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Paper No. 45

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PARSE BIOSCIENCES, INC.,

Petitioner,
v.

10X GENOMICS, INC.,

Patent Owner.

IPR2023-00955 (Patent 10,240,197 B1)
IPR2023-00958 (Patent 10,697,013 B1)

Record of Oral Hearing
Held: November 6, 2024

Before MICHAEL J. FITZPATRICK, SHERIDAN K. SNEDDEN, and DEVON ZASTROW, *Administrative Patent Judges*.

APPEARANCES:

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The above-entitled matter came on for hearing on Wednesday, November 6, 2024, commencing at 1:00 p.m., at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia.

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

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3 JUDGE FITZPATRICK: Good morning or afternoon, as the case
4 may be. I'm Judge Fitzpatrick. Joining me, I'll let you look at all -- there's a
5 lot of -- we're doing this virtually. There's a lot of images you may see here.
6 But we have Judges Newman and Snedden also here. We have the record
7 before us. We also have the demonstratives that each party has sent us. We
8 have a court reporter, of course.
9 And we're here for two cases and -- well, yeah, we have two cases
10 and that's IPR2023-00955, followed by IPR2023-00958. And the Petitioner
11 in both cases is the same. That's Parse Biosciences and Patent Owner is
12 10X Genomics.
13 Can we have an introduction of counsel for Petitioner first, followed
14 by Patent Owner? Mr. -- oh, there you go. Okay. Please start over.
15 MR. WALTER: Can you hear me? All right, Your Honor.
16 JUDGE FITZPATRICK: Yes, we can now.
17 MR. WALTER: All right. Your Honor, this is Derek Walter for
18 Petitioner Parse Biosciences from Weil, Gotshal & Manges.
19 MS. RAYMOND: And good afternoon, Your Honor. This is Megan
20 Raymond with Groombridge, Wu, Baughman & Stone for Patent Owner.
21 And with me is Steve Baughman. Also Groombridge, Wu, Baughman &
22 Stone. We'll be splitting the argument today. And on the public line we
23 have representatives of the client 10X.
24 JUDGE FITZPATRICK: Thank you. That reminds me, I'm going to
25 be doing the same thing to try to mute when I'm not talking. If everybody
26 could do that, it makes for a clear listening experience for everybody. And

1 this is an open line so there is -- and there is nothing under seal filed in this
2 case, so I don't think that's any concern. But just wanted to remind
3 everybody of that.
4 In the order setting oral argument we had because of -- we already
5 knew that there was a lot of overlap, so we had 45 minutes per side per case
6 for a total of three hours. And we stated that we were going to start with the
7 '955 case first, take a short break, and then go to the '958. We've now
8 looked at the entire record and perhaps there's even more overlap of issues
9 than we anticipated. So I know that there may be duplication, you might say
10 something and it's relevant to both cases. I don't want it to get, you know --
11 I don't want to change course at the last second right before we start. So I
12 think we should stick to the '955 and then take a short break and then do the
13 '958. But I want to let both sides know we're obviously cognizant of the
14 arguments are typically going to be relevant to both cases.
15 MS. RAYMOND: Your Honor, if I might ask one question about the
16 details of that.
17 JUDGE FITZPATRICK: Sure, sure.
18 MS. RAYMOND: Which is, is there going to be -- I understand we're
19 going to be doing the arguments separately as it was laid out. Will there be a
20 single transcript for both of these proceedings or is there going to be a
21 separate transcript such that only the argument from the '197 ends up in the
22 '197 patent, the '955 case ends up in that proceeding, and only the transcript
23 for the second proceeding ends up in that proceeding?
24 JUDGE FITZPATRICK: Understood. I think we should do -- I'm not
25 sure if it'll be the -- let's say for now it's the same transcript. Okay? It's a
26 single document. But if, for example, it was two different documents, I have

1 no problem with filing them both in each case, so that for appeal purposes
2 or, you know, request for reconsideration, you have something to point to
3 that's in the case that you are appealing or requesting rehearing on.
4 MR. WALTER: Your Honor?
5 MS. RAYMOND: Understood. Thank you.
6 MR. WALTER: Your Honor, this is Derek Walter. Just to follow up
7 on that point. We agree with that. That makes sense to either file the
8 transcript in both cases or file both transcripts in both cases so that we can
9 try to avoid some duplication today. And that makes sense.
10 JUDGE FITZPATRICK: That's what we'll do. So I just -- yeah, if
11 you make a case and you're talking about ligation, for example, we
12 understand that that's relevant to, I think, the independent claims in one case
13 and thus all of them, and then the dependent claims in the other case. You
14 know, you won't have to repeat that in detail or at all. You know, we're
15 aware of that. That's just an example.
16 So why don't we start with that? We'll start with the '955 case.
17 Petitioner you have 45 minutes. Of course, you can reserve some time for
18 rebuttal, and both sides will get the chance to reserve time for rebuttal.
19 MR. WALTER: Thank you, Your Honor. I'm going to go ahead and
20 reserve 10 minutes for rebuttal, if that's all right.
21 JUDGE FITZPATRICK: Perfect.
22 MR. WALTER: And I'm going to share my screen so you can see our
23 presentation. Your Honor, are you able to see our slide presentation? I
24 think you're on mute. Can one of the Judges confirm that they can see our
25 presentation?

1 JUDGE FITZPATRICK: I can. I'm sorry. Yes, I was on mute. And
2 I also have access to -- all three of us, we have access to the demonstratives,
3 too, if you want to call them out or if you need to bounce back and forth.
4 You don't always need to show us the slide if you tell us the slide.
5 MR. WALTER: So thank you, Your Honor. And there is a lot of
6 overlap between the two cases we're going to be hearing today and the
7 previous case that's already been decided, so there is going to be some
8 material that the Board's already seen. With that in mind, I'm going to try to
9 emphasize the material that's new and/or what the other side has
10 emphasized. And I'm going to try to go lighter on the stuff that the Board's
11 already seen.
12 So as background, the claims are directed to tagging, specifically this
13 idea of using two tag sequences. This is slide 3. The patents in this case, as
14 you recall, they're not about tagging. They're about this thing called the
15 "reflex method." That's on slide 5. The reflex method is what the patent
16 characterizes in the invention. And the tagging claims in this case were only
17 drafted years after 10X took control the portfolio.
18 The tagging concept, that's actually described in the patent as prior
19 art. That's on slide 7. Here they say they "previously described methods
20 that enable tagging." You also see it in slide 8 and you see it on slide 9 as
21 well, where they talk about these prior art references that disclose tagging.
22 There's a couple of references on this slide. The '473 patent and the '665
23 patent that are incorporated by references. Those are prior art references that
24 disclose tagging. Keep a pin in those two references.
25 So the patents tell you that these are prior art and it's not just tagging
26 that's in the prior art. It's the specific dual tagging method, where you use

1 two tags, that we know is in the prior art. How do we know that? Well,
2 their expert has told us that in district court litigation. I'm showing you slide
3 31. This is an excerpt from their expert's report from the parallel litigation.
4 And he's trying to identify where the patent discloses support for this
5 contract concept of two tag sequences. And he says it's in the '473 and the
6 '665 patent. These are the two patents that I'm showing on slide 9. And he
7 says these patents "disclose the use of unique tags to identify the origins of
8 the sample polynucleotide and to distinguish it from other polynucleotides in
9 the same cell." And he says these are providing support for that for two tag
10 sequences.
11 This wasn't a mistake or a typo. If you recall, in the '981 case, we
12 asked him what's inventive about any of these claims? And if you recall
13 from that case, as I'm showing on slide 27, he says, I don't know. He says, I
14 wasn't prepared to offer an opinion. And we asked him the same question
15 again in this case about the '197 or the '013 patents. We asked him, you
16 know, what's the inventive contribution? He says, that's "outside the scope
17 of my reports." He punted on it. He says, "I'm not really prepared to offer
18 an opinion today." That's on slide 29. We asked him multiple times just to
19 be sure. Slide 30. "I'm not prepared to offer an opinion about the inventive
20 concepts in the patent today."
21 That speaks volumes. The Board noted it in the prior final written
22 decision. We have the same evidence here today. But, of course, we can't
23 just stand on this. We have to go through the analysis and address the
24 arguments they make.
25 With regard to the '197 patent, there really isn't anything new that
26 they've raised. There's one argument that they emphasize, however, and it's

1 this idea that we haven't shown that in *Linnarsson* the entire tagged
2 polynucleotide is sequenced. You see that on slide 34 of their Patent
3 Owner's response. And so I'm going to address that.
4 Now, I want to be clear about what their argument is and what it's
5 not. The argument is not that the claims require sequencing the entire
6 tagged polynucleotide. How do we know that? Well, their expert has
7 acknowledged it. That's on slide 76. He said in the parallel district court
8 proceedings that the claims "do not require sequencing the entirety of the tag
9 polynucleotides." And at the last hearing, which was regarding the '981
10 patent, they disavowed any construction that would require sequencing the
11 tagged polynucleotides in their entirety. And that's on slide 77. And they're
12 not going to do anything different here, I can guarantee you that.
13 The argument that they're making is rather a gotcha sort of argument,
14 that the theory of the petition was at its core based on sequencing the
15 entirety of a tagged polynucleotide and that we didn't show that *Linnarsson*
16 did that. They focus on one line I'm showing on slide 35. They focus on
17 one line of our petition where we said, "A POSA would have understood
18 that such sequencing is performed on the entire tagged polynucleotide."
19 They feature that on the first page of their surreply. And again, that's on
20 slide 35.
21 Now, what I'm going to do is I'm going to first going to assume that
22 they're correct about the petition being based on sequencing the entirety of
23 the tagged polynucleotide. I'm just going to assume that. And I'm going to
24 show that even under that assumption, their rebuttal fails. And then I'm
25 going to circle back and explain that they're probably reading too much into
26 the petition, and the petition really wasn't locked into some sort of theory

1 about sequencing the entirety of the tag polynucleotide. So I'm going to start
2 under the assumption that they're right about the petition.
3 Now, they make one argument to support their contention that
4 *Linnarsson* doesn't disclose sequencing the entire tagged polynucleotide.
5 One argument. And that one argument is that *Linnarsson* only discloses a
6 method based on fragmentation and capture that uses biotin. Okay. This is
7 something the Board's familiar with. And this is -- I'm showing that
8 argument that they present on slide 37. They say in their header,
9 "*Linnarsson*'s STRT Method Consistently Discloses Fragmentation and
10 Capture." And this is the method that's disclosed in figure 11, which I'm
11 showing on slide 38. The idea is that in this method you only sequence part
12 of the molecule and that this is the only method that *Linnarsson* discloses.
13 Now, this argument is, of course, no different from the argument
14 they previously presented for the '981 patent and it's incorrect. I'm showing
15 that on slide 40, the previous final written decision. The Board said, hey,
16 you don't require the biotin. That's part of that fragmentation and capture
17 method. And they quoted the portion of the *Linnarsson* reference that says
18 that those steps in figure 11, which include the biotin and the fragmentation
19 and capture, are optionally used.
20 The Board's decision to this effect, it was correct. And the evidence
21 is overwhelming. And I'm just going to hit that evidence real quickly again
22 on slide 39, I just alluded to this. Figure 11, it shows a graphical
23 representation of steps that are optionally used. Let's look at figure 3 and
24 figure 4. There's no biotin in figure 3. That's on slide 39 -- excuse me, slide
25 48. On slide 49 in figure 4, there's no biotin, nor is there a restriction
26 enzyme. And these particular examples, these are things we cited

1 throughout the petition. You can see that on slides 50, 51, 52, 53, 54, and
2 55.
3 Now, how do they deal with figures 3 and 4? And this is something
4 that's maybe a little bit new, but not terribly new relative to the previous
5 case. They make the argument that figures 3 and 4 must use a biotin and
6 restriction enzyme because they're discussed in the context of example 1.
7 And in example 1, there's an example where you use a biotin and a capture
8 method. And that argument's incorrect and I'm going to show you why.
9 The text of example 1, it discusses alternatives. If you look at the
10 example, it does indeed contemplate an approach where you use a biotin,
11 and you can see that in *Linnarsson*. I'm showing page 1003.24 of
12 *Linnarsson*. And if you look at lines 13, you can see that there's a biotin
13 there. You can see this bio. Okay? So that's clearly there in this one
14 example. But this is not the only thing that's there. Okay.
15 One thing that's worth noting about this CDS that we're looking at
16 here, that has a biotin, it doesn't have a cell tag. And keep a pin in that.
17 That's important. Right below that is the TSO that they use in this example.
18 And this has a cell tag as well.
19 Now, let's look now at figures 3 and 4. Here's figure 3. Okay?
20 JUDGE FITZPATRICK: Counsel? Mr. Walter, in that prior, you just
21 - I think you just said the CDS does not have a tag, correct?
22 MR. WALTER: Yes. And the TSO does have a tag.
23 JUDGE FITZPATRICK: Does have a tag. So I think you said "as
24 well," which made -- which confused me there.

1 MR. WALTER: You're right. That was an error on my part. In this
2 example, the CDS does not have a tag and here the TSO does have a tag.
3 That was my mistake.
4 But now let's look at figure 3. And here's the contrast I wanted to
5 draw out. Here's figure 3. It's a TSO, that has a cell tag. It doesn't have the
6 biotin. Here's figure 4. Here's the CDS. This does have a cell tag. Okay.
7 So what's being disclosed in example 1 are sets of different approaches.
8 Let's look back at page 1003.24. No cell tag in the CDS. It's a different
9 approach. Figure 4, again, as you can see, it does have the cell tag.
10 So what is contemplated in example 1 is not one approach that's
11 based on fragmentation and capture. It's multiple different approaches that
12 do different things. There's a reason figures 3 and 4 don't have biotin, one's
13 got a cell tag, one doesn't. It's because it's contemplating different
14 approaches.
15 Now, let's talk about the restriction enzyme. Of course, that
16 restriction enzyme, that's an essential part of the figure 11 approach. You
17 can see that here. If you look at figure 11, you can see that there's the
18 restriction enzyme BTS. It's called out over the place -- all over the place.
19 But as you scroll down further to slide 57, what 10X calls out is this
20 restriction enzyme called BtsI. Okay? That restriction enzyme doesn't
21 appear anywhere in figures 3 and 4. The argument they make is that, well, if
22 you look at the sequence, if you look at the sequence and you go and analyze
23 it, if you look at the sequence, that's in figure 3 and figure 4, if you look at
24 this APS sequence, okay, if you go and you analyze this figure, what you'll
25 find is that there is a sequence in there for this BtsI. That's what they say, is
26 if you go and analyze this, you'll find this BtsI sequence buried in there. The

1 trouble is that BtsI, it's never mentioned once in the patent. If you look at
2 figure 11, when it wants to use that restriction enzyme, it calls it BTS, but
3 that's not BtsI, that's a different enzyme. That's an enzyme called BtsCI.
4 Okay?
5 And if you look at figures 3 and figure 4, unlike figure 11, it doesn't
6 call out the BTS restriction enzyme. It calls out the APS, the cell tag, the
7 RCX, but it never says, here's the restriction enzyme cut site. And so the
8 idea that someone would think, hey, if you go and analyze this, there
9 happens to be coincidentally a restriction enzyme sequence in here and
10 you're supposed to use it, that makes no sense because it's never called out.
11 It's never called out anywhere in the patent.
12 Let me tell you -- give you another reason why it doesn't make sense.
13 With regard to restriction enzymes, it turns out there's thousands of these
14 enzymes. And if you take any sequence, any random sequence, and you ask
15 does it happen to include a sequence that corresponds to a restriction enzyme
16 cut site, the answer most likely is going to be yes. And so if you do that
17 analysis for figures 3 and 4, and you look to see what restriction enzymes are
18 there, restriction enzyme cut sites are there, you find that there's actually five
19 different restriction enzyme cut sites that are there. Okay?
20 So if you follow their argument, their argument would be, well, look,
21 someone would know that you're going to use the fragmentation and capture
22 method because the sequence that's disclosed here happens to include a
23 fragmentation site for a restriction enzyme. Never mind the fact that the
24 restriction enzyme you're supposed to use is not mentioned anywhere in the
25 patent. And never mind the fact that, in fact, there's five different random
26 restriction enzymes that could be used to make the cut here, including

1 TspRI, BtsIMutI, Nt.CviPII, Nb.BtsI. All these different ones, under their
2 theory, they would have you believe someone of skill in the art would think
3 are supposed to be used with the invention, even though none of these are
4 mentioned once in the patent. Okay.
5 So this argument about fragmentation and capture, to sum up on this
6 particular point, it's wrong. As shown on slide 40, the Board already
7 concluded it's wrong. And this puts an end to the overwhelming majority of
8 the arguments that they make in this case. Now, that's the only argument,
9 that is the only argument they make to try to suggest that *Linnarsson* doesn't
10 disclose sequencing the entire tagged polynucleotide. That's the only
11 argument.
12 I'm going to go a step further. Okay? One thing that's very
13 important to know, they're not arguing that the sequencing was difficult or
14 that *Linnarsson* doesn't disclose the technology to sequence the whole
15 tagged polynucleotide. I'm not arguing that. The argument, like I said
16 earlier, is this gotcha argument, the petition was based on this. Now, you
17 know, their argument on his face is a bit odd. And it would be even odder to
18 suggest that *Linnarsson* doesn't actually teach sequencing the tagged
19 polynucleotide or that someone of skill in the art would have some difficulty
20 doing it. That would be a crazy thing to suggest. And neither their attorneys
21 nor their expert make such a suggestion. And I want to show you why that's
22 the case and I want to do it using evidence in the patent itself, 10X's own
23 admissions, and, most importantly, affirmative disclosure in *Linnarsson*.
24 So let's go to slide 85. The first thing to note is that the patent admits
25 that as of 2009, the priority date, you could use the Roche 454 sequencer to
26 sequence a molecule that's as long as 40 [*sic*] bases and do it in a single run.

1 In a single run. Even though these are short read sequencers, you could do
2 400 bases in a single read. Okay? And there's no real dispute that that's
3 enough if you wanted to sequence the entire tagged polynucleotide.
4 I'm sure you know page 1003.20. This is *Linnarsson*. And if you
5 look at the bottom here, it's referring to multiple different sequencing
6 technologies, commercial sequencing technologies, the Applied Biosystems
7 solid platform and the Illumina sequencer system.
8 JUDGE FITZPATRICK: And Mr. Walter, without -- on this issue, on
9 slide 73, which you showed us earlier, that had that statement that began, "A
10 POSA would have understood about the entire" -- I'll wait for you to get
11 there. I think it was 73.
12 MR. WALTER: Yeah, I'm going to get -- I'm going to try to -- I don't
13 think it was 73. I think it might have been something else. Is it --
14 JUDGE FITZPATRICK: Or maybe it's a duplicate content. If you
15 could turn to 73. Because in my copy that's where my question is coming
16 from.
17 MR. WALTER: Okay.
18 JUDGE FITZPATRICK: Unless I got the cases mixed up. So you're
19 on 82, right? Yeah, yeah. So if you go to --
20 MR. WALTER: Yeah, I don't think I've shown slide 73, so I want to
21 show you --
22 JUDGE FITZPATRICK: If you don't mind, could you just for a
23 moment show slide 73?
24 MR. WALTER: Yes.
25 JUDGE FITZPATRICK: Oh, I'm sorry. You don't have it in
26 chronological order. I didn't mean to mess you up.

1 MR. WALTER: It's okay. It's okay.
2 JUDGE FITZPATRICK: Let me read it. Let me read it.
3 MR. WALTER: I'm going to be there just a moment and then I can
4 switch back. It's right there.
5 JUDGE FITZPATRICK: It's the one with the word -- that one. Yeah,
6 "sequencing is performed."
7 MR. WALTER: Okay. So I did show that earlier. Yes.
8 JUDGE FITZPATRICK: Gotcha. Okay. So that sentence, "A POSA
9 would have understood that such sequencing is performed on the entire
10 tagged polynucleotide," and it goes on. What does -- what did Petitioner
11 factually mean by that?
12 MR. WALTER: Right. Okay. And so that's something I was going
13 to get to a little bit later --
14 JUDGE FITZPATRICK: Okay.
15 MR. WALTER: -- but since you've asked, I'll skip to that right now
16 and I'll lay out what it is we're getting at with this. So here is this slide, and
17 this comes from one sentence in the petition. And all it says is that
18 "sequencing is performed on the entire tagged polynucleotide." That doesn't
19 mean you have to get the whole sequence. What's important to note is if you
20 look up here at the top, what's the claim element? The claim element is
21 "sequencing the tagged polynucleotide to determine the sample sequence,
22 the first tag sequence, and the second tag sequence. Okay?
23 And the key point here is that the sample sequence, nobody contends
24 this means it's the whole sequence of the sample. Any portion of the
25 sequence of the sample would suffice. And that's what they're accusing in
26 the district court. And they're never going to stand up and say that this claim

1 language means you have to sequence the entire length of the sample
2 sequence. Any portion of the sample sequence would suffice. And what
3 we're trying to say here is that someone would know that you're subjecting
4 the entire molecules to sequencing such that you're going to be able to get
5 that. Okay.
6 And it cites paragraph 176 of Dr. Cooper's declaration. That's at the
7 end here. Let's look at what he actually said. Okay. He says, a POSA
8 would have understood that the sequencing step of *Linnarsson* discloses
9 determining the sample sequence, the first tag sequence, and the second tag
10 sequence. He never says you have to get the sequence of the entire
11 molecule. That's just a statement that's consistent with the general and
12 robust sequencing disclosure in *Linnarsson*. This isn't a lock into some sort
13 of narrow theory that the petition was based on getting the whole sequence
14 of the polynucleotide.
15 So that's what we're trying to say here. It's just that the sequencing is
16 being applied to the whole of the molecule such that you would get the
17 sample, the first, and the second. That's all we're trying to say.
18 Now, if there's no questions, I want to circle back. Go ahead.
19 JUDGE FITZPATRICK: Let me just then -- so it is not your position,
20 though, that a POSA would have understood that such sequencing is
21 performed on the entire tagged polynucleotide, such that the entire
22 polynucleotide is sequenced like, so that they know the whole sequence.
23 MR. WALTER: Yeah. So --
24 JUDGE FITZPATRICK: What I'm wondering is if there's a
25 concession, at least; it doesn't seem like it would matter based on the claim
26 scope. But I want to know, in Petitioner's view, does *Linnarsson* teach

1 sequencing the entire tagged polynucleotide in the most literal sense of that
2 phrase or not?
3 MR. WALTER: It actually does. It actually does. And that's where I
4 was going before you asked your question.
5 JUDGE FITZPATRICK: Okay.
6 MR. WALTER: Now, if I want to circle back to that, it teaches both.
7 It teaches getting partial, but it also teaches getting the whole thing. It
8 actually does.
9 And that's why I was bringing up all this sequencing technology that
10 was available. There's no real question that this sequencing technology that
11 was available at the time, that their expert, as I'm showing on slide 84, says
12 was known unconventional, could actually generate that whole sequence.
13 And so I want to show where *Linnarsson* actually teaches that.
14 I'm showing now slide 79, and it states, "The cDNA library can be
15 sequenced by any suitable screening method." And again, it brings up this
16 Applied Biosystems and the Illumina system, and it says the "library can be
17 shotgun sequenced." Okay. Now, what is shotgun sequencing? Okay? It
18 tells you what that is. That's on slide 80. This is from *Linnarsson*. So the
19 shotgun sequencing is a method where the DNA you sequence, you first
20 shred it into smaller fragments, okay, which you can sequence individually.
21 And then it says this, and this is the key point, "The sequences of these
22 fragments are then reassembled into their original order based on their
23 overlapping sequences, thus yielding a complete sequence." A complete
24 sequence. That's shotgun sequencing. Our expert explained this. He
25 walked through the process of shotgun sequencing.

1 And what's important is on slide 82, he states, after you do the
2 sequencing, the algorithm methods for reassembly can be used to generate
3 longer stretches of sequencing germane information corresponding to the
4 entire original tagged DNA fragments. And he says *Linnarsson,* in fact,
5 mentions precisely this. So it does. It actually teaches all the alternatives.
6 And that's not surprising because the sequencing technology at this time was
7 developed.
8 You know, the argument that, you know, *Linnarsson* doesn't tell you
9 how to sequence the entire tagged polynucleotide, it's kind of an odd
10 argument. At the time, people were able to sequence the entire human
11 genome. They could sequence the entire tagged polynucleotides from
12 *Linnarsson*. And it teaches you the shotgun sequencing method for doing it.
13 As the Board found in the previous -- in its previous decision, the
14 sequencing disclosure is robust. And so there's -- it's all there. Doing it
15 partially or doing the whole thing, it's all there. The disclosure is general.
16 And nobody would contend that -- nobody of skill in the art would
17 reasonably contend that the *Linnarsson* reference doesn't disclose
18 sequencing the entire tagged polynucleotide. But just as important, the
19 petition wasn't limited to that. You know, taking one line out of the petition
20 and saying, oh, look, the petition is based on this and this is the theory of the
21 case, and you have to pursue -- show every time that the entire tagged
22 polynucleotide is sequenced, that's a stretch.
23 All right. So the next argument that I want to address is this question
24 of motivation to combine. And for that I'm going to go to slide 90. I'm
25 going to try to hit this quicker and quickly get to some dependent claims that

1 are at issue in this case, and maybe I'll be able to wrap up a bit early and
2 maybe address what they want to address in reply.
3 The motivation to apply *Linnarsson* is clear. If you look at slide 90,
4 the Board found in its final written decision that Petitioner had argued
5 persuasively. The *McCloskey* teaches a MID with two tag sequences, okay.
6 And the motivation to apply that to *Linnarsson*, that was clear. On slide 91,
7 *McCloskey* teaches that its methods can be used for single cell analysis.
8 That's the same thing that *Linnarsson* is doing. So, you know, they're two
9 peas in a pod.
10 Slide 92, the Board found that the Petitioner's rationale that a skilled
11 artisan would have made the combination to solve amplification bias, that
12 was persuasive.
13 Slide 93, with regard to the specific ligation method, the Board said
14 that was an obvious design choice as well.
15 So the one argument they make against the motivation to combine is
16 the incompatibility argument. And that's the argument that the *Linnarsson*
17 method is limited to the approach that uses biotin. Well, as we saw earlier,
18 the Board found previously, and as I just walked through, *Linnarsson* is not
19 limited to that approach.
20 And what's just as important as I'm showing on slide 103, the Board
21 found that a person of ordinary skill in the art would have known how to use
22 biotin in a manner that didn't interfere with the proposed modification. So,
23 you know, the Board rejected the bodily incorporation argument that they
24 made. So the motivation to combine is there.
25 The next argument they make on motivation to combine is that
26 *McCloskey* doesn't have enough barcodes to tag each mRNA molecule. The

1 Board rejected that, too. That's on slide 109. *McCloskey* is not limited to
2 16,384 unique barcodes. As the Board found, it teaches precisely how to
3 manipulate the number as needed. That was correct.
4 I'm showing you their slide 36. And here they make another
5 argument along the lines of, hey, the petition was based on tagging
6 substantially all mRNA molecules of a cell. So you have to show that you
7 tag all substantially all mRNA molecules of a cell. And they're showing
8 something from page 55 from the '197 petition. That's not what the petition
9 was based on. This is a specific argument directed to claim 14 of the '197
10 patent, which specifically requires tagging substantially all the molecules in
11 the cell. We're not saying that's the only thing *Linnarsson* does and that this
12 is the heart of the petition. We're saying you can do this.
13 Look at the portion that we quote from *Linnarsson*. It says you can
14 do "direct sequencing of all, or parts." all or parts, "of the mRNA content of
15 a tissue." *Linnarsson*'s not limited to all of it. So the whole premise of the
16 argument is wrong. And then there's just several other errors with the
17 petition as well.
18 If you look at slide 110, the Board noted, this is the last oral
19 argument. The claims just require "generating a plurality of tagged
20 polynucleotides from the plurality of sample polynucleotides." It doesn't
21 have to be all. That's something they admitted in the district court in slide
22 111.
23 And then there's this idea that you need more than 16,000 tags to tag
24 all the molecules in a mammalian cell. That's on slide 112 from the Patent
25 Owner's response. But as the Board found, "*Linnarsson* is not limited to
26 mammalian cells." That's slide 113.

1 Slide 115, *Linnarsson* tells you you can use it with prokaryotic cells.
2 And as Dr. Cooper explains, this is on slide 118, bacteria have, you know,
3 just a few thousand, and so even with 16,000, you could tag them all.
4 And yes, it's a reasonable thing to use *Linnarsson* with prokaryotes
5 because prokaryotes have poly(A) tails. They make the argument that
6 because *Linnarsson* uses poly(A) tails and bacteria don't have poly(A) tails,
7 it wouldn't make sense to apply *Linnarsson* to prokaryotes, even though
8 *Linnarsson* says do that. That argument is wrong. The literature is clear.
9 Bacteria have poly(A) tails. That's on slide 119.
10 Dr. Cooper confirmed that over and over on slide 120, Slide 121,
11 122, 123, 124, 125. They're going to tell you that Dr. Cooper admitted it.
12 He didn't. He said just the opposite. That's on all the slides I just showed
13 you.
14 And finally, as the Board noted, the disclosure in *McCloskey* is
15 general. It tells you how to manipulate things. So that argument is wrong.
16 Finally, on this point, I want to show you their slide 41. The
17 argument they make here is that for ground 3, we used a reference called
18 *McCloskey II*, and *McCloskey II* was a reference that included a very clear
19 disclosure of using very, very long tags. And the idea is that because ground
20 2 invokes *McCloskey II*, ground 1 must be limited to 7. That's without
21 merit. Because we used a reference with a more detailed disclosure to
22 address a set of very specific dependent claims regarding the number of tags,
23 that doesn't mean we agree that *McCloskey* is necessarily limited in some
24 certain way.
25 And what's notable here is you look at these claims 13 to 19. You
26 know, they're not even really challenging those on the basis of the number of

1 tags. Under their theory what they would have you do is they would have
2 you find the dependent claims obvious, but not the independent claims. That
3 doesn't make any sense.
4 So I want to skip to some dependent claims now. And for that I'm
5 going to go and skip ahead. And I think, you know, one issue I'm skipping
6 is this question of ligation. I'll address that in connection with the '013
7 patent. And, you know, it'll be filed in both cases. That'll save us some
8 time. It makes sense to address that in the '013 patent because the
9 independent claims require ligation in that case.
10 I'm showing you their slide 49. And this is talking about claim 8.
11 And claim 8 requires that you generate the tagged polynucleotide by
12 hybridization and then extension. And the argument they make, as you see
13 in the header, is that the theory fails because in ground 1, the CDS is not
14 sequenced.
15 Okay. So a few things on this. First, whether the CDS is sequenced
16 or not doesn't matter because claim 8 doesn't require it. Claim 8 just
17 requires that you generate the tagged polynucleotide by hybridization and
18 extension. And that happens in every single embodiment in *Linnarsson*.
19 And it even happens in the figure 11 embodiment. You always do the
20 hybridization and then the extension. Maybe there's some other steps
21 afterwards, but you do always do the hybridization and extension. And
22 whether the CDS is sequenced doesn't matter because that's not required in
23 the claims.
24 And also the argument fails because it's based on the assumption that
25 the CDS is not sequenced because it remains stuck on a bead. You can see
26 that here. Okay. That's the argument is that the CDS isn't sequenced

1 because it remains stuck on a bead. Well, that bead that they're talking
2 about, that's the streptavidin-B that binds to the biotin. And as the Board
3 previously concluded, as I'm showing on slide 40, *Linnarsson* doesn't require
4 biotin. So the argument on claim 8 is just wrong on multiple levels. And it's
5 premised on at least two incorrect assumptions.
6 I'm now going to go to claims 23 to 25. Here on -- I'm showing you
7 their slide 53. And the argument for claims 23 to 25 is that the ground 1
8 theory doesn't have enough second tag sequences. That's wrong.
9 *McCloskey* is not limited to 16,384 unique barcodes. The Board found that.
10 That's on slide 137. And this is addressed fully in our reply.
11 And then finally, on claim 26. Here's claim 26. This claim requires
12 that the plurality of sample polynucleotides comprises a subset of
13 polynucleotides of the cell having the same sequence. And they say we
14 didn't show that a cell has multiple RNA molecules. That's the argument
15 they make. You see that in their Patent Owner's response. That doesn't
16 make any sense. Let me tell you why.
17 The key rationale for claim 1 was that you use the tag from
18 *McCloskey* to distinguish the copies. I'm showing that on slide 177. And
19 this is discussed in detail on pages 42 and 43 of the petition. Here we're
20 talking about the different cell or allele copies. That's right here. And that's
21 for claim 1. That's the whole idea. That's the whole reason you introduce
22 the different tags from *McCloskey* is so that when you have two molecules
23 that are the same, you can tag them differently and distinguish them later on
24 down the road. And so the idea that we had to show that for claim 26 makes
25 no sense because that's part of claim 1.

1 And then on top of that, Dr. Cooper showed that it would be obvious
2 to target a subset of sequences using a range of technologies that were
3 available. And that was on slide 178. And none of this was ever rebutted in
4 the slightest.
5 JUDGE FITZPATRICK: Mr. Walter, you're at your, you know, your
6 time less your rebuttal.
7 MR. WALTER: Well, that's perfect, because that's exactly where I
8 wanted to stop. And I'll stop there, and then I'll address any points I need to
9 in rebuttal. And then pick this up for the '013.
10 MS. RAYMOND: Good afternoon, Your Honor. Are you ready for
11 Patent Owner to begin?
12 JUDGE FITZPATRICK: Yes, we are. And we have -- I'll just
13 remind you, we have your whether you want to show demonstratives the
14 way Mr. Walter did or not, we have the -- we have them.
15 MS. RAYMOND: Wonderful. Thank you. I think we will be pulling
16 some of them up.
17 Good afternoon, Your Honors. We thank the Board for your time
18 today on behalf of 10X. And while we'll likely cover only certain of the
19 disputed issues today, we'll rely on and stand by our objections, arguments,
20 and evidence we've put forward in this proceeding, in our briefs, and our
21 other submissions.
22 So unless the Board has other guidance as to how you'd like us to
23 proceed today we'll plan to focus on the following topics. First, some of the
24 differences in the arguments and record between this proceeding and the
25 '981 proceeding. Mr. Baughman will cover that topic. Second, the
26 motivation to combine argument. Mr. Baughman will also cover that topic.

1 Third, sequencing the entirety. I'll plan to cover that topic. Fourth, ligation.
2 I will cover that topic if there's time. And then fifth, the motion to exclude
3 *McCloskey,* and Mr. Baughman will cover that if there's time. And of
4 course, we're happy to answer any questions on other topics.
5 JUDGE FITZPATRICK: And did you want me to remind you of a
6 rebuttal time? Do you want to reserve some?
7 MS. RAYMOND: Thank you, Your Honor. Yes, we'd like to reserve
8 three minutes for rebuttal.
9 JUDGE FITZPATRICK: Got it.
10 MS. RAYMOND: And as we go through today, I just ask the Board
11 to keep in mind that their obviousness theory that's been set forth by
12 Petitioner needs to be a consistent one across the limitations and across the
13 dependent claims. And, of course, the burden is always theirs. I think I
14 heard some things today that suggested some burden shifting, but we will
15 call that out as we can as we go along.
16 And with that, I will turn it over to Mr. Baughman to discuss the
17 differences in the record between this proceeding and the '91.
18 MR. BAUGHMAN: Thanks very much. And Your Honors, before I
19 do that, I want to make sure I don't forget to respond to Mr. Walter's
20 comment about dual tagging. If I could ask my colleague to put up their
21 slide 31, please, Parse's slide. I think Mr. Lamb is going to share his screen.
22 There we go.
23 I heard Mr. Walter arguing that this is somehow a concession that
24 what he calls dual tagging was already known. And I think it's important to
25 say that dual tagging as we understand it means two tags. Dual tagging as
26 Mr. Walter is understanding it or arguing it as though it means the claimed

1 invention. What Mr. Quackenbush testified about here in reality is that the
2 '473 patent has one tag, the '665 has the other. There is no showing here of a
3 single patent that discloses the particular combination of tags and the
4 benefits and the procedures that we've laid out in our claims. If there were,
5 there'd be an anticipation claim, and there isn't one. This is also not part of
6 Mr. Walter's grounds.
7 And respectfully, this --
8 JUDGE FITZPATRICK: Mr. Baughman, if I could condense this
9 argument. Like the part that's highlighted here, if it said "comma,
10 respectively" at the end. Is that your point? That one patent of scope?
11 MR. BAUGHMAN: I think that's right. I'd have to check to see
12 which one is which, your Honor, but I believe that's correct. Yes.
13 JUDGE FITZPATRICK: Okay. Okay, thank you.
14 MR. BAUGHMAN: And I think, also, just while we're on this topic,
15 the sort of idea of asking Mr. -- Dr. Quackenbush, excuse me, to opine
16 about the features of the patent that are patentable is literally reversing the
17 burden. It's requiring Patent Owner to show patentability. It's exactly what
18 the Office and its reviewing courts have said is not allowed. The burden
19 begins, remains, and ends with Petitioner to show unpatentability. It doesn't
20 come to Dr. Quackenbush to say, well, here are the three patentable things.
21 And by the way, in district court, he actually did opine that the MID was the
22 dual MID as claimed was inventive. It just wasn't his burden to do that here.
23 And it wasn't his burden to sort of lay out all the things that Patent Owner
24 believes are patentable. Just it's a complete inversion of the rules and the
25 burdens in this proceeding.

1 If I could turn now to the things that are different here. We did hear
2 from Mr. Walter over the last few minutes about how the Board can just rely
3 on the '981 decision to reach an outcome. And he talked about a few things
4 that are, in his view, changed. I want to talk about four significant ways,
5 four pillars the Board relied on as support for its '981 final written decision
6 that have all explicitly been removed by Petitioner Parse here in this '197
7 proceeding. They're gone. I will quickly walk through the four of them.
8 One has to do with sequencing. Mr. Walters talked about it a little
9 bit. Three have to do with motivation to combine. And those four
10 differences underscore why the Board's decision here should be different.
11 We're happy to talk about the scientific reasons. They aren't trivial. They're
12 not gotchas. And they are part of the theory of Petitioner's obviousness
13 combination or why they matter to those theories. We'll talk about those.
14 We plan to talk about those after identifying the four things. But we're
15 happy to take this however Your Honors wish. So let's just turn to those
16 now.
17 If we could turn to Parse's slide 72, please. And this is the argument
18 Mr. Walter was making about *Linnarsson* having a robust disclosure of
19 sequencing. And turning to their slide 78, he's highlighting part of the
20 Board's final written decision. I want to focus -- because that's sort of an
21 alternative comment the Board makes in any event. What the Board actually
22 said was that the claim doesn't require sequencing the entirety, which we've
23 never argued. And the second sentence here that the Petitioner didn't assert,
24 that *Linnarsson*'s sequences tagged and unfragmented DNA molecules in
25 their entirety. That's what the Board relied on for this part of its final written
26 decision.

1 If we turn to the petition, I know you've already looked at Your
2 Honors, but I want to pull up page 44 of the petition. And I think I heard
3 Mr. Walter say this is just one line. The claims aren't limited to this. This is
4 the entire mapping of limitation 1G in the petition. Whole thing. And what
5 does it say? They are relying on the understanding of *Linnarsson* that
6 sequencing is performed on the entire tagged polynucleotide, which includes
7 the sample sequence of both tag sequences. Why did they put in the word
8 "entire"? What does that do in the sentence if it doesn't mean the entire
9 thing?
10 It lists the sequences. It lists the tags. What does "entire" mean? It
11 means what it says. And the fact that in the other proceeding, Petitioner was
12 going to take the view I've never heard of this theory, this is crazy, in this
13 petition, we have it written out in plain words. It is the entire mapping for
14 limitation 1G. It's what they build their whole petition on. Let's take a look
15 now at --
16 JUDGE FITZPATRICK: Mr. Baughman, can I pry a little bit there?
17 So let's assume that, you know, I can see this statement here. It's in their,
18 you know, in their petition. Let's assume it's factually wrong that a POSA
19 would not have understood that sequencing is performed on the entire tagged
20 polynucleotide. But certainly there's evidence, and they cite to it, of
21 sequencing. And that sequencing is of the tagged polynucleotide. Maybe
22 it's 40 percent of it, maybe it's 30. I have no idea. Let's just keep the
23 hypothetical. That'll be gray. Kind of like the limitation itself is gray. I
24 don't think any numerical amount has been proposed in district court or here
25 for how much of the polynucleotide needs to be sequenced.

1 So, but let's say that they're factually wrong, that *Linnarsson* only
2 teaches what I'll just call partial sequencing of the tagged polynucleotide.
3 But they've still pointed to it. They've still pointed to the teachings in
4 *Linnarsson* of that. Even if they were factually incorrect in asserting that not
5 only does it teach partial, but, in fact, teaches entire sequencing. Why -- I
6 don't understand how that would be helpful to your position.
7 MR. BAUGHMAN: Sure. Your Honor, I have two quick responses
8 and I might turn it over to Ms. Raymond if you want to talk about that in
9 detail now, which we can do.
10 First, I heard Mr. Walter say that both are disclosed, that just using
11 the entirety was done. I think he also said it'll be in the transcript. No one
12 would ever do that, but it's in *Linnarsson*. And now he's saying, well, he
13 said entire, but he didn't mean it here for this mapping. So I think, to begin
14 with, in fairness, we're allowed to know what the position is before we have
15 to respond to it. And I feel like we're having to respond to all kinds of
16 different ever-shifting positions about what they're actually mapping. But
17 Ms. Raymond can talk about what changes with this mapping.
18 This is their obviousness combination. This is what they're pulling
19 out of *Linnarsson* to put into it. They're obligated under the case law, we
20 pointed out, *Intelligent Biosystems* and *Arctic Cat*, to actually prove the
21 things they say for their obviousness argument. And it has downstream
22 consequences about where to put the tags, what's available for sequencing,
23 and whether the entirety of the polynucleotide sequence. And I'm happy,
24 Your Honor, to turn it over to Ms. Raymond if you want to go into detail
25 now and I'll come back to the other things that are different in this petition.

1 MS. RAYMOND: So to elaborate on that, Your Honor, if it would be
2 helpful, so Petitioner has argued as part of their obviousness combination of
3 the petition that a POSA would have been motivated to have a first tag in the
4 CDS and a second tag in the TSO or vice versa, or both in the CDS or both
5 in the TSO. So this suggests this flexibility of a combined system as to
6 where the tags can go. But this only works if the entirety of the
7 polynucleotide is sequenced.
8 So in the petition, perhaps for simplicity, Parse argued that the
9 whole, you know, the whole tagged polynucleotide is sequenced. In the
10 POR, we explained that while *Linnarsson* teaches something is sequenced, it
11 doesn't teach sequencing the entire polynucleotide and it also doesn't
12 disclose sequencing the CDS end. And even if the CDS end is sequenced, if
13 the whole tagged polynucleotide isn't sequenced, then the two ends are
14 separate and there's no disclosure of associating the 3-prime sequence tag,
15 the CDS end, with the 5-prime sequence tag, this TSO end, to know which
16 cell goes with which polynucleotide if the tags are put on different ends. So
17 all you know for one end is which cell the attached fragment came from and
18 for the other side you have a polynucleotide tag.
19 In reply Parse doesn't defend its citations from the petition regarding
20 the sequencing of the entire polynucleotide. And I didn't hear them defend
21 those here. Instead, of course, it's argued that the whole thing is sequenced
22 as fragmentation is optional. We disagree. They don't provide any further
23 explanation as to how their original cites disclose the sequencing of entirety.
24 And second, they say it doesn't matter, of course, if the whole thing
25 isn't sequenced. But the issue, again, is that they haven't shown disclosure of
26 the sequencing of the CDS end. We pointed this out in the POR and their

1 only response was that it would not make any sense if it's not sequenced if it
2 has a tag. That doesn't meet their burden. The burden is on the Petitioner.
3 They didn't show it's disclosed and they didn't make an obvious argument to
4 say it would have been obvious to sequence the CDS end.
5 And I heard today them arguing about figures 3 and 4, which, of
6 course, are disclosed only in the context of example 1. And I think there
7 was a new argument about example 1 actually is, you know, maybe several
8 different embodiments, you know, in the same place. And again, we haven't
9 heard them ever articulate some sort of combination of what aspect of these
10 different embodiments you would combine. And neither Petitioner nor Dr.
11 Cooper identified indeed a complete embodiment without fragmentation and
12 capture. And again, where do they show the CDS in figure 4 without a
13 biotin sequence?
14 So, you know, we have a lot of interrelated issues here sort of going
15 on that interplay with other claims. For instance, if we go to claim 8 that
16 Mr. Walter was arguing about earlier in their petition, they rely only on
17 sequencing the CDS end. Again, no disclosure of *Linnarsson* in that.
18 Petitioner's slide 135 quotes the petition, but that's not the portion of the
19 petition that addresses claim 8. In their petition in claim 8, they only address
20 the CDS. They say the CDS -- they map the CDS for claim 8, not the TSO.
21 There's a reason for that, and that's because the claim requires hybridization
22 to the sample polynucleotide.
23 And if we look at figure 11, for example, of *Linnarsson*, what we see
24 is that what the TSO is hybridized to in *Linnarsson* is not the sample
25 polynucleotide itself, but indeed a piece of cDNA. So by mapping to the

1 CDS, they've avoided issues about the TSO, but again, they haven't shown
2 the sequencing of the CDS itself.
3 Just to -- let's -- and then I guess just one other thing about the
4 interpretation of figures 3 and 4, I do think we're hearing some new
5 argument, but again that it's only disclosed in the context of example 1. I
6 don't think we've heard before today that example one is in itself multiple
7 different embodiments, which is, I think, what we were hearing today. And
8 there's no disclosure of those tags, those TSOs and the CDS's and the tags at
9 the end shown in figures 3 and 4, being sequenced anywhere outside of the
10 context of example 1 and 2. So we have no disclosure that says, you know,
11 outside the context of example 1 and 2 sequences. All we have is we do
12 have sequencing of the TSO end, but we do not have sequencing of the CDS
13 end. The sequencing details matter because there are different issues with
14 ligation depending on where the tag is attached and which end is sequenced
15 or if the whole thing is sequenced. That also relates to, you know, what is
16 and isn't sequenced.
17 What sequencing in entirety does, of course, is give us false sense of
18 simplicity of the case. The late theories on sequencing ignore the aspects of
19 recombination that require the sequencing of the entirety to work.
20 And then finally, just a point on the restriction enzymes, they argued
21 before that there was no restriction enzyme cite at all. And they point to
22 nothing special about BtsCI, the particular restriction enzyme discussed in
23 *Linnarsson*. And their own expert relies on *Hug*, which itself uses or would
24 require a BamHI restriction enzyme. And then just to note, their own expert
25 also admitted, and I'm trying to find it, that restriction enzymes other than

1 BtsCI are within the scope of *Linnarsson*. And that's, excuse me, example
2 20 40, 3716 to 21.
3 So I apologize, Your Honor. I think that's probably more than you
4 were asking for at this point. And if that doesn't answer your question, I'm
5 happy to, you know --
6 JUDGE FITZPATRICK: Yeah.
7 MS. RAYMOND: -- try to give it to you.
8 JUDGE FITZPATRICK: Let me follow up with a couple things.
9 There are a lot of things that are interrelated, as you mentioned. I want to
10 make sure I heard you right. Did you say that or are you contesting that in
11 *Linnarsson* that the CDS, it does not get sequenced or you said only the 5-
12 prime end gets sequenced in *Linnarsson*?
13 MS. RAYMOND: So there is no disclosure --
14 JUDGE FITZPATRICK: And I'm talking about *Linnarsson* -- I'm
15 sorry, *Linnarsson* unmodified. Let's just leave it as *Linnarsson*, okay?
16 MS. RAYMOND: They have pointed to no disclosure in *Linnarsson*
17 of sequencing the CDS. They have also not tried to combine any disclosure
18 of sequencing with a disclosure about the CDS. So in terms of meeting their
19 burden, I have not seen them meet their burden, nor am I aware of any
20 disclosure in *Linnarsson* that says the CDS is sequenced or, you know, that
21 end of the polynucleotide is sequenced.
22 JUDGE FITZPATRICK: But the tag can be part of the CDS, right, in
23 *Linnarsson*?
24 MS. RAYMOND: The tag is part --

1 JUDGE FITZPATRICK: Would it make sense when you use the
2 CDS with a tag in *Linnarsson* to not sequence it? Then wouldn't there be no
3 purpose of the tag?
4 MS. RAYMOND: That sounds, Your Honor, like an obvious
5 argument to me that they haven't made, that I haven't seen, that I still haven't
6 seen --
7 JUDGE FITZPATRICK: Well, could you --
8 MS. RAYMOND: -- in this case.
9 JUDGE FITZPATRICK: Okay. I mean, so -- I mean, do you -- but
10 do you, does your cite contest that in *Linnarsson*, the CDS tag, the CDS
11 introduced tag is not sequenced? Did you contest that it's sequenced? I'm
12 sorry about the double negative.
13 MS. RAYMOND: We contest that there's any disclosure of complete
14 embodiment in which the CDS is sequenced.
15 JUDGE FITZPATRICK: Okay. And then back to slide 73. I just
16 want to get -- like zoom right in on that. That highlighted sentence about the
17 POSA, right? Let's scratch that sentence and let's just pretend that the
18 petition didn't even include it and didn't include the cite to paragraph 176 of
19 Dr. Cooper's first declaration. Let's assume it just had that first sentence. So
20 that that leaves only one sentence for this whole section, right? But it's got
21 evidence cited. It says, "*Linnarsson* teaches that after generating the tagged
22 polynucleotides, 'sequencing is performed' thereon." And it cites to Exhibit
23 1003, multiple places. If it just said that, and I think we can take it -- you
24 know, we may interpret it as just saying that.
25 If the second sentence is not true and you're contesting that's not true
26 factually, that the person of ordinary skill in the art would not understand

1 that the entire tagged polynucleotide is sequenced, so then we just ignore
2 that. It wasn't proven. But what if we look at just the first sentence? I think
3 that's pretty good evidence that this limitation is met if the limitation, in fact,
4 only requires partial sequencing.
5 MS. RAYMOND: Yes, Your Honor, but --
6 JUDGE FITZPATRICK: I'm inviting you to tell me why that
7 wouldn't be the case.
8 MS. RAYMOND: Sure, Your Honor. So those disclosures there,
9 they do not tell us what is sequenced or how much is sequenced. So we still
10 don't know. We don't --
11 JUDGE FITZPATRICK: And we know -- yeah. And I'm sorry --
12 MS. RAYMOND: There is something sequenced. We don't dispute
13 that there is something that is sequenced. But those --
14 JUDGE FITZPATRICK: I want to go back to that how much that you
15 just said, but you don't tell us how much is required.
16 MS. RAYMOND: Right. And that would be the burden of Petitioner
17 to establish how much is required and that they have established that in their
18 petition or at least in their reply.
19 JUDGE FITZPATRICK: I don't think it's their burden if the claim
20 doesn't require a numerical amount. And it seems like the claim doesn't
21 require a numerical amount because I think in court you have failed to
22 identify that.
23 MS. RAYMOND: So, Your Honor, it would certainly require, and I
24 don't think this is disputed, at least the CDS is sequenced and the TSO is
25 sequenced because their theory is we get flexibility because we can put it on
26 one, either, or both, and the sample polynucleotide. Right? And so if part of

1 it -- you need to know, for example, enough about the sample polynucleotide
2 to know what it is, how much sample polynucleotide is actually being
3 sequenced to know that I have enough. Is the entire CDS being sequenced
4 such that even assuming it has, you know, the tags in it, I know what those
5 tags are? And the same for the TSO.
6 And again, there's no way -- like, there's no way to put those
7 together. You know, part of their theory is you could put some on one tag
8 and some on the other. There's no way to marry those two back together.
9 And that's -- in *Linnarsson*, *Linnarsson* itself, of course, says for the cell tag,
10 you can put a tag on the CDS and/or a tag on the TSO. But all you're trying
11 to do in *Linnarsson*, all you have to do is have a tag that is associated with
12 the cell. Right? So if I've divided up the CDS and the TSO, that's okay
13 because I'm still going to have a tag on each that tells me this is the cell it
14 came from. Right? Assuming I can sequence, I can sequence enough of it.
15 But I don't know how those two things fit together. I can't put those two
16 pieces back, the CDS and the TSO. There's no need in *Linnarsson* for that.
17 And there's no -- you know, there's been no argument of how you would sort
18 of put Humpty Dumpty back together again, so to speak.
19 JUDGE FITZPATRICK: I hear you. I just -- one of the purposes of
20 *Linnarsson* is to make a cDNA library, I think. And they're trying to study
21 gene expression in single cells. So it seems to me they would also be --
22 when they're talking about sequencing, they would also be sequencing
23 enough of these polynucleotides to know -- to be able to distinguish them
24 from each other.
25 MS. RAYMOND: Sure, Your Honor, but now we also have as part of
26 their theory the modification of the CDS or TSO itself. And I think now

1 they're also saying make -- just make the CDS and TSO longer, right? Make
2 the polynucleotide tag longer because, oops, seven isn't enough, so add
3 more. Right? So now I'm adding more. Now I have something longer. If I
4 have a longer tag, I have a shorter sample polynucleotide that I'm
5 sequencing, if I'm sequencing, you know, 100 base pairs. And so as a result
6 of that -- you know, again, this is sort of, you push one part of the balloon
7 and it pushes the other part of the balloon in terms of what this combination
8 really is.
9 JUDGE FITZPATRICK: Thank you. Will you guys -- will one of
10 you speak -- oh, I'm sorry. Go ahead, Mr. Baughman.
11 MR. BAUGHMAN: Sorry, Your Honor, I didn't mean to interrupt
12 your question. I'm sorry.
13 JUDGE FITZPATRICK: I was just going to say, will one of you
14 speak to claim 8 in more detail, the distinction that that claim makes versus
15 claim 1?
16 MS. RAYMOND: Sure.
17 MR. BAUGHMAN: Could I just -- one quick thing about -- before
18 we move off this point, Your Honor, I just want to --
19 JUDGE FITZPATRICK: Yeah.
20 MR. BAUGHMAN: Because you made a comment about burden. I
21 just want to be clear, it is not our burden because it's not a claim construction
22 issue. It is their burden to show that the story they tell for obviousness is
23 true. The story they tell for obviousness, half of it is the sentence saying the
24 entire polynucleotide is sequenced. I don't think you can excise that and say,
25 we're going to just look at the rest. The Supreme Court has said you can't

1 rewrite the petition, which is Petitioner's choice at the beginning under SAS
2 (phonetic 1:04:31), and rises to the end.
3 It is their job to show that the factual theory, which has
4 consequences, it's not just a random fact they assert, it has consequences, as
5 Ms. Raymond laid out, for the other limitations in the claims and the other
6 dependent claims, and it makes some of their other jobs easier and they take
7 advantage of that. So I don't think you can just say we're going to just excise
8 the thing they got wrong because it's their theory, not just, you know, it's
9 blue or red. It's not just a fact statement that doesn't matter. It's part of how
10 they mapped this claim affirmatively.
11 I'm sorry to interrupt and make it longer, but that's -- I want to just
12 get that into the record, and back to Ms. Raymond on claim 8.
13 MS. RAYMOND: Certainly. So if we could go to slide -- our slide
14 49, which just has the language of claim 8 on it. And just as a reminder, in
15 the petition, they mapped only the CDS. So although we have this up, you'll
16 recall that In *Linnarsson* figure 11, what happens is that the CDS anneals to
17 the mRNA molecule, the poly(A) and the poly(T), you know, match up with
18 each other and anneal, and that starts this process.
19 And then as part of sort of the next step, after there's an extension
20 step, there's an annealing of the TSO. Right? There's a poly(C) and a
21 poly(T) that we see on the left side of portion B of figure 11 that show that
22 matching up.
23 And my point here is that I think there's a reason why they map the
24 CDS in the petition, and that's because the CDS does, I said anneal,
25 hybridize to the sample polynucleotide. It hybridizes to the mRNA
26 molecule. However, the TSO anneals to the cDNA that has been reverse

1 transcribed. So it is not hybridized to the sample polynucleotide itself. And
2 that's something that, you know. never seen Parse deal with, except to say,
3 well, you know, well, if it's not the CDS, it could be the TSO. But again,
4 every change has a consequence on, you know, another portion of the claim
5 or a different claim. And here it breaks this requirement that you hybridize
6 to the sample of polynucleotide.
7 So unless CDS itself is sequenced and enough of it is sequenced,
8 you're not going to be able to meet claim 8 with a TSO. You can't meet
9 claim 8 with the CDS if not enough is sequenced either, of course.
10 JUDGE FITZPATRICK: I think I followed all that. I just had one
11 clarification. CDNA and mRNA are both are both capable of being
12 polynucleotides, but the issue is it would be a different polynucleotide.
13 MS. RAYMOND: That's correct. What has been identified as the
14 sample polynucleotide, right, which must be consistent throughout the claim.
15 And we see claim 1 early on picks up the language of the sample
16 polynucleotide, and it is no longer the sample polynucleotide in later aspects
17 of the claim, you know, it's like the tagged polynucleotide or --
18 JUDGE FITZPATRICK: Instead it's this thing that's been generated -
19 -
20 MS. RAYMOND: Correct.
21 JUDGE FITZPATRICK: -- the tagged polynucleotide. Okay. All
22 right, understood.
23 MS. RAYMOND: And with that, unless there are other questions on
24 sequencing, I'll turn it back to Mr. Baughman to talk about motivation to
25 combine and the number of -- the length of the tag.

1 MR. BAUGHMAN: Thanks. And if we could go to Parse's slide
2 107, please. Petitioner slide 107.
3 So Mr. Walter was talking about whether *McCloskey* has no barcodes.
4 This is another place, Your Honor, where there are three changes in the
5 record here that impact the Board's '981 decision. I know that's what Mr.
6 Walter is relying on. So let's take a look at their slide 109.
7 This is actually little Roman 3. I know Your Honors are familiar
8 with this, but there were three reasons in the '981 petition -- or, sorry, '981
9 final written decision. I'd like to talk about all three because they're all
10 raised here. So let's go back actually to their slide 113 and start with little 1.
11 And what Mr. Walter highlighted is that -- from the decision is that
12 *Linnarsson* isn't limited to mammalian cells.
13 What we are interested in talking about is the second unhighlighted
14 sentence again, and whether Petitioner's reliance on *Linnarsson* is limited to
15 mammalian cells. If we take a look at the actual underlying decision here at
16 page 37, cited there at the top, you'll see Your Honors wrote, "In fact, we
17 reviewed the petition for the words 'mammal, mammalian, eukaryote,
18 eukaryotic,' and could not locate any of them." This is another situation
19 where this petition is different. So let's take a look at petition page 67.
20 This is for claim 13. It's in ground 3. But it builds on the same
21 combination --
22 JUDGE FITZPATRICK: So the petition in this case?
23 MR. BAUGHMAN: In this matter. In this matter, Your Honor.
24 Exactly.
25 JUDGE FITZPATRICK: Okay.

1 MR. BAUGHMAN: In this '197 proceeding, and we'll see it again in
2 '013, they affirmatively map the sample to mammalian cells. You can see it
3 right here. "Each sample polynucleotide from a single cell is tagged with a
4 unique tag sequence typical mammalian cell comprises," and they give the
5 numbers. This is the sample when you get to claim 13. Right? But the
6 sample is the same here as it was in ground 1. It's coming from *Linnarsson*.
7 They're not saying oh, I modified *Linnarsson* or I focus only on this aspect
8 of *Linnarsson* and there's a reason I'm pointing to mammalian cells. They
9 map mammalian cells for the sample in *Linnarsson* here. Let's turn to their
10 slide 115.
11 On reply, Petitioner talks about lines 14 to 16. There's some other
12 examples in *Linnarsson:* prokaryotic bacteria and yeast. But importantly,
13 they never cited lines 14 to 16 in the petition or in Dr. Cooper's mapping.
14 Let’s take a look at the petition at 28.
15 Let's see, at the top here, *Linnarsson*, the sample can be obtained
16 from a tissue of interest. And if we look at the cite below the block quote,
17 it's lines 11 to 12 of column 13, not 14 to 16, which is on Mr. Walter's slide.
18 Let's take a look at what Dr. Cooper does in paragraph 127 of
19 Exhibit 1002. Paragraph 1-2-7, Exhibit 1002. Go to the next page, please.
20 He says, *Linnarsson* explains, rolling over to page 61, "*Linnarsson* explains
21 that the analysis is performed on cells obtained from a tissue of interest."
22 And then he says, "Such 'tissue of interest' constitutes a recited sample." So
23 they're affirmatively mapping this thing to a tissue of interest. We know
24 from Dr. Quackenbush's undisputed testimony in Exhibit 2013, paragraph
25 63, note 10, the tissue of interest is a eukaryotic cell.

1 And let's take a look at what Dr. Cooper is relying on here. It's lines
2 11 to 12 of *Linnarsson*, not 14 to 16. Okay. Now let's take stock of what
3 that means. This is the first of the three reasons the Board decided there
4 were enough tags in the '981 final written decision explicitly removed by
5 this mapping. And of course it matters because the Petitioner can't run away
6 from having enough tags for the mammalian and other eukaryotic cells it
7 affirmatively mapped as its theory here.
8 Let's look at little Roman 2. So, final written decision, page 37.
9 There's been talk about this already today. I'd like to clear it up. This is the
10 '981 final written decision, page 37. The heading here is, "Not all the
11 mRNA's present in cells must be tagged."
12 Let's look at the next page 38, bottom of that page. The Board
13 concluded, consistent with the petition, Dr. Cooper doesn't state that all
14 polynucleotides within a cell must be differentiated. Neither the claims and
15 then nor Petitioner's rationale requires all of the mRNA's present in a cell to
16 be tagged.
17 Let's look at petition page 55. This is ground 1, and it's not a
18 modification of *Linnarsson*. I'm sorry, page 55 of the, yeah, the position
19 here in the '197 proceeding. The paragraph starting, "Further." The purpose
20 of *Linnarsson*'s method, as Your Honor said earlier, is gene expression
21 analysis. That's why you're doing it. You're trying to count what's in the
22 cell. A person of ordinary skill would have understood that contemplates the
23 analysis of substantially all mRNA molecules of a cell. By the way, this
24 isn't weird *Linnarsson,* modified *Linnarsson*. This is *Linnarsson* straight up.
25 In the last sentence, "A person of skill would have understood that such a

1 method was designed to be applied to substantially all mRNA molecules of a
2 given cell."
3 Now, in our '981 argument, Mr. Walter said, pay no attention to this.
4 It's for another case. Not relevant here. Doesn't have anything to do with
5 anything. For '013, we submit this as an admission about what *Linnarsson*
6 means, but it sure as heck in this proceeding. Let's take a look at what Dr.
7 Cooper says about it, paragraph 222 in Exhibit 1002. And at the end of it he
8 says, next page, "A POSA would understand that *Linnarsson* describes a
9 method which is designed to be applied to substantially all mRNA molecules
10 of a given cell." And again, we know the purpose of that, as is discussed in
11 paragraph 222, is because gene expression analysis needs that.
12 So the second of the three reasons the Board used in deciding in the
13 '981 that there were enough tags has been explicitly removed by these papers
14 in the '197. And they can't run away from having to tag a sample that
15 includes substantially every mRNA in the cell. Obviously it matters because
16 the Petitioner itself explains this is necessary for *Linnarsson*'s purpose of
17 gene expression analysis, which depends on how many mRNA are actually
18 in the cell. And as the whole basis of Petitioner's obviousness combination
19 failing to do this would break *Linnarsson*'s gene expression analysis and the
20 whole proposed combination. It would change its principle of operation. So
21 if we look now --
22 JUDGE FITZPATRICK: Mr. Baughman?
23 MR. BAUGHMAN: Yes, Your Honor.
24 JUDGE FITZPATRICK: Mr. Baughman, were you just reading from
25 what were you just a moment ago reading from?
26 MR. BAUGHMAN: Just my notes, Your Honor.

1 JUDGE FITZPATRICK: Just your notes? Yeah, I'm sorry. Okay.
2 What is the evidence for the statement that you made that gene expression
3 requires all -- you know, a proper gene expression analysis requires that all
4 sample polynucleotides, you know, be sequenced. And let me just preface
5 this with saying I would think that you could still have -- you could still get
6 a useful analysis even if you didn't get all of them. Although --
7 MR. BAUGHMAN: What I'm saying, Your Honor, is that --
8 JUDGE FITZPATRICK: -- if you got all of them, it would be better.
9 MR. BAUGHMAN: I'm sorry, Your Honor. So they're talking about
10 the combination here is supposed to be improving *Linnarsson*'s gene
11 expression analysis. And if we take a look at our slide 55 -- sorry, yeah, 36,
12 quoting from their petition at 55. The very purpose of *Linnarsson*'s method
13 is gene expression analysis. I think we're all agreed on that. And what they
14 say that is, Cooper, paragraph 65, Exhibit 1002, is detecting mRNA
15 molecules. It's critical to the study determining the count. There's lots of
16 testimony from Dr. Cooper about how important it is to be able to count how
17 many mRNA are being produced by a cell.
18 And then if we go back here to what is on pages 54 and 55 of the
19 petition, and then we'll go to Cooper as well, Your Honor, I think we need to
20 start in this paragraph specifically. So it includes the step of releasing
21 mRNA from each single cell to provide a plurality of individual mRNA
22 samples. And by the way, this is what they're mapping. They aren't
23 mapping -- there's a version of things in *Linnarsson* that does some
24 targeting. That is not what they're doing here. What they're doing is
25 random, nonspecific tagging. It's in claim 20, which is petition 51. They

1 don't make any changes for that to happen. They're saying, let the tags loose
2 and we're going to try to tag as much as we can.
3 And what the Petitioner said here, because the mRNA is
4 indiscriminately released from each single cell without any elimination or
5 filtration, the released mRNA sample that is tagged, amplified, and
6 sequenced comprises substantially all mRNA molecules of said cell. So
7 that's what *Linnarsson* is making. That is the sample they map from
8 *Linnarsson*. It goes all the way through the claim.
9 And it goes on to say that people of ordinary skill understand you tag
10 substantially all of that for because of the purpose of being gene expression
11 analysis. It matters here because it's claim 25. They need that. They need
12 that coverage. But is this a special change from the mapping before now?
13 This is ground 1. It's not unchanged from claim 1. They can't -- this is
14 another example of, you know, show me a problem, I'll make up a solution.
15 This is the same mapping from the very beginning of ground 1 through
16 claim 25. They say they got it already. They're tagging everything. They're
17 tagging substantially all molecules and it has a purpose.
18 And if we look at Dr. Cooper, paragraph 222 again, the lead-in to
19 why he says what he says. "As discussed above, *Linnarsson*'s method tags
20 sample polynucleotides, which are substantially all mRNA molecules of the
21 cell." So if we go up a couple lines there, released -- the released mRNA
22 sample we were talking about from the petition comprises substantially all
23 mRNA molecules of the cell. It's about five lines up from the bottom.
24 Then *Linnarsson*'s method tags these sample polynucleotides for the
25 purpose of gene expression analysis. A person of skill would understand the

1 purpose of such a method would be to analyze substantially all mRNA
2 molecules of a cell.
3 So, Your Honor, are there other analyses you could do? Yes. What
4 is the theory of what they're doing with *Linnarsson*? This. And they say so.
5 And they don't say, oh --
6 JUDGE FITZPATRICK: Suppose --
7 MR. BAUGHMAN: -- (inaudible; overtalking 1:18:31) theory only
8 for claim 25, Your Honor.
9 JUDGE FITZPATRICK: What about the last sentence of paragraph
10 221? That seems to cut against your argument by using the word "can".
11 MR. BAUGHMAN: That's a summary of his opinion that it teaches --
12 that it can comprise -- if you look at the formula, he says "can" before
13 everything all the way through the declaration. They're going to have an
14 obviousness problem if they only go with can instead of will, Your Honor,
15 respectfully, because to be obvious, it better be will or does.
16 JUDGE FITZPATRICK: Well, it also can signify something else,
17 that it can be one or more things.
18 MR. BAUGHMAN: Understood, Your Honor. But there's -- I don't
19 see any --
20 JUDGE FITZPATRICK: I understand everybody's very careful with
21 their language. I get it. But that does seem to cut the other way to say that
22 it's not limited to it.
23 MR. BAUGHMAN: And we agree, Your Honor, that there are other
24 disclosures. By the way, the passage I think Mr. Walter was talking to about
25 some are all, that's talking about prior methods, not *Linnarsson*'s method,
26 that quotation. I know he was laying a lot of weight on what was bolded and

1 what wasn't, but what's actually mapped here, I mean, *Linnarsson* does teach
2 other things. We all agree to that. But what it teaches and what they rely on
3 is this for ground 1.
4 And we can let them keep changing, but that's, respectfully, not
5 something we're going to be able to respond to. That's not fair. It's not the
6 rules, and it's not a gotcha. We have things to say about this, but we need to
7 know what this is.
8 To keep going with this, Your Honor, once we've got the cell with
9 substantially everything in it tagged by *Linnarsson*, then we get passed off to
10 adding *McCloskey*, which they say uniquely tags everything in that sample
11 that comes from *Linnarsson*, the sample being substantially all the mRNA
12 from the cell. So we see that on their slide 30 -- our slide 37. And if we
13 actually zoom out. Let's zoom out to petition page 40, please, 40 and 41.
14 And again, the reason that this is happening is because it's important
15 to gene expression analysis. They say so. It typically relies on limited
16 amounts of template DNA, amplification bias is particularly important to
17 correct. And they say that *McCloskey* -- that *Linnarsson* only partially
18 solves the problem. It pools things together because otherwise you'd have
19 too few mRNA in each cell and you'd have to do more amplifying. But by
20 tagging where they come from, putting them together and amplifying
21 together, you can reduce the number of amplification steps, reduce that kind
22 of error. But they say that only reduces amplification bias right on the
23 bottom of 41. It doesn't actually solve the problem, bottom of that
24 paragraph.
25 *McCloskey*, however, provides the exact solution by incorporating a
26 second tag that uniquely identifies each sample polynucleotide in the

1 sample. So that's their theory. That's what they ride all the way through.
2 And it's pretty clear.
3 If we take a look at our slide 38, this is where Dr. Cooper is
4 explaining to solve the problem, you need to uniquely tag. That lets you
5 count the number of unique tags. The same is true on a bunch of other spots.
6 I'll put up their slide 99, please. This is where Dr. Cooper is saying,
7 under the highlight as always, "to measure true sample complexity/template
8 diversity," you tag "each sample polynucleotide uniquely" unless you
9 analyze it. So again, that's the reason, Your Honor, that these aren't trivial
10 changes that they made.
11 And now let's quickly turn -- I know -- I don't know where we are on
12 time, Your Honor, but I'd love to touch on the last thing that they have on
13 slide 109, if I could.
14 JUDGE FITZPATRICK: Yeah, I think you got a couple minutes
15 before -- five minutes left total, including your rebuttal.
16 MR. BAUGHMAN: Thanks, Your Honor. Okay. I'm going to go
17 real quick. But on their slide 109, this is where we get to the number of
18 codes. If we look at the actual part of the final written decision, they're
19 pointing to at page 39 at the bottom. The Board pointed out that the petition
20 -- this was disputed by Petitioner. But they said, Your Honor said it clearly
21 proposes using seven polynucleotides. This is the final written decision,
22 page 39 at the bottom. But the Petitioner didn't limit that to just seven. That
23 was Your Honors' conclusion there.
24 If we look at our slide 41 now, please. Mr. Walter pulled this up.
25 I'm pulling it up, too. Ground 1, I'm happy to show it to Your Honors. It's
26 quite clear that is 4 to the 7. That's what they relied on. And what they say

1 about ground 3 is when you need to increase the number of tags, you apply
2 the 4 to the n formula and you add *McCloskey II*.
3 We can see that on our slide 42. This is ground 3. It's the same
4 sample of mRNA that's in ground 1. It's the same stuff tagged by
5 *Linnarsson*. And the only change here is the number of tags they're going to
6 use to tag it from 4 to 7, to 4 to the 30th. And that's the first time they ever
7 mentioned 4 to the n. And if they meant it, they knew how to say it. There
8 it is. And on the right is the first time they mentioned *McCloskey II*. It is
9 literally, back to our slide 41, a different ground from ground 1. And its
10 only purpose is to have more tags.
11 Now, we actually see Dr. Cooper essentially acknowledge this in his
12 reply declaration. Let's look at their paragraph 128 -- their slide 128, excuse
13 me. Here we have he's talking about ground 1. He says, well, *McCloskey II*
14 talks about having a lot more bases and he quotes from that. And he says,
15 thus a person would find it obvious from *McCloskey*'s method to expand
16 barcodes to different lengths. When they wanted to change their ground 1
17 theory, they knew how to do it. He's trying to cite *McCloskey II* to change
18 ground 1 into ground 3. Can't have it. It's not what they said, not what they
19 did. And it's quite clear that they meant to and did map 7.
20 I'm happy to talk with Your Honor about why that fails. But we
21 know it fails even for bacteria because, as they say in paragraph 77 of Dr.
22 Cooper, a person of skill would know you need about 100 times more to
23 actually uniquely tag everything. That's their theory. For a reasonable
24 expectation of success, you need 100 times more based on paragraph 77 and
25 their disclosure. And so bacteria fails even if you're allowing their new

1 theory, yeast fails even if you're allowing the new theory, and certainly
2 mammals fail.
3 And I think we might be at time, Your Honor, but I'm happy to
4 answer questions. So let's just say it's quite clear that the record here,
5 although we think lots of it bears on what's in '981 is certainly different and
6 expressly undercuts all three reasons for this conclusion and eliminates
7 about a bunch of other things as well.
8 JUDGE FITZPATRICK: And I have a question about *McCloskey*
9 unmodified and about this barcode. And they say we currently use 7
10 nucleotides giving 16,384 possible barcodes. What are they tagging in
11 *McCloskey*? And does that same 100-to-1 ratio apply there?
12 MR. BAUGHMAN: My understanding, Your Honor, is they're
13 tagging alleles, so they have a lot fewer. This is in our Patent Owner
14 response. They're tagging a lot fewer things. This is banging a square peg
15 into a round hole. They didn't need more. What is happening here is they're
16 saying, well, take *McCloskey*. And they're literally saying, take its seven
17 position barcode, you can see it on our slide 40 quoting Dr. Cooper, like the
18 next seven, that's the barcode. And they're saying, bang it in there. But that
19 doesn't -- it doesn't work for what they're trying to do. This is ground 1, use
20 seven. When they wanted to go to ground 3 and change it, they knew what
21 to do.
22 JUDGE FITZPATRICK: I, you know, I understand that argument.
23 I'm just wondering what would *McCloskey* -- I mean, they're working with
24 cells. Are they tagging some real unique cells -- things within -- you know,
25 why would they use only 16,000 if it's not even enough for a bacterial cell?

1 MR. BAUGHMAN: I think the answer, Your Honor, I'm sorry to
2 interrupt, I'm just conscious of the time because *McCloskey* is a targeted
3 method. Your Honor will recall there are five pieces of that hairpin and
4 they're only bringing in one. So unlike *Linnarsson*, the method that they're
5 mapping from *Linnarsson*, which is just a random tagging, *McCloskey* can
6 target things. So they're trying to look at something that's much smaller in
7 number and only two alleles per cell are tagged. So it's a lot smaller
8 universe.
9 But on the other hand, I mean, I do want to again make the point, I
10 know we've said before in the prior proceeding, the *Virtek* (phonetic
11 1:27:18) case makes pretty clear that you can't just say *Linnarsson*,
12 *McCloskey*. If we keep changing things in *Linnarsson*, if we keep changing
13 *McCloskey*, is there anything we can come up with that might render this
14 claim obvious? We think the claim is not obvious, but we need to know in
15 advance what the argument is going to be before we can respond to it and
16 have due process.
17 JUDGE FITZPATRICK: Thank you. You know, what I'm going to
18 do is I like to -- you know, we'll switch it over to Mr. Walter for his rebuttal.
19 He had 10 minutes. I'm going to give him 12 because I want to give you 2
20 so that you can at least respond since we had some questions back and forth
21 just now.
22 MR. BAUGHMAN: Thanks, Your Honor.
23 MR. WALTER: Your Honor, can you hear me?
24 JUDGE FITZPATRICK: Yes, thank you.
25 MR. WALTER: Let me see, this is the wrong one. Let me show the
26 right one. Hold on just one moment here. Let me get my -- okay.

1 JUDGE FITZPATRICK: Okay.
2 MR. WALTER: Can you see my slides, Your Honor?
3 JUDGE FITZPATRICK: Yes. Figure 4.
4 MR. WALTER: All right. Thank you. So I'll start at the beginning
5 of the argument. There was the argument that there was no disclosure of
6 sequencing the CDS. I'm showing you slide 49. This is the CDS and, as
7 you noted, it includes a cell tag. *Linnarsson* tells you, you sequence the cell
8 tag so you can determine which fragment -- which cell a particular fragment
9 came from. Any place where *Linnarsson* says you sequence the cell tag,
10 that's a disclosure of sequencing the CDS because *Linnarsson* tells you the
11 cell tag can have a CDS.
12 You know, we asked our expert about this issue and what we find
13 here is -- here's slide 153. It tells you -- excuse me, this is slide 43.
14 *Linnarsson* tells you the tag is present in the CDS or the TSO and that the
15 synthesis of the CD of the tag can use -- operate as a barcode to identify the
16 cDNA. So it's telling you you're going to sequence it to identify it. We
17 asked our expert about this issue in response to the argument they were
18 making as to this idea that you would never sequence it. And what their
19 expert said was, why would -- we asked them why would you tag the CDS if
20 it was never going to be sequenced? He says he doesn't know. Why would
21 there be a cell tag if it was never going to be sequenced? He doesn't have
22 any response on that point. It doesn't make any sense to suggest that the
23 CDS is going to be there but not sequenced.
24 Let me show you now page 1003.005 of *Linnarsson*. It's got a
25 general description of figure 1. It says that the single cells are placed in a
26 separate well, you tag them, and you perform reverse transcription to

1 generate those tagged cDNA molecules and then you sequence them. This
2 isn't limited to an approach that uses fragmentation or capture. It's a
3 completely general disclosure of doing sequencing and you're going to
4 sequence the tag. It doesn't say it's only one or the other.
5 Now, there was also some question of we never show that you can
6 sequence the entire molecule. Well, I walked through the shotgun
7 sequencing disclosure during my presentation. I explained how it worked
8 and I explained how --
9 JUDGE FITZPATRICK: Mr. Walter, and that stuff was not in your
10 petition, right?
11 MR. WALTER: This was something we added in reply. We added
12 this in reply. And you know, I don't think there's any question that this is
13 fair reply. They're arguing that the sequencing disclosure that's otherwise
14 completely general in the patent, this disclosure here, column 4, lines 8 to
15 13, sequencing is performed to obtain 100 million reads. And then we get a
16 response that says, well, gosh, we don't know how much of this we're going
17 to sequence. And it's fair for us to come back and say, hey, listen, the
18 disclosure in *Linnarsson*, it's general. It discloses commercial sequencing
19 platforms, Applied Biosystems and Illumina. And it says you can do the
20 sequencing by any suitable screening method. And it teaches the shotgun
21 sequencing approach where you can fragment molecules, sequence them,
22 and then put them back together to get the entire sequence. And during the
23 argument there was no response, no suggestion that, no, this wouldn't work
24 to get the full sequence. It does work to get the full sequence.
25 Let's look at the language that we actually -- this is the one line from
26 the petition. And you're right, even if this only line -- this first line was here,

1 that would be enough. This one line here at the end we've highlighted that
2 they rely upon, it just says that the entire molecule is subject to the sequence.
3 It doesn't mean you need to generate the entire tag sequence. Dr. Cooper
4 never said anything to the contrary. That's what he said. He said the
5 sequencing step of *Linnarsson*, which is disclosed in a general way at page
6 4, lines 8 to 13, says you're going to get the sequence of the sample
7 sequence, the first tag sequence, and the second tag sequence. And it
8 discloses in the patent the methods that would allow you to do that.
9 Now, there's been some suggestion that we need to come along and
10 we need to say, listen, the *Linnarsson* method, the *Linnarsson* patent, it
11 needs to say more than sequence the tagged molecules. They need to tell
12 you precisely how much you're going to sequence. And it needs to tell you
13 what method you're going to use. And it needs to give you like a precise
14 fraction or precise portion. That argument, I think, turns obviousness on its
15 head. Someone is going to read *Linnarsson* based on the knowledge of the
16 person of skill in the art. And the patent admits at the relevant timeframe,
17 you could go by a Roche 454 sequencing instrument and you could sequence
18 in a single run, without even doing assembly or shotgun sequencing, you
19 could do in a single run 400 bases. And there's no contention that that's not
20 enough to get the tag, the sample sequence, and the second tag. There's been
21 never any dispute to that regard. And in fact, that would be a kind of a
22 strange thing to argue because, as our expert confirmed, and I think I saw
23 this earlier during my original presentation, he acknowledges that
24 sequencing at the time was conventional, and that's something they
25 acknowledge in the Becton-Dickinson case.

1 So, you know, any argument that we need to establish that
2 *Linnarsson* comes out and says, okay, you're going to sequence X-number of
3 bases, you're going to go and sequence 70 percent of the molecule, that turns
4 obviousness on its head. The patent says you're going to seek sequencing on
5 the tagged molecules. It actually does teach a method that allows you to get
6 the entire tagged molecule. But a person of skill in the art would read this,
7 with his or her background knowledge they would see the disclosure of the
8 commercial sequencing platforms, and, as Dr. Cooper confirmed, they
9 would know that you're going to be able to get the sample sequence, the first
10 tag, the second tag, and the entire molecule if you want.
11 Let me go back to claim 8. There were some questions on claim 8.
12 The claim 8 argument, I still don't understand it. They say it fails because it
13 doesn't sequence the CDS. Well, it does sequence the CDS. The whole
14 point of sequencing the CDS with the tag is so you can get the sequence of
15 the tag. But it doesn't really matter because claim 8 doesn't require
16 sequencing the CDS. It only requires that you generate the tag by
17 hybridization and extension. And as their own slide shows here on the right,
18 that's done. That's done in every embodiment. Here's the hybridization and
19 here's the extension. That's done in every embodiment. It doesn't matter if
20 there's other steps. The claim is still satisfied.
21 And then finally, I want to get to this question of gene expression
22 analysis and whether you have to tag every single molecule in the cell.
23 Well, again, the claims don't require it. And this idea that the petition was
24 locked into this because we made this argument for a dependent claim, I
25 think that lacks merit.

1 Here's what the petition says. It says it contemplates the analysis of
2 substantially all mRNA molecules in a cell. It doesn't say it's limited to it. It
3 says *Linnarsson* is designed to be applied to that. Yeah, it is. You can apply
4 to that, but that's not the only. Again, I'll point you to what we quoted,
5 "Direct sequencing of all or parts of the mRNA content." We relied on the
6 "all" for claim 50 -- claim -- the dependent claim, whichever one this is, we
7 relied on that for this. But it also says "or parts". It's not limited to that.
8 So gene expression, the idea that gene expression requires every
9 single molecule in a cell to be studied, that's wrong. It's gene expression.
10 You're trying to figure out what genes are being expressed. That doesn't
11 mean you need to analyze every single gene. Maybe there's genes you're
12 interested in.
13 And then finally, at the end, they showed on their slide 40 an
14 argument regarding the number of tags. And the contention here on their
15 slide 40 was that the theory of the petition was always based on 7. I would -
16 - you have to read the slide that they point to, the portion of the petition that
17 they point to very carefully. If you look at page 40, page 40 of their
18 presentation, the sentence --
19 JUDGE FITZPATRICK: Mr. Walter, you're at your time, so wrap it
20 up quickly.
21 MR. WALTER: I'll wrap up. Yeah, I'm going to wrap up. The key
22 thing to note is that on slide 40 it says, "for example". That's an example
23 that we're giving. We're not saying the petition is limited to this. We're
24 giving an example. And then they come along and say, look, your example
25 says seven. You're limited to that. You didn't show anything else. Well, in
26 our reply, we said, hey, that's crazy. Nobody of skill in the art would think

1 this is limited to seven. *McCloskey* instead tells you that you can be 4 to the
2 n. The Board noted that and that's the right analysis. And that's a fair
3 response to the argument they made in response to ours.
4 And with that, I'll wrap up unless there's questions.
5 JUDGE FITZPATRICK: Thank you. Let's turn it over to Patent
6 Owner.
7 MR. BAUGHMAN: Thanks, Your Honor. Really quickly, I'm not
8 going to try to put the slides up because I'm not sure there's time. But if you
9 look at the petition pages 37 to 38, they point to the hairpin from *McCloskey*.
10 They say that's the barcode, the yellow highlighted part with -- seven Ns
11 (phonetic 1:40:24) in it. If you take a look at Cooper, paragraph 117, he's
12 pulling out *McCloskey*'s figure 1. He's showing the seven base pair codes
13 over and over again. If you take a look at paragraph 159 where he starts
14 mapping to the claim limitation, he pulls up that same yellow highlighted 7N
15 figure from *McCloskey*. There's no question that *McCloskey* says what we're
16 using now is seven. And that's what he uses and he doesn't modify it.
17 And he -- on slide 40, our slide 40, he absolutely says, what's the
18 theory? I can conceptually, Your Honors are very familiar with this, I can
19 conceptually divide *Linnarsson*'s existing tag using six to eight position
20 positions for the cell tag and using seven, the next seven, to distinguish the
21 polynucleotides. If there's another theory, if there's another "for example,"
22 I've yet to see it. And this is why Your Honors concluded in the '981 that
23 that's definitely what they relied on. But you let them have some space,
24 understandably, that was your view, to make changes if they wanted to. We
25 disagree. And now we know from what they said in '197 when they wanted

1 to make a change, they explained it. They cited 4 to the n for the first time
2 to do it. And they brought in *McCloskey II*.
3 If we look at their slide 36, please. Their slide 36 -- I'm sorry, their
4 slide 46. I'm sorry. Could you put up our slide 46? I think I have the wrong
5 ones up. Nope. Okay. I've got the wrong numbers. I'm going to just say it
6 because I can't find the slide, Your Honor, but the bold he was referring to,
7 again, the all or some, if you look at the end of that sentence, it says "is
8 increasingly being used." It's not *Linnarsson*'s method. It's summarizing
9 what's going on. So the whole idea that, oh, they're doing something
10 magical and they're saying, well, we're simultaneously saying there are other
11 choices and we're making this one, that's just a quotation of what was
12 possible in the art at the time.
13 If we could put up their slide 73, please. Their slide 73. What I
14 heard Mr. Walter say was, you know, why don't you just take out that
15 second sentence? What he's basically saying is, change my obviousness
16 theory. I don't want to say that anymore. But again, this is what they said.
17 If you look at the paragraph of Dr. Cooper that he's comparing it to, if those
18 are different, we can't bring in what Dr. Cooper says. That's incorporation
19 by reference. This is their theory. This is what controls. They only had a
20 paragraph to write about this whole limitation, and that's what they said. It's
21 been in there from the beginning. They had to explain how they could do it
22 from the beginning, not just respond to us. It's always been their theory
23 from the day they filed this, the sequencing was performed on the entire
24 tagged polynucleotide to satisfy 1G.
25 And unless there are other questions, Your Honor, I think I'll leave it
26 there. I'll pass it to Ms. Raymond if there's anything else.

1 MS. RAYMOND: Nothing here. I suspect our time is up. Thank
2 you.
3 JUDGE FITZPATRICK: Let's close the record, you know, or at least
4 temporarily, and take a break. Let's -- in the interest of moving this along,
5 let's not start at 3 Eastern, even though that might be a nice time. Let's -- can
6 we shoot for 2:55?
7 SPEAKER: Yes, Your Honor.
8 JUDGE FITZPATRICK: That gives you a little over 10 minutes. Is
9 that enough?
10 SPEAKER: Yeah.
11 MS. RAYMOND: Certainly, Your Honor.
12 SPEAKER: Thanks, Your Honor.
13 MS. RAYMOND: Thank you.
14 JUDGE FITZPATRICK: All right. Thank you.
15 REPORTER: We're off the record.
16 (Recess)
17 JUDGE FITZPATRICK: We'll go on the record. This is IPR2023-
18 00958. We've already discussed a related case and this transcript will be
19 filed in that case as well, and that case will be filed in this case.
20 Looks like we have the same counsel. And so why don't we just
21 jump right into this? We'll start with Mr. Walter on behalf of Petitioner.
22 MR. WALTER: Thank you, Your Honor. I'd like to reserve 15
23 minutes.
24 JUDGE FITZPATRICK: Okay.
25 MR. WALTER: Are you able to see my slides?
26 JUDGE FITZPATRICK: Yes.

1 MR. WALTER: Okay. In this one, I'm going to address kind of the
2 only real issue that might be different relative to the previous case. The
3 claims in the '013 patents, they require ligation in their independent claims --
4 in the one independent claim. So I'm going to address that ligation issue
5 and, in particular, the question of motivation to combine, which is really the
6 only thing they argue with regard to ligation.
7 So the first thing to know is that the specification of the '013 patent,
8 it tells you that ligation is a prior art technique. It identifies several
9 references that disclose ligation dating all the way back to 1979. That's on
10 slide 39. And it, in fact, characterizes ligation as a conventional technique.
11 That's on slide 40. In other words, this is a tried and true method that
12 everybody knows how to do and the patent admits it.
13 And the Federal Circuit has made clear that you're going to be on
14 pretty safe ground in finding obviousness in view of this alone. That's on
15 slides 41 and slides 42, where we cite the *I/P Engine* case and the *McCoy v.*
16 *Heal Systems* case. Of course, the evidence on ligation goes far beyond this.
17 10X and its expert have admitted how well known and conventional it was.
18 I'm showing slide 43. This is from the *Becton-Dickinson* case. I'm showing
19 slide 43. And this is where they said everything was routine and
20 conventional. Here they said "ligation will be known to those of skill in the
21 art."
22 Slide 44. This is Dr. Quackenbush's expert report from the parallel
23 district court litigation in this case. And here he's opining the conventional
24 techniques include ligation. There's much more to this effect.
25 Slide 45. Dr. Quackenbush, their expert, "ligation was a
26 conventional technique."

1 Slide 46. "I'm not contesting that ligation was a well-known method
2 of attaching oligonucleotides."
3 Slide 47. As of 2009, their expert admits he had done it himself and
4 he had done it for the purpose of sequencing.
5 Slide 48. "Ligation is a method known in the art." And this is all
6 further evidence confirming obviousness. And here's the law on this, *KSR*,
7 "A person of ordinary skill 'has good reason to pursue known options.'"
8 Ligation, as we've just shown through extensive evidence, was a known
9 option.
10 Slide 50. "A person of ordinary skill is a person of ordinary
11 creativity, not an automaton." So we're going to talk about this later. They
12 make the argument that, well, there's problems because biotin gets in the
13 way. Well, a person of ordinary skill in the art would be a person of
14 ordinary creativity and would be able to use ligation notwithstanding that.
15 Slide 51, *I/P Engine* case. The fundamental flaw by non-obviousness
16 when we're talking about a technique, that's a technique that's widely applied
17 in the art.
18 Now, there's expert testimony on this. The path and the motivation
19 for using ligation is straightforward. I'm showing slide 52. This is
20 paragraph 149 of Dr. Cooper's declaration. He says that, "Using ligation to
21 add the tag after extension would allow for increased flexibility" during your
22 experiment. And he likewise explained, I'm showing page 1070, Exhibit
23 1070, page 61, paragraph 74. And he says, look, if you're going to put a
24 second tag on, there's only really two ways to do it. Okay? You're either
25 going to include the second tag as part of the CDS or TSO when you

1 synthesize it or you're going to make it separately and you're going to attach
2 it by a ligation. Okay?
3 And so the record here we have it proves obviousness. A POSA
4 would have combined *McCloskey*'s barcode with *Linnarsson* to avoid
5 amplification bias. That's the basic general overarching motivation for why
6 you'd combine *McCloskey* with *Linnarsson*. *McCloskey* is bringing in that
7 second barcode and there's only a small number of ways to introduce that
8 barcode. The method was routine and conventional and it offered a clear
9 flexibility benefit. That's like the recipe for obviousness. That's the
10 canonical set of ingredients that establish obviousness.
11 And there's multiple cases of this effect: slide 54, the *Uber*
12 *Technologies* case; slide 55, *Nike v. Adidas;* slide 56, *Almirall v. Anneal;*
13 slide 57, *ACCO Brands v. Fellowes;* slide 58, *Ball Aerosol*. All of these
14 cases are right on pay point.
15 Slide 60. Patent Owner's response to this is to contend that the tag
16 can't be ligated to the CDS because the CDS has a biotin at the end, and the
17 CDS with the biotin apparently is going to block ligation. Essentially, this is
18 the argument that the only embodiments disclosed in *Linnarsson* are the
19 figure 11 embodiments. And you see that in their Patent Owner's, surreply.
20 That's effectively the argument they make. It is the argument they make.
21 They say *Linnarsson*'s method consistently discloses fragmentation and
22 capture. The argument, it's limited to these approaches. But as we know
23 and as we discussed earlier, and I'm going to move through this more
24 quickly, that's not true. The steps in figure 11 are optional. The Board
25 found that already. That's shown on slide 64.

1 And further, the law is clear that bodily incorporation is not required.
2 Someone of skill in the art, wouldn't look at *Linnarsson* and say, oh, the only
3 thing I can do is use this one example that has biotin and there's a biotin in
4 the way. And so since the biotin is in the way, I'm stuck. That's not the law.
5 A person of ordinary skill is a person of ordinary creativity, not an
6 automaton.
7 And as I'm showing on slide 98, Dr. Cooper explains precisely what
8 someone would do. It would be an easy thing to do. You wouldn't sit there
9 like someone who doesn't understand what a biotin is and try to ligate a
10 DNA molecule to a biotin. But a skilled artisan would understand that the
11 biotin would have to be moved. If you still want to use, you'd have to put it
12 on the additional tag sequence to make sure that it doesn't block it. He says
13 such modifications would have been routine and obvious to the skilled
14 artists.
15 We asked our expert about this. This is slide 99. We asked them, do
16 you have an opinion whether or not a person of skill in the art would be able
17 to do that? And by that I mean ligate a tag to the CDS before placing biotin
18 on the 5-prime end. Would someone be able to do it out of order? And Dr.
19 Quackenbush, their own expert, he didn't answer. And that tells you
20 basically what the answer is. The answer is yes, someone would be able to
21 do it.
22 Would a person of ordinary skill in the art be able to adjust the
23 process? This is another set of questions that we asked Dr. Quackenbush,
24 and he obfuscated and ultimately said, "I haven't done the analysis." He
25 says, "It's a complex question that doesn't have a 'yes' or 'no' answer." That's

1 a non-answer. That's an admission that, in fact, someone would be able to
2 do it. That's on slide 100.
3 Here's slide 101. Would it be within the scope of the competency of
4 a skilled artisan to modify *Linnarsson* so the tag is located before the biotin
5 is added? "I'm having trouble giving a simple 'yes' or 'no' answer." So we
6 have Dr. Cooper, on the one hand, who's clear and straightforward, yes,
7 someone could modify it. And then we have Dr. Quackenbush, who is
8 refusing to answer. He's certainly not standing up and saying, oh, boy, this
9 would be challenging and this would be difficult.
10 Slide 102. There's more on this. "I haven't done an analysis to
11 understand whether it would actually completely disrupt the process." He
12 didn't look at it. If it were really non-obvious, he'd have more to say than
13 this. And the Board concluded this as well. The Board concluded in its final
14 written decision, as I'm showing on slide 65, that a person of ordinary skill
15 in the art would know "how to use biotin in a manner that didn't interfere
16 with the proposed modification."
17 And so to sum up, on ligation, there's clear evidence that it's a
18 known, routine, and conventional technique. It was obvious, and they
19 provided no substance rebuttal except to pursue an approach based on bodily
20 incorporation of a method in *Linnarsson* that's not even required.
21 All right. So we're now treading into area that's already been
22 covered, and I'm going to try to move through this stuff really quick, and I'll
23 use most of my time on rebuttal. So first there's the question of sequencing
24 the entire the tagged polynucleotide. The record here is the same. You
25 know, the only difference is they don't even have the gotcha argument at all.
26 That one line that they relied upon in the '197, that's not even present here.

1 And so this is, in essence, no different from the '981 patent that's already
2 been found invalid.
3 In any event, the petition satisfies the claims. Page 44 of the petition
4 makes clear that sequencing is performed thereon. That's a general
5 disclosure. And their argument is, well, it doesn't tell you the details or how
6 much is sequenced. Well, that's the point. It tells you sequencing is
7 performed thereon.
8 In the context of a disclosure like *Linnarsson* that says you do
9 sequencing and it tells you in 2007, you're going to use a commercial
10 sequencing platform like Illumina or Applied Biosystems, and it teaches you
11 that you can do shotgun sequencing so you can get complete sequences,
12 that's all you need to tell someone of skill in the art to understand that if you
13 want, you're going to be able to get the sequence of the entire tagged
14 polynucleotide. To suggest otherwise and to suggest that someone is skilled
15 in the art wouldn't understand from *Linnarsson* that you can do this and that
16 *Linnarsson* teaches that you can do this, like I said in the previous case,
17 would turn obvious on its head and ask someone to be an automaton. To
18 read *Linnarsson* outside the context of the knowledge of the skilled artisan
19 and expect *Linnarsson* to tell you, okay, to do the sequencing, you have to
20 use this instrument and you're going to do these many polynucleotides and
21 you're going to do this portion of the polynucleotide and it has to be this
22 exact percentage, that's not obviousness and that's not how someone with
23 skill in the art would read *Linnarsson*.
24 I also want to say on this point that they say the petition doesn't
25 provide details or specify what or how much is sequenced. There's a lot of
26 argument along the lines of, well, since you didn't include that in petition,

1 anything you say beyond this is improper reply. And that's not a fair
2 argument either. A person of ordinary skill in the art, like I said, reading
3 *Linnarsson* in the context of its full disclosure, where it's disclosing
4 commercial sequencing instruments, wouldn't need to have more disclosure
5 than that. And for them to come back and make a contention that the level
6 of detail we included on the sequencing disclosure in our initial petition was,
7 frankly, surprising.
8 Again, we're talking about a technology at a timeframe where there
9 are multiple commercial instruments, where we have a general disclosure,
10 and where even the patent itself admits that at the relevant timeframe, you
11 could use the Roche 454 to get 400 reads. For them to come back and say
12 there's some sort of deficiency in the level of detail we provided with regard
13 to the sequencing disclosure, that, frankly, was a very surprising and
14 unexpected argument. And it's not unreasonable, nor is it unfair for us to
15 say, hey, look, the sequencing disclosure is robust and it's more detailed and
16 the claims aren't limited to this. That's a fair response. And they haven't
17 really done anything to undermine that response except to complain that
18 there's something additional in our reply that's beyond the petition and
19 complain that it's unfair.
20 I'd like to go on now to this numerosity of tags argument that we
21 dealt with previously. Again, the argument that we see in the '013 patent is
22 that the seven nucleotide barcode theory would not provide enough unique
23 tags to satisfy the motivation. The Board already rejected that. *McCloskey*'s
24 not limited to 16,384 unique barcodes. You see that on slide 142.
25 The posture we have here is the exact same posture that we have in
26 the '197 patent case and the exact same posture we have in the '981 case. In

1 the '981 case, they made the same argument they're making the '197 and '013
2 patent with which is that the original petition relied only on seven barcodes
3 and that it was unfair and improper for us to say, hey, *McCloskey*'s not so
4 limited. The Board rejected that very argument in the '981 patent case, and
5 the Board should reject it here.
6 As I pointed out previously, the petition provided an example to
7 provide an example of how you could use the seven nucleotide barcode in
8 conjunction with *Linnarsson* to do the tagging. That was an example. It
9 wasn't limited to seven nucleotides. And for them to come in later on and
10 say, hey, someone of skill in the art would read *Linnarsson* and think it's
11 limited to seven and think that when you set an example you were limiting
12 your case to seven, that would, again, turn obviousness on its head.
13 And what I recall from the previous IPR oral argument is that the
14 Board didn't accept that. The Board didn't accept the notion that by
15 providing an example of using seven and pointed the example of using seven
16 that we're locked into seven and someone with skill in art wouldn't know
17 that you can use more than seven. It's a fair response to say, hey, the notion
18 that we're limited to seven and that *McCloskey* is only limited to seven, that's
19 inaccurate and that turns obviousness on its head. Someone of skill in the art
20 would know how to use more. And in fact, *McCloskey* does post -- disclose
21 more. That was fair. That was fair then and it's fair now.
22 And I think that there's not really any other material difference
23 between this case and the '981 case or the '197 case that merits further
24 discussion at this point. So I'm going to stop now and let them respond, and
25 then I'll address anything that comes up in reply, for which I reserve 15
26 minutes. Unless there's questions.

1 JUDGE FITZPATRICK: No questions. Thank you.
2 MS. RAYMOND: Thank you, Your Honor. May I proceed?
3 JUDGE FITZPATRICK: Please. Thank you.
4 MS. RAYMOND: Thank you. As with the '197, while we'll likely
5 cover only certain of the disputed issues today, again we rely on and stand
6 by our objections, arguments, and evidence that we've put forward in the
7 proceeding, in our brief, and other submissions. Unless the Board has other
8 guidance as to how they'd like to proceed, we'll plan to start with ligation,
9 which I will cover, and then Mr. Baughman will address some of the other
10 issues that Mr. Walter just covered, as well as the motion to exclude.
11 As a more general matter, we won't plan to walk through the
12 arguments that we just made for the '197, of course, unless Your Honors
13 have additional questions or would like us to.
14 So then turning to ligation, the bottom line is they haven't shown a
15 benefit that comes out of making all of these modifications. And if we turn
16 to slide 2,7 in the petition they just argued you'd ligate. Right? They don't
17 include in their grounds any art disclosing ligation. They do provide an
18 example of *Hug* providing a way that tags can be ligated, generally without
19 an explanation of how it would work in *Linnarsson*. And they say that this
20 ligation would allow "added flexibility." That's the benefit. That's why
21 they're saying you would ligate.
22 In the Patent Owner response, we pointed out the biotin issues with
23 ligating the CDS, and I know we've talked about those before. We pointed
24 out issues regarding ligation to the TSO, issues with incompatibilities
25 between *Hug* and the petition theory. And we explained how the biotin
26 fragmentation and capture disclosure of *Linnarsson* is not optional. But

1 also, importantly, we pointed out their flexibility argument and that even
2 though they said, you know, ligation would allow you flexibility, it didn't
3 identify any benefit of that flexibility.
4 If we turn to slide 59, in the reply they proposed more modifications.
5 They repudiate the petition that drew a box around a CDS with a biotin and
6 identified it and relied on it as the CDS that they were ligating to. And they
7 made additional changes that create more complexities and have more issues
8 and create other inconsistencies. But importantly, once again, they said, you
9 know, you would have this benefit of flexibility because the reason why
10 flexibility is good is because it would let you know mid experiment that, you
11 know, you could add a shorter tag and you wouldn't waste reagent. So
12 again, it creates flexibility so you can have shorter tags and not waste
13 reagent if you have fewer molecules.
14 But here's the problem. The problem is that you don't magically
15 discover in the middle of *Linnarsson* how many tags you need. You don't
16 know. So this idea that there would be a benefit to being able to somehow
17 make shorter tags doesn't make any sense because it's not until you get to the
18 end of *Linnarsson* that you figure out how many molecules there actually
19 are. So this whole idea that there would be some benefit by, you know,
20 being able to make a shorter tag at the ligation staff as opposed to making --
21 you know, having a shorter tag earlier, it just -- it simply doesn't make any
22 sense.
23 And if I could touch on a couple other issues here, they also argue
24 you don't need biotin, right? You could change *Linnarsson* and remove the
25 biotin where it's not necessary. But again, why are they continuing to rely

1 on figure 11 if the biotin isn't required? This biotin, of course, has
2 advantages. Biotin is how you purify and they're removing that.
3 And I think I heard Mr. Walter say that -- I think he talked about Dr.
4 Quackenbush's testimony and criticized Dr. Quackenbush for not
5 considering whether you could remove or change the biotin that was -- you
6 know, whether you could remove or change the biotin. And again there,
7 there was no such theory that had been presented for Dr. Quackenbush to
8 respond to at that point. That's a burden-shifting attempt.
9 And finally, an argument that someone could modify it by their
10 expert doesn't meet their burden. If we could turn to slide 60 -- excuse me,
11 slide 29 in this proceeding and talk a little bit about *Hug*. And this also
12 relates to this argument that you can make a shorter tag.
13 So while they argue for a motivation that allows this shorter tag and
14 less racist reagent, *Hug* uses an entire additional linker molecule. And part
15 of what we said in our Patent Owner response is you couldn't use *Hug* to
16 ligate, you know, the molecule of *Linnarsson* right to the ligated tag. And
17 they say, oh, wait, that's no problem because *Hug* uses a linker molecule.
18 Okay. So now we have a modification, a proposed, you know, motivation
19 that says use less reagent and now we have to use more reagent.
20 And another thing they say is, oh, well, you said that there was a
21 problem with how you would actually basically connect the tag to the
22 *Linnarsson* molecule. And they say, oh, you could use some non-random
23 portion of *McCloskey*'s barcode. What is that? So now are we now adding
24 to *McCloskey*'s barcode? They've argued you could have a shorter molecule,
25 you could have a shorter tag by using ligation, and now we're making a
26 longer tag in order to ligate? It just makes no sense. And I'd invite you to

1 look there at Exhibit 1070, paragraph 77 and paragraph 93 on page 73
2 talking about this modification and design to *Hug*'s linker molecule. Fails to
3 ignore *Hug*'s --
4 JUDGE FITZPATRICK: Ms. Raymond?
5 MS. RAYMOND: Yes?
6 JUDGE FITZPATRICK: What's the benefit to your client's invention
7 to having that step involving ligating the second tag? How do they do it?
8 MS. RAYMOND: Your Honor, I don't know the answer to that
9 question, but I'm happy to think about it and try to give you an answer on
10 reply.
11 JUDGE FITZPATRICK: Thank you.
12 MS. RAYMOND: I apologize. With respect to the -- again, with
13 respect to these modifications that are required by *Hug*, *Hug* requires this
14 BamHI restriction site to create a site for the linker to attach to. And again,
15 they haven't identified any such site in *Linnarsson*, nor have they proposed a
16 modification to *Linnarsson* that require that. And again, this is yet another
17 thing you'd have to change, more reagents you'd have to use in order to
18 introduce this cite in order to do this ligation.
19 And in addition, they say, of course, ligation is so simple. But even
20 just using their chosen example of *Hug* shows that ligation of a random tag
21 to *Linnarsson* is not so simple. You know, just as a reminder here, of
22 course, we're not simply ligating the same thing. You know, we don't have a
23 bunch of the same thing that we're ligating a bunch of tags that are all the
24 same to. We need -- we're talking about ligating these randomly generated
25 tags to the polynucleotide. So we're not going to be able to use unless you
26 somehow change the tag. And I guess you have this non-random sequence

1 that they've now added in, you can't -- and I guess what I'll -- I'll get into
2 some details, which is that when you cut with this restriction enzyme, you
3 end up with what's called a sticky end. And that's basically you have these
4 two. You have a DNA molecule, right, with two strands and you've ended
5 up with one strand that sort of sticks out more from the other.
6 And this ligation process in *Hug* involves you basically -- you take a
7 linker molecule and you add the linker molecule to the shorter strand and the
8 linker molecule anneals, it matches up to the bottom strand that's longer in
9 the overlapping part where, you know, the C's match the G's and the T's
10 match the A's. You anneal that and then you can ligate that new linker to the
11 top strand of the DNA. So what you need is you need a linker that's going to
12 match up to the end of the molecule that you're ligating to.
13 And so, you know, this is all -- and that's again another process that
14 you have to go through, more reagents, more complications, more
15 opportunity for issue. So they haven't shown that a POSA would go through
16 all these modifications, especially when this flexibility benefit they point to
17 of shorter tags doesn't exist and is, frankly, internally inconsistent with the
18 arguments that they've made.
19 And just to note, too, I think I heard Mr. Walters say that there are
20 only two ways that you could add a tag. I just note that, of course,
21 *Linnarsson* itself talks about, you know, you can add a tag to the CDS or the
22 TSO or both, for example. *Linnarsson* itself says you could insert a tag.
23 And then we're talking about ligation. But again, you know, the question of
24 how you would do this ligation, it's not that there's one simple way that you
25 would do this ligation. It's, as you can see, this ligation to *Linnarsson* is a
26 complicated process.

1 Finally, or maybe not finally quite, but I'd like to just draw Your
2 Honors' attention to *ExtractionTek*. I think that we've seen an attempt by
3 Mr. Walter today to sort of try to wash out any requirement to show
4 motivation to combine or reasonable expectation of success because linear --
5 or because ligation is known in the art. But you know, as *ExtractionTek*
6 says, a person of skill would have to make changes to implement a teaching
7 and this Petitioner failed to explain what the changes the person of ordinary
8 skill in the art would have made. They need to explain the reasons why you
9 would make all these changes and, frankly, they need to explain a benefit.
10 And once you look at these changes there is no benefit to the ligation here.
11 And unless Your Honors have questions, I know we have the one
12 pending question, I will turn it over to Mr. Baughman.
13 MR. BAUGHMAN: Thanks. And I want to just touch briefly, I don't
14 want to repeat things that we've done already in the '197 proceeding, just as
15 Mr. Walter acknowledged has happened.
16 I do want to say that in terms of how many tags are needed the same
17 three changes of record are present here. Two of them are explicit changes
18 in '013 from what was in '981. So again, just as in '197 Petitioner mapped to
19 mammals for the same sample coming in from claim 1. Again, Petitioner
20 mapped to tissue of interest and didn't point to those extra lines that came up
21 in reply about other theories for prokaryotes and bacteria and so forth. Still
22 don't have enough tags. But that first prong of the '981 decision is again
23 contradicted by what they did here.
24 The second prong is based on the admissions that we talked about in
25 the '197 proceeding. They're in '197 but they're admissions about
26 *Linnarsson* and not some other reference that isn't at play here. And there

1 are admissions about why it's important for gene expression analysis and
2 how a person of skill would interpret *Linnarsson* knowing what its purpose
3 is, knowing the disclosures that they're relying on here, which are the same
4 ones they relied on in '197, why it matters.
5 And again, if we hear again about that boldface word, the end of that
6 phrase on page 105 of Dr. Cooper's declaration, Exhibit 2022 here, says,
7 "All or parts of the mRNA content of a tissue is being increasingly used."
8 It's not limiting or characterizing *Linnarsson*. It's just it's not an argument
9 that belongs here.
10 And then the third piece about tagging seven, relying on the seven-
11 nucleotide barcode that's actually in *McCloskey*, again, that's what happened
12 here. I don't think if you actually look at the Cooper declaration that cites
13 the two parts of figure 1 showing the seven positions calling it the barcode, I
14 think it's page 33 of the petition, that's what's being brought in. That's what
15 they relied on. And again, unlike in '981, here we have an explicit change in
16 ground when they wanted to adjust, where for the first time they bring in the
17 4 to the n formula and use *McCloskey II* to say you can get to 20 or 30. So,
18 again, we have that juxtaposition that we would argue it's revealing for '981
19 as well, but understanding it's not in the record there as an argument for '91,
20 it certainly is in the record here.
21 So those three things I just wanted to mention in terms of *McCloskey*
22 having enough barcodes, the same arguments apply here.
23 In terms of the motion to exclude, I did want to touch on some things
24 that are different here as well. Give me one second because I put the wrong
25 pile in front, so pardon me.
26 JUDGE FITZPATRICK: Before we get into the motion to exclude --

1 MR. BAUGHMAN: Yes, Your Honor.
2 JUDGE FITZPATRICK: -- is there any argument to the contrary that
3 ligation, in this context, ligation to polynuclear nucleotides, ligation of tags
4 to polynucleotides was not known at the relevant time, pre-critical date?
5 MR. BAUGHMAN: I think I defer to my colleague, Ms. Raymond,
6 on that because it sort of falls into the arguments she's been making.
7 JUDGE FITZPATRICK: (Inaudible; overtalking 2:16:07) her answer,
8 and I would direct her to that. You know, Mr. Walter had like some
9 excerpts from the deposition of Dr. Quackenbush. Is there some explanation
10 to say, hey, wait, this is -- he's talking about totally something else, this is
11 out of context, or is he saying what it looks like he's saying?
12 MS. RAYMOND: I don't think there's any dispute as to whether
13 ligation itself was known at the time, Your Honor. The question is you have
14 two very particular things that are being combined here and using ligation to
15 combine those two particular things, or, you know, they have -- using
16 ligation to combine these types of two things together has not been
17 established as being, you know, known and, you know, typical and well
18 used. I mean, I think one of the distinctions in *I/P Engine*, for instance,
19 which I know Mr. Walter was relying on, is that there, the way in which the
20 combination was used was routine, and here they're proposing something
21 that makes it vastly more complicated. And there hasn't been anything to
22 establish that, you know, for instance, ligating these -- again, there's this
23 complication that you're trying to ligate a whole bunch of tags, each of
24 which are different, to a whole bunch of polynucleotides, each of which are
25 different. And as part of that process you need to do some matching up of

1 sequences in order to get them to overlap so that you can get them to anneal
2 to each other and then you can ligate.
3 And so this isn't -- you know, I used to -- and I apologize for this
4 maybe diversion, but I used to work in a lab where we did, you know,
5 ligation and we would cut the DNA and we would -- and this wasn't the --
6 for us at least, this wasn't the way and the reason why we would use ligation.
7 This would have been a much more complicated thing than just say I'm
8 going to take -- you know, usually you take a batch of something, you cut it
9 with a restriction enzyme. So you have in *Hug* it would be BamHI right?
10 And then you ligate all the same things to those sticky ends, all the same
11 tags. But here we have different tags that we're ligating. They're all -- the
12 whole purpose, right, of the *McCloskey* tag that we're trying to add is the
13 *McCloskey* tag is randomly generated. And so the ends of those tags -- most
14 of the ends of those tags are not going to be the same.
15 And I appreciate that Parse has now tried to argue that you would
16 use some sort of non-random portion at the end of *McCloskey*, but, frankly, I
17 don't know what that is. I don't see where that disclosure is in *McCloskey*.
18 And again, that would make this tag longer, you know, not shorter, which is
19 what they say this, like, flexibility benefit would be.
20 JUDGE FITZPATRICK: To the extent I'm following all of that, it
21 sounds like -- I mean I could definitely -- a message that's definitely getting
22 across is that it would be very tedious. But I don't know if that translates
23 into, you know, into, you know, countering that, you know, there will be no
24 reasonable expectation of success because they have -- there seems to be like
25 a significant amount of evidence to say that ligation in this context is
26 conventional ligation in gene sequencing and gene analysis, and, you know,

1 working with polynucleotides. That ligation is not just known but
2 conventional and was in the past before the critical date. And it sounds like
3 it would be very tedious to practice or to have, you know, modified the
4 asserted prior art to, you know, render claim 1 obvious. But it doesn't -- but
5 the tediousness of it, I don't know if that translates into making it not
6 obvious.
7 MS. RAYMOND: I think the issue is the tediousness of all of it. And
8 I don't think, frankly, we've seen them explain actually how you get all the
9 way from point A to point B with this ligation. Every time we come up with
10 an issue, they say, okay, modify it a little bit more, modify it a little bit more.
11 But, you know, again, the question is, is there -- there still has to be a
12 motivation, right? And there has to be a motivation in view of what your --
13 what the proposed modification is. If the proposed modification is very
14 complicated, then this benefit that they're saying, which doesn't even pan out
15 as I've stepped through, but this benefit of flexibility because you can have a
16 shorter tag, even if we assume for a moment that you could somehow have a
17 shorter tag, they haven't shown that it would be worth -- that that small
18 amount of flexibility, again, I dispute that there is flexibility, that that small
19 amount of flexibility would be worth it.
20 To go through all of this like complicated, tedious, you know,
21 process of making all the modifications you would need to *Linnarsson* and
22 making apparently the modifications you would need to *McCloskey*'s tag to
23 have, for example, a non-random code at the end of *McCloskey* in order to
24 ligate them together. And we know, I mean, *Linnarsson* itself says you can
25 insert tags. So like, why aren't we inserting them? You know, we've already
26 seen *McCloskey* is saying, you know, you can add the tags on the CDS or

1 TSO. So without there being a real, you know, a true benefit to making this
2 modification, that benefit has to be looked at in view of all the complications
3 that are caused by doing this addition in this way.
4 JUDGE FITZPATRICK: What if we -- what if I, you know, at least
5 hypothetically, just said, I agree there's no benefit or no net benefit to doing
6 this? I don't know if that for sure takes away their reason for the
7 combination because they also cite law that suggests that you don't need to
8 articulate a specific benefit to make a modification when the modification is
9 substituting in something that was conventional or implementing something
10 that was conventional. So what would be the response to that? Forget that
11 that --
12 MS. RAYMOND: Respectfully, Your Honor, that's not how I read
13 those cases, I read those cases to say if you're going to make a change, you
14 still need a reason to make those change. And with respect to the sort of the
15 design --
16 JUDGE FITZPATRICK: I agree and that's what I said, you still need
17 a reason. But the reason I think is built in. The reason is that it was
18 conventional. But what I'm trying to separate is reason from benefit. Let's
19 say for this hypothetical I agree that this benefit seems too attenuated to do
20 all this tedious work. And in reality, this person of ordinary skill in the art
21 wouldn't have done It. But -- you know, for that -- for this benefit, wouldn't
22 have gone through all this work for this benefit. But there's -- I think there's
23 a problem still in that the law says that if something is conventional, it's
24 pretty much obvious.
25 MS. RAYMOND: So I believe, Your Honor, perhaps what you're
26 referring to is the design choice law, which I don't think we've seen design

1 choice presented in the context of something like molecular biology, of
2 course.
3 JUDGE FITZPATRICK: It was a case, you know, and I'll ask Mr.
4 Walter to put it up when he comes up, it was a case that I've seen today and
5 I've seen in the briefing. But so it wasn't a necessary design choice. It was -
6 - I think it was right out of *KSR*. It's a quote from *KSR*.
7 MS. RAYMOND: Mm-hmm.
8 JUDGE FITZPATRICK: In fact, I'm sure of it. You know, for the
9 benefit of this and just, you know, did not -- Mr. Walter, do you -- can you
10 tell us the slide that that's on, if you know it?
11 MR. WALTER: Yes, in just a moment. It is -- yes, it's slide 49.
12 JUDGE FITZPATRICK: Of yours in this case?
13 MR. WALTER: Yes.
14 JUDGE FITZPATRICK: Thank you. Let's pull that.
15 MR. WALTER: Do you want me to share my screen or --
16 JUDGE FITZPATRICK: Wait. Petitions. Oh, got the wrong file.
17 Okay. This is what it says, Ms. Raymond, I don't know if you're on it, but I
18 can read. A person of ordinary skill "has good reason to pursue the known
19 options within his or her technical grasp," such that Section 103 bar, the
20 patentability of obvious variations. So I apologize, it did not use the word
21 "conventional". But this is what I was thinking about.
22 MS. RAYMOND: Sure. I mean, I don't think this gets us there, Your
23 Honor, because this -- there's also this requirement of anticipated success.
24 And I also think you -- I mean, if we take this to the extreme, then this
25 means at any time we have a known option, it's going to be obvious. Right
26 I mean, that's -- the second -- the secondary references are always a known

1 option. I don't think *KSR* does away with the requirement that there has to
2 exist a motivation to combine the various prior art references.
3 JUDGE FITZPATRICK: Okay.
4 MS. RAYMOND: Yeah.
5 JUDGE FITZPATRICK: I don't think we can hammer it out
6 anymore. Yeah. And I just wanted you to respond to it. It sounds like the
7 parties agree that this is conventional and known. And so it may be an
8 uphill battle, but.
9 MS. RAYMOND: And, well, I mean, maybe what we'll say to that is,
10 yes, ligation on its own, again, is conventional and unknown. But the
11 known options to add a random tag, you know -- the way I would frame the
12 question is, were there known options as to how to add a random tag? And I
13 think by virtue of the discussion about how complicated it would be, saying
14 this is just something that would be -- that was out there and you could
15 easily reach on the shelf floor is perhaps a stretch.
16 You wouldn't use -- there wouldn't -- you know, if you look at your
17 different options that are out there, there would be no reason to reach for
18 ligation because it would be complicated. You could use the CDS and the
19 TSO, you could insert a tag. But, you know, of the known options, why
20 would you go out there and reach for something that has no, again, in my
21 view, no benefit and that greatly complicates the process?
22 You know, they've said themselves that it's good to have, you know,
23 fewer reagents. Why would you now go and introduce all of these reagents
24 through this process? I don't think that we can. We can't look at this in a --
25 with our blinders on, right, as if, you know, this was the only way to ever
26 accomplish it. And I agree. I understand. I appreciate their arguments.

1 And the case law that says it doesn't have to be the best way to do -- you
2 know, an obviousness combination doesn't have to be the best way to do
3 something, but you still have to have a motivation to do it that way. And
4 what we're saying here is there would be no motivation to do it that way
5 because it is so complicated and because there are not benefits.
6 JUDGE FITZPATRICK: Thank you. And if, before you guys go, if
7 either of you could tell me why the Patent Owner does it, that might be
8 helpful.
9 MR. BAUGHMAN: Could I quickly add something to the design
10 pattern?
11 JUDGE FITZPATRICK: Yeah.
12 MR. BAUGHMAN: And if there's time to reach the motion to
13 exclude, I'd love to. I don't know where we are on time, Your Honor. If
14 there isn't, I understand that as well.
15 Two things I wanted to just add that *Virtek* is a cite for the
16 proposition that *KSR* doesn't get rid of the requirement of a motivation to
17 combine. I think we've cited that to Your Honors.
18 I heard Mr. Walter talk about the *ACCO* case. I just want to remind
19 everybody what that that is. And it's representative of the design choice law
20 he's citing. This is a sensor and a paper shredder. Do you put a thickness
21 sensor before or after the pressure sensor? That's the choice. There are only
22 two places you could possibly put it, and is it A or B? That is absolutely not
23 what is happening here with ligation. It's like saying, you know, taking that
24 sensor here or there into something like, how do I detect anything? Is
25 detecting anything an option? The ligation possibilities here are just not
26 comparable to these mechanical cases that Mr. Walter is citing.

1 And if I could turn to the motion to exclude, I'm happy to do that. I
2 don't know where we are in time, Your Honor.
3 JUDGE FITZPATRICK: You got time. I think you got about -- I
4 think, doing my math here, I think you got 16 minutes, actually.
5 MR. BAUGHMAN: Great. Thanks, Your Honor. Our slide 53, I
6 want to talk about something where the record has changed a little bit. The
7 question I want to raise is about *McCloskey* and whether *McCloskey* itself
8 should be excluded here.
9 Looking at their reply brief at page 4, their argument here is that
10 *McCloskey* is an online publication, published online in October 2007.
11 They're not arguing the print copy.
12 And if we turn to our slide 54, you know, I know the Board's
13 familiar with these arguments. They don't have any kind of declaration.
14 They thought they needed one. They put one in. But it doesn't say anything
15 about *McCloskey*. Apparently, it's from the wrong proceeding. So there's no
16 admissible evidence with the petition that *McCloskey* was ever disseminated
17 or made publicly available under the Federal Circuit's test for what that
18 means as of the priority date in 2009. The date on the face of *McCloskey* is
19 hearsay. And even if it were considered, that date alone wouldn't show
20 actual accessibility for this online document.
21 And I think it would be helpful just to call out the *Medivis* (phonetic
22 2:30:16) case we've cited to Your Honors. If we could actually put up, yeah,
23 footnote 6 here. The document that was excluded by *Medivis*, this is, I
24 think, in March of this year, was actually supposed to be a purported journal
25 article. Okay. So it isn't something handwritten or just some webpages. It's

1 a journal article. And there was a -- it was a copyright date that was cited.
2 That wasn't enough.
3 And so turning back to our slide 55, what did they do here when they
4 realized that because we briefed it, that their declaration was the wrong one?
5 They responded to our reply citation basically saying there's no evidence
6 with a brand new declaration, I know Your Honors know this, improperly
7 incorporated by reference. And *Medivis*, again, says you can't do that. You
8 can't just say, here's a new declaration, period. If they want to rely on things
9 from the declaration, they have to say it. As we demonstrated last time and
10 the Board found it should be excluded because it's late and it's certainly not
11 responsive to something we said. Just like in *Sirius XM*, we just pointed out
12 the failure.
13 Turning to our actual motion on slide 56, our slide 57, we objected to
14 *McCloskey* itself, the underlying prior art reference as irrelevant and its date
15 as hearsay. And what we said, because I'm hearing complaints about this
16 now, to the extent the Petitioner attempts to rely on any date that may appear
17 in Exhibit 1004, that's *McCloskey* to establish public accessibility as a
18 printed publication, any such data is hearsay. So we got printed publication
19 cheat up right there. And what are they relying on? The data is hearsay.
20 They failed to serve supplemental evidence within the time period it was
21 required. They were more than four months late and they didn't ask the
22 Board's permission. So let's look at the hearsay issue because it's never been
23 addressed. It's not addressed in the '981 final written decision, respectfully.
24 Turning to our slide 58, there is no hearsay exception that they've
25 ever identified that would let them rely on the publication date to show the
26 truth of what's asserted there. And we actually went and looked in the

1 declaration that they thought they needed and put it on reply, but it was
2 improper and they never sought permission For. Dr. Hall-Ellis referred to
3 three websites where she said what this online thing might be. We went to
4 the Wayback Machine and looked. The earliest you ever get is 2016. So
5 there's no evidence of any kind in the record of public accessibility as of
6 2000, even if you look at the date on the face of it.
7 If you look at our slide 59, the conventional markers of publication
8 arguments they're making are not about hearsay or proving public
9 accessibility. And they don't point to any evidence other than the date that
10 actually gets them where they need to be in 2009. So let's look at their slide
11 167.
12 This is what they're pointing to. Each of these is a date on the face
13 of this online document, and they're relying on it for the purported truth of
14 the matter.
15 Turning to our slide 60. What does *Medivis* say about that in 2024?
16 Anybody can say I'm available online on a date. It's not good enough. And
17 even if it were online on a date, that's not good enough either. You have to
18 show that it was actually published and made available to the extent that
19 people interested and of ordinary skill could get it. That's what the Federal
20 Circuit tells us. And we put law about that in our motion. Let's see what
21 they said about it in response.
22 This is their opposition to the motion to exclude, page 9. This is
23 paper 40. At the bottom here they're talking about the *Acceleration Bay*
24 case. This is how they conceded it came out. A reference wasn't publicly
25 accessible because it was uploaded to a website. But it wasn't a reputable
26 publisher and only provided a list of authors and years. So the search feature

1 was deficient and it wasn't functionally available for the purpose of the
2 Federal Circuit test of being reasonably available to those who needed it. So
3 the only evidence here that they're relying on of public accessibility is a
4 hearsay date on the face of *McCloskey* itself. I'll come to the three
5 documents that they're talking about as sort of corroborating that. But none
6 of them show anything in 2009
7 On slide 61, *Schlumberger*, a copyright notice doesn't establish when
8 something was publicly accessible for patent law. It's on the left. *Celltrion*
9 on the right, merely demonstrating publication on the Internet isn't good
10 enough.
11 Now let's look at their other couple arguments. The *McCloskey II*
12 argument wasn't one they made in the '981. It was the basis for the Board's
13 ruling, but we didn't have a chance to brief it because nobody briefed it. But
14 if we look at slide 62, they're arguing it now affirmatively in their paper.
15 We responded to it.
16 Their argument is that because *McCloskey* had what appear to be
17 similar authors and might have been writing about the same subject matter,
18 that means that anything else like that was publicly accessible as of
19 *McCloskey II*. That just can't be the case. You know, *McCloskey*'s authors
20 could have written about the same subject matter in a lab notebook. And the
21 fact that *McCloskey II* was available doesn't mean that the lab notebook was.
22 It certainly doesn't show it as of the time required.
23 And the Fodor patents that they're talking about are both after the
24 critical date. So they're not even making mention of this cite until 2010 or
25 2014. We don't have any proof of public accessibility of the online
26 document as of the critical date.

1 And slide 61 just repeats the points that confirm the Hall-Ellis
2 declaration should be excluded. It was four-plus months late. There's no
3 reason to waive the requirements. They didn't even ask for permission and
4 they waited five months.
5 I guess I'll close with their slide 176. They talk about indicia
6 supposedly confirming publication. The only one here that I think isn't just a
7 hearsay statement from *McCloskey* itself is this idea of citations in the
8 literature. And again, those are too late and don't prove accessibility of this
9 document.
10 Their slide 178. All the cases they cite have more evidence than just
11 a single copyright date on the face of the document that we have here. They
12 cite copyright evidence in the -- Copyright Office evidence in the *Vidstream*
13 case. On slide 175, their *Trend Micro* case isn't even a hearsay case.
14 Respectfully, there's no evidence. They've never tried to show that they can
15 satisfy the hearsay exception and *McCloskey* itself should be excluded.
16 Happy to pass back the podium to Ms. Raymond. I don't know if we
17 have something further to say or not. Unless there are any questions on this,
18 Your Honor.
19 JUDGE FITZPATRICK: No questions.
20 MS. RAYMOND: I'd be happy to do it in rebuttal. I'm trying to sort
21 out a couple of items on this end.
22 JUDGE FITZPATRICK: Okay. So I think it -- you know, I'll just
23 point out that I have not heard a reason why, although I would love to know
24 why Patent Owner ligates, why they do that step of ligation that's in claim 1.
25 Maybe you can get to it. Is that an answer that you guys want to provide or
26 you can't provide?

1 MS. RAYMOND: Your Honor, I -- if your question is why do -- why
2 does -- I take that question as the (inaudible; overtalking 2:37:23).
3 JUDGE FITZPATRICK: Not -- yeah, you can exclude -- I'm sorry,
4 you can exclude businesses purposes and whatever. I'd just like what is the
5 benefit of doing it if there -- if it -- you know, if there's no benefit to doing it
6 with the prior art?
7 MS. RAYMOND: Right. I think there may be very particular use
8 cases where adding the tags in various steps can allow one to include error-
9 resistant tags at each step. Of course, here we're adding *McCloskey*, which
10 gets rid of the error-resistant tag, aspect of the tag. But the combination of
11 each of the tags added in multiple steps can allow for unique identification
12 of polynucleotides with potentially more precision and might avoid errors
13 that could be introduced during, you know, an amplification step. And I
14 don't know if this approach would be advantageous in all the situations, but,
15 you know, the addition of tags in multiple steps, including by ligation, might
16 have benefits for particular approaches.
17 I think in the patent we see a little bit of disclosure in column 7, in
18 lines 24 to 26, talking about MIDs can be generated in a variety of different
19 ways, e.g., by combinatorial tagging approach in which one MID is attached
20 by ligation and a second MID is attached by primer extension. Thus MIDs
21 can be designed and implemented in a variety of different ways to track
22 polynucleotide fragments during processing and analysis, and thus no
23 limitation in this regard is intended.
24 So I think we're simply trying -- you know, we're trying not to be
25 limited here in the reasons why someone, you know, someone might do it.
26 Of course, this isn't in the record. They haven't said that's the reason here.

1 But I think, you know, there could be use cases where it would be
2 appropriate. I don't know that this is that use case. I don't think there's any -
3 - there's nothing in the record to address that, and so we'd have to speculate
4 that.
5 JUDGE FITZPATRICK: Thank you. I appreciate you answering
6 that. I know it wasn't part of the record. No questions from me. Can we
7 turn over to Mr. Walter then?
8 MR. WALTER: Yes, Your Honor. Thanks.
9 JUDGE FITZPATRICK: All right.
10 MR. WALTER: Your Honors, can you see my slide?
11 JUDGE FITZPATRICK: Yes, but before -- while we stay on the
12 same subject, if I could interrupt right from the get-go. Presumably, your
13 client has been accused of doing this ligating, since this, I believe, claim 1 of
14 this patent is asserted in the related lawsuit. Am I correct in that
15 assumption?
16 MR. WALTER: That's right. Yes, we're accused --
17 JUDGE FITZPATRICK: Okay.
18 MR. WALTER: -- of infringing.
19 JUDGE FITZPATRICK: And if -- you know, I'm sure you're
20 pleading non-infringement, but is there -- is this -- if, in fact, you do a
21 process that involves ligation, why? If you can answer that.
22 MR. WALTER: Right. So, you know, the answer, Your Honor, is
23 that it's basically the rationale that we have been providing and that Dr.
24 Cooper has been providing. This is a conventional way to add tags to DNA
25 molecules that gives you flexibility during the course of your experiment.

1 That's why. And that's something that people have known for quite some
2 time.
3 I think what was telling on this, you asked the same question to the
4 Patent Owner, and, you know, they later came along with some sort of
5 answer that I, quite frankly, couldn't follow. But at the beginning there,
6 there was no answer whatsoever.
7 You know, what's the benefit of litigation, you asked? And it's --
8 you know, what this reminded me of was this. This is Dr. Quackenbush,
9 what's inventive about these patents? And he says, I'm not really prepared to
10 offer an opinion today. And I kind of felt like when you were asking the
11 Patent Owner that same question, what's the benefit of ligation, and there
12 was no answer. It's kind of the same thing. There's no answer because there
13 isn't really anything inventive about it. It's a conventional technique that
14 people knew how to use, and it would offer this flexibility benefit. And
15 that's why everybody does it. And that's why everybody's been doing it for a
16 long time. That's why the patent doesn't even bother to tell you what the
17 benefit is. It's just because it's a conventional technique, it's easy to use, and
18 everybody's known how to use for quite some time.
19 You asked a question about, you know, what is the benefit? And
20 they actually -- I actually have to have -- do you actually have to have a
21 benefit? The answer is no, you don't have to have a benefit. *KSR* said that.
22 Here's another quote from *KSR*. It's discussing a case called *Sakraida* from
23 1976. And the Court says in that case, the Court derived from the
24 precedents the conclusion that when a patent simply arranges old elements
25 with each performing the same function it had been known to perform and

1 yields no more than one would expect from such an arrangement, the
2 combination is obvious.
3 That's what we have here. That doesn't say you have to have like a
4 clear benefit. That's not a requirement. There's no rigid formulation in *KSR*.
5 We got rid of that. We got rid of that. *KSR* is an open, flexible test. And
6 the reason someone would use it here is because it's an easy, straightforward
7 thing to do to add a tag. There's only a small number of options. People
8 have been doing it for years, and it does happen to give you a little
9 flexibility.
10 So I don't think there's really any question on the ligation.
11 The next point I want to address real briefly is there was a segment
12 where Mr. Baughman reiterated some of the arguments about what the
13 petition was based on. And he said, look, they relied upon mammals and
14 then they relied upon *McCloskey*. And *McCloskey*, we had seven barcodes
15 and the number of tags that would be available to tag all the number of
16 messenger RNA molecules. But if you only have seven nucleotides, it
17 wouldn't be enough. So I want to say a few things in response to this.
18 You know, first, this notion that the way someone would do obvious
19 is to say, well, look, you pointed to mammals, an example, and you pointed
20 the example of seven and seven might not be enough for every molecule in a
21 mammal, so you lose. That's not the way we do obviousness. A person of
22 ordinary skill in the art would know that the disclosure in *Linnarsson* isn't so
23 limited. A lot of the things they pointed to say you're limited to mammals.
24 It doesn't even say it's limited to mammals. It says it refers to something like
25 a cell culture. It says it can come from a tissue, it can come blood, it's not
26 necessarily limited to mammals.

1 And the whole discussion here about the number of nucleotides, that
2 was an example. I feel like I keep reiterating this. The Board was correct to
3 conclude that *McCloskey*'s not so limited. And you know, to walk in and
4 say, hey, you lose because you pointed to an example as mammals and you
5 pointed to seven nucleotides and that doesn't fit and everybody would be
6 stuck, that's not obviousness. And it was fair for us to come back and reply
7 and say, hey, look, people with skill in the art aren't stupid. They would
8 know that if you have to tag a larger number of molecules, you're going to
9 use more than seven. Our petition wasn't limited to seven and *McCloskey* is
10 not limited to seven either. That's a fair thing to say in response.
11 And for them to say, oh, my goodness, we're stuck, we had no idea
12 how to respond to the petition, that's not a fair reading of the petition. The
13 petition wasn't based on the notion that this is all about tagging mammals
14 with seven nucleotides. The petition was based on the broad disclosure
15 that's in *McCloskey* and *Linnarsson.* In *Linnarsson* it's talking about
16 analysis of single cells. It discloses a wide range of single cells. And
17 *McCloskey* is teaching generally the use of a second tag to distinguish
18 molecules within a cell. That's what the petition is based on. It's not based
19 on seven and mammals.
20 And then finally, I want to hit the motion to exclude. The issue here,
21 there's really only one issue is *McCloskey* prior art printed publication. The
22 Board already found that it was. They found that it was in the '981 patent
23 case.
24 I'm showing you slide 166. The indicia establishing that it's prior art
25 is extensive. The date the publication was received, the date the publication
26 was accepted, the date of online publishing, the copyright date, the fact that

1 it's a peer-reviewed journal, the edition identifier, the citations in the
2 literature that corroborate things, the fact that it's a reputable publisher, and
3 the fact that the document bears the overall conventional attributes of a peer-
4 reviewed publication, that's enough in this case and that's consistent with the
5 cases that we cite on this point.
6 *Trend Micro* case, here it states a date appearing on a reference is
7 sufficient when dealing with documents from recognized sources with
8 conventional markers. That's exactly what we have. The *Vidstream* case,
9 copyright registration, copyright date, presence of an established publisher,
10 listing for sale books, existence in the MARC record, all of these things are
11 things that someone could say are hearsay. But this was still accepted as a
12 printed publication.
13 And then finally, I want to address the *Medivis* case they point to.
14 Now that *Medivis* case is interesting. If you go look at that *Medivis* case,
15 what actually happened in that case was the IPR, it was either -- the decision
16 was actually either in favor of the Patent Owner or there was no institution.
17 But in that case there was actually multiple prior art references that were at
18 issue. At least two of them were not your normal, run-of-the-mill scientific
19 publications, like the *Chen* reference in *Medivis* or the *McCloskey*
20 publication that we have here. There was something else and there was a
21 legitimate question as to whether this was prior art. I think there were
22 system-type references that pertain to a system and there were references for
23 which there wasn't the conventional indicia. And the reason that case was
24 either decided in favor of the Patent Owner ultimately or not instituted was
25 really driven by these other references.

1 And there was a petition for rehearing in that case. And if you look
2 at that petition for rehearing, you look what the Board said, when you read
3 between the lines, I'm not so sure that that case really believes -- the judges
4 who wrote that decision are really fully convinced of how they decided that
5 *Chen* reference.
6 The reason that case was decided the way it was was because of the
7 other references, not really because of *Chen*. The *Medivis* treatment of the
8 *Chen* reference, that's an outlier. That's contrary to *Trend Micro*, it's
9 contrary to *Vidstream*. It's contrary to the other cases that we've decided.
10 That's an outlier.
11 So I don't have anything more unless there's questions. Otherwise, I
12 think we're done.
13 JUDGE FITZPATRICK: No questions.
14 MR. BAUGHMAN: Your Honor, can we use our brief response,
15 please?
16 JUDGE FITZPATRICK: Certainly. Yeah.
17 MR. BAUGHMAN: So if we could turn to our slide 45, please. So
18 their obviousness combination here is quite clear. There are only two
19 grounds. And the second ground is when they wanted to increase the
20 number of tags beyond 4 to the 7. So all this having a person of ordinary
21 skill change their combination, make edits, do whatever, has nothing to do
22 with the actual petition that they argued here. When they wanted to change
23 from 4 to the 7 to 4 to the 30, what did they do? They added *McCloskey II*
24 and cited 4 to the n. So I just think it speaks for itself.
25 Let's turn to their slide 176, please. I think I said this before, nobody
26 testified about any of this stuff. These indicia supposedly are all Mr.

1 Walter's interpretation from the face of the document. They're all hearsay
2 except for the citations in the literature, which are too late. If we look at
3 *Medivis*, I think we don't need to read between the lines. We can just read
4 the lines. The Board said what it said, and it's pretty clear. And I don't
5 know that Mr. Walter can vibe into a different result.
6 And if we look at our slide 40, you know, the Board and the Federal
7 Circuit have been pretty clear that if you tell a story for obviousness, you
8 have to prove that story, not a different one. This is the Intelligent
9 Biosystems case. There are others.
10 I think unless you have questions, Your Honor, or Ms. Raymond has
11 something to add?
12 MS. RAYMOND: Nothing here.
13 MR. BAUGHMAN: That's all from us, Your Honor.
14 JUDGE FITZPATRICK: Okay. Just to button this up, I'm going to
15 name both cases because this -- whatever transcript or transcripts generated
16 from today will be filed in both cases, and that's IPR2023-00955 and
17 IPR2023-00958.
18 I'm going to take a second while we're -- well, we can go off the
19 record, but I'm going to have everyone stay on and ask the court reporter if
20 she has any spelling questions that she's ready to ask.
21 REPORTER: I have all my spellings. Thank you.
22 JUDGE FITZPATRICK: Great. Well, I think that concludes our call
23 then. Thank you very much. I really appreciate the preparation that went
24 into this, and it's certainly helpful to our decision.
25 MS. RAYMOND: Thank you, Your Honor.
26 MR. WALTER: Thank you, Your Honor.

1 MR. BAUGHMAN: Thanks, Your Honor.

2 JUDGE FITZPATRICK: Have a good day.

3 REPORTER: Thank you. We are off the record at 4:03.

4 (Whereupon, the proceedings at 4:03 p.m. were concluded.)

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