the issue. And it's that latter half, canceling
9 "the effect of bias in consensus base call accuracy," that Petitioner's
10 truncated evaluation or, you know, summary of the problem the '730
11 patent was trying to solve fails to consider.

12 And, Judge Mitchell, your question to Petitioner about whether
13 or not barcodes alone versus target differentiator tag combinations, as
14 claimed and described in '730 patent, is right on point, because it is a
15 distinction with a difference and it is something that McCloskey does
16 not disclose. So I'd like to turn to that now.

17 So if we could flip ahead to slide 57.

18 JUDGE MITCHELL: Can I ask one quick question?

19 MR. WUESTE: Yes.

20 JUDGE MITCHELL: So if you're just trying to solve the
21 problem of bias, would there be any reason to do that, sort of, by
22 itself? I mean, does that get you anything in the lab that -- that's
23 useful if you're not doing a consensus read later? Like, is it useful, in
24 and of itself, to know there was, you know, 20 extra of this particular

1 nucleotide that was, you know, amplified versus others that were only
2 five?

3 MR. WUESTE: It certainly could be, depending on the type of
4 experiment you're trying to perform, right? The issue here is that, in
5 the context of next generation sequencing, those effects of
6 amplification bias and skew have greater imports or greater, you
7 know, impact upon subsequent downstream analyses like consensus -
8 base calls. So you can address for bias without also including a novel
9 step that enhances the accuracy of your downstream analyses as well.

10 JUDGE MITCHELL: Okay. Thank you.

11 MR. WUESTE: So slide 57. And it's important to note here
12 that Petitioner is relying solely on McCloskey for the correcting step,
13 and that's what I want to start with. McCloskey does not disclose
14 correcting, because it does not disclose the claimed, the plain as day,
15 claimed target:differentiator tag combinations. Everybody admits it.

16 Petitioner relies solely on McCloskey. If you look at slide 57
17 we have an excerpt there from their petition at Page 56, and they're
18 relying only on McCloskey for this, right? They say, "McCloskey
19 teaches correcting for errors or bias." And frankly, that makes sense
20 because Bignell is not really directed to correcting for error. Bignell
21 is interested in reducing cost efficiencies by pooling lots and lots of
22 samples together, millions of samples together, and making sure you
23 know which molecule came from which sample. Bignell is not
24 interested in correcting for error in the same way that they allege
25 McCloskey discloses.

1 But as we heard Petitioner's counsel say earlier, everybody here
2 agrees that McCloskey uses barcodes alone. This is throughout their
3 Reply, for example, their Reply at 3 to 4, we're on slide 58 of
4 Molecular Loop's presentation, "After amplification sequencing
5 McCloskey uses the barcodes." Or their Reply at 5, "By using the
6 barcodes McCloskey allegedly collapses." And I confirmed this with
7 Dr. Gabriel, Petitioner's expert.

8 I asked her: "In your opinion, McCloskey identifies target
9 barcode combinations using the barcode alone, correct?"

10 And she said: "Yes."

11 Petitioner wants to say that if you use the barcode alone, it ends
12 up in the same result, right? That was their slide -- I believe it was
13 Demonstrative 15, if I'm remembering correctly. That's not actually
14 accurate, right? And it's not what the '730 patent discloses. The
15 claims require combinations and that is important because, when you
16 use the information from both the differentiator tag and the target
17 sequence itself, as opposed to just the barcode, that allows for the
18 correction of bias and more accurate genotyping and consensus base
19 calls. That is what is happening in Exhibit -- in figure 5 from the '730
20 patent, EX1001. And we're looking at slide 59 here, right?

21 When you look at both the target sequence as well as the
22 barcode, you're -- you can make that correct call, right? What
23 happens when you correct for bias in the middle step -- before you
24 correct for bias, after amplification, you can get an over-amplification
25 of certain molecules or an under-amplification of others, and that can

1 lead to incorrect calls. After you collapse them, as long as you have
2 the correct sequence information still in your read, you can make the
3 correct call, because now you're linking up both the barcodes to the
4 sequence itself. You got two Ts, two As, and that allows you to make
5 the correct call of a heterozygous AT.

6 Petitioner, again, wants to say that that doesn't matter, because
7 if you collapse on the barcode, you are necessarily also collapsing on
8 the target sequence. But that's not actually true and I'll show you,
9 because I asked Dr. Gabriel this same question. At her deposition, we
10 presented her with two experiments, shown on slide 61 as EX2026
11 and EX2027. All right? And we ran through a sequencing analysis
12 with Dr. Gabriel. EX2026 on the upper left-hand side, we have two
13 original target nucleic acids, an A assigned to barcode 1 and a C
14 assigned to barcode 2. We amplify them.

15 Now, there are multiple areas in the -- or multiple phases in the
16 sequencing read in which error can be introduced. One of them can
17 be during amplification, in which you are getting or misreading the
18 wrong sequence, right? So after amplification, we have the amplified
19 products, and we walked through this with Dr. Gabriel, and we
20 noticed that barcode 1 was amplified four times, but there was an
21 amplification error introduced during amplification, which everyone
22 acknowledges can happen. And so instead of four As, associated with
23 the barcode of 1, you have three As and one T. And when you have
24 both this target information, the target sequence information, as well

1 as the barcode, you're able to identify that error and make the correct
2 call.

3 And that's -- I asked her this at her deposition. EX2025, Lines
4 4921 through 58, "You can look at the reads themselves," this is her
5 testimony, "you can look at the reads themselves and understand that
6 there's one outlier T where you have a bunch of As, and you're able to
7 do that because what you're looking at is the sequence information
8 and their results."

9 Then we ran a --

10 JUDGE YANG: I'm sorry. I have a question.

11 MR. WUESTE: Yes.

12 JUDGE YANG: So the last step, it says, "Correcting for error
13 or bias." Would correcting one of them here, say, just correcting the
14 bias, would that not meet the Claim limitation?

15 MR. WUESTE: So I don't think that is -- I don't want to step
16 on Mr. Matty's toes because he's going to address this as well, but
17 what I will say is, you can correct for error, you can also correct for
18 bias. What the advantage of the '730 patent invention is, is that with a
19 novel step of collapsing target:differentiator tag combinations, you are
20 addressing both.

21 JUDGE YANG: But that's not what the Claim says, right? It
22 doesn't say, correcting for error and the bias. It says, "Or."

23 MR. WUESTE: That's true. That's true. And so what I would
24 say is, the novel step of collapsing target:differentiator tag
25 combinations allows you to do either. And there's a distinction

1 between Claim 1 and Claim 2, because there's a temporal distinction
2 between the collapsing step and making the consensus base call.

3 With the combination of both the target sequence information,
4 as well as the differentiator tag, you can do what Dr. Gabriel was able
5 to do in EX2026, which is, both correct for bias, right, after you've
6 collapsed, and also identify error. If you rely on the barcode alone, as
7 McCloskey does, and you're locating just the barcode, I asked her to
8 identify which one had an error and she was unable to do so.

9 JUDGE MITCHELL: So is that "bias or error," is that because
10 maybe there's not an error? That it may be biased, but there's not an
11 error?

12 MR. WUESTE: That's true. You could have bias without
13 introducing error. You can also, presumptively, have error without
14 introducing for bias. The advantage of the '730 patent invention is,
15 with this step, you can do either and do so in an efficient fashion.

16 All right. So what are we dealing with here? McCloskey uses
17 barcodes alone because, at heart, McCloskey is primarily directed not
18 to correcting for amplification bias, but mostly towards authentication.
19 All right? It's throughout McCloskey. This is -- we're looking now at
20 slide 62 from Molecular Loop's presentation. EX1012 is McCloskey.
21 McCloskey was addressing a need in the art for methods for verifying
22 the authenticity of PCR products. And that's -- you can use that to
23 correct for error, but that's primarily, when I have a set of sequences at
24 the start, am I getting the same set at the end of my sequencing run?
25 And that's why McCloskey introduces barcodes. But if you're doing

1 that, right, if you're doing that, you only really need the barcode
2 information itself.

3 McCloskey is directed towards counting. So Petitioner's
4 counsel pointed you to Paragraph 93 of McCloskey. So if we look at
5 that, this is EX1013 -- oh. Sorry. My apologies. EX1012 at
6 Paragraph 93. The very bottom of that paragraph, there's a sentence
7 that begins, "Each genomic fragment." And what that reads is: "Each
8 genomic fragment is marked prior to amplification, allowing us to
9 identify contaminant and redundant sequences and quantify accurately
10 the proportion of cells carrying a particular sequence variant by
11 counting only distinctly tagged sequences." Everybody agrees that
12 "counting only distinctly tagged sequences" in McCloskey, is using
13 the barcode alone.

14 But McCloskey is primarily interested in counting and a
15 counting application is not necessarily the same thing as an
16 application that also corrects for error. I asked Dr. Gabriel this at her
17 deposition, EX2025, 5414 through 21.

18 My question to her was: "So in the scenario in which you're
19 using just the barcode alone, like an accounting application, like
20 McCloskey, you would not be able to identify error, correct?"

21 And her answer was: "You wouldn't be trying to. It's a
22 different type of experiment. That's a different application."

23 And that's the reason why McCloskey's use of barcodes alone
24 makes sense for McCloskey, but doesn't disclose what the '730 patent
25 claims, which is collapsing target differentiator tag combinations.

1 Combinations. And that has a real effect that is a distinction with a
2 difference, because it allows you to do both, correct for error and fix
3 downstream problems. I should say, increase the accuracy of
4 downstream analyses. Let me be more precise.

5 I'm happy to answer any other questions you, Your Honors,
6 may have about the collapsing step, otherwise I'll move on to the
7 motivation to combine, the lack thereof. Okay.

8 So if we can move back to slide 41.

9 Each of Petitioner's grounds, 4 through 7, is based upon this
10 combination of McCloskey and Bignell and the problem that
11 Petitioner has is, they consider it one way, but not the other.
12 Petitioner says, "If I had McCloskey, would I add it to Bignell?"
13 What Petitioner fails to do and address in any meaningful way is,
14 would a POSITA looking at Bignell have wanted to add McCloskey?
15 And Petitioner failed to show that, has failed to carry their burden, to
16 show that a POSITA would've been motivated to do that for three
17 different reasons, and they all, kind of, build off each other, right?

18 So to begin with I, kind of, want to start, we're on slide 43, with
19 what they say McCloskey is supposedly missing, okay? This is the
20 petition at 47, right? What they say is: "McCloskey does not require
21 specific sequencing technology, but notes that methods for sequencing
22 are standard in the art." And therefore, they assume that to implement
23 McCloskey's method, a POSA would've looked at other references for
24 details on known standard sequencing technologies. And they cite
25 Bignell as one of those.

1 The problem with that is, the reason McCloskey says, "Methods
2 for sequencing are standard in the art" is, it knew how to sequence
3 things. McCloskey has six experiments, six examples, described in
4 specification, in which they run how their tagging method would work
5 in different experiments. Those experiments are run on, and
6 sequenced on, ABI 3100 machines. Those are Sanger sequencing
7 platforms. So McCloskey, when it says, "Methods for sequencing are
8 standard in the art," it's talking about the methods for sequencing that
9 were known to McCloskey that it ran its own experiments off. And
10 those are Sanger sequences.

11 Now, Sanger sequencing, everybody agrees, are detailed, but
12 they're slower and they have low throughput. At slide 44 we have
13 excerpts from both Dr. Gabriel's deposition and Dr. Puglisi's
14 Declaration. Dr. Gabriel agrees that -- compare a Sanger sequencing
15 was capable of roughly on, you know, the level of hundreds of reads,
16 whereas next gen sequencing was capable of millions. Dr. Puglisi
17 agreed, EX2023 at Paragraph 30, this is his Declaration, "The Sanger
18 method suffers from drawbacks including the limited throughput and
19 the cost per nucleotide sequencing." And if you look at the example
20 set forth in McCloskey, right? The six experiments that I was
21 describing earlier, they're all on the level of 100 to 150 reads, right?
22 So low, low throughput.

23 Conversely, Bignell is directed to something different. In a
24 different context. Bignell is interested, this is -- we're at slide 45 in
25 Molecular's presentation. Bignell is EX1013. And if you look at the

1 quote from Bignell at 2, 3 to 8, this is describing what Bignell is going
2 after. It's "seeking an ability to genotype large populations in a small
3 number of reactions while retaining the information relating to the
4 source of the individual samples. Would yield the information
5 content of a full, non-pooled population screen in the time and at the
6 cost of a pooled reaction."

7 What Bignell is contrasting its method from was prior
8 approaches that did separate serial analysis of individual DNA
9 samples. If you look at Bignell, EX1013 at 151 to 58, "Large-scale
10 genotyping," NGS genotyping of the type that Bignell is talking
11 about, "is demanding in terms of the cost of both materials and labor
12 involved and the time taken to perform the study, especially if the
13 methodology employed involves separate serial analysis of individual
14 DNA samples." What Bignell is saying its pooled reactions and its
15 sample-specific tags are good for is providing information that is at a
16 cheaper cost than doing each individual DNA sequence read one by
17 one. Dr. Gabriel confirmed this as well, EX2025, 8711 to 15.

18 I asked her: "Bignell's method is designed to provide better
19 information using a sample-specific barcode at a lower relative cost
20 than sequencing all of those DNAs one at a time; is that right?"

21 "Yes."

22 So what's the problem here? A POSA looking at Bignell with
23 its emphasis on costs, on cost-efficiency and cost reduction, especially
24 in comparison to the costlier, separate serial analysis of DNA samples
25 one by one, would have recognized that McCloskey's method, which

1 applies a tag to every individual molecule, would've increased costs.
2 It would've increased costs. Petitioner is quibbling over how much
3 that would be, but in Petitioner's -- in the original petition, neither
4 Dr. Gabriel nor Petitioner analyzed that at all. They didn't address the
5 issue of the cost at all.

6 It is Petitioner's burden to disprove -- it is a petitioner's burden
7 to show that the claims are unpatentable. *Unified Patents,*
8 *Incorporated v. Velos Media, LLC*, this is IPR2019-00710. The board
9 said, "It is not Patent Owner's burden, however, to disprove
10 Petitioner's alleged motivation. Rather, Petitioner must demonstrate,
11 by the preponderance of the evidence, that the claims are
12 unpatentable. This burden of persuasion never shifts to Patent
13 Owner." Petitioner has to show that a POSITA looking at Bignell
14 would've been interested in adding McCloskey. Failing to address
15 costs does not prove that -- does not carry that burden. They
16 compound upon this.

17 So petition -- the original petition, Dr. Gabriel's original
18 Declaration, didn't address costs. We brought that up and in reply
19 they said, as we heard Petitioner's counsel say, well, okay. Sure, there
20 may be some additional costs. We're on slide 48 now. If you look at
21 EX1065, this is Dr. Gabriel's Reply Declaration. She says, "Adding
22 random barcodes to the sequencer reach would not have significantly
23 increased the cost of next generation sequencing," acknowledging that
24 there are some cost increases, "but to the extent that some additional

1 cost is incurred in use-cases where high accuracy is required, the
2 added cost is warranted by the improved analytic accuracy."

3 The problem with that is, they never tell us, neither Dr. Gabriel
4 nor Petitioner ever tell us, whether a POSA, using and looking at the
5 proposed McCloskey-Bignell combination, would've been interested
6 in improved accuracy. That's situation-dependent.

7 I asked her at her deposition, EX2025: "If very high accuracy
8 was not the intent of the experiment using the McCloskey-Bignell
9 combination, then the cost would not be worth it, correct?"

10 And her response was: "Yeah. It may or may not be,
11 depending upon what a person was trying to do."

12 But she never tells us what a person would be trying to do. So
13 we don't know whether a POSA would have been willing to accept
14 those higher cost increases for higher accuracy. Maybe the
15 experiment being run is one where you're trying to get lots of
16 information, but you don't care about the accuracy as much. Would a
17 POSA have been willing to absorb those higher costs then? She didn't
18 do that analysis. Petitioner didn't do that analysis.

19 Slide 49.

20 JUDGE MITCHELL: Let me ask you this --

21 MR. WUESTE: Yes.

22 JUDGE MITCHELL: -- so I mean, we always, sort of, look in
23 the art, like, we always assume people are going to want to make
24 improvements. We assume a POSA's going to want to do that.
25 Wouldn't this be an improvement? I mean, even if you're not as

1 concerned with accuracy -- I mean, I would think almost any scientist
2 in the field would love to have the highest accuracy they could have,
3 you know, with the tools available.

4 So why can't we take that and say, well, of course somebody
5 would look to improve accuracy?

6 MR. WUESTE: Because there's always a trade-off, all right?
7 I -- what's the old adage? You can have it fast, cheap, or good, right?
8 You're making a trade-off in every single scenario. Depending upon
9 what you're trying to do, you can maybe only get two out of those
10 three.

11 Sure. People would be interested in higher accuracy, but -- and
12 this leads me to the next point -- so I'm going to -- your question is
13 right on point because it segues me in -- when -- into why -- what I
14 want to say. Petitioner's failure to consider these whys and hows of
15 what experiment will be run, whether or not accuracy is worth it, led it
16 to ignore that Bignell's focus is on cost reduction, right? Bignell says,
17 I -- I'm returning to this quotation, we're on slide 52 now, from
18 Bignell, EX1013 at 151 to 58, "Large scale genotyping is demanding
19 in terms of the cost of both materials and labor involved and the time
20 taken to perform the study, especially if the methodology employed
21 involves separate serial analysis of individual DNA samples."

22 Bignell is more interested in cost reduction. I'm not saying it's
23 not interested in accuracy, but cost reduction is a major part of it,
24 right? And so it was aware of methods like McCloskey's that added
25 molecule specific tags. That's the Brenner approach.

1 Petitioner wants to say, well, Bignell is not that concerned with
2 Brenner, because Brenner is really about how you do it as opposed to
3 whether or not you do it.

4 But the point here is that Bignell knew that you could provide
5 tags for individual molecules. This is EX1013, Bignell at 320 to 35.
6 If you apply that method, the tags are synthesized in a combinatorial
7 manner, meaning that all 16,777,216 different sequences, that has a
8 cost increase. Bignell knew that individual tagging with different tags
9 for each individual sample at this level, at this magnitude of
10 sequencing runs, led to in cost increases, and they did not want to do
11 separate serial analysis of individual DNA samples.

12 Doctor?

13 JUDGE MITCHELL: But does that -- the reason to do it
14 doesn't necessarily have to come from, you know, for lack of a better
15 word, a base reference. I mean, you can look at, you know, what is a
16 POSA out there, what would they look at, you know, and what would
17 they combine looking at, you know, different rationales for what is
18 combined. It's almost like -- to me, it seems like you're almost saying
19 it's sort of a teaching away and I read this as, like, yeah, I'm going to
20 consider costs.

21 And, you know, Bignell's telling me, hey, this is going to cost
22 you to do it this way.

23 But why would that be to a level where a POSA would just say,
24 okay, I wouldn't -- I wouldn't go there?

1 MR. WUESTE: Well, so I think there's a distinction there.
2 One, Bignell says, we don't want to do it, right?

3 And so when Bignell says that, sure, a POSA with the proper
4 amount of analysis and evidence can get around that and demonstrate
5 why, in this scenario, increased accuracy would be worth it.

6 The problem we have here is Dr. Gabriel admitted that she did
7 not perform that analysis, right? And so it's Petitioner's burden to
8 carry this.

9 And we can speculate as to whether or not a POSA might have
10 been willing to do that and say, sure, I recognize that Bignell wants to
11 reduce costs. I recognize that Bignell doesn't like separate serial
12 individual molecule-by-molecule analysis. I could get there.

13 They haven't provided the evidence or the analysis to show how
14 you would do that or why a POSA would do that. They have a
15 conclusory statement that a POSA would have been able to do that,
16 but not how, and that's the issue.

17 JUDGE MITCHELL: So yours is a -- you're saying it's a lack
18 of proof regardless of whether you could do it or there might have
19 been a way on a different record you could show it. It's not on this --

20 MR. WUESTE: On a different record, maybe it's possible. I
21 agree completely. But that's not the record we have before us.

22 JUDGE MITCHELL: Okay. Thank you.

23 MR. WUESTE: All right. And with that, so because Petitioner
24 nor Dr. Gabriel failed to consider the costs, neither Petitioner nor
25 Dr. Gabriel provided evidence showing when the trade-off between

1 cost can actually be worth it. And because Petitioner, Dr. Gabriel,
2 failed to address Bignell's rejection of prior art molecule specific
3 approaches, they have not carried their burden. They have not shown
4 the evidence.

5 I'm happy to answer any other questions Your Honors may
6 have. Otherwise, I'm going to gratefully turn it over to my colleague,
7 Mr. Matty.

8 JUDGE MITCHELL: I'm good.

9 MR. MATTY: All right. Good afternoon, Your Honor. It's
10 Brian Matty again on behalf of Molecular Loop. So as Mr. Wueste
11 noted, I'll be handling the grounds that have to do with the Chee
12 reference and my plan with the time that I have today is to focus on
13 three main issues there. There's other issues that are addressed in the
14 briefing. We heard about some of them in the argument already
15 today. I'm sure we won't get to them all, so we'll likely rest on our
16 papers for some of the issues.

17 The three that I want to focus on are, first, the issue of
18 conception. This is a pretty narrow dispute on whether the March 6th,
19 2009 documents disclose correcting for errors or bias. And when you
20 look at those documents, when you look at the figures, and when you
21 look at the expert's testimony about those documents and about what
22 error is, I think it becomes pretty clear that the full scope of the later
23 provisional claims is shown in the March 6th conception documents.

24 The second issue is the reasonable diligence through the critical
25 period. Here we have ample evidence of diligence on -- from both the

1 inventors and the prosecuting counsel for what is a relatively short
2 period that they need to show diligence for. The petitioner's
3 arguments and most of the nitpicking that they do in their responses
4 really just fall into traps that the federal circuit has indicated is not the
5 correct way to do that analysis. That's highlighted in the *Perfect*
6 *Surgical* case, and I want to spend some time on that case just to
7 highlight those points because I think Petitioner's arguments really fall
8 apart once you get through that case.

9 And then last, if we have time, I'll disclose -- I'll discuss the
10 collapsing and determining consensus base calls terms and show how
11 Chee lacks disclosure of those, particularly for Claim 2, which
12 requires both steps and requires the collapsing to happen before
13 determining a consensus base call.

14 So with that, I'll turn to the issue of the swear behind. And
15 Chee is not prior art to this patent for Claims 1 to 3 and 9 for the
16 reason that those claims were conceived prior to Chee's priority date
17 and were constructively reduced to practice during the critical period.

18 There's also an additional issue for all claims, Petitioner has not
19 shown that the specific portions of Chee that it relies on in its
20 invalidity attacks were disclosed in Chee's earlier provisional.

21 So I'm going to take those issues in turn. First on the
22 conception issue and the documentation going back to March 6th,
23 2009, Patent Owner demonstrated evidence of how the draft and
24 figures on that March 6th date fully showed conception of Claims 1 to
25 3 and Claim 9 of the '730 patent. I have here on Patent Owner's slide

1 18 a copy of the figures that was included in that March
2 6th documentation. It's Exhibit 2008.

3 And that figure and some of the surrounding discussion of that
4 figure in the draft, which is Exhibit 2006, is, I think, central to this
5 issue. Dr. Puglisi analyzed that evidence and he walked through step-
6 by-step, explained how it showed conception for Claim 1, and he did
7 that in his declaration at Paragraph 61 to 73 and 84.

8 For the other three claims, obviously Claim 2 and 3 are
9 dependent claims, so they include all the limitations of Claim 1. They
10 have some additional limitations. Those were also shown in that
11 March 6th documentation. That document shows how you do a
12 collapsed barcode step before you do a correct call, a consensus base
13 call, as is claimed in Claim 2. It also explains that the random
14 barcode sequences were used to detect and correct biases which maps
15 to Claim 3.

16 And then for Claim 9, that's a separate independent claim.
17 Again, a lot of overlap with Claim 1, but a couple limitations that are
18 worded a little differently. The March 6th documentation shows those
19 differences, too. It notes that incorporation of a barcode at a given
20 step allows the detection of biases and that the barcodes are randomly
21 incorporated, and those map to those, sort of, tweak limitations in
22 Claim 9.

23 And again, Dr. Puglisi walked through all of that and he
24 explained it at Paragraph 74 and 84 in his declaration.

1 JUDGE YANG: Counsel, can we go back to the slide where
2 you showed the figures in the traditional -- could you point out
3 where -- perhaps where we would see the collapsing or error part?

4 MR. MATTY: Yes. So it's in the top part. There are a couple
5 of things going on. What the top part of that figure shows is the
6 amplification step that we've been talking about a lot, and then sort of
7 a middle column where you have a bunch of amplified nucleic acids
8 that were sequenced.

9 And if you just use that column and you go down to the bottom
10 of that column, it leads to an incorrect call, a homozygous T, where
11 the patient was actually heterozygous at this particular spot. It was
12 a -- an allele in the genome, this can happen, you know, in all diploid
13 organisms. It happens when you get an A from your mother and a T
14 from your father. At that particular point in the genome, you can have
15 either an A or a T depending on which of the copies of the diploid
16 genome you're looking at.

17 So in that middle column, before things are collapsed, there's a
18 call that this is a homozygous T. We know that's incorrect because in
19 the sample as it started, there were As and Ts. The correct call would
20 be heterozygous. So that incorrect call of a homozygous T is an
21 inaccurate result. That's an error. And that terminology, "inaccurate
22 result," is the exact wording that Dr. Gabriel, Illumina's expert, used
23 when she was describing her understanding of error in the '730 patent.

1 She said, I looked at this patent, I see the word error, I'm
2 interpreting it along -- right along with its traditional understanding of
3 an inaccurate result.

4 So in that top figure, when you do the collapsing. And then at
5 the end, you have the collapsed reads. Now, you do the correct call,
6 you find a heterozygous A/T. You're not calling it a homozygous T
7 anymore. You're realizing it's a heterozygous A/T.

8 That corrects the inaccurate result that you would have gotten at
9 the beginning, that is correcting for error, and that's shown and
10 described in the March 6th documentation.

11 JUDGE MITCHELL: Excuse me. In that middle step where
12 you get the incorrect call, is that because somebody reading it just
13 thinks the A is noise or was just a missed -- you know, it was
14 amplified wrong? Is that --

15 MR. MATTY: It's -- I think it's the noise, Your Honor. When
16 they look at -- reads and say, at this location, I have to figure out if it's
17 an A or a T.

18 And if you see a bunch of As and just a few Ts, you think those
19 are wrong and you say, it -- it's a homozygous A.

20 But if you see 50/50, you might say that's heterozygous. We
21 know this should be 50/50 because that's how it started, but because of
22 the amplification introducing the error, it's closer to the, you know,
23 90/10 or whatever you want to call it that leads to the incorrect
24 homozygous call.

1 And the collapsing is what corrects for that. It gets it back to
2 the 50/50 on the right column, so you can realize, oh, this is
3 heterozygous.

4 JUDGE MITCHELL: Okay. Thank you.

5 JUDGE YANG: So just to make sure I understand this part, so
6 in your explanation, the error isn't a sequence error. Do I understand
7 that correct? It's the column part.

8 MR. MATTY: That's correct. It's the inaccurate result that
9 comes out of the column. And I'll jump ahead to Patent Owner's slide
10 22 because I think this gets to exactly the question that you just asked.

11 When Petitioner is arguing that there's not conception shown in
12 the March 6th document for error, they're taking a pretty limited read
13 of what error can be. In their reply, they don't really do a claim
14 construction to really define it, but if you read their argument, they're
15 limiting an error to errors that occur in DNA synthesis during
16 amplification or sequencing in which a nucleotide is incorrectly
17 incorporated in the complementary strand.

18 They're sort of zeroing in on that specific type of one example
19 of error and saying, aha, that wasn't disclosed in the March 6th
20 application, therefore, we can get out of conception.

21 But the error that is claimed and described in the patent is not
22 limited in that way. The patent describes more broadly that it's using
23 a method of correcting for errors or bias, and specifically a step of
24 correcting for errors or bias, and the specification explains that the

1 error and bias are overlapping, and the same method can correct for
2 both.

3 As I mentioned earlier, it's also consistent with how both
4 experts are reading these terms. In Dr. Gabriel, this is her testimony
5 that I referenced earlier, she acknowledged that she understood error
6 in the '730 patent consistent with "the traditional understanding of an
7 inaccurate result." That's from Exhibit 2025 at 37 to 13.

8 Also elsewhere in her testimony, she volunteered over-
9 representation, which we've been talking about a lot today, as an
10 example of what she understands to be PCR errors. So in her own
11 words, "Characterizing over-representation as an error." That's in
12 Exhibit 2025 starting at Page 20, Line 18 through 21, 15.

13 So even under Dr. Gabriel's understanding, this is broader than
14 just the wrong base gets thrown in during sequencing. There are other
15 types of errors, and it's simply an inaccurate result based on the plain
16 meaning of the term. That's why that March 6th document shows
17 correcting for errors when it's correcting for those inaccurate results.

18 Dr. Puglisi, again, explained the same thing. Consistent with
19 Dr. Gabriel, he agrees that over-representation can be a type of error,
20 and he explained that in his declaration at Paragraph 72.

21 JUDGE MITCHELL: How much is disclosed in the spec itself
22 as to what constitutes error?

23 MR. MATTY: It -- the spec, it doesn't detail error. It doesn't
24 laundry list errors. It describes this method that we're showing in the
25 figure and explains how it works to get to the right result, but it

1 doesn't laundry list all the different types of errors that you might find
2 or that you might address, nor was it required to. The law just
3 requires that you disclose enough to show conception sufficient for a
4 person of ordinary skill to make and use and practice the invention,
5 and this figure and the discussion around this figure does that even if
6 it doesn't explain all the different types of errors that you might
7 address using the method.

8 And I think -- I zero in so much on this figure because I think
9 it's important. That figure in the March 6th document is the same
10 figure that showed up in the provisional application as figure 2. It's
11 ultimately the one that showed up in the '730 patent as figure 5,
12 consistently describing this method of correcting for errors or bias in
13 the same way.

14 And, you know, I think an important point, both parties have
15 noted that during prosecution of this patent, the PTAB actually had an
16 appeal come up from examiner rejections. That's in the record in the
17 file history at Exhibit 1004, starts at Page 1172. And there, the board
18 was dealing with an examiner rejection of whether there was written
19 description support for the correcting step.

20 In analyzing that issue, the board looked at this exact figure,
21 and I think what it found is telling. It looked at figure 5 and says --
22 this figure, it's figure 5 in the patent, was figure 2 in the provisional,
23 was all the way back in the March 6th document, "Illustrates how
24 target differentiator tag combinations are collapsed to correct for
25 errors or bias, and thus provide a correct determination of a

1 heterozygous sequence of genomic DNA." That's at Page 1178 of
2 Exhibit 1004.

3 And they went on at Pages 1178 over to 79. They said,
4 according to figure 5, "If the analysis stopped at this point with seven
5 amplicons," referring to that middle column, "corresponding to target
6 T and two amplicons corresponding to target A, error and bias may be
7 introduced wherein an inference is made that the two amplicons
8 corresponding to A are erroneous and therefore lead to an incorrect
9 conclusion that the gDNA was homozygous for T."

10 It's exactly that step that we were just talking about, and the
11 Board looked at the figure and said, "This method shows that errors
12 and bias may be introduced in the process that's shown there in that
13 middle column."

14 So with that, I'll turn over to diligence, and I promised to spend
15 some time in the *Perfect Surgical* case, so I'll do that now. I would
16 submit to Your Honors that the *Perfect Surgical* case is the single
17 most important case that the parties cited on this issue in the briefing,
18 particularly Pages 1007 through 1011 of that Federal Circuit decision,
19 go through a detailed discussion of the proper way to do a diligence
20 analysis.

21 It addresses situations and arguments that are very similar to the
22 facts that we have in this case, and it repeatedly faults the board for
23 accepting arguments that are very similar to the ones that Petitioner is
24 trying to ask you to accept here today. The Federal Circuit there was
25 dealing with a Board decision that found there was no diligence in a

1 swear behind argument. It found flaws in the Board's analysis of that
2 issue and overturned or vacated that finding of no diligence.

3 And the reasons that the Board -- that the Federal Circuit did
4 that and pointed out the flaws in the Board's analysis are directly on
5 point with what Illumina is trying to argue here.

6 And the main point in -- you know, sort of overarching all of
7 this analysis is, as the Federal Circuit said, "A patent owner need not
8 prove the inventor continuously exercised reasonable diligence
9 throughout the critical period. It must show that there was reasonably
10 continuous diligence."

11 And it went through a number of situations, both in the *Perfect*
12 *Surgical* case and in some prior case law, where courts and parties
13 have fallen into this trap of zeroing in and trying to argue about
14 continuous exercising diligence. Some of those pitfalls are on the
15 slide, on Patent Owner's slide 24. The Federal Circuit noted the
16 inventor is not required to work on reducing his invention to practice
17 every day. If there's periods of inactivity within the critical period,
18 those periods of inactivity do not automatically vanquish a patent
19 owner's claim for reasonable diligence. And the absence of evidence
20 that an inventor and his attorney revised or discussed the application
21 on a daily basis is insufficient to determine that the invention was
22 abandoned or unreasonably delayed.

23 And what the Federal Circuit was looking at in that case was a
24 situation of an inventor and a prosecuting attorney working together,
25 just like we have here. They explained in the *Perfect Surgical* case at

1 Page 1007 that the inventor had hired James Heslin, who was his
2 prosecuting counsel, to draft and file an application for him.

3 The counsel sent an initial draft of the application right at the
4 beginning of the critical period, had drafted the application already,
5 and then later he filed that application with the PTO.

6 Now, the time between those two events was 93 days, and so
7 the Federal Circuit noted, you know, during that 93-day lapse of time,
8 you had to analyze the evidence of what was going on to determine if
9 there was reasonable diligence.

10 The Federal Circuit explained, this is at Page 1009 in the
11 decision, "When you're doing that analysis to determine if there is
12 reasonably continuous diligence, the point of the diligence exercise is
13 not to scour the patent owner's corroborating evidence in search of
14 intervals of time where the patent owner has failed to substantiate
15 some sort of activity."

16 The point instead is to assure that, in light of the evidence as a
17 whole, the invention was not abandoned or unreasonably delayed.
18 That's how you're supposed to do this analysis.

19 And the Federal Circuit there faulted the Board for doing the
20 opposite and doing something similar to what Illumina is doing here.
21 The Federal Circuit noted at Page 1010, "The Board fixated on the
22 portions of the critical period where the patent owner did not provide
23 evidence of specific activities to conclude that there was no
24 diligence."

1 And so that's what the Federal Circuit lays out in *Perfect*
2 *Surgical*.

3 And if you look at the evidence here in this case, in light of
4 some of those guiding principles and some of those warnings against
5 some of the pitfalls that the Board fell into in that case, I think it
6 shows that Patent Owner's evidence of diligence is far and above high
7 enough to meet the standard here.

8 JUDGE MITCHELL: I'll ask you a question because
9 Petitioner's counsel talked about the 20-day critical period being fairly
10 short versus, I think you said 93 days for *Perfect Surgical*.

11 MR. MATTY: Yeah.

12 JUDGE MITCHELL: Does that make a difference, in your
13 mind, how short or how long that period is in determining the
14 reasonable diligence?

15 MR. MATTY: I think it does, but I think the effect's actually
16 opposite of what Petitioner suggested. I think Petitioner was
17 suggesting that if the time period is shorter, you have sort of a higher
18 bar to show your activity and your diligence.

19 They said some of those longer, 93, you know, *Monsanto* was, I
20 think, even longer than that. Some of those longer periods, there was
21 more leeway given because of the length of time. I don't think there's
22 any case law to support that. It's a rule of reason analysis, and the
23 longer the period that you're trying to show diligence for, I think the
24 more evidence you need to show that you're reasonably continuously

1 diligent for that period of time. I think it's harder to be reasonably
2 continuously diligent for 100 days than ten days.

3 And I think where Petitioner goes wrong, they latch onto the
4 *Mulder* case. We heard about the *Mulder* case. That was the one that
5 had a two-day critical period that was found to not have any activity
6 and therefore no diligence. That case is a very specific finding and a
7 very specific situation, and it's nothing like what we have here.

8 And again, we can go back to my favorite case, *Perfect*
9 *Surgical*, to see that. *Perfect Surgical* analyzed *Mulder*. And at Page
10 1009 of the *Perfect Surgical* case, they explain that in *Mulder*, the
11 patent owner did not produce any evidence of diligence during the
12 critical period.

13 What happened in *Mulder* is the patent owner said, it was only
14 two days. We were diligently working on the invention, you know,
15 we shouldn't be -- that shouldn't count against us for prior art.

16 But they provided zero evidence of any activity during the
17 diligence period.

18 So the court said it's just a complete lack of proof. There's no
19 evidence showing any diligence. You can't meet your burden.

20 That's nothing like we have here with all the evidence and
21 testimony in the record, all the correspondence between the inventors
22 and the -- and Prosecuting Counsel that Your Honors are familiar
23 with.

24 What *Mulder* said is, if you have no evidence, you're going to
25 lose.

1 It doesn't matter if it's a two-day window, a 20-day window, or
2 a 200-day window. You have to have some evidence of diligence in
3 order to start to reach that bar of reasonably continuous diligence. So
4 that's what *Mulder* was limited to and that was a situation where a
5 two-day critical period was found to lack diligence, because there was
6 simply no evidence at all.

7 All right. I'll turn then to Patent Owner's slide 26. We have, in
8 slides 26 to 28, a pretty detailed walkthrough each day of the critical
9 period where there's evidence going back and forth of some of the
10 work that's going on. And I think if you look at that evidence and
11 look at that summary across the board, you see a couple of things.
12 There is substantive work being done on this patent application
13 throughout that critical period. We heard some suggestion from
14 Petitioner that everything was done by April 23rd or April 24th before
15 the critical period.

16 We know that's not true because if you look at these
17 communications, which, again, are very similar to the types of
18 communications that the Federal Circuit looked at in *Perfect Surgical*.
19 If you look at those communications, you see them discussing the
20 application, sending paragraphs back and forth, sending claims,
21 sending edited documents, asking questions, setting up calls to
22 discuss. They're continuously working on the substance of the
23 application right up until the day it's filed.

24 On May 18th, there's still correspondence going back and forth
25 of updates to the specification, updates to the claim, and updates to the

1 figures to get it ready for filing that day. That day, when the
2 substantive work was done, it was filed right away. There was no
3 period of waiting. There was no gap between when the application
4 was ready and when it was filed. And we'll see that in the timeline in
5 slides 26 to 28.

6 And importantly, if you put that timeline up next to Illumina's
7 slide, I think it was slide 56 where they had red boxes for certain days,
8 I think you'll see repeatedly, there are days where there is evidence of
9 work being done that Illumina is simply ignoring to fill in more of
10 the -- those cells in red. They're going through that exercise that the
11 Federal Circuit has warned against of putting up each day and just
12 trying to fill in as many in red as they can to find periods of inactivity.
13 It fails to do the proper rule of reason analysis and think about the
14 evidence as a whole.

15 So I won't go through each day in the interest of time, but there
16 are days that they're calling red where we have evidence of work
17 being done. We noted that and called it out in our sur-reply. And we
18 also called out that a number of the days that they're faulting the
19 inventors and Counsel for not working are weekends, they're
20 Saturdays and Sundays that they have filled in red.

21 That actually, again, is an issue that was addressed in *Perfect*
22 *Surgical*. At Page 1011 of that decision, the board says -- I'm sorry,
23 the Federal Circuit said that "the board's focus on gaps of inactivity
24 led it to make fact findings unsupported by substantial evidence."
25 This is at Page 1011. The Federal Circuit says, "The most egregious

1 of these errors concerns the Board's finding of inactivity between
2 March 12th and March 15th." The Federal Circuit noted March 12th
3 was a Thursday.

4 On that Thursday, there was correspondence going back and
5 forth, to set up a meeting to discuss the draft. There was nothing over
6 the weekend. And then on Monday, there was evidence that counsel
7 and the inventor met. It's very similar to a couple of the weekends
8 that we have here that Illumina's faulting us for. And the Board in
9 *Perfect Surgical* determined that that Thursday to Sunday was a gap
10 in a gap of inactivity that supported its finding of no diligence.

11 And what the Federal Circuit said at 1011 of its decision, "The
12 Board's finding that this long weekend amounted to a period of
13 inactivity is unreasonable on its face."

14 Illumina is asking Your Honors to make that same unreasonable
15 finding, and we would just implore you to follow the guidance in
16 *Perfect Surgical*, because I think you'll see that there's more than
17 enough evidence of diligence here.

18 So I see I'm into rebuttal time. Unless Your Honors have
19 questions, I'll stop there for now and save the rest of our time.

20 JUDGE MITCHELL: Thank you.

21 Okay. Whenever you're ready.

22 MR. BROUGHAN: Okay. Just give me one moment, please.

23 JUDGE MITCHELL: Sure.

24 MR. BROUGHAN: May I begin?

25 JUDGE MITCHELL: Yes.

1 MR. BROUGHAN: I'd like to address a number of points
2 Counsel made in particular about the McCloskey reference, but let me
3 start by looking at Claim 1. And this was reproduced in our slide 4.
4 And if you look at that last element, "Correcting for error or bias
5 introduced during said workflow by collapsing target differentiator tag
6 combinations, observed more than once into a single count." Nothing
7 in that claim element requires genotyping, and nothing in that claim
8 element requires making a consensus base call.

9 A number of Counsel's arguments referred to this element
10 somehow being different than McCloskey because it allowed the
11 genotype calls that allowed the base calls, but there's nothing in that
12 claim that actually requires doing so. And when we asked their
13 expert, Dr. Puglisi, whether Claim 1 requires making a genotype call,
14 he agreed that it did not. And this can be seen in Exhibit 1066, Page
15 83, Lines 2 to 6.

16 What Claim 1 here says is that you collapse target differentiator
17 tag combinations into a single count. It doesn't say what you look at
18 to do that. It specifies that the combinations, if they're observed more
19 than once, are collapsed into a single count. There's no instruction on
20 what you look at or how you do it. And this becomes more clear, I
21 think, when you look at what's in the specification of the '730 patent.
22 Hopefully, I have my slides right here. Yes.

23 So if you look at our slide 60, this shows figure 5 of the '730
24 patent, along with the description and the specification of what's in the
25 figure 5. And you can see in the highlighted box, figure 5 says,

1 "Collapsing differentiator tag sequences." It doesn't say collapsing tag
2 target combinations. It says, "collapsing differentiator tag sequences."
3 When you look in the specification that it's describing to see how it
4 describes what is happening there, it states that repeat target
5 differentiator tag combinations are collapsed. So by looking at the
6 tags alone, the '730 patent is recognizing that that will collapse
7 combinations into a single count.

8 If we go on to look at the claim language itself, the first thing I
9 want to point out is that Claim 1, which recites consensus-based call
10 with respect to the grounds based on McCloskey and Bignell,
11 Molecular Loop has not contested that our combination discloses the
12 elements of Claim 2.

13 We relied on the combination of McCloskey, Bignell, and
14 Bentley to meet Claim 2, and they've raised no arguments specific to
15 that ground for any element in Claim 2. All of Molecular Loop's
16 arguments about the combination are directed to Claim 1, and, in
17 particular, the collapsing stuff and the motivation to combine, which
18 we'll get to in a minute. But in terms of the limitations of the claims,
19 it's all about collapsing in Claim 1, and collapsing in Claim 1 does not
20 require genotype call or consensus-based call.

21 JUDGE MITCHELL: Can I ask you a question?

22 MR. BROUGHAN: Yes.

23 JUDGE MITCHELL: So how would I read correcting for error
24 or bias as, I'm not telling you what I'm doing with that collapsed set of
25 target differentiator tag combinations?

1 MR. BROUGHAN: With the collapsed tags, you can correct
2 for error. With the collapsed tags, you can correct the bias.
3 Correcting for bias is, you know --

4 UNIDENTIFIED SPEAKER: (inaudible).

5 MR. BROUGHAN: Yes. Well, we agree that the claim is
6 describing what you do with the collapsed reads, and you can do
7 either one. That doesn't say you have to do both. It says you have to
8 collapse to correct for error or collapse and correct for bias.

9 Does that answer your question or is that --

10 JUDGE MITCHELL: Yeah, but I guess you were saying it
11 doesn't -- you know, it just talks about collapsing and nothing else, but
12 can't I read into the claim, when it's talking about error or bias, that
13 then I can do a consensus read, or I can, you know, do other things
14 with the collapsed target:differentiator tag combinations?

15 MR. BROUGHAN: You can, but that is -- but those specific
16 additional operations are not required by the claim. You know,
17 correcting for bias can be done without making a consensus-based
18 call, for example. It can be done without making a genotype call.
19 Correcting for biases can be done without either of those things, and
20 those things aren't required by the claim in order to achieve that.

21 JUDGE MITCHELL: Okay. I got you.

22 MR. BROUGHAN: So when McCloskey -- well, we'll come
23 back to McCloskey in a second.

24 The other point about -- and if I may, kind of, revert to the
25 combination point, the Claim 2 recites collapsing all sequence reads

1 comprising the same differentiator tag into a single read. If Claim 1
2 required collapsing based on the combinations, looking at the
3 combinations and not alone -- looking at the combinations and did not
4 cover looking at the tags, then Claim 2 would be invalid because it is
5 of a different scope than Claim 1. So their read of Claim 1 can't
6 possibly be right in view of what's in Claim 2.

7 I'd like to go to their slide 59 next. And I think this goes back
8 to the -- your question a moment ago, I -- Your Honor. They point to
9 this slide and say that the -- what's important about the invention is
10 that it allows for -- let's see, allows for correction of bias and more
11 accurate genotyping and consensus base calls. And then there's that
12 highlighted box on the bottom, on the right. That step, as I just
13 mentioned, it's not required by the claim. You can correct for bias
14 without doing those additional operations. So that's not something
15 that's required within the scope of the claims.

16 JUDGE MITCHELL: So you're saying, correct me if I am
17 wrong, any error or any type of bias would be encompassed within the
18 claims?

19 MR. BROUGHAN: That's correct. And, like McCloskey, does
20 explicitly state that it corrects for skewing and amplification bias by
21 removing redundant sequence reads. And although McCloskey
22 doesn't explicitly say -- I mean, but more than that -- and maybe this
23 confuses a little bit, but I do want to make the point. McCloskey does
24 actually do genotype calls, doesn't call it a genotype call. But
25 McCloskey is looking at the FMR1 locus, which is associated with

1 fragile X syndrome, and McCloskey says it's attempting to quantify
2 the proportion of cells that have different sequences in it.

3 So what McCloskey is doing there is trying to determine
4 whether the person is carrying that fragile X mutation that's associated
5 with the disease. So although McCloskey isn't calling it out, that's
6 what McCloskey is doing. This is explained by Dr. Gabriel in her
7 reply declaration in -- which is Exhibit 1065 in Paragraph 16, and it's
8 described in McCloskey itself in Paragraphs 92 to 93.

9 If I could go on and make a -- talk about their slide 61. These
10 figures that they've shown in slide 61 are incomplete, and you can see
11 that there's two steps in the figures at the top. What's not shown is a
12 collapsing step. There's no collapsing whatsoever shown on these
13 slides. And so how McCloskey would operate on the collapsed
14 sequence reads is not accurately shown here.

15 The other thing that's not shown is that McCloskey sequences
16 both the target and the barcode. While this figure -- these figures
17 don't show you the entire sequences, in McCloskey, McCloskey is
18 sequencing the entirety of the target and the tag. So when McCloskey
19 performs analysis, McCloskey does have all of the information needed
20 to identify errors or to identify what sequences are there or to quantify
21 the number of molecules that were in the starting sample. That is all
22 available to McCloskey. It's just not shown in these figures, and so
23 these are inaccurate and don't really show anything about how
24 McCloskey is actually running.

1 If I could turn now to some of their arguments about motivation
2 to combine McCloskey and Bignell. Their failure of proof argument
3 is a bit surprising to us because we think there is quite a bit of
4 evidence on the motivation to combine. For example, Dr. Gabriel has
5 11 paragraphs dedicated to this in her opening report declaration, this
6 would be Exhibit 1005, Paragraphs 247 to 57, and she has four
7 paragraphs in her reply declaration, which is Exhibit 1065, those are
8 Paragraphs 17 to 21.

9 In the petition, we also dedicated a number of pages to
10 addressing this exact issue. This is -- in the petition we have this on
11 Pages 46 to 51. And not only did we -- not only did we rely on
12 Dr. Gabriel's testimony, we also relied on industry trends at the time.
13 For example, the industry trends, as discussed in the Shendure
14 reference, which is Exhibit 10 -- well, I -- I'll have to look up the
15 exhibit number more because I didn't write that down, but the
16 Shendure exhibit, which extensively discusses how NextGen
17 sequencing techniques reinvigorated the industry and made people
18 more interested in adapting old techniques for the new -- for the new
19 sequencing regime.

20 We also, in the petition, addressed simultaneous -- in the
21 petition and in the reply, simultaneous invention that she came up
22 with the same idea of using tags to address bias, and that the fragile X
23 reference also came up with the same idea of using unique tags to
24 address bias.

1 And finally, just to comment on Bignell and cost savings.
2 While Bignell does describe cost savings, next generation sequencing,
3 like Bignell, provides cost savings because it allows multiple samples
4 to be sequenced at the same time. And McCloskey, which includes
5 both the batch tag, which is the sample tag, and the unique identifier,
6 the barcode, preserves those cost savings from McCloskey. So
7 nothing of -- or so those cost savings from Bignell by doing next-
8 generation sequencing. So there's nothing in McCloskey that would
9 destroy any cost savings that Bignell is describing. And just to go
10 back to the Shendure reference that I mentioned a moment ago, that is
11 Exhibit 1014, and it describes industry trends at the time.

12 If there are no further questions, we'll rest on papers.

13 JUDGE MITCHELL: I think that's good. Thank you very
14 much.

15 MR. BROUGHAN: Thank you very much.

16 JUDGE MITCHELL: Looking for your (inaudible).

17 Whenever you're ready.

18 MR. WUESTE: Thank you. Good afternoon. Once again,
19 Your Honor, it's Michael Wueste on behalf of Patent Owner
20 Molecular Loop. I'll make this brief and let everyone get on with the
21 rest of their, at least around here, cold day.

22 Want us to turn to where Petitioner's counsel left off, and that is
23 the argument that somehow, because McCloskey discloses batch
24 stamps already, that it would not have added additional costs to
25 Bignell's technique for adding sample-specific stamps. And frankly,

1 I'm a little bit confused by that, because if a POSITA, looking at
2 Bignell, also looks at McCloskey, which already discloses batch
3 stamps, why would they add McCloskey to Bignell? That seems like
4 a redundant combination, and so the only benefit that Petitioner has
5 alleged is that you would also add McCloskey's molecule-specific
6 tags, but that raises a problem for them, because they admit, and you
7 should take them at their word, that that will attribute additional costs.

8 And Bignell, with its emphasis on cost reduction and its
9 rejection of molecule-specific approaches like McCloskey's, opposed
10 to looking at that with all those disclosures about why it is cost-
11 prohibitive to do serial sequence-by-sequence analysis, and molecule-
12 specific tags would not have been motivated combined McCloskey
13 and Bignell.

14 Petitioner introduced -- or described a large section of its
15 petition and Dr. Gabriel's declaration, in which they say they
16 addressed the motivation to combine, but noticeably absent in that
17 was any discussion of whether or not Petitioner and Dr. Gabriel
18 accurately assessed or analyzed the cost of the combination, especially
19 in view of Bignell's emphasis on cost reduction, right?

20 And so that's the failure of proof, right? When you have a
21 situation like you do at Bignell, where you're concerned about cost
22 reduction and you're introducing a combination that they admit, and
23 you should take them at their word, would increase costs, you have to
24 do some sort of analysis show why a petitioner would -- why a

1 POSITA would still be motivated to combine the two references
2 regardless. They haven't done that.

3 JUDGE MITCHELL: Can I ask you, though?

4 MR. WUESTE: Yes.

5 JUDGE MITCHELL: You know, we always say, even if it's an
6 imperfect combination, it's still a combination a POSA would make --
7 you know, it doesn't have to be perfect. A lesser one is just fine too,
8 something that's maybe not as great. Would -- could we not look at
9 the combination that way here and say it costs you more money.
10 There might be companies that are very willing to pay the cost for
11 various reasons. It may not be the best solution for, you know, all
12 different scenarios, but a POSA would look and go, yeah, it's going to
13 cost me some more, but I would do it.

14 MR. WUESTE: In a vacuum, I would agree with Your Honor,
15 but that's not the evidentiary record we have here. And the failure to
16 provide that motivation, go through that analysis of when you would
17 make that trade-off, is what Petitioner has failed to do.

18 So in a different -- in a different scenario, had they had
19 Dr. Gabriel say, yeah, this may be imperfect, but here are the reasons
20 why you would still go forward with it, that may hold true. But
21 Dr. Gabriel admitted that she did not do that. She never listed out
22 what a POSA -- what a POSITA would be trying to do with this
23 combination. She never analyzed what kind of experiment would be
24 run to determine whether or not you want to make that trade-off of

1 cost for accuracy. She does not -- she leaves it as an unsupported and
2 conclusory statement that you could do that.

3 Well, that's not sufficient. It's particularly where, as here, and I
4 know I'm beating a dead horse a little bit here, Bignell recognized that
5 there were molecule-specific tagging approaches in the prior art and
6 said, I don't want that because they are too cost -- they are too cost-
7 prohibitive.

8 JUDGE MITCHELL: Okay. Thank you.

9 MR. WUESTE: Petitioner, with regards to the collapsing -- the
10 correcting via collapsing step, Petitioner's counsel said Claim 1 does
11 not require genotyping calls, and I would respectfully submit that
12 Petitioner's counsel is getting it wrong.

13 Sure, Claim 1 does not explicitly recite genotyping calls. What
14 Claim 1 does recite is the invention that solves the problem the
15 patent -- the '730 patent is trying to solve, which is both correcting for
16 bias and doing so in a way that improves the accuracy of downstream
17 and analyses. And so the correcting for errors or bias -- and Your
18 Honor, you pointed that out to Petitioner, and you were absolutely
19 right to do so.

20 Correcting for errors or bias by collapsing serves that goal,
21 right? The inventors of the '730 patent need not have explained that
22 this is the problem they're trying to solve in the description of the
23 invention, as recited by the claim limitations. What they recited was
24 the invention that allowed them to solve that problem.

1 And frankly, that's also borne out by Claim 2. I know
2 Petitioner pointed you, Your Honors, out to slide 16. They brought
3 this one up where they put up both the bottom of Claim 1 and the
4 top -- and the top of Claim 2. Claim 1, they're right, we don't
5 disagree, does not recite consensus base call. But Claim 2 -- and this
6 is where their claim's instructional argument falls apart, introduces a
7 temporal limitation, a temporal narrowing on the steps and the
8 performance of Claim 1.

9 Claim 2 should not be -- it is not read and should not be read to
10 say, oh, even though Claim 1 recites target differentiator tag
11 combinations, we should interpret that to be narrower because
12 Claim 2 also says collapsing all sequence reads. What Claim 2 is
13 actually about is saying, after you collapse all the sequence reads,
14 after you perform that correcting step, after you perform the
15 collapsing step using target differentiator tag combinations, as recited
16 plain as day in Claim 1, then you determine a consensus base goal.

17 And that is how we get to Claim 1 describes the invention,
18 Claim 2 shows how you apply the invention in order to -- in order to
19 get the goal or the result of more accurate consensus base calls. You
20 do it. Collapsing first, then determine the consensus base call.

21 Petitioner pointed out figure 5 and said, oh, figure 5 doesn't say
22 combinations, it says sequences. And I would respectfully submit
23 that, one, that is incorrect because, as Petitioner showed, the
24 description of claim 5 -- of figure 5 also describes using target
25 differentiator tag combinations. And frankly, that's both wrong on the

1 merits and wrong procedurally. You should not be interpreting target
2 differentiator claim -- target differentiator tag combinations, a clear
3 ordinary-meaning claim limitation, based on an importation of some
4 narrow description of the specification. That's wrong as a matter of
5 claim construction, and frankly, it's wrong because it's now a claim
6 construction they've introduced too late in the proceedings.

7 And with that amount of time, so I'll leave you to it. Thank you
8 very, very much. I appreciate it.

9 JUDGE MITCHELL: Great. Thank you so much.

10 JUDGE YANG: Do have a question.

11 JUDGE MITCHELL: Go ahead. Go ahead.

12 MR. WUESTE: Yes.

13 JUDGE YANG: So it's about your argument just now saying
14 about the Claim 2, there is a temporal element, and I do see the claim
15 language saying that you collect before you determine the consensus
16 sequence.

17 I'm just curious: Does the specification actually describe any
18 other way determining the consensus sequence, either simultaneously
19 as with a collapsing step or after?

20 MR. WUESTE: I don't --

21 JUDGE YANG: The --

22 MR. WUESTE: -- I don't believe so.

23 JUDGE YANG: Okay. Do you -- I do understand you're a
24 lawyer, but just in case you're so deep into this, do you know a -- like,
25 give me an example or was that ever done?

1 MR. WUESTE: Well, you're talking about in the prior art as
2 opposed to within describing '730 patent?

3 JUDGE YANG: Correct.

4 MR. WUESTE: What I would say --

5 JUDGE YANG: Because you just said in the '730 patent, there
6 was no such description, right?

7 MR. WUESTE: Of doing it -- doing the collapsing step before
8 performing a consensus base call, no. And I would say -- respectfully
9 submit that there was no description of that in the prior art either,
10 because the prior does not disclose collapsing target differentiator tag
11 combinations. That is part and parcel of the innovative and inventive
12 step claimed by the '730 patent.

13 JUDGE YANG: Okay. Thank you.

14 MR. WUESTE: Thank you very much, Your Honors.

15 JUDGE MITCHELL: Thank you so much, and thank you all
16 for coming out on -- as someone that's in D.C. We really appreciate
17 it, love having people come in person and argue, and it's -- this has
18 been very helpful from both sides, so thank you very much. And safe
19 travels home for everyone. And we are adjourned, but if you all
20 would wait around just a few minutes, to make sure the court reporter
21 doesn't have any spellings or things that she needs from you all. So
22 thank you very much.

23 MR. WUESTE: Thank you, Your Honors.

24 THE REPORTER: I don't have any spelling questions. Thank
25 you.

1 (Whereupon, the above-entitled matter went off the record.)
2
3
4