

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CHARLES RIVER LABORATORIES, INC.,
Petitioner,

v.

SEIKAGAKU CORPORATION,
Patent Owner.

IPR2025-00440 (Patent 11,236,318)
PGR2025-00023 (Patent 11,959,109)

Oral Hearing Held: June 9, 2026

Before: MICHAEL J. FITZPATRICK, SUSAN L. C. MITCHELL, and
TAWEN CHANG, *Administrative Patent Judges*.

IPR2025-00440 (Patent 11,236,318)
PGR2025-00023 (Patent 11,959,109)

APPEARANCES:

ON BEHALF OF THE PETITIONER:

SCOTT MCKEOWN, ESQ.
CHELSEA A. LOUGHRAN, ESQ.
Wolf, Greenfield & Sacks, P.C.
smckeown-ptab@wolfgreenfield.com
fluo-ptab@wolfgreenfield.com

ON BEHALF OF THE PATENT OWNER:

ALEXANDER STEIN, ESQ.
CHRISTOPHER BETTI, ESQ.
ALISON SLAUGHTER, ESQ.
MARIA E. DOUKAS, ESQ.
WAN-SHON LO, ESQ.
Morgan, Lewis & Bockius LLP
alexander.stein@morganlewis.com
christopher.betti@morganlewis.com
alison.patitucci@morganlewis.com
maria.doukas@morganlewis.com

The above-entitled matter came on for hearing on June 9, 2026,
commencing at 1:30 p.m.

P R O C E E D I N G S

- - - - -

JUDGE MITCHELL: Okay, good afternoon, everyone.

We have a final hearing this afternoon and inter partes review and a post grant review, IPR2025-00440 and PGR2025-00023.

I am Judge Mitchell and with me by video conference we have Judges Fitzpatrick and Chang.

I would like to get appearances for the parties on the record, and I want to start with Petitioner.

MS. LOUGHRAN: Good afternoon, Your Honor, Chelsea Loughran from Wolf, Greenfield, and Sacks here for Petitioner, Charles River Laboratories.

With me today is Scott McKeown, also from Wolf, Greenfield, and Flora Luo, also from Wolf, Greenfield, and we have Christine Norris from Charles River Labs.

JUDGE MITCHELL: Thank you and welcome.

JUDGE FITZPATRICK: Judge Mitchell, can I interject and maybe we're going to have to have that -- I couldn't hear all that, but I don't see -- I don't have a camera on the speaker.

JUDGE MITCHELL: Oh yes, it wouldn't. I'm sorry because they're -- it's going to face me. But you'll see them at the podium.

But I'm sorry, yes, I don't know how to do that for you to see who's there.

JUDGE FITZPATRICK: Right now, I don't even have a view of podium, I don't know, so, I didn't know that that was not --

1 JUDGE MITCHELL: No, we're not.

2 JUDGE FITZPATRICK: --were not.

3 JUDGE MITCHELL: No, you need to have a view of the podium.

4 I guess you cannot see the podium?

5 JUDGE CHANG: I can see from my end in San Jose.

6 JUDGE FITZPATRICK:

7 No. So right now, I've have four windows that are just blank one,
8 and I would like to substitute that for the podium one, but I don't know how
9 to do that.

10 PARTICIPANT: Okay, how about now? Do you see the podium?

11 JUDGE FITZPATRICK: No, instead, I just lost -- I lost Judge
12 Mitchell.

13 Oh, yes, yes, yes, I have the podium, I'm sorry, but I lost Judge
14 Mitchell.

15 PARTICIPANT: There you go, yes, I believe you have it back
16 now.

17 JUDGE FITZPATRICK: Now, I have most--could you just have
18 them -- let's ask the Counsel to make -- can we have introductions when
19 you're at the podium?

20 JUDGE MITCHELL: Yes.

21 JUDGE FITZPATRICK: Then I can see who's talking and I can
22 put a face to a name.

23 Thank you.

24 MS. LOUGHRAN: Good afternoon, Your Honors.

25 My name is Chelsea Loughran from Wolf, Greenfield, and Sacks

1 arguing today on behalf of the Petitioner, Charles River Laboratories.

2 With me also from Wolf, Greenfield are Scott McKeown and Flora
3 Luo, and from Charles River Laboratories is Christine Norris. Thank you.

4 JUDGE MITCHELL: Thank you.

5 And let me see who we have from Patent Owner.

6 Go ahead.

7 MS. DOUKAS: Hi, good afternoon, Your Honors.

8 Maria Doukas from Morgan, Lewis on behalf of Patent Owner.

9 With me is Christopher Betti, also from Morgan, Lewis and I'll let
10 my co-counsel introduced herself because she will also be arguing today.

11 JUDGE MITCHELL: Great, thank you.

12 MS. LO: Good afternoon, Won-Shon Lo here from Morgan,
13 Lewis on behalf of Patent Owner, Seikagaku.

14 JUDGE MITCHELL: Great, thank you and welcome.

15 So, as set forth in our oral hearing order, each side has 90 minutes
16 to present its case for both cases.

17 Just to remind, to assist us in following along with your argument
18 and, certainly for the clarity in the record when we go back and rely on it,
19 make sure if you refer to an exhibit, you give us the number or the page
20 number to which you're referring in your demonstrative, and including, you
21 know, state the slide number.

22 And also, if you're referring to an argument that just goes to a
23 particular case, just make sure you put that on the record that you're talking
24 about one of the specific cases.

25 So, the Petitioner will present argument first as it's their burden of

IPR2025-00440 (Patent 11,236,318)

PGR2025-00023 (Patent 11,959,109)

1 showing unpatentability of the challenged claims.

2 And I want to ask Petitioner, do you want to reserve any time for
3 rebuttal?

4 MS. LOUGHRAN: Yes, Your Honor, I would like to reserve 40
5 minutes for rebuttal, please, 40.

6 JUDGE MITCHELL: Forty? Okay.

7 And Patent Owner, you will have the last word today. Would you
8 like to reserve any of your time for rebuttal?

9 MS. DOUKAS: Yes, Your Honor, we'd like to reserve 15 minutes,
10 please.

11 JUDGE MITCHELL: Okay.

12 MS. DOUKAS: Thank you.

13 JUDGE MITCHELL: And I just need to get the clock set and
14 then, when you're ready, we can begin.

15 Whenever you're ready.

16 MS. LOUGHRAN: Good afternoon, Your Honors, I'm going to
17 start with the inter partes review challenging Claim 21 of U.S. Patent
18 Number 11,236,318.

19 That will cover the petition and then, also Patent Owner's revised
20 Contingent Motion to Amend and then, I will go into the PGR.

21 May it please the board?

22 Okay, this is the challenged '318 Patent. As you can see it issued
23 on February 1st, 2022. It was filed on April 30th, 2019, and claims priority
24 through a series of identical applications to a PCT filed on December 10th,
25 2013.

1 That PCT is materially identical to the first application filed in the
2 U.S., the '767 application.

3 There's a 2012 priority document that had less disclosure than the
4 later filed application.

5 So, the core dispute in this case is whether the challenged Claim 21
6 is entitled to that '767 application filing date of December 10th, 2013.

7 And in view of that, there are two instituted grounds, when
8 afforded a correct priority date of no earlier than the actual filing date of the
9 '318 Patent, which again, is April 30th, 2019, the challenged claim is
10 obvious over prior art Mizumura in view of the '498 PCT or is obvious
11 -- and/or is obvious over Mizumura and in view of McClymont.

12 Now, Mizumura is the 2015 publication of that priority document,
13 that '767 application, that we'll talk about today.

14 So, when afforded a 2019 earliest effective filing date, the
15 teachings in that disclosure, combined with other art that published in the
16 interim, renders Claim 21 obvious.

17 Now, this is challenged Claim 21, it recites a Factor C protein that
18 has the activity of Factor C, that is more commonly produced in HEK293
19 cells, and has a particular function.

20 It has to have a residual activity in the presence of two broad and
21 open-ended ranges when the Factor C protein is in the presence of one of
22 two ionic solutions.

23 So, it covers any recombinant *Limulus polyphemus* Factor C
24 protein whose residual activity falls within either of those two open-ended
25 ranges.

1 Now, there are 21 claims in the '318 Patent, and I'm on
2 Demonstrative Number 5 right now.

3 There are two other independent claims, one and two, and a set of
4 dependent claims, but all of these other claims recite the one structural
5 limitation that the inventors offered for the functional property that they
6 claimed.

7 This limitation highlighted here wherein the Factor C protein
8 contains an α -2, 3 terminal sialic acid in a greater amount as compared with
9 the corresponding native horseshoe crab Factor C and/or corresponding
10 Factor C recombinant protein recombinantly expressed using Sf9 as a host
11 cell.

12 That limitation was added during prosecution to all of the pending
13 claims to overcome various 112 and 103 rejections.

14 However, at the very end of prosecution of this patent, Applicant
15 added Claim 21 without this greater sialic acid limitation, without any other
16 explanation or teaching as to why the recombinant Factor Cs claimed have
17 any particular residual activity value.

18 And Claim 21 was inexplicably allowed.

19 Okay, so, the petition argues that the reason Claim 21 should not
20 be afforded that December 2013 filing date of the '767 application is
21 because it does not -- that application does not describe or enable that claim
22 for the requirements of 112.

23 And we'll start with written description.

24 Now, you can search and search the '767 application for this
25 purported invention, a HEK expressed *Limulus polyphemus* protein, having

IPR2025-00440 (Patent 11,236,318)

PGR2025-00023 (Patent 11,959,109)

1 the full scope of these claimed residual activities or even an example of
2 those activities, you will not find it.

3 There's no working example that's undisputed. There is no
4 prophetic example. There's no description of this protein as an embodiment
5 of the invention.

6 Now, of course, Patent Owner is going to show you the words of
7 this claim.

8 JUDGE MITCHELL: Can you -- I am so sorry to interrupt you, I
9 think I've lost California, I'm so sorry.

10 MS. LOUGHRAN: Oh, I'm sorry.

11 JUDGE MITCHELL: Can we make sure we have Judge Chang?
12 I'm so sorry to interrupt you in the middle of your argument.

13 MS. LOUGHRAN: Should we stop the clock?

14 JUDGE MITCHELL: I'm so sorry, yes, I should.

15 JUDGE FITZPATRICK: Yes, you should.

16 MS. LOUGHRAN: Thank you.

17 JUDGE MITCHELL: Are we able to get California back?

18 PARTICIPANT: Hold on a minute.

19 JUDGE MITCHELL: Okay, thank you.

20 PARTICIPANT: We might need to work on it because she can't
21 hear us.

22 JUDGE MITCHELL: Okay, yes, thank you.

23 We should be able to get her back.

24 Can you hear us, Judge Chang?

25 JUDGE CHANG: I can hear you.

1 JUDGE MITCHELL: We just lost you.

2 I can hear you, okay, now we can hear you.

3 Okay, and I have judge Fitzpatrick.

4 JUDGE FITZPATRICK: I'm still here, yes.

5 JUDGE MITCHELL: Okay, okay.

6 JUDGE CHANG: Sorry about that.

7 JUDGE MITCHELL: Go ahead when you're ready.

8 MS. LOUGHRAN: Sure.

9 So, as I was saying there's no description of this protein as an
10 embodiment of the invention now.

11 And Patent Owner will show you the words of this claim and
12 disparate parts of the specification.

13 Now, *Limulus polyphemus* crabs were certainly known. HEK293
14 was our recombinant system that the inventors used to express all their
15 species of Factor C.

16 And the claimed residual activity percentage ranges appear in a
17 laundry list of possible such ranges unlinked to the species of the method of
18 recombinant production.

19 But the sum of that disclosure is not sufficient under cases such as
20 *Novozymes*, which hold that formal textual support for each individual
21 limitation is not sufficient where there is no description of the actual quote,
22 actual function, and composition that those limitations together define.

23 Now, Patent Owner will show you a single working example of a
24 protein from a different species of crab, but that's not what the Applicant
25 claimed here in 21.

1 And so, they get from what's in the '767 application to the subject
2 matter of this claim, additional information needs to be read into that
3 application.

4 And Patent Owner has a lot of information to read in, but it is
5 improper.

6 The thing they want to read in was not well known, and it does not
7 serve to create written description of this claim in the '767 application where
8 there is none, for two reasons, either of which is sufficient to find no written
9 description.

10 So, first, this highlighted yellow material recombinant production
11 of *Limulus polyphemus* Factor C, it's not described in the application and it
12 undisputably has not been accomplished or produced by anyone before
13 2013.

14 Patent Owner argues that despite this, it was somehow quote,
15 unquote, well known.

16 Now, was it an obvious thing to try to do? Possibly.

17 Certainly, several years later, it was likely an obvious thing to try
18 to do, and that is what animates the European opposition discussed in the
19 papers in this case.

20 But as Your Honors know, obviousness does not amount to written
21 description. *Ariad* says this as does *Lockwood*.

22 Just because a person of skill in the art could have accomplished it,
23 does not mean Applicant gets credit for it where Applicant did not describe
24 it.

25 You will see --

1 JUDGE CHANG: I have -- let me ask a question.

2 MS. LOUGHRAN: Sure.

3 JUDGE CHANG: So, I think Patent Owner does say, and I think
4 this is true, that it is not required for written description -- for adequate
5 written description to have a reduction to practice.

6 So, is it a case that the fact that no one has actually done it that
7 produced an actually competent, *Limulus polyphemus* Factor C, is that
8 dispositive for written description?

9 MS. LOUGHRAN: Well, if you don't have an actual reduction to
10 practice, if you have a claim to like genus of proteins with particular
11 function as this claim recites, you have to have one of two things, a
12 representative species, or some structural explanation for why you're getting
13 that functional protein.

14 So, if the Applicant didn't have a reduction to practice but had
15 those things, then you could -- you would be in the in the vein of cases like
16 *Ariad*, et cetera, where you could, you know, where you could say, well,
17 they had envisioned the genius, right?

18 Like *Teva* says that as, as Patent Owner has recently cited, but they
19 don't have any of that here.

20 It's not even that they don't have an actual reduction to practice,
21 they don't have a species. They don't have a structural feature explaining the
22 function.

23 And so, they can't then import what became later known into their
24 application to solve their written description problem.

25 JUDGE CHANGE: So, would it be sufficient, in your view, would

1 it be sufficient for them to say, well, if you express this particular Factor C
2 protein in this particular cell, then you will inherently result in the, you
3 know, recite that residual activity, is that sufficient for written description?

4 MS. LOUGHRAN: Well, I would say, they would have a different
5 problem at that point regarding inherency, but yes, they would have to have
6 evidence of that, which then gets to our enablement issue, which is, if they
7 had said, when you were recombinantly reproduce *Limulus polyphemus*, you
8 are always going to get something within this range.

9 That still does not suffice to show that they have enabled the full
10 scope of that range, including that they had not -- and that they had not
11 described it.

12 That would get them closer for *Teva* where the, you know, it was
13 undisputed that all of the agonists treated headache, but that is definitely not
14 what they have here.

15 In fact, the record here shows the exact opposite, it was completely
16 unclear then and today per their own experts why it is that you get particular
17 residual activities when you recombinantly express these proteins.

18 JUDGE CHANG: I'm sorry, just one more question related to
19 this.

20 Would you say it is the Petitioner's burden to show that the claim
21 is not described or is it Patent Owner?

22 There is a little bit of a burden of production and burden of
23 persuasion issue.

24 So, would you say it's Patent Owner's burden to show that it's, you
25 know, that it's inherently going to have this residual activity or is it the

1 Petitioner's burden?

2 MS. LOUGHRAN: Well, under *Tech Licensing*, it's the
3 Petitioner's burden to make the challenge, but Patent Owner does have to
4 demonstrate entitlement to that date.

5 So, they do have to come forward with evidence where they would
6 say, you know, okay, maybe we are in a *Teva* case where it is undisputed
7 that we have an example and then we have a link.

8 In *Teva*, they had an example of the humanized antibody and then,
9 they had a link to the fact that all such proteins treated headache.

10 I think that they would have to show that, yes, and then, the burden
11 would shift to us to either disprove that or call into question its credibility.

12 But here, they don't have either of those elements, they don't have
13 a representative example, and they have not shown, and they cannot show,
14 that every single protein that you express is going to fall within this specific
15 claim range.

16 So, you know, part of the burden shifting of *Tech Licensing*, they
17 have not demonstrated entitlement to that date.

18 JUDGE CHANG: Okay, thank you.

19 JUDGE MITCHELL: Are you reading the residual activity
20 limitations to be, what, 10 percent to 15 percent to a hundred?

21 MS. LOUGHRAN: Where, however, the evidence of record is
22 that they can be even higher than a hundred.

23 So, it is it is much like *MagSil* in which it is 10 percent to -- and I
24 wouldn't say infinity when I asked Patent Owner's expert this, they said yes,
25 it could be over a hundred, and indeed, you know, they point to after arising

1 evidence of unexpected results with numbers over a hundred, there is not a
2 known upper limit, it truly is an open-ended range.

3 And there's no explanation for how you get anywhere within that
4 range other than produce the protein and then, measure what you get and
5 that is not sufficient for written description or enablement.

6 JUDGE FITZPATRICK: And Counsel, I had the same question,
7 but I also have a follow up question.

8 Your denominator for making these calculations, so, with respect
9 to Claim 21, the claim we've been talking about, would be, you put the same
10 concentration or the same amount of native *Limulus polyphemus* Factor C
11 into an identical solution and measure that activity and that is that is what is
12 a hundred percent?

13 MS. LOUGHRAN: So that is unclear.

14 The record shows that there is -- there are ways to standardize to
15 calibrate these proteins. And so, you -- it would not be, you know, X
16 concentration of recombinant protein and the same concentration of native
17 protein and compare, you know, what the results you get in an ion solution
18 to what you get in *Limulus*.

19 There are all of these balancing factors about what particular
20 concentration you use for each of these proteins.

21 A lot of those distinctions are why we say their unexpected results
22 cannot be relied on. But, you know, the idea that you're that you're
23 advancing, Your Honor, is correct, it's just there is not a one to one
24 relationship between these proteins in terms of concentration and function.

25 JUDGE FITZPATRICK: Thank you.

1 And I have an unrelated question, bigger question, I -- when I read
2 the record, from the beginning, I got the sense that, when somebody first
3 discovered that these horseshoe crabs had this reaction, to endotoxin,
4 someone figured out, hey, we can use this to, you know, to -- for human
5 biological safety, medical safety.

6 And maybe it was an American that invented it or someone in the
7 Western Hemisphere and that's why it started with the *Limulus*, it seems like
8 that in the literature, it was the *Limulus* horseshoe crab that was bred and
9 harvested for this technology.

10 And yet, it seems like the advances, recombinantly, started with at
11 least one or more of the Asian species and that there is something difficult
12 about recombinant -- applying that recombination technology to the
13 American horseshoe, the *Limulus* horseshoe, you might even had -- so, it
14 sounds like you -- that that is pretty consistent with your view -- with
15 Petitioner's view of kind of the background here.

16 And then, I'm going to ask Patent Owner the same thing, but here's
17 the question, do -- what is it, in your view, that it was so difficult about the
18 recombinantly expressing, than -- let's stick with Factor C, since that's all
19 that's at stake in this case?

20 MS. LOUGHRAN: Yes, so --

21 JUDGE FITZPATRICK: And it's all *Limulus*?

22 MS. LOUGHRAN: Yes.

23 So, Charles River's expert would welcome this question, and I will
24 do my best to explain it to Your Honors.

25 Obviously, recombinant technology involves taking proteins or

IPR2025-00440 (Patent 11,236,318)

PGR2025-00023 (Patent 11,959,109)

1 gene sequences from a horseshoe crab and putting them in a hamster cell or
2 a human cell.

3 There are a lot of things about the machinery of the cell that
4 happened to try to express a protein and then express it with a particular
5 function.

6 Some of the recombinant systems, mammalian ones, have very
7 complex glycosylation profiles, that is what led to the hypothesis in this
8 patent that, if you add these terminal sialic acids, maybe that would help
9 with ion resistance.

10 You have the Patent Owner abandoned that theory, but I think
11 what my understanding of how this developed was that, you're correct,
12 *Limulus* native protein was viewed as available for the assay for a native
13 protein assay.

14 Folks on the other -- in Japan and Singapore started to work on
15 recombinant technology but ran into a bunch of hurdles, some with certain
16 mammalian cells, COS-1 was one of them, found out that a couple worked
17 in certain species of crab but ran into challenges there as well.

18 And I think the -- what was happening was that things were
19 starting to catch up with *Limulus*, that's why the research hasn't been done on
20 *Limulus* in 2013.

21 Several years later, you see the field starting to catch up with
22 respect to the *Limulus* protein and having it be recombinantly expressed.

23 And then, you see the inventors of this patent in 2016, say, ah, we
24 have finally done it.

25 You also see Karen McClymont who, you know gets her thesis for

1 having, you know, delineated that sequence, and recombinantly expressed it.

2 So, I just -- I think that there was a push in Singapore and Japan to
3 do this for recombinant expression. There were certainly difficulties,
4 particularly in getting functional protein expressed.

5 And then, when you get to 2014, 2015, 2016, they worked to
6 backfill and catch up with the *Limulus* protein.

7 And then, you see the inventors' '498 PCT where they, you know,
8 when they say we have finally accomplished it.

9 JUDGE FITZPATRICK: Thank you.

10 And can I, somewhat telling you, wouldn't want to change this, but
11 is it your position that the Asian species, in other words, it had to start with
12 them.

13 But we could also say -- and say, yes to this genomic -- what,
14 there's something inherently more difficult about the *Limulus* -- the
15 American horseshoe crab to work with those genes, to get those, you know,
16 proteins recombinantly expressed.

17 Is there something more difficult about that species or is it just that
18 the Asian species -- the technology was applied to the Asian species earlier?

19 MS. LOUGHRAN: Well, I think it's both of those things.

20 I think what he's getting -- I think it's -- let me just -- I can show
21 Your Honor in terms of evidence in the record.

22 So, yes, there was definitely a head start with the Asian species,
23 but I think what you're looking at is, you know, is sort of the variance and
24 genetic differentiation between these species because you've got a bunch of
25 them over in sort of the Asian area and they're being researched and there

1 are similarities, genetic similarities with respect to those horseshoe crabs.

2 But *Limulus* has diverged, I think it's like 130 million years ago

3 and so, the genes with respect to that crab are different. They're -- it's

4 clearly documented that there are subpopulations where there are

5 physiological differences.

6 And you know, I mean, I think from a commercial perspective or a

7 technical perspective, getting to those sequences and then recombinantly

8 producing them was, you know, was more challenging.

9 And so there were -- there was a, you know, sort of a lag in being

10 able to do it as the inventors on this patent themselves stated in 2016.

11 JUDGE CHANG: Sorry, I do -- I have two related questions, I'll

12 just ask them.

13 MS. LOUGHRAN: Of course.

14 JUDGE CHANG: So is it the case, and this is just a technical

15 question, which I am not sure about, is it necessary to have either the gene

16 sequence or the amino acid sequence in order to produce the recombinant

17 protein or is it possible, if you -- even if you did know the complete

18 sequence to be able to produce a recombinant Factor C protein from *Limulus*

19 *polyphemus*?

20 And that's the first question.

21 And the second question is, regardless of the answer to that

22 question, is it Petitioner's view -- there's a lot of evidence and both from

23 both parties about whether or not the sequences were available.

24 But is it necessary, in your view, for adequate written description

25 for either the genetic sequence or the amino acid sequence to be described in

1 the Spec in order for there to be adequate written description?

2 MS. LOUGHRAN: So, I'll take both of those in turn, Your Honor.

3 So, in terms of do you need to know the sequence? Well, they
4 claimed *Limulus polyphemus*, so they didn't claim a sequence with like a 10
5 percent variation on that sequence, where you could say, well, I know what
6 the sequence of *Tachypleus* is and I can change some of the amino acids and
7 still be within 10 percent variance and I'll just produce that recombinant
8 protein. Right?

9 No, they claimed *Limulus polyphemus*, so yes, you do have to have
10 the *Limulus polyphemus* sequence and amino acid information in order to
11 describe and enable this claim, that is how they claimed it.

12 They could have chosen a different way, but that's how they
13 claimed this.

14 Now to your second point that I was sort of starting to get to this in
15 my argument, but I'll skip right to answer your question.

16 No, the answer is no, this claim is not described, even if Your
17 Honors find that, oh, you know, they didn't really need to have this
18 sequence, or the sequence was fully well known, or they could have
19 recombinantly produced this protein.

20 If Your Honors agree with that, this claim is still not described and
21 enabled, because that's not where they stopped.

22 The inventors did not just claim that protein, they claimed that
23 protein with a particular function, and they did not describe an example of
24 that protein getting that function. They did not describe any reason or
25 structural feature or correlation of that protein to this function.

1 And as Your Honor said, there's definitely a lot of evidence on the
2 record about how a person of skill in the art would get the protein. But Dr.
3 Schaefer and Patent Owner argue that, well, the reason that you, you know,
4 can get to the residual activity is because there are similarities between
5 proteins, right, between the species.

6 Now, that is not the correct question to answer, because let me see
7 here, if I can -- sorry, if you look at Figure 7 of the patent itself and I -- if
8 you -- everybody knows what Figure 7 looks like, I say, probably, at this
9 point, you will see all those bars, all that variation of residual activity, that
10 was all for *Tachypleus*, it's a whole host of proteins were produced from an
11 identical species, they all had the same protein structure, the same motifs,
12 the same amino acid sequences, and you're seeing that variation in residual
13 activity as a result of other things such as type of recombinant system, such
14 as, you know, differences in cell culture medium, et cetera.

15 There's a very unexpected property, residual activity per Patent
16 Owner's own explanation.

17 And so, it is not enough just to have the protein in hand, because
18 they claimed this protein having a very broad open-ended range of residual
19 activities and they didn't teach those, you know, those functions.

20 This is not like a well-known genus, for example, in *Teva* or a
21 scenario like, as you as a gene model where, you know, the characteristic
22 was sort of already well known that the record evidence here is that residual
23 activity was a very unpredictable, very nuanced, and very highly variable
24 feature of these proteins, very sensitive to ionic solutions.

25 And so, to say, oh, well, just because you can say *Limulus* and

1 *Tachypleus* are generally similar in terms of their ability to detect endotoxin
2 does not lead a person of skill in the art to conclude, oh, I would get a
3 similar residual activity.

4 And indeed, when you look at the data, the residual activities are
5 quite different.

6 JUDGE CHANG: So, this goes a little bit to your obviousness
7 argument, but there are evidence on the record, I think, that, you know, the
8 similarity is something like 97.7 percent or something like that above.

9 And then, your obviousness in this case for your reasonable
10 expectation of success, I believe they argued inherency, Petitioner did not
11 argue inherency, but argued that if you compare the sequences, now that you
12 have both sequences, you will be able to reasonably expect that it will have
13 similar residual activity based on the similarity in sequence.

14 How does that -- if it's so unpredictable and it's not identical
15 sequence, why would you be able to reasonably expect that you will have
16 that residual activity?

17 MS. LOUGHRAN: So, couple answers to that, thank you for that
18 question.

19 So, again, when we're talking about the unpredictability of this for
20 purposes of whether they sufficiently described and enabled it, they do have
21 to describe and enable the full scope, and full scope requires a correlation
22 which was not provided.

23 Now when you get to 2019 and you have the sequence
24 information, you have the inventor's own admission that, per that sequence
25 similarity, a person skilled in the art would expect to get the similar value of

IPR2025-00440 (Patent 11,236,318)

PGR2025-00023 (Patent 11,959,109)

1 ion inhibition, plus you have the '498 PCT where they successfully were
2 able to express and successfully able to show that you could get this -- that
3 you could get these proteins.

4 At that point in 2019, a person of skill in the art would be able to
5 say, I don't know that I'm going to get every -- that I could get every value,
6 that I certainly can't enable that entire range, but a person would have a
7 reasonable expectation of success that they could get a protein somewhere in
8 those goal posts, and that's what's required for obviousness by 2019.

9 The field had developed by that point, more information was
10 known, success with these proteins was actually demonstrated, and that
11 informs what a person of skill in the art would have understood by that point
12 in time.

13 JUDGE CHANG: Okay, thank you.

14 MS. LOUGHRAN: Okay, so, I just -- that was a lot of questions,
15 so let me jump back into my presentation and see if I can provide some more
16 help for Your Honors and understanding this case.

17 So, just in terms of whether a person of skill in the art would have
18 known this sequence and would have known to produce for comment Factor
19 C, I think Your Honors are very aware of, you know, from the record
20 evidence, of the evidence that we have that says it was not well known by
21 2013.

22 Now, you know, it's hard to prove a negative as of 2013, but what
23 we can prove is what actually came about later, and those are the things that
24 Your Honors have seen in the record, and I won't belabor the point, but we
25 have the inventors themselves filing a patent application, not just having

IPR2025-00440 (Patent 11,236,318)

PGR2025-00023 (Patent 11,959,109)

1 later reduced it to practice, right, they have filed a patent application which
2 they have said, this thing is new and not obvious because and they put all of
3 these statements in the record.

4 And again, I'm not going to go through all of them, but there's
5 three important things about this document.

6 It says *Limulus* has not been known before, and the reason is, is
7 because there was difficulty, that you could see the last sentence of
8 paragraph 13, the fact demonstrates the difficulty in accurately determining
9 the full length sequence structures of these proteins, this gets to your -- to
10 Judge Fitzpatrick's question, there is difficulty in doing so, the inventors put
11 that on the record as support for their invention.

12 They say they had succeeded in doing it for the first time, so it's
13 the second thing that they say in this application.

14 And then, they say, we have also not just gotten this sequence, but
15 we have, for the first time, expressed it and expressed it in Factor C, Factor
16 B, and pro-clotting enzyme to demonstrate for the first time that these
17 proteins can be used to detect endotoxin.

18 So, that's what the inventors say as of 2016.

19 Now, you have -- also, you have McClymont, so independent she
20 doesn't know, to my knowledge, she doesn't know the inventors,
21 independently going out and saying, we need to understand more about these
22 proteins so that we can make recombinant Factor C.

23 She talks about contradictory results about their particular binding
24 functions, which contradicts Dr. Schaefer's opinion that all of these
25 characteristics were well known by 2013.

1 And she says the sequence of *Limulus polyphemus* Factor C is not
2 publicly available, so consistent with the inventors, the inventors'
3 statements.

4 She talks about having gone out to a database in which both
5 sequences were known, and her thesis is to create from that both bulk
6 sequence and the Factor C coding sequence.

7 And then, too, she talks about exactly how she did it. She had
8 some challenges along the way. She failed to produce it -- the sequence the
9 first time she tried again, she gets it.

10 Again, this is leading to a 2017 thesis and then, she produces
11 recombinant Factor C for *Limulus*.

12 Now, also, if we go forward a couple of years you've got the Patent
13 Owner, who is now prosecuting the claim that will ultimately issue as Claim
14 21 and they file a declaration in which they tell the Patent Office in 2020,
15 we've succeeded in cloning cDNA encoding Factor C from *Limulus*
16 *polyphemus*.

17 Now, there's the inventor filing the declaration with the Patent
18 Office saying that they have succeeded in doing something when that thing
19 is common knowledge and when they claim to have already done that thing
20 seven-odd years later.

21 Now, you can move ahead to another year, another year ahead
22 where the Patent Owner actually goes ahead and puts Claim 21, at that point
23 it was 24, on the record and we can talk about what Patent Owner said.

24 And we're now on Slide 16.

25 The Patent Owner said, because that '498 PCT gave rise to a patent

IPR2025-00440 (Patent 11,236,318)

PGR2025-00023 (Patent 11,959,109)

1 in Europe that, as I noted at the beginning of this presentation, was
2 challenged as obvious, that that getting this protein by 2016 should have
3 been obvious, would have been obvious.

4 And Patent Owner argues in Europe that claimed subject matter is
5 not obvious. They say opponent has provided a lengthy explanation as to all
6 the experiments that a skilled person could have done prior to the effective
7 filing date of 2016 to determine the sequence of *Limulus polyphemus* Factor
8 C, but that's the wrong test.

9 Opponent has failed to demonstrate that there was any motivation
10 to arrive at the claimed subject matter, with the expectation of some
11 advantage.

12 And Patent Owner goes on to say, you would not read the
13 sequence information, if you see paragraph 53, D3 is the sequence
14 information that Patent Owner put in the record, you would not read that
15 with D1, which is the '767 application, the contents of the priority document
16 to get to this claim, to get to Claim 21.

17 So, I think it's clear, as you move forward in time, all of this
18 information, the Patent Owner characterizes the sequence as unknown, and
19 they say it's a previously unknown sequence.

20 All of this information is consistent with there being a later
21 obtaining of this sequence information and recombinant production until you
22 get to 2025, where Patent Owner files Dr. Schaefer's declaration and he says
23 no, no, no, in 2013, a person of skill in the art could have done it.

24 You'll see the words, could have, a lot in Patent Owners
25 presentation. Could have is not sufficient for written description.

1 As the *Enzo* Court says, that a Patent Owner could have done it
2 was not sufficient to show that the inventor described it.

3 JUDGE CHANG: So, I have another question related to this.

4 So, the Patent Owner does cite to an EPO notice of opposition, I
5 think it's Exhibit 1048 --

6 MS. LOUGHRAN: Yes.

7 JUDGE CHANGE: -- which Patent Owner says is filed by
8 Petitioner.

9 MS. LOUGHRAN: Yes.

10 JUDGE CHANG: And in Patent '155, they do -- it does say that
11 D1, which I think is a particular document that's cited in that opposition,
12 already discloses that recombinant Factor C protein derived from *Limulus*
13 *polyphemus*.

14 And I think Patent Owner's position is that D1 is substantially
15 identical, if not exactly identical to the specs of the '767 Patent.

16 So how do you respond to that, seeing the contradictory
17 statements?

18 MS. LOUGHRAN: So, the response there is yes, D1 is the '767
19 application, but they're looking at it through the eyes of somebody in 2016.

20 And I know the slide that you're talking about, Your Honor, and
21 they use quotes around the idea that *Limulus polyphemus* could be derived,
22 that is not a quote from that application. That is a quote from the
23 prosecution history.

24 So, it's a bit misleading that they say, oh, this quote comes from
25 the application, it does not, it's just what Patent Owner had -- it was a

1 statement in the prosecution.

2 But all of this is in the context of was this claim obvious by 2017?

3 If you look at Slide 11 of Patent Owners demonstratives the quote
4 is, points the skilled person to, and I think what was being argued there was,
5 as Judge Fitzpatrick was suggesting earlier, the field was moving forward,
6 the field was definitely -- there was a lot of energy and work towards this in
7 the in that time frame.

8 By 2016, sure, it would have been obvious to get this protein.

9 By 2013, it was -- it may have been obvious, but the full scope of
10 this claim, in terms of a protein that has this unpredictable residual activity
11 value, was certainly not described.

12 JUDGE CHANG: So, I would say that, I mean, it's not just a
13 statement in prosecution, right, it's a statement in the notice, it's a quote from
14 the opposition, which I think Patent Owner says is filed by the Petitioner.

15 And that D1, I understand it's, you know, this is 2016, but when he
16 says the D1, the '767 application already discloses the recombinant Factor
17 C, that seems to suggest it's not just a question whether it makes it obvious,
18 but it actually discloses --

19 MS. LOUGHRAN: Well --

20 JUDGE CHANG: -- the recombinant Factor C.

21 MS. LOUGHRAN: Well, I mean, I think that the point there was
22 -- I mean you can look at the '767 application, it doesn't disclose it from a
23 written description standpoint.

24 I think what Patent Owner was -- what the opponent was arguing
25 there was, if you take the information that was known by 2016 and that

1 disclosure, you would say, okay, that -- nobody has, nobody -- again,
2 nobody had actually done it.

3 There's no evidence that it was done or that anybody wrote out that
4 sequence or that it was -- that it appeared in the public record, like in some
5 of the cases, the Patent Owner cites, but that person of skill in the art as of
6 2016, reading that application would say, okay, that's a disclosure for
7 purposes of this being an obvious invention.

8 JUDGE CHANG: Okay, thank you.

9 MS. LOUGHRAN: But again, Your Honors, separate and apart
10 from the question of whether Factor C was known and whether the
11 recombinant production of Factor C was known, we have the fact that this
12 claim includes a functional requirement.

13 Now, these residual activities are not described in the '767
14 application for *Limulus polyphemus*.

15 And again, as I noted before, their argument is, well, you could
16 have looked at results from the *Tachypleus* example and made an
17 extrapolation.

18 Now, that extrapolation is not backed up by the evidence. In fact,
19 the evidence suggests otherwise. Right?

20 So, Applicant got this claim by arguing that it was unexpected to
21 get any particular value of residual activity for these claims.

22 They say the factors here, the claimed invention provides
23 unexpected effects in terms of salt tolerance.

24 They -- let's see, as we said, the Figure 7 of the application
25 provides significant variants in these in these results for data from the same

1 species of horseshoe crab.

2 And then, there's a number of -- and then, Dr. Jain explains in his
3 declaration why any differences in amino acid sequence would lead a
4 personal of skill in the art to look at, with skepticism, on extrapolation of the
5 residual activity function.

6 These horseshoe crabs diverged over millions of years, structure
7 and function are highly variable, Dr. Jain explains all of this in his
8 declaration.

9 And so, I guess I'll just sum up on the written description point,
10 you know, there's no species here, there's no example, prophetic or a
11 working example, of the Patent Owners. The Applicants abandoned the one
12 structural feature that would have pointed to a residual activity correlation
13 because they, I guess, they found that that wasn't a good explanation, but
14 they didn't offer any other explanation.

15 And so, under cases like *Novozymes* then the Claim 21 is not
16 sufficiently described.

17 I know my time is running short, so I'm going to move on to
18 enablement.

19 Now, what I want to say about enablement is just that enablement
20 requires for a claim like this, enablement requires a person -- requires the
21 Applicant to demonstrate that they have just put it in a disclosure on how to
22 make and use the full scope of this claim.

23 This is an open-ended claim range, I think Your Honors were quite
24 apt in your institution decision about the fact that, in order to enable this
25 claim, you have to show, not just a single value within the scope of that

1 claim, but that you can get a value around that number, you know,
2 something moderately higher and something much higher that comes
3 directly out of cases like *Fisher* and *MagSil*.

4 And I think Your Honors were spot on in the institution decision
5 about the fact that we maybe need more factual development on this issue.

6 The point I want to make here is that there has been no additional
7 factual evidence put in on this enablement issue.

8 So, Dr. Schaefer and Patent Owner have not put in any evidence
9 that there's anything in the '767 application that you could modify or change
10 or do to drive that value higher, a little bit higher, moderately higher, or
11 much higher. There is no explanation in that application and Patent Owner
12 has offered none.

13 The evidence on this from Dr. Schaefer is found at pages
14 -- paragraphs 106 to 118 of his declaration. And if you look there, he
15 criticizes Dr. Jain. He points to aspects of the specification that show you
16 how to make a recombinant Factor C protein and measure it, but not to get
17 any particular result.

18 And so, I guess, I'll just say that the record -- the evidence has not
19 been moved down the field, so to speak, on this issue from where the
20 institution decision is, there's just no evidence that a person of skill in the art
21 would read the '767 application and understand how to get, you know, the
22 full scope of values in this range under case law like -- such as *MagSil* and
23 *Fisher* and *Butamax*, et cetera.

24 Okay --

25 JUDGE CHANG: One quick question, actually, let me ask about

1 that.

2 MS. LOUGHRAN: Sure.

3 JUDGE CHANG: So, is it -- do you -- is it -- do we need to
4 construe the claims in order to decide whether this is, in fact, a range?

5 Because I think in some cases that you mentioned, there was
6 actually either a claim construction, or the Patent Owner had adopted a
7 position that required it to be a range.

8 Is that, in your view, is that necessary and is it possible to construe
9 it so that it's essentially, I think, what Patent Owner is arguing, essentially,
10 says threshold?

11 MS. LOUGHRAN: I don't think that there needs to be a
12 construction here, Your Honor, because the claim is clear what the values
13 are. They -- these values do show up in the specification, again, unlinked to
14 any particular embodiment.

15 And it's very clear that Patent Owner points to the one working
16 example Figure 7 as an example of something that falls within the scope of
17 this claim.

18 So, I don't see there needing to be claim construction on this issue.
19 This, you know, I understand in, in *MagSil* and some of those other cases
20 there was claimed construction, but it was not necessary to the finding.

21 This claim is clear on its face, and it recites a very broad, open-
22 ended range. And Your Honors, already asking about reasonable
23 expectation of success. So, unless there are other questions on the point
24 about obviousness for the '318 Patent, I'll use my remaining opening time to
25 discuss the PGR.

1 Oh, before I get there, the revised Motion to Amend, so, Patent
2 Owner has put in a motion -- a new claim, Claim 22 in which, essentially,
3 they've rearranged to the limitations of Claim 21.

4 The only material difference is that they have included a limitation
5 that shows that -- or that that recites that the Factor C has to be higher than
6 the comparator proteins.

7 So, you'll recall when they put their first motion in, they just
8 decided that it was higher. We showed that that was broader.

9 And then they put their second motion in, and they put those
10 percent ranges back in the claim and added in this comparative value.

11 But if you look at the data in the '767 application, it's very clear
12 that their comparative values are very low. Right?

13 So, this claim covers the same scope as Claim 21, because the
14 comparators are lower than both of the thresholds that they put back into the
15 claim.

16 So, you know, for the 16 millimolar mag sulfate, both of the
17 comparators are lower than 15, and for sodium citrate, they're lower than 10.

18 So, there's no protein that would not fall within the scope of this
19 claim that would fall within the scope of Claim 21, given that information is
20 provided in the patents.

21 But even setting that aside, you know, whether it's technically a
22 little bit narrower or the exact same scope, the Patent Owner offers the same
23 evidence of written description and enablement with respect to Claim 22 as
24 it did it for Claim 21.

25 Other, you know, the word higher, higher than residual activity is

1 certainly found in the specification, but again not in any particular
2 embodiment.

3 So, they have the same problem with claim -- with respect to
4 Claim 22 as they do with Claim 21, particularly on enablement, because
5 those percentage thresholds, that range, 10 percent or higher and 50 percent
6 or higher, it's worded differently, but the claim encompasses the same scope.

7 So, how does it solve the enablement problem with this
8 amendment? It still does not describe or enable the claim, just like it did not
9 for Claim 21.

10 All right, that will get me to the PGR, same technology, same
11 specification, same priority document, same inventors, and I'll say, here's the
12 challenge, and just to level set, the instituted ground is essentially that the
13 claim -- challenged claims here are not described and enabled for some,
14 certain of the same, but also different reasons, as with respect to the '318
15 Patent.

16 And then, when they're not afforded their 2013 priority date, Patent
17 Owner is not arguing for any interim priority date, they should be afforded
18 their actual filing date, I believe 2023.

19 In that scenario, they're anticipated by the '629 publication, which
20 is the U.S. publication of the '498 PCT.

21 Now these are the claims, all of that is to say, there are there are 10
22 claims in the '109 Patent. They all depend from Claim 1 and Claim 10 was
23 independent, but this claimed all the dependent claims provide limitations
24 that do not narrow these claims in any way that solves the written
25 description and enablement issues that I'm about to go into.

1 So, this is challenged Claim 1, it claims a method of producing an
2 endotoxin assay agent that broadly covers expression, not just of Factor C,
3 but all three proteins in the coagulation cascade.

4 Now, as we heard with the '318 Patents, the inventors described
5 expressing Factor C from *Tachypleus* and HEK and CHO mammalian cells
6 in the '767 application.

7 But this claim goes far, far beyond that, it also covers *Limulus*
8 *polyphemus* horseshoe crabs, which we've discussed. The inventors did not
9 possess those proteins as of 2013.

10 And then, as shown in blue and pink here, it also requires the
11 production of Factors B and pro-clotting.

12 And I'm in on Slide 50.

13 Even though the '767 application doesn't actually describe the
14 inventors having done this, and to the contrary, the specification and the
15 evidence discusses just how challenging it was to express Factor C in
16 mammalian cells.

17 You know, when they provided their working example, they did
18 express Factors B or pro-clotting enzyme in mammalian cells, they used
19 insect cells.

20 And to make matters worse, it's not just expressing these proteins,
21 right, this claim requires those proteins to be functional, to have their
22 activity, meaning that they have to be activated by their upstream protein
23 and work to activate their downstream protein and recombinant technology
24 is challenging as Your Honors intimated earlier.

25 But the specifications had nothing about expression of these

1 proteins other than, well, just do what you did for Factor C, right, and
2 *mutatis mutandis* language regarding Factors B and pro-clotting enzyme.

3 But the point here, and the point that the inventors were making, it
4 was difficult to do this in the mammalian cells.

5 They solved the problem for Factor C by showing that, if you
6 secreted these proteins by using HEK and CHO cells, then you could get
7 back to Factor C.

8 But they didn't do anything and they didn't describe anything in the
9 '767 application that says you could -- that any of that would work for
10 Factors B and Factor C, and particularly across all mammalian cells.

11 And so, that includes mice and hamsters and humans and primates,
12 they claim all of that, even though it was known that making these proteins
13 was difficult to do, and they don't describe how to do it.

14 And then, they say, well, now we want to claim covering that. But
15 a lot of --

16 JUDGE CHANG: Let me -- I'm sorry, let me distinguish between
17 the description and enablement.

18 So, as you acknowledge, I think, that the spec -- the '767
19 application does say, do the same thing as we do for Factor C with respect to
20 the other proteins.

21 So, is that sufficiently -- so, you may say it's not enabled, it sounds
22 like that's what you're arguing, but would you say that's, nevertheless,
23 described because they tell you basically do what we did for this Factor C
24 for the other protein?

25 MS. LOUGHRAN: It's not.

1 It's not because that actually contradicts the other evidence in the
2 specification.

3 And so, you know, when you have evidence that says, well, our
4 theory is do X, but X contradicted by the specification, you -- that is not
5 adequate written description and I believe that's the *BASF* case, the canola
6 case, I think.

7 That what they say here is expressing any mammalian cell, you
8 could do it in any mammalian cell, but the specification says no, you can't do
9 it in at least mammalian cell, CHO cells, right?

10 So, they don't reconcile that that contradiction -- that can't be
11 adequate written description.

12 And as Your Honor has intimated, it definitely is not enablement.

13 Just finally on the written description point, I just want to make
14 one more point and then I will cede the floor to opposing Counsel.

15 This last limitation right, may be the same or different, meaning I
16 think it says, wherein the host cell for expressing Factor C, Factor B, and
17 pro-clotting enzyme may be the same or different.

18 Now, that is a limitation that Applicants added during prosecution
19 of this claim to get around the prior art.

20 Now, they didn't -- you can search the '767 application for those
21 words, they're not there. You can search the application for anything that
22 talks about expressing these proteins in different host cells, and then, putting
23 them together in this assay agent, it is not there.

24 We pointed this out, they know that there is no written description
25 for this feature, either explicitly or in an example or prophetically, we

1 pointed it out in our petition.

2 They said nothing in their Patent Owner response.

3 Then, we pointed that out in our reply.

4 And in their surreply, they said, well, there is support and they
5 listed a couple of paragraphs. None of those paragraphs talked about doing
6 this limitation. The stuff that they point to talk -- is related to other
7 dependent claim limitations.

8 What they point to is, well, you could use host cells that include
9 animals and insects and things like that, but there's nothing in this
10 specification that says what they have explicitly put in here in their claim
11 during prosecution, that you could do this by expressing in different host
12 cells.

13 Again, host cells are in other parts of the claim, host cells are
14 mammalian cells, HEK cells, kidney cells, human or CHO cells, but there's
15 nothing in the specification that says that the inventors had possessed the
16 ability or enabled the ability to make this endotoxin detection assay, where
17 each of those things is expressed in different cells.

18 So, even if, you know, there's some, you know, even if there's
19 some proclivity to saying, well, some of these other elements of this claim
20 are described, that one absolutely is not, the record has no evidence of that
21 being described.

22 And for that reason, Your Honors should find that this claim is not
23 entitled to a 2013 priority date and, that being the case, it is anticipated by
24 the '629 publication.

25 And I will sit down, thank you very much, Your Honors.

1 JUDGE MITCHELL: Thank you.

2 JUDGE FITZPATRICK: Sorry, I have just a couple of questions
3 about this.

4 One is to see your response, what's highlighted in purple, what you
5 were just talking about, maybe the same or different and it's cut off.

6 MS. LOUGHRAN: Yes.

7 JUDGE FITZPATRICK: Isn't that implicitly described, if, assume
8 the rest of the claim is described, and we know you don't want to, right?
9 Okay?

10 But for example, the light blue limitation, "expressing the
11 horseshoe crab Factor B having activity of Factor B in a mammalian cell as
12 a host cell."

13 I think you agree with that that limitation covers expression in any
14 mammalian cell. Right?

15 So, for example, hamsters, right?

16 MS. LOUGHRAN: Yes, yes.

17 JUDGE FITZPATRICK: And then, the limitation immediately
18 below it, I think you would also agree covers the expression of what's recited
19 there in an embryonic human kidney cell, right?

20 MS. LOUGHRAN: Yes, yes.

21 JUDGE FITZPATRICK: Okay.

22 So, those are different cells, so isn't it -- I -- you know, I think, you
23 know, there's definitely some issues here, and I just don't see why the purple
24 language, "may be the same or different," is an additional issue here for that
25 one.

1 Because I feel like it's -- I mean, every limitation is a limitation, it
2 seems to me like it really doesn't have any effect.

3 I don't even know how it was used to get around the art, because if
4 the art used the same cell, it reads on that, and if the art used different cells,
5 it also reads on that.

6 MS. LOUGHRAN: Yes.

7 JUDGE FITZPATRICK: Yes.

8 MS. LOUGHRAN: Yes, my response --

9 JUDGE FITZPATRICK: Tell me what you think about that?

10 MS. LOUGHRAN: Yes, my response to that is just, you know, the
11 Applicant was using its own choice of language and getting around the prior
12 art, right?

13 So, you know, the -- there are certainly -- you could look at it as
14 sort of types of host cells, right, in the specification they talk about host cells
15 being animals or insects, whatever, et cetera.

16 You can envision a scenario where you express Factors C, B, and
17 pro clotting enzyme all consistently in HEK cells, because, let's say because
18 the Applicants knew that for HEK for Factor C, that was a workable model.

19 I think that's where you would say, okay, the Applicants have
20 described how to do this in the same cells.

21 Now not saying they did, because they only expressed Factors B
22 and pro-clotting enzyme in insects cells.

23 But I think what they said was, with respect to the prior art is, well,
24 actually, you know, we think you could make all of these proteins in
25 different host cells. So, you could make one in HEK and one in CHO and

1 maybe one in some other type of host cell.

2 And that is the limitation that they used during the prosecution
3 history to get around the prior art.

4 I also find it a bit inexplicable that, yes, the Patent Owner -- that
5 the examiner didn't say well, wait a second, where have you described that?
6 But they certainly did not, there's nothing in the -- in this specification that
7 says that they described these, you know, these elements in any mammalian
8 cells.

9 But they didn't even -- it's not even like they said in the '767
10 application, even though they hadn't made anything, so they said, let's just
11 make some *in haec verba* description. It's not like it came from the '767
12 specification where they said, you could do this in the same or different
13 cells. It comes from nowhere and, you know, they used it to get this claim
14 issued, but they certainly didn't describe or enable it.

15 Thank you.

16 JUDGE FITZPATRICK: And one other question, sorry, about the
17 same demonstrative, it -- there's the green -- the largest highlighted
18 language, the green one, earlier you said, as part of your arguments, you
19 talked about how they're actually claiming stuff that they say that didn't
20 work. Right?

21 But I read this -- so, the Factor C is enormous in this thing, right?

22 MS. LOUGHRAN: Correct, yes.

23 JUDGE FITZPATRICK: Because you have to have one of these
24 two cell lines, and then, the factor is limited to two of the four horseshoe
25 crab species.

1 MS. LOUGHRAN: Yes.

2 JUDGE FITZPATRICK: And if I can direct your attention to
3 Column 2 of the Patent, the '109 Patent, in lines 44 to 53 or 54, it sounds
4 like, you know, that there, they're admitting a problem with Factor C when
5 you use the same horseshoe which is two different scientific names, one of
6 them is *Tachypleus* and then --

7 MS. LOUGHRAN: Yes.

8 JUDGE FITZPATRICK: -- one is *rotundicauda*.

9 And then expressing the cell is the monkey cell, COS-1?

10 MS. LOUGHRAN: Yes.

11 JUDGE FITZPATRICK: And so, those are carved out, right, of
12 Claim 1 there?

13 MS. LOUGHRAN: Correct, yes, well, yes, exactly.

14 JUDGE FITZPATRICK: Okay.

15 MS. LOUGHRAN: So, what they did was, they knew that they
16 were hitting a roadblock with respect to COS-1.

17 And so, they tried a couple other Factor C -- or expression systems
18 and they also, and this is why this secreting the horseshoe crab Factor C into
19 the supernatant, they -- that also comes into play.

20 They say well, when you secrete the protein and you've made it in
21 these two specific ones, then we get functional Factor C.

22 That's what they managed to show and claim and then, they
23 ignored all of that when they got to the rest of the coagulation cascade and
24 said well, you know, we'll claim the rest of it very, very broadly, yes.

25 JUDGE FITZPATRICK: Thank you.

1 MS. LOUGHRAN: Thank you, Your Honor.

2 JUDGE MITCHELL: Thank you.

3 And whenever you're ready.

4 MS. DOUKAS: Good afternoon, Your Honors, Maria Doukas for
5 Patent Owner, and I'm going to start with the IPR and then, I'm going to turn
6 it over to my colleague, Ms. Lo, who will present on the PGR.

7 And just for the record purposes for the IPR, the Patent Owners,
8 demonstratives, or Exhibit 2109.

9 May it please the board, if you could turn to Slide 2, please?

10 For the IPR, Petitioner has not met its burden to demonstrate Claim
11 21 is unpatentable, and this is for a few reasons.

12 First, we believe that Claim 21 is entitled to a December 2013
13 priority date, and if the board agrees with that, then there's no dispute
14 amongst the parties.

15 The art that's relied upon for the two grounds is not prior art, the
16 unpatentability grounds to become moot.

17 Second, and I'll touch on this later, should the board find that the
18 December 2013 priority date is not applicable here, we believe the Petitioner
19 has failed to meet its burden to demonstrate unpatentability because it has
20 not shown a reasonable expectation of success.

21 And as Your Honors alluded to this during Petitioner's arguments,
22 we believe that the arguments made by Petitioner's expert with respect to
23 Section 112 and why there's no section 112 support, contradict the
24 arguments made for why reasonable expectations of success exists to
25 support obviousness.

1 And separately from that -- yes?

2 JUDGE FITZPATRICK: Well, I'm sorry.

3 MS. DOUKAS: No, no, no.

4 JUDGE FITZPATRICK: The IPR, yes.

5 MS. DOUKAS: Yes. Because it is Your Honor's anticipation and
6 I was confused for a moment, I'm sorry.

7 JUDGE FITZPATRICK: No problem.

8 MS. DOUKAS:

9 And then, the second reason with respect to patentability to the
10 extent we are looking at Grounds 1 and 2, we do believe that there are
11 unexpected results of non-obviousness.

12 And then, finally, to the extent that the board does find Claim 21
13 unpatentable, I do want to touch on Patent Owner's contingent Motion to
14 Amend and revise Claim 22, which we believe would alleviate any potential
15 concerns, particularly with respect to should the board find the residual
16 activity limitations encompass a wide range, that are either not enabled, do
17 not have description support, we believe that Claim 22 narrows that and does
18 have sufficient 112 support to be entitled to the December 2013 priority
19 date.

20 So, I want to start with the priority date and the written description
21 arguments, if we turn to Slide 5?

22 JUDGE CHANG: Actually, before we go there, can I just ask the
23 same question to you that I asked Petitioner?

24 So, who's for that -- so, I think it's fairly clear that Patent Owner
25 has a burden of production in terms of showing the entitlement to a priority

1 date.

2 Is it -- does Patent Owner agree that Patent Owner also has a
3 burden of showing lack of written -- or the existence of adequate written
4 description for purposes of showing that priority date?

5 MS. DOUKAS: Yes, so, we believe that Petitioner has the burden
6 to show that there is a lack of written description and enablement.

7 The burden can shift, but we do believe that Patent Owner, in this
8 case, has shown that there is sufficient written description and that there is
9 sufficient enablement for the full scope of Claim 21 and Petitioner has not
10 come back with any evidence undercutting the evidence the Patent Owner
11 has put forth.

12 So, we do believe, ultimately, I think that the burden does rest with
13 Petitioner to show that Claim 21 in this case would not be entitled to its
14 December 2013 priority date.

15 JUDGE CHANG: Okay.

16 MS. DOUKAS: So, on Slide 5, we have one of the arguments that
17 we've heard from Petitioner with respect to the IPR and Claim 21, and it
18 focuses on the lack of examples, that there is no examples of a recombinant
19 protein from the *Limulus polyphemus* sequence, and this lack of examples is
20 not dispositive.

21 The case law is very clear, examples, reductions of practice are not
22 required to show written description support.

23 And I'm going to jump to Slide 8 just to reorient, I know we
24 touched on the -- Petitioner touched on the PGR at the end.

25 We have challenged Claim 21 of the '318 Patent for the IPR and I

IPR2025-00440 (Patent 11,236,318)

PGR2025-00023 (Patent 11,959,109)

1 just want to reiterate what Claim 21 actually requires, because we do believe
2 it is not a broad genus claim, it's a single -- it's a narrow species claim, it
3 requires a specific Factor C protein from a specific species of horseshoe
4 crab, *Limulus polyphemus*.

5 It does not require any sequence informations directed to the
6 recombinantly produced protein.

7 It requires the expression of this protein to be in a specific cell line,
8 HEK293 and then, it requires specifically claimed residual activity threshold
9 values and specifically claimed salt solutions, each of which we believe
10 shows up in the '767 priority application to provide written description
11 support.

12 So, looking at the priority application and starting first, and this is
13 the '767 application on Slide 9, the '767 application has a section titled
14 modes for carrying out the invention.

15 And within that section, it notes that the Factor C of the present
16 invention is derived from a horseshoe crab. And it expressly identifies the
17 claims *Limulus polyphemus* is one of those examples.

18 There is disclosure of a Factor C protein from the claimed species
19 of *Limulus polyphemus*.

20 The '767 application also includes an entire example dedicated to
21 steps for expressing Factor C in the specifically claimed HEK293 cells.

22 And as our expert Dr. Schaefer explains, a person of skill in the art
23 reading the '767 application would have understood that there is description
24 support for recombinantly expressing Factor C from *Limulus polyphemus* in
25 HEK293 cells.

1 JUDGE CHANG: So, let me -- okay, so, the -- putting aside the
2 question of the sequence information, it seems that the '767 applicant, the
3 point where they mentioned the *Limulus polyphemus*, basically, it's in the
4 statement that says, you know, it's in the description, the mode of invention.

5 But there's no description, I think you mentioned that, you know,
6 there is a description of recombinantly expressing in HEK cells, but that is
7 not the particular *Limulus polyphemus* species.

8 And I think the Petitioner has mentioned, and I believe this is the
9 law, that it's not sufficient to make something obvious, you have to actually
10 describe it.

11 So, how would you respond to that argument that, even if you have
12 made something -- made that obvious, you have not actually put together the
13 entire claim and described it in the spec?

14 MS. DOUKAS: I mean, I think our view is that the invention does
15 contemplate and the inventors, within the four corners of the specification,
16 contemplate that as part of the invention, is a *Limulus polyphemus* Factor C.

17 While they don't provide any specific examples, under the law,
18 examples are not required and the identification that this is what the
19 inventors viewed as part of their invention, we think is sufficient for written
20 description support in order to meet the burden without the lack of examples.

21 And as we talked about and, I'll bring this to the *Teva* case, that we
22 did supplemental briefing as our papers discussed, even though -- as our
23 papers discussed, there was information in the arts regarding sequence
24 deposit information with respect to Factor C for *Limulus polyphemus*, a
25 person of skill in the art would have been capable of using routine methods

1 to identify that, as Petitioner's expert discusses in the European opposition
2 expression of *Limulus polyphemus* would have been routine.

3 So, we do feel that this discussion and the modes for carrying out
4 the invention and just what was known in the art, because the knowledge of
5 a person -- the knowledge of a person of skill in the art, also goes into the
6 analysis of written description that it does meet the burden. It does show
7 that there was written description support.

8 JUDGE CHANG: And sorry, going that to what you just
9 mentioned in terms of what's in the prior art, I just want to confirm, that I
10 know there was a lot of evidence cited as to what was in the prior art, but
11 there was -- do you -- does Patent Owner agree that there's no description or
12 no disclosure in the prior art of the actual sequence of either the genetic
13 sequence or the amino acid sequence of *Limulus polyphemus* Factor C
14 protein, is that true?

15 MS. DOUKAS: So, and I was going to touch on, I know that
16 Petitioner raised the statements made in Patent Owner's '498 PCT that has
17 some overlapping inventions with the '767.

18 So, Patent Owner agrees that there had not been, as of 2013, the
19 full length cDNA sequence for *Limulus polyphemus* Factor C published.

20 However, in the art, we do believe that there was sequence
21 information example -- for example articles like Tokunaga which was
22 Exhibit 1022 in the IPR was from 1991. The authors compared the sequence
23 of *Limulus polyphemus* to sequences of *Tachypleus tridentatus* to determine
24 the sequences were indistinguishable.

25 So, there was some identification of sequences that must have been

1 done in order to do that characterization.

2 Similarly, with all this, which is Exhibit 2036 from 2006, again,
3 they did -- the authors of that publication did homology studies. They
4 compared -- they did homology comparisons using *Limulus polyphemus*
5 sequences, so they must have identified the sequences.

6 And then, deposit information, which I can jump ahead --

7 JUDGE CHANG: Just to -- just the two that you have already
8 mentioned, but those are not publicly available, right?

9 Even -- so, we are making assumption that the right -- the authors
10 of those papers have sequence information, but that at least is not publicly
11 available, and therefore, would not be available to a person of skill in the art,
12 which is a person we want to confirm with for written description.

13 Is that -- do you agree with that?

14 MS. DOUKAS: Well, I think a person of skill in the art would be
15 able to obtain the sequences, but the publication and whether we do concede
16 that the full length cDNA sequence had not been published as of 2013.

17 But there was information that a person of skill in the art would be
18 aware of.

19 And when we're looking at written description and also
20 enablement, we're looking from the lens of a person of skill in the art.

21 And for example, as we have on Slide 13, there was deposit
22 information that was published and available as of October 31st, 2013.

23 And as Patent Owner's expert discussed and walked through, and
24 then moved -- jumped ahead to Slide 15, from this deposit information, the
25 person of skill in the art could have confirmed 97.2 percent of the full Factor

1 C coding sequence, the remainder of the sequence could have been obtained
2 by routine methods, and this could have been used.

3 This would have been known to a person of skill in the art used by
4 a person of skill in the art using routine methods to obtain the sequence and
5 express factors with recombinant Factor C from *Limulus polyphemus* as of
6 the December 2013 date.

7 JUDGE CHANG: And so how -- so, this is a claim to the actual
8 Factor C protein cell. So, how would you respond to case law that, *Eli Lilly*,
9 that says, when you are -- when you have claimed a biological molecule, you
10 actually have to describe the biological molecule, not just tell POSA, a
11 person of skill in the art, how it could be isolated or obtained.

12 Do you agree with that statement of the law, or do you think that,
13 you know, it's sufficient if you are able to obtain -- somehow obtain that
14 molecule?

15 MS. DOUKAS: We believe it's sufficient if you're able to obtain
16 the molecule.

17 I mean this -- the case law says, for written description, examples
18 are not required.

19 So, while we -- while Claim 21 may be directed to this specific
20 species of horseshoe crab, the '767 application contemplates *Limulus*
21 *polyphemus* Factor C as a mode of the invention, and may not describe and
22 include examples, but a person of skill in the art, just based on all the
23 knowledge in the art, would be able to recombinantly express the *Limulus*
24 *polyphemus* Factor C.

25 So, we don't think that, under the law, you'd need to describe

1 -- you need to have sequence information necessarily described especially
2 for this claim, which is directed to a protein.

3 We think that what is described in the '767 application is sufficient
4 for the written description inquiry.

5 JUDGE CHANG: One other question, and I think this is a
6 technical question I also asked the Petitioner.

7 So, are you able to actually obtain a recombinant Factor C protein
8 if you do not have the full sequence? I'm not saying that you could not have
9 obtained the sequence first, I mean if you don't have the -- do you have to
10 have the full sequence before you can obtain the recombinant Factor C
11 protein?

12 MS. DOUKAS: I don't think you need to have the full sequence.

13 I mean, I think that the deposit information, as Dr. Schaefer
14 explained, could be used -- you could use the, for example, this
15 transcriptome deposit, assemble the full factor coding sequence, and then,
16 that could be used to create cDNA that could be then used for expression in
17 the, for example, the HEK293 cells.

18 So, we do think that what is known in the art between the deposit
19 information, the publications, that this all folds into the analysis in
20 conjunction with what is actually disclosed in the '767 application and then,
21 a person of skill in the art would have believed that there was written
22 description support for the invention as claimed.

23 JUDGE CHANG: Okay, thank you.

24 MS. DOUKAS: So, just on this subject and I'm just going to go
25 back to Slide 10 of Patent Owner's demonstrative, and I believe this was

1 touched on during Petitioner's presentation.

2 So, as I said, Patent Owner's view is that there is written
3 description support that the '767 application contemplates, that the invention
4 includes recombinant Factor C protein from *Limulus polyphemus*.

5 And as was discussed during Petitioner's presentation, if we look
6 at what we have on Slide 10, these are statements that Petitioner presented to
7 the European Patent Office during the opposition proceeding.

8 These are Petitioner's words, and Petitioner's words in paragraph
9 155 is, Petitioner concedes D1, which it says corresponds to the '767
10 application, has the same description, already discloses a recombinant Factor
11 C protein derived from *Limulus polyphemus*.

12 Now, it talks about that the sequence is not known, but it does say,
13 and this is Petitioner's view before the EPO, that D1 did disclose the
14 recombinant *Limulus polyphemus* Factor C protein and that is precisely what
15 we have in Claim 21.

16 JUDGE CHANG: So, sorry, but this is in front of European Patent
17 Office.

18 So, what is the -- why is that -- and I am assuming -- I do not know
19 European patent law, but I'm assuming that is a different legal system with
20 different legal requirements.

21 Why is that necessarily -- Patent Owner's are directly translating
22 that into written description in -- under American patent law?

23 MS. DOUKAS: No, I -- understanding that there are different
24 patentability standards, we don't think that this goes to the patentability
25 standard presented before the EPO versus U.S. law.

1 We think this goes directly towards what Petitioner -- the state of
2 the art, what Petitioner believes and what it told the EPO D1 actually
3 discloses.

4 It doesn't touch on the patentability standards in this paragraph, it's
5 just a statement of they've read D1 and this is what Petitioner, before the
6 EPO, this is the position they took, D1 discloses this.

7 So, it's just a disclosure and what Petitioner's view was in a
8 different forum when it wanted to make a different argument, how it read the
9 same document that it now says doesn't have written description support for
10 the recombinant Factor C protein from *Limulus polyphemus*.

11 If we go to Slide 11, we just have one more statement, again, this
12 is Petitioner's view before the European opposition, and again, the intent of
13 this is not to apply patentability standards before the EPO to this proceeding,
14 but more to show what positions Petitioner took when it was in a different
15 form, when it needed to make different arguments to support its opposition
16 to Patent Owner's patents.

17 And there at the EPO, Petitioner again talks about D1, that's the
18 '767 priority application. It says it discloses methods for commonly
19 producing Factor C, which I think we all agree on, and then, it directly
20 points the skilled person to carry out this method with Factor C derived from
21 *Limulus polyphemus* species.

22 So, Patent Owner, I'm sorry, Petitioner, when it was reading and
23 interpreting D1 and telling the EPO what it discloses, it took opposite views
24 as to what it's telling Your Honors, we believe, in this proceeding.

25 So, just to sum up, as this portion right here, we believe -- Patent

1 Owner believes that the skilled artisan reading the '767 application, would
2 have understood that the inventors had possession of HEK293,
3 recombinantly expressed Factor C from *Limulus polyphemus*.

4 And we believe that Petitioner's statements to the European Patent
5 Office, while, again, it is a different patentability standard, we think it goes
6 to the credibility of Petitioner's arguments in this proceeding.

7 They took different views, they interpreted the document
8 differently, they made different arguments, and we think that this does
9 undercut their opinion here as to the lack of written description support for
10 recombinantly produced *Limulus polyphemus* Factor C.

11 So, if we just jump ahead to Slide 17, I want to go back to the
12 challenged claim and focus on the residual activity limitations.

13 Now, the -- as we've discussed the Claim 21 it describes it requires
14 recombinantly expressed Factor C, but it also requires that this
15 recombinantly expressed Factor C meet threshold residual activity values in
16 specifically claimed salt solution.

17 And Patent Owner believes, if we turn to Slide 18, that the '767
18 application provides written description support for these thresholds residual
19 activity values.

20 We have an excerpt on Slide 18 from the '767 application and it
21 describes the Factor C of the present invention may have low susceptibility
22 to inhibition of activity by an ion and then, it identified specific examples of
23 what that means.

24 And those examples of what this low susceptibility to inhibition of
25 activity by an ion includes Factor C exhibiting what we have claimed, a

1 residual activity of 10 percent or higher in the 21 millimolar sodium citrate
2 or residual activity in 15 percent or higher in the 16 millimolar magnesium
3 sulfate.

4 JUDGE CHANG: So going to that point –

5 JUDGE FITZPATRICK: Oh, I'm sorry, go ahead, Judge.

6 JUDGE CHANG: Yes, I'm sorry.

7 So, in that particular section that you just read, it says the Factor C
8 of the present mentioned may have low susceptibility of inhibition activity
9 by an ion -- to inhibition of activity by an ion.

10 So, that doesn't tell you which Factor C, right, it just says, it may
11 have. And given that the only discussion of residual activity is in a different
12 species, right, would the skilled artisan reading this spec, expect that the
13 *Limulus polyphemus* Factor C also have these particular those low
14 susceptibility?

15 MS. DOUKAS: So, that goes to another point, and I'll just jump
16 ahead, one, an argument that Petitioner's raised is that you can't translate.

17 We have data in the '767 application, the patent with respect to
18 *Tachypleus tridentatus*, an entirely different species.

19 How can you equate that to possession of the *Limulus polyphemus*?

20 And I, again, I'm going to go back -- I have a few points on that as
21 to why you can actually make that leap and why you would expect that there
22 would be residual activity and *Limulus polyphemus* with the data and the
23 information that's in the '767 application.

24 JUDGE CHANG: Well, I guess I just mean even the statement
25 itself, right, the Factor C of the present invention may have that quality, that

1 property.

2 That doesn't suggest that all Factor C will have that property.

3 Is that true or do you read that differently?

4 MS. DOUKAS: I -- sorry to move around so much going back to
5 -- I read that differently.

6 I think it is saying -- I think that's an intro and I think that it's
7 explaining that the Factor C of the present invention, which is we've
8 established the '767 application, talks about modes for carrying out the
9 invention include Factor C from all the species.

10 So, to include *Limulus polyphemus* and that the low susceptibility
11 to inhibition of activity in ion is defined by these specific examples and
12 that's what we have claimed.

13 And I think that this shows that there is possession, that there was
14 -- that the inventors did present that these threshold values of claims residual
15 activity -- of claims residual activities that are based on the specific
16 examples.

17 That's what they identified as being correlated to this low
18 susceptibility to inhibition of activity by an ion.

19 And then --

20 JUDGE CHANG: But those are examples, though, I don't see a
21 definition here. Do you read this as a definition of what loss of the
22 capability means?

23 MS. DOUKAS: Not -- no, not necessarily, but I do think that this
24 is the focus of the invention and this is what the Claim 21 is trying to
25 encompass, that the idea of the invention is that you want to have this low

1 susceptibility to the inhibition of activity by an ion.

2 So, even in the presence of ion solution, the Factor C will still
3 work as intended to detect the endotoxins.

4 And it's giving different examples, and the passages do continue
5 with different salt solutions, and we do believe that Claim 21 then is
6 narrowly tailored to be exactly what is described in the specification, these
7 specific salt solution concentrations, the sodium citrate magnesium sulfate as
8 the threshold values you need to hit of residual activity to achieve that -- the
9 focus of the invention to achieve that low susceptibility to the inhibition.

10 JUDGE FITZPATRICK: And with that, I'm looking up at this
11 slide that you have highlighted, and I see *in haec* support for the limitations,
12 but I don't see this as a description of how to achieve these.

13 There's no reduction that -- there's no actual reduction to practice
14 in the patent described where they did this with respect to one of these
15 -- with respect to what they claim, which is a Factor C that's derived from
16 *Limulus*.

17 And so, is there something else in the patent specification where it
18 described how to achieve, not that you would -- not that we found, for
19 example, you could get 10 percent or higher description. How do you
20 achieve that or one of the -- what are the factors that are going to affect the
21 residual activity that you're claiming?

22 MS. DOUKAS: In the claim itself, no, and I think that's where we
23 go to Figure 7.

24 I mean that is where they achieved it and I understand Figure 7 is a
25 different species, of horseshoe crab, but then, if you look at in the context of

1 what a person of skill the art would understand, they would understand that
2 these species evolve slowly, they would expect that the residual activity
3 would be maintained.

4 And that's what both of our experts testified would be maintained
5 across these two species of crabs.

6 JUDGE FITZPATRICK: If someone was able to figure out how to
7 do it with respect to *Limulus*.

8 And that brings me to my next question, which is, if there's a
9 concession on your part and it's reasonable to do so, that there is no
10 description in the patent of, for example the mRNA, encoding or any other
11 genetic information encoding Factor C from this -- from the *Limulus* species.

12 And you have -- your side is relying on, I think, that you take the
13 position that the majority of that genetic information was available in some
14 sort of deposit, although your spec doesn't point to it, that you're saying a
15 POSITA would know that it exists and then could fill in the gaps.

16 And my question is, if that's all true, what exactly did you guys
17 invent that's in the claim?

18 You could have the claims going back, what aspects were actually
19 invented?

20 Because I struggle to find what possibly could be, if that's the case,
21 if you don't need the genetic information because the person with skill in the
22 art could obtain that, who could figure out how to get it, and then, a person
23 of skill in the art could figure out how to have it expressed in either in the
24 -- well, in the HEK cell line, like it's the only one that's mentioned here.

25 And then, I think you do relative things and we certainly could

1 measure the residual activity, you know, then afterwards, just see whether or
2 not they hit these minimums, if indeed, that's what they are there.

3 What is left to claim as inventive?

4 MS. DOUKAS: Well, I think, in terms of the broader view of the
5 invention, it talks about the difficulty with expression in the mammalian
6 cells in the COS-1.

7 So, the patent is directed to and describes, that's why they describe
8 expressing the Factor C protein in HEK293 cells and then, that sort of tied to
9 the inventive concept that when they were expressing these Factor C
10 proteins in these cells, they were observing that there would be the -- at least
11 meeting the threshold residual activity.

12 So, I think it's a combination of everything all together and the
13 being able to express in the mammalian cells.

14 JUDGE FITZPATRICK: So, it sounds like then, the invention is
15 the expression because it's difficult. So, I mean, if it's -- if it was difficult,
16 then why on earth should we assume that a person of skill in the art was
17 enabled when you didn't even -- you actually do it with *Limulus*, and if it
18 was difficult it, it seems then, that kind of informs in the other direction of
19 enablement.

20 MS. DOUKAS: But I think they did, the inventors did do it. I
21 know they did it with a different species, they did it with *Tachypleus*
22 *tridentatus*.

23 So, I don't think our position is not that it would be difficult if you
24 switch over to a *Limulus polyphemus* instead and express it, I think it's the
25 being able to express in the mammalian cell with this horseshoe crab species

1 and they were able to do that.

2 The examples talk about expression of the *Tachypleus tridentatus*
3 in the HEK293.

4 So, and then --

5 JUDGE FITZPATRICK: So, just so I can understand the position
6 of the moment ago, we said difficult, I took that to mean that the inventors
7 found it difficult to express *Tachypleus* Factor C in the HEK293 cell lines.
8 Is that right?

9 MS. DOUKAS: I misspoke, that is the -- I think that's what they
10 talk about in the background of the patents that, before mammalian
11 expression, that the COS-1 cells were not with respect to expression, the
12 COS-1 cells and what they figured out a way to express in the mammalian
13 cells instead of the HEK29.

14 And while the --

15 JUDGE FITZPATRICK: But if -- I'm sorry, I admit that I'm a
16 layperson in this technology, but it -- I've seen these cell lines come out over
17 and over in different cases and different technologies. It seems like there's
18 like a set of well-known and established expression systems, and all the ones
19 that are in the specification are among them, the human, whether they are
20 kidney, the COS, which is a -- derived from African green monkey kidney
21 cells, the Chinese hamster ovary, and then, outside of the mammalian,
22 there's this insect line.

23 Those are -- it just doesn't seem -- something doesn't add up to me
24 that -- so, this -- it's solely is the inventors had trouble expressing
25 *Tachypleus* Factor C in a COS-1 expression system.

1 And then, they figured out eureka, hey, why don't we do this in the
2 human embryonic kidney?

3 I don't see what was invented because the person of skill in the art
4 knew that that was an available expression system.

5 And then, even if that was a kind of a eureka moment, just because
6 they thought of doing it with the *Limulus* cell line, but they never actually
7 did it, excuse me, I misspoke, the *Limulus* Factor C, you mentioned here, I
8 don't -- I just -- I can't envision how they should get a patent for that, the
9 way it's been framed and I'm struggling to follow.

10 MS. DOUKAS: So, I -- and I'm probably not doing a good job of
11 explaining.

12 So, if we if we go to Exhibit 1001, which is the '318 Patent, and
13 I'll direct your attention, and I have it up on the screen as well, Column 3,
14 this is the mean -- so, it's sort of the means for solving the problem at line 10
15 is where it starts.

16 So, I think this is sort of the combination of everything that comes
17 into Claim 21. So, the inventors found that recombinant horseshoe Factor C
18 can be produced by, for example, the HEK cells.

19 And that endotoxin can be measured, while reaction inhibition, the
20 presence of the salt is mitigated.

21 So, it's the combination of determining you can recombinantly
22 express the Factor C in now the HEK293 cells if we're looking just to Claim
23 21. And when you do that, the reaction inhibition, which is measured by
24 residual activity, is being mitigated.

25 In other words, the Factor C that's being expressed is able to still

1 detect endotoxin even in the presence of the various salt solution ions.

2 JUDGE CHANG: And I have a question with respect to the
3 residual activity.

4 Is it Patent Owner's position that it's an inherent property of the
5 Factor C protein of the particular species or is it dependent on various, you
6 know, various other factors?

7 MS. DOUKAS: We have -- I think we have not taken a specific
8 position on that, I think it would be an inherent property of the specific
9 species of Factor C of recombinant -- of the species of Factor C as our
10 expert, Dr. Morris, explained in her declaration that when she talks about
11 unexpected results, a person skilled in the art would expect that you would
12 see similar residual activity values between the two species of *Tachypleus*
13 and *Limulus* and what was actually observed measuring the residual activity
14 in HEK293 cells, is that the residual activity of *Limulus polyphemus* was
15 much significantly higher, so, yes.

16 JUDGE CHANG: Okay, but this is not a position you've taken in
17 your papers, correct?

18 MS. DOUKAS: Correct.

19 JUDGE CHANG: Okay, thank you.

20 MS. DOUKAS: So, just going back to residual activity, and I
21 know I alluded to this and we've seen Figure 7.

22 Figure 7, as we've discussed is related to a different species of
23 horseshoe crabs. There's residual activity values shown for the two claimed
24 salt solutions.

25 This demonstrates the claimed residual activity in the two salt

1 solutions in HEK293 cells, yes, it is *Tachypleus tridentatus*. The inventors
2 achieved the threshold level of 10 percent or higher in the sodium citrate,
3 which is Column 5, or 15 or higher in the 16 millimolar magnesium sulfate,
4 which is Column 2.

5 So, while we understand that this is a different species of
6 horseshoe crab, if we jump to Slide 21, we, again, have statements from
7 Petitioner itself, this is before the EPO, and Petitioner told the EPO, again,
8 when Petitioner was talking about D1, which is the '767 application, it
9 argued that D1 highlights Factor C expressive mammalian cells can have
10 this low susceptibility to activity inhibition by ions and that this property
11 may be expected for recombinantly produced Factor C from any source,
12 including *Limulus*.

13 So, we just wanted to highlight this, that here, we understand that
14 Petitioner's view is that the data in Figure 7 and the examples in the '767
15 application are directed to an entirely different species so, you can't
16 extrapolate and get to residual activity values in the claimed *Limulus*
17 *polyphemus* before the EPO.

18 Again, just looking at applied patentability standards, but just
19 looking at what they view D1 as describing and what they view the state-of-
20 the-art, their view was that this property would be expected if you
21 recombinantly produced Factor C from *Limulus polyphemus*.

22 And this tracks, if we turn to Slide 22, with what Petitioner's -- I'm
23 sorry, Patent Owner's expert explains. Patent Owner's expert, Dr. Schaefer,
24 explains, first of all, those skilled in the art understands that horseshoe crabs
25 evolve slowly. They would expect the key regions encoding function

1 argument, to be highly conserved across species.

2 And if we turn to Slide 23, Dr. Schaefer went a step further, he
3 actually compared the amino acid sequences between species to assess the
4 presence of conservative substitutions, and one of Petitioner's, expert Dr.
5 Jain's arguments, to support his view that you would not expect residual
6 activity values to translate between species, is that there would be non-
7 conservative substitutions that could potentially impact the residual activity.

8 So, our expert, Dr. Schaefer, actually ran the analysis. He
9 compared the sequences and he identified only 11 non-conservative
10 substitutions out of the 1,020 amino acids.

11 And if we go to --

12 JUDGE CHANG: So, but this is not available to a skilled artisan,
13 in taking the tape, right, the full sequence. So, he could not -- you could not
14 have done this analysis and determined what was or was not conservative.

15 MS. DOUKAS: Yes, but it -- correct.

16 But he did -- he used techniques that were -- a person of skill
17 -- actually, strike that.

18 A person of skill in the art could have used the deposit information
19 to obtain the full sequence. And as Dr. Schaefer explains, the person of skill
20 in the art could have run this comparison between the species because they
21 could have obtained the cDNA sequence of *Limulus polyphemus*.

22 They could have compared it to sequence of the other species of
23 horseshoe crabs and could have identified how many non-conservative
24 substitutions existed and then where those non-conservative substitutions
25 resided and that --

1 JUDGE CHANG: So, but I guess, it seems to me, though, that
2 reading the spec without doing any additional information, additional work,
3 and even considering what's available in the prior art, and that's assuming
4 that we consider that, just without doing any additional work, you will not be
5 able to say I reasonably expect there to be, you know, 11, you know, non-
6 conservative substitutions, is that true?

7 MS. DOUKAS: Yes, I mean without doing -- you would need to
8 do work in order to identify exactly how many non-conservative
9 substitutions existed.

10 And the reason I just wanted to bring this to Your Honors'
11 attention is that, Dr. Schaefer did do that work as this again maybe goes to a
12 burden question.

13 Petitioner's, expert Dr. Jain, makes a statement in his declaration
14 that there could be non-conservative substitutions that potentially could
15 impact the residual activity, but he doesn't provide any supporting evidence,
16 he doesn't do any analysis, he doesn't quantify that value.

17 So, Dr. Schaefer did that work, he identified the sequences or he
18 used the sequences to identify how many non-conservative substitutions
19 existed and was able to determine that they actually are very conserved and
20 that there were only five non-conservative substitutions in the conserved
21 domains and based on that, a person of skill in the art, in his view, would
22 believe that the functional domains are very highly conserved between
23 species.

24 JUDGE CHANG: So, is it -- I'm sorry, and Petitioner -- I think
25 that Petitioner does make the argument I think this is true, that even now,

1 right, we do -- and certainly in 2013, there's no description of what
2 determines residual activity, is that correct?

3 MS. DOUKAS: Not that we've briefed your, Your Honor, not that
4 I -- that we have put in our papers in terms of a correlation between a
5 structure function.

6 JUDGE CHANG: Okay, thank you.

7 MS. DOUKAS: So, just to wrap this up on the written description,
8 we do believe that a person of skill in the art, reading the '767 priority
9 application, would have understood the inventors possessed the full scope of
10 Claim 21.

11 And I'm going to jump to enablement and turn to Slide 28.

12 As I touched on before, our view is, Claim 21 is not broad, it's a
13 narrow species. You have a specific species of crab, specific host cell,
14 specific salt solution concentration for the claimed residual activity.

15 Slide 29, one of Petitioner's arguments is that the '767 application
16 doesn't describe or instruct a person skilled in the art how to make or use for
17 recombinant proteins from this species of crabs, the *Limulus polyphemus*,
18 and that there are no working examples.

19 So, this argument just, again, goes back to the similar arguments
20 that Petitioner makes in written description as to a lack of working
21 examples.

22 But the law does not require examples for adequate description or
23 enablement, examples are not required.

24 It's really is there undue experimentation that would need to be
25 used in order to make or use the full scope of the invention, and in Patent

1 Owner's view, there's not.

2 Slide 30, I've covered some of these excerpts already. The '767
3 application provides a road map. It tells a person skilled in the art step for
4 expressing Factor C in mammalian cells, in the HEK293 cells, that are
5 specifically claimed.

6 It provides Figure 4, which explains how to measure residual
7 activity.

8 It provides data from Figure 7.

9 This, in our view, provides a road map that a person of skill in the
10 art could follow to make and use the scope -- the full scope of the invention.

11 And if we turn to Slide 31, again, I do want to go back to
12 statements that Petitioner made before the EPO.

13 Before the EPO, whereas here, Petitioner's arguing that there
14 would be undue experimentation required that there is no enablement, again,
15 these are not focusing on patentability standards, but really the state-of-the-
16 art and what Petitioner told the EPO, the state of that was.

17 In Slide 31, Petitioner told the EPO that it's a matter of routine
18 practice to determine the sequence of a known protein and there's, I don't
19 think, any dispute that *Limulus polyphemus* Factor C was a known protein
20 has been known for decades.

21 The Petitioner also said that a person skilled in the art could derive
22 the sequence in a matter of routine analysis, and again, the same statement
23 about D1, what it already discloses.

24 And if we switch to Slide 32, Petitioner retained an expert in the
25 EPO proceeding, Dr. Froman, different than the expert they retained here.

1 But even Doctor Froman, Petitioner's expert, said that, no, he said,
2 the skilled person could follow the teaching described in two examples, and
3 these two publications D23/D24 predates 2013, and that he believes that,
4 using these protocols, there's every reason to believe a person would have
5 been successful in obtaining the *Limulus* Factor C cDNA.

6 So, to the extent the sequence would have been required to
7 recombinantly express, Petitioners expert, Dr. Froman, in the EPO
8 proceeding said that a person skilled in the art could do this, could use
9 methods known well before 2013 and would be successful in obtaining the
10 cDNA.

11 And if we turn to Slide 33, what we have highlighted in the box
12 above, it goes to the concept of expressing, if we have the patent, the '767
13 application describes expression of *Tachypleus tridentatus* and HEK293.

14 Petitioner's, expert Doctor Froman, wrote -- this is his declaration
15 that we have excerpted here, he wrote out the question, is there any reason to
16 believe that this protein, and it would be referring to *Limulus polyphemus*,
17 would have been difficult to express after obtaining the cDNA sequence?

18 And he said no. He talks about the HEK293 cells, and he says at
19 the bottom of paragraph 47, if I follow the example of D1 using the *Limulus*
20 sequence, he would not anticipate experiencing any difficulties.

21 JUDGE FITZPATRICK: I mean, I agree that this -- that Dr.
22 Froman's testimony is helpful for you.

23 Both sides are putting in evidence into the record showing
24 inconsistent positions that have been taken and might be released.

25 This is one of them.

1 The other is the one that Petitioner has highlighted, and I'd like to
2 draw your attention to it, that's in the '498 that the -- I think it's Exhibit 1005
3 in this case, is that right? Does that ring bell? The '498 -- the application
4 ending '498?

5 MS. DOUKAS: Yes, Exhibit 1005.

6 JUDGE FITZPATRICK: And if you go to page, you know, 2,
7 which has paragraph 7 through 12, and then, page 3 which shows paragraph
8 13.

9 So, I'm about to -- so, I'm going to read it all, but it is included and
10 put into the record and I didn't see -- and I'm going to summarize, it
11 basically says *Limulus polyphemus* was really hard to work with and still it
12 is as of the time of this writing, it is hard to work with.

13 And I have to quote a part of paragraph 13, "the full-length
14 sequences of all proteins and genes involved in the coagulation mechanism
15 of *Limulus polyphemus* has not yet been elucidated."

16 This fact also demonstrates the difficulty in accurately determining
17 the full length sequence structures of these proteins and genes in *Limulus*
18 *polyphemus*.

19 Now, this is a document that belongs to patent -- to your client, to
20 Patent Owner, so, this is the position that they have taken.

21 I understand that Dr. Froman says, you know, says, hey, I would
22 have expected it to be, you know, readily -- you could readily extract from
23 one species to others.

24 But this is saying no, it's much more difficult and it has been
25 difficult.

1 So, what is -- and I've read all the briefs in both cases, and I've
2 never really seen a -- I've seen an attempt to rebut this evidence, but they
3 were broadly characterizing, hey, look at these other sources that they're
4 showing how advanced the technology with respect to what *Limulus* was
5 prior to, you know, priority date.

6 I never do -- and I don't see anything on your side squarely
7 addressing these inconsistent statements that are in the '498 application.

8 MS. DOUKAS: Yes, I mean, I think one thing is they -- the
9 statements that you just read, paragraph 13, with respect to, it talks about the
10 full sequence of all proteins and genes involved in the coagulation
11 mechanism of *Limulus polyphemus* has not yet been elucidated.

12 I mean, it's not specific to Factor C, I will say we do concede that
13 before, as far as we're aware, the full sequence, the full cDNA sequence of
14 *Limulus polyphemus*, had not been published.

15 I don't believe -- we don't believe that the inventors that overlap in
16 the '498 PCT necessarily were taking the position that couldn't be done, that
17 wasn't sort of the focus of the EPO proceeding.

18 But it had not been published, and we have conceded that in our
19 briefing that the full length sequence of *Limulus polyphemus* Factor C had
20 not been published before, as of 2013.

21 JUDGE FITZPATRICK: Yes, I mean, this obviously goes beyond
22 that. It doesn't just say it hasn't been done, this is clearly stating that it has
23 been -- it has proven difficult. I read, Your paragraph 12.

24 “However, in *Limulus polyphemus*, even though more than 20 years have
25 passed since the report in the genus of *Tachypleus*, complete identification

1 of these proteins and genes in terms of both structure and function has not
2 been achieved. This is because,” there's a typo here, I'm just going to read it
3 as is, “this is because due to the various differences in diversity of
4 biomolecules depending on the genus and species of horseshoe crab, it has
5 not been possible to accurately determine the full-length sequence structure,
6 expression, and function of these proteins and genes using conventional
7 methods.”

8 And the proteins and genes are referring to the three endotoxin
9 assay, the serines, the B, C, and pro-clotting.

10 MS. DOUKAS: Okay.

11 JUDGE FITZPATRICK: So, it's not just that they didn't have it, I
12 think your position is, okay, even though the cDNA where -- or the
13 sequence, the genetic sequence for *Limulus* Factor C, even though the
14 inventors did not really possess that, and it wasn't published somewhere else,
15 they had a sequence for different species and it would have been routine to
16 get it for this particular species, *Limulus*.

17 However, the same party, had also said in its other statements, that
18 were just 180 degrees opposite than that here.

19 MS. DOUKAS: Yes, and our view is, and just with our expert,
20 and we don't think reading these, I think they are -- they're broad and it's not
21 -- we don't believe it contradicts the positions that we're taking here.

22 We do concede that the full length sequence had not been
23 elucidated and that they had not determined the full length sequence of and
24 for Claim 21, I'll just focus on Factor C for *Limulus polyphemus*.

25 But we don't think that there was a position taken that you couldn't

1 do it, that the intent was really that this is the first time the full length
2 sequence had been published for the Factor C, *Limulus polyphemus* Factor
3 C.

4 And I guess --

5 JUDGE FITZPATRICK: And you take my message, and I'll give
6 you just full responses because it says, it has, quote, "it has not been
7 possible," unquote, that's in paragraph 12.

8 And I know this is difficult evidence for, you know, probably to
9 reconcile with your case, but I sit here and I think that this is really
10 inconsistent with the claims at issue with the position that you're taking to
11 defend the claims at issue that are being challenged in these two
12 proceedings.

13 MS. DOUKAS: Yes, I do think, though, I think that the '767
14 application, when we're looking at it under the written description standard
15 in the U.S., I do think that it contemplates with the most recurrent the
16 invention, *Limulus polyphemus*, as I've discussed, it has examples.

17 We have identified the deposit information that our expert in this
18 proceeding said that a person of skill in the art could use to identify parts of
19 the sequence and then, use routine methods to get to the rest of the sequence.

20 And I do want to -- not to sort of be throwing things at each side,
21 but just going back to Petitioner's arguments and Petitioner did address this
22 paragraph 12 that you identified from the '498 PCT to the EPO.

23 And on Slide 26 of our demonstrative, Petitioner's view was that
24 that statement was generic and entirely unsupported.

25 And the only reason I bring this up is, Petitioner has -- is taking

1 contrary positions between the two proceedings, and whereas, here, wants to
2 rely on that statement, say that this shows that there is no written description
3 support, no enablements.

4 It told the EPO that that statement is generic and unsupported, it
5 included a footnote, talks about it being factually incorrect, and as the party
6 that bears the burden of demonstrating, we think lack of 112 support, and
7 ultimately, unpatentability, we do think that this does go to the credibility
8 that should be afforded Petitioner's arguments.

9 JUDGE CHANG: Okay.

10 I just want to turn quickly to -- I know you probably have
11 something else you wanted to discuss for the PGR, but for the enablement, I
12 don't think you've actually addressed, I think, the major point of the
13 Petitioner's argument, which is the range issue.

14 Are you relying on claim construction for that or are you saying
15 -- how are you addressing that point, that you have not enabled the entire
16 scope of the range, assuming it's read as the range?

17 MS. DOUKAS: So, our view is that it's not, it should not be read
18 as a range.

19 For Claim 21, our view is that it is describing a threshold that
20 needs to be reached, and we think that the '767 application explains how to
21 achieve that.

22 The data shows that, the evidence shows that, even though it's for a
23 different species, you would expect that residual activity be maintained in
24 the *Limulus polyphemus*.

25 We think that, even though it does -- Claim 21 does say at least 10

1 percent or higher to 15 percent or higher, that when you look at it within the
2 scope of the invention, it's a threshold, you don't have to be enabling the full
3 scope.

4 JUDGE CHANG: And what is the -- what is -- what within the
5 intrinsic evidence are you relying on to argue that it's a threshold as opposed
6 to a range and how do you distinguish that between the cases that Petitioner
7 has cited, like *MagSil*, that reads similar language as the range?

8 MS. DOUKAS: I think it would be -- it would be in the -- and I
9 apologize, I only have the '767, but it correlates the discussion of , in Slide
10 18, the Factor C of the present invention with the low susceptibility to
11 inhibition of activity by an ion.

12 That that is the scope of the invention having this low
13 susceptibility and it's achieved, and what you illustrated by is these residual
14 activity values meeting this threshold amount, that that's all that you need to
15 achieve, that's what the claimed invention is directed to.

16 JUDGE CHANG: And what --

17 MS. DOUKAS: So -- I'm sorry.

18 JUDGE CHANG: Okay, but would you agree, if we do read it as a
19 range, then there's no description of the -- no enablement of the full scope,
20 that there is not the description of how you could achieve different points
21 within that range, assuming that limitation's construed as a range?

22 MS. DOUKAS: I mean, we think of, based on the data that was
23 shown -- I'm sorry, I'm going to jump to -- and I believe we briefed this in
24 our paper with the unexpected results, but it kind of ties to it just to get to the
25 data. In the opposition, data submitted after there was data measured for

1 residual activity of *Limulus polyphemus* and Factor C, and that it did show a
2 range that went above 100 percent for the residual activity, and that a person
3 of skill in the art would understand that if you were going to make and use
4 *Limulus polyphemus* as the recombinantly expressed Factor C, that you
5 would be able to achieve 10 percent and even greater than that.

6 But if -- and I'll jump ahead, just cognizant of time, our revised
7 contingent motion to amend, should Your Honors find that there is a wide
8 range of residual activity, and should you find that there is not written
9 description support or enablement support for the residual activity, we do
10 believe and ultimately find unpatentability, because we do have a backup
11 -- sorry, not a backup.

12 But we do have an argument that if there is -- if we are not entitled
13 to the priority date for claim 21 and the unpatentability grounds come into
14 play, we do believe that Petitioner takes contradictory positions with respect
15 to 112 and obviousness from reasonable expectation of success, that their
16 expert's credibility is undercut. He does take contradictory positions.

17 So just because we're on the topic of residual activity, I'll jump
18 ahead to the revised claim 22. So in this scenario, claim 21 has no priority
19 date of December 2013. It's been found unpatentable. We believe that
20 claim 22 would resolve -- if the lack of priority date is based on the residual
21 activity limitations, it would resolve that issue. Claim 22 puts this in scope
22 of requiring the residual activity in the two specifically claimed solved
23 solutions to be higher than a residual activity in control Factor C. So that
24 would be Factor C in SF9 cells or native Factor C.

25 And this, we believe, takes us into the land of *Alcon*. Wherein

1 *Alcon*, the Federal Circuit said that even if -- even though in *Alcon* the
2 Federal Circuit said that the claim was enabled, you didn't have to show a
3 magnitude of being greater. You just had to show that there's a greater
4 value. So in this case, the claim is written that all you would need to show,
5 which we believe that the '767 application describes with the examples and
6 all of the disclosures, that you have a higher residual activity than the control
7 Factor C.

8 So to the extent there's concerns about the -- and it's determined
9 that the residual activity as claimed in claim 21 lacks priority date support
10 and the claim is found unpatentable, we do think that amended claim 22
11 does resolve that residual activity limitation. And just on that, just real
12 quick, just to go back, I just wanted to just highlight, and this is slide 36. To
13 the extent claim 21 is not entitled to a December 2013 priority date and we
14 are looking at whether Petitioner has met its burden to demonstrate
15 obviousness.

16 We do believe that Petitioner's expert has taken, and Petitioner
17 itself, has taken opposite views. For section 112, they argue that a person of
18 skill in the art would have been reluctant to extrapolate the residual activity
19 between different species, and that you can't extrapolate that. Proteins claim
20 residual activity based on information about other species. But for 103, the
21 only prior art they rely on, if it is prior art, is Mizumura, which is the same
22 figure 7. It's data from *Tachypleus tridentatus*.

23 And here, they take an opposite view. They say that a person of
24 skill in the art would reasonably expect now the two to be comparable, and
25 that's talking about *Tachypleus* and *Limulus*. You would have comparable

1 residual activity values. So we think that this undercuts the weight of the
2 evidence and is Petitioner's burden to demonstrate unpatentability and
3 cannot just rely on conclusory assertions. We think this does go to that and
4 does undermine that point.

5 JUDGE CHANG: Well, I think that they did respond to that by
6 saying that, well, now you have -- it's not just the '767 publication, but
7 actually the full-length sequence. You could actually do the comparison that
8 Dr. Schaefer did, for example, and say, okay, now we see that there's only
9 five. They did not do that, but they are saying that based on the comparison
10 of the full sequence and given the difference in the timeframe, 2013 versus
11 2019, that it's not inconsistent. So would you -- does that still strike you as
12 inconsistent?

13 MS. DOUKAS: Yeah, I mean, Dr. Jain -- in the first statement up
14 above, Dr. Jain says in paragraphs 181 to 182, that's what Petitioner cites,
15 that he would reasonably expect. But he didn't actually do the sequence
16 analysis. He didn't do a sequence comparison. So he makes a conclusory
17 assertion. Our view is, in this case, he concludes that one would reasonably
18 expect that this would occur. But he didn't present any evidence himself of
19 sequence comparison or anything showing that there would be sort of
20 sequence overlap to support his conclusion there of the reasonable
21 expectation.

22 And then if you contrast that with then what he said for Section
23 112 and what Petitioner relies on with respect to a person of skill in the art
24 wouldn't want to extrapolate, we do think that there is a missing piece on the
25 Section 103. So unless there are any questions, I will turn it over to my

1 colleague, as well, for the PGR.

2 JUDGE MITCHELL: Thank you.

3 MS. DOUKAS: Thank you.

4 MS. LO: Good afternoon. All right, let me just plug in.

5 JUDGE MITCHELL: Sure.

6 MS. LO: So good afternoon. This is Shon Lo, and I will be
7 discussing the PGR issues. So in the interest of time, I'm going to put up
8 claim 1. You've seen claim 1 already here. It's a method for producing an
9 endotoxin assay that comprises combining three recombinantly expressed
10 proteins that may be expressed in the same or different mammalian cells.

11 So in its argument, Petitioner focused on the last limitation, the
12 same or different, and I'd like to say that that limitation was added to address
13 a 112 rejection, not a 103 or prior art-based rejection, but 112, and it was
14 because claim 8 did not further narrow the scope of claim 1. And so Patent
15 Owner revised that claim, and that's Exhibit 1002 at 123.

16 And the basis of patentability of these claims was the inventor's
17 discovery that Factor C could be expressed in soluble, functional form from
18 mammalian cells, contrary to what the prior art described for Factor C from
19 the *rotundicauda* species of crab, where others had failed in 1997 to express
20 them in monkeys. So I think I wanted to address Judge Fitzpatrick's
21 question about patentability and the inventiveness of these claims.

22 So here I'm now on slide 7. This is a timeline showing the
23 extensive knowledge and information in the prior art concerning these three
24 proteins that was available and known prior to the December 10, 2013,
25 priority date, starting in the late 1970s when the native lysate-based

1 endotoxin was first commercialized.

2 So there's a lot of information on this slide, a lot of references here.

3 The take-home message is that the three proteins in the cascade, along with
4 their endogenous target, the coagulogen protein, were thoroughly
5 characterized in terms of structure and function after the priority date.

6 Factor C was known to be highly conserved across crab species, with
7 multiple reports of approximately 90 percent sequence identity. The
8 robustness of Factor C's functions had been established for both native and
9 recombinant proteins.

10 In fact, a recombinant version of the *C. rotundicauda* Factor C, a
11 commercial version of that assay, was launched in 2004. And further, SKK,
12 the Patent Owner here, showed in 2008 that recombinant *C. rotundicauda*
13 Factor C activated native *T. tridentatus* Factor B, and therefore this cross-
14 species interaction was also known. Patent Owner SKK also showed that a
15 fully recombinant reaction in 2012, in a patent filing in 2012.

16 Therefore, a POSA, in 2013, understood and expected that Factor
17 B and pro-clotting enzyme, like Factor C, would be highly conserved across
18 species and were functional in their recombinant forms. What's missing
19 from this timeline is the 1997 disclosure that *C. rotundicauda* Factor C was
20 not expressed in soluble form in cross-crab cells.

21 Now, importantly, Petitioner's expert Dr. Jain did not consider the
22 majority of these disclosures in reaching his opinions. Only the three that
23 are identified with an asterisk, two references from 1991 and one reference
24 from 1995. Petitioner, therefore, has not and cannot controvert Patent
25 Owner's evidence of how all of this information would inform a POSA's

1 understanding of the '767 application, or that a structured function
2 correlation was known.

3 So I think I will skip ahead in the interest of time to slide 13. Now,
4 you've heard some argument concerning whether a POSA would be able to
5 extrapolate or predict successful or functional protein expression across
6 species. So Petitioner says, oh, a POSA would not simply extrapolate or do
7 that. However, that is just attorney argument. The specification in fact
8 teaches extrapolation, and the evidence, the preponderance of the evidence,
9 supports successful expression of these proteins.

10 And here on slide 14, we have an overview of the evidence on
11 either side. So for Petitioner, we have Dr. Jain who opines that you cannot
12 predict success for Factor C or pro-clotting enzymes and you have to -- in
13 order to support claims directed to expression in mammalian cells, you have
14 to do the experiment and express all of those proteins in the mammalian
15 cells. So that is the wrong legal standard for written description.

16 As the Federal Circuit found in the *Amgen v. Hoechst Marion* case
17 314 F.3d 1313, that case found that examples of expression in two types of
18 cells supported claims of expressing this protein in any vertebrate or
19 mammalian cell. And in addition to incorrectly understanding or applying
20 the law of written description, Dr. Jain did not have the proper perspective
21 for his opinion. He only considered 22 references from the voluminous prior
22 art, several of which were outdated, overly general, or outright inapplicable,
23 as Patent Owner has explained in its papers.

24 Rather than focusing on the recited proteins, Dr. Jain based his
25 opinion on the general complexity and unpredictability in the field of

1 biology, and that's found in his deposition transcript, Exhibit 1065, pages 87
2 and 92 to 93. Now, so we have Dr. Jain and Petitioner's evidence on the one
3 hand. On the other hand, we have the evidence supporting Patent Owner
4 that contradicts his uninformed and overly general opinions.

5 First, the '767 application itself, which teaches extrapolation of
6 successful expression of Factor B and pro-clotting enzyme. We have
7 Petitioner's Opposition expert, Professor Frohman, who testified, as you just
8 saw, with respect to the Opposition, that he would extrapolate and predict
9 successful expression of at least *Limulus* Factor C. And on that point, Dr.
10 Jain agrees with Professor Frohman that a POSA would be able to
11 successfully express *Limulus* Factor C in CHO and HEK293 cells after the
12 disclosures of the '767 application. And that's Exhibit 1068 at page 87.

13 We also have Patent Owner's expert, Professor Schaefer, who
14 conducted an extensive and thorough literature review and concluded the
15 similarities and close relationship between the proteins to support successful
16 expression of Factor B and pro-clotting enzyme. And also in that literature
17 review, he found no reason to expect or any evidence of difficulties in the art
18 with expressing Factor B and pro-clotting enzyme. And certainly Petitioner
19 does not come forward with anything.

20 Some of those reasons why Professor Frohman would expect no
21 difficulties -- excuse me, Professor Schaefer would expect no difficulties is
22 because Factor B and pro-clotting enzyme are smaller and less complex
23 proteins. And so the difficulties that were known in the prior art with
24 respect to Factor C would not be expected for proteins that were like half the
25 size.

1 So in sum, Patent Owner's evidence shows '767 application
2 discloses representative species, and a POSA would understand the
3 inventor's possessed what Petitioner says is missing, *Limulus* Factor C,
4 functional Factor B, and pro-clotting enzyme expressed in mammalian cells,
5 and the Board's written description analysis can end here.

6 JUDGE CHANG: So I have two questions for you. One, you
7 have not mentioned -- I believe in your papers, you argue that there is a
8 claim construction issue that you do not believe, Patent Owner, does not
9 believe that the claim has a functional requirement. And are you dropping
10 that argument? And if not, how can you square that with the fact that the
11 claim itself requires the Factor C and Factor B to actually have that activity?
12 And also, what does it mean to have an endotoxin assay agent if it cannot
13 actually assay endotoxin?

14 MS. LO: Sure. So utility is not a ground that Petitioner has raised
15 here. We are maintaining that the proper interpretation or proper
16 understanding of the claims is that it requires each individual protein to have
17 their canonical function, but that the claim does not require performance of a
18 cascade reaction or performance of an endotoxin assay agent. That is in a
19 different -- that requires additional steps and is recited in a different claim.

20 JUDGE CHANG: Right. Do you agree, though, that it has to be
21 capable of assaying endotoxin? It does not actually require the assay to be
22 performed, but do you agree that the endotoxin assay agent that's claimed
23 must be capable of performing that assay?

24 MS. LO: We do agree. However, we think -- we do agree with
25 that. The difference here is the Petitioner's expert, his understanding of the

1 claim, he imported a functional requirement where there isn't one. And also
2 not requiring the endotoxin assay agent to be functional as a whole actually
3 eliminates the need for trial-and-error experimentation. That was the basis
4 for all of Petitioner's argument on the enablement side.

5 JUDGE CHANG: I'm sorry, the last sentence confused me. So
6 you do agree that there is the requirement that it's capable of performing that
7 assay? Not that the assay has to be actually performed, but it has to be
8 capable of such performance, right?

9 MS. LO: Right, we do agree.

10 JUDGE CHANG: Okay. Thank you.

11 MS. LO: Unless there are some questions about written
12 description, in the interest of time, I will move on to enablement. Okay. So
13 I'm going to skip ahead to slide 29, which is a summary of the evidence on
14 either side for enablement. Well, let me -- sorry, I will go back on slide 28.
15 So these are the reasons why Petitioner's evidence concerning enablement
16 deserved little weight.

17 First of all, Petitioner did not attempt to explain or reconcile the
18 arguments and evidence that it submitted in the opposition concerning
19 expression of *Limulus* Factor C. Its expert imported limitations into claim 1.
20 He conducted a limited literature review, and he also relied on outdated or
21 irrelevant support for unpredictability in the art. There is no evidence of
22 difficulties or inadequacy of routine techniques in terms of obtaining Factor
23 B or pro-clotting enzyme. And for the Petitioner, who's not definitive, it's
24 genus size calculation.

25 So with respect to enablement, Dr. Jain really focused on the

1 difficulty in obtaining the sequences. He said it was nearly impossible to
2 obtain unpublished sequences. And cloning *Limulus* Factor C alone
3 constitutes undue experimentation. Now, on the other hand, we have
4 un rebutted testimony from Dr. Schaefer. We have the '767 application's
5 disclosures, and it describes expressing Factor C in mammalian cells and
6 instructs skilled artisans that those techniques could be used for Factor B and
7 pro-clotting enzymes.

8 The '767 application also teaches how to confirm functionality of
9 these individual proteins and then combine them into an endotoxin assay
10 agent. There's no dispute that a POSA's level of skill, knowledge, and also
11 the level of routine experimentation are high.

12 And so we also have testimony from Petitioner's own expert.
13 Professor Frohman, again, their European opposition expert, opined that it
14 was routine to determine sequences of known proteins, and he expected no
15 difficulties in expressing *Limulus* Factor C by following the '767 application.

16 We also have Dr. Jain agreeing with Professor Frohman with
17 respect to expressing *Limulus* Factor C in CHO and HEK cells used in the
18 '767 application example. And we also finally have Dr. Jain admitting that
19 he could only speculate about how a POSA would obtain unpublished
20 sequences, because he has not done any gene sequencing. So therefore he
21 lacks knowledge and experience of routine techniques that a POSA would
22 have used to obtain those sequences, and that, I believe, it should undermine
23 the weight of his testimony about the degree of experimentation required.

24 Now, Dr. Jain is qualified to opine on protein expression. He has a
25 lot of experience in that field. However, and so importantly, he conceded

1 that it was routine to express proteins after their sequences were known. So
2 in sum, we think that the evidence shows only routine experimentation is
3 required to practice the full scope of the challenge claims of the '109 patent,
4 and this conclusion is confirmed by post-priority date evidence, the '629
5 publication and the McClymont thesis.

6 As Patent Owner presented in its brief, the '629 publication
7 includes less detailed information and refers back to the '767 application
8 with respect to the techniques that were used to express Factor B in pro-
9 clotting enzyme, as well as Factor C from *Limulus polyphemus*.

10 And finally, the McClymont thesis shows that someone with less
11 skill than a person of ordinary skill did what Dr. Jain said was undue
12 experimentation in and of itself, which was to clone *Limulus* Factor C at the
13 beginning of her thesis work, which was contemporaneous with the priority
14 date. So I think that ultimately that document, which is Exhibit 1011 in the
15 PGR, just confirms that only routine experimentation is required.

16 And as far as Grounds 1 and 2, I believe Petitioner has not proved
17 those grounds here because, again, it failed to submit any evidence as of the
18 July 2023 filing date of the application issuing of the '109 patent. So I will
19 -- does the Board have any questions about enablement?

20 JUDGE CHANG: Well, it's actually a question for both written
21 description and enablement. So is there any difference between the Patent
22 Owner's position with respect to enablement and written description
23 specifically with respect to the existence of the full sequence of Factor C
24 protein for *Limulus polyphemus*? Because it seems to me, I think those two
25 are different standards, and I think it has been agreed that as of 2013, the full

1 sequence of *Limulus polyphemus* Factor C has not been published. And so
2 does that make a difference in your argument with respect to enablement
3 versus written description?

4 MS. LO: I think for written description, it certainly makes a
5 difference. In view of the *Teva v. Eli Lilly* decision from the Federal Circuit
6 from this past April, the Federal Circuit found that sequences that were
7 merely routine steps away from known proteins could be determined to be in
8 the possession of a POSA. So again, the specification in that case had
9 murine antibodies, but the claims were directed to humanized antibodies.

10 However, because at the time it was routine to determine the
11 sequence of a known protein, the Federal Circuit determined that the
12 sequences necessary to carry out that humanization were in the possession of
13 the inventors and that supported written description of the humanized
14 antibodies.

15 JUDGE CHANG: Okay. So then it's Patent Owner's position that
16 essentially that determining the sequence of *Limulus polyphemus* from the
17 other species is essentially equivalent to what the Federal Circuit found in
18 *Teva*, is that correct?

19 MS. LO: Yes, that's correct. There are multiple, as Professor
20 Frohman in the opposition, Petitioner's expert in the opposition, opined in
21 which Patent Owner's expert, Dr. Schaefer, agreed there were multiple
22 routine techniques available to determine the sequence of a known protein.
23 That included the RACE PCR technique, screening a lambda phage library,
24 and also standard PCR.

25 And that bears on enablement as well. Again, these are routine

1 techniques. They were well known. That RACE PCR technique was first
2 published in 1988. So this is not -- this is well within the skill level of a
3 person of ordinary skill in December 2013, as well as within the realm of
4 routine experimentation as opposed to undue. Thank you very much. We
5 will reserve our remaining time for --

6 JUDGE FITZPATRICK: I'm sorry. I have a question. I don't
7 know if Judge Chang -- I wanted to give her an opportunity to follow up, if
8 needed. My question is in relation to -- I'll put one on the end -- excuse me,
9 sorry, column 3, lines 25 to 31. And I think you paraphrased this during the
10 presentation because you talked about the basis of the invention. First of all,
11 does that make sense? Would you agree with that?

12 MS. LO: Yeah.

13 JUDGE FITZPATRICK: Okay, so I'm going to read it. It says,
14 "the present inventors have found that a recombinant horseshoe crab Factor
15 C can be produced by use of human cells or Chinese hamster cells as host
16 cells, and that endotoxin can be measured by use of the thus-produced
17 recombinant Factor C while reaction inhibition in the presence of a salt ion
18 is mitigated. The present invention has been accomplished on the basis of
19 these findings."

20 And that is in contrast to a problem that is discussed in column 2
21 about using the green monkey kidney cells for the expression. If this is true,
22 kind of taking this at face value, is there an explanation from Patent Owner
23 for why in both patents, and we can start with '109 patent, why is the Factor
24 C that's recited in the claim, why is it species-limited?

25 MS. LO: In terms of crafting the claims to be directed to *Limulus*

1 and *Tridentatus*?

2 JUDGE FITZPATRICK: Yes, and in the other case it's just
3 *Limulus*. Whereas the whole basis of the invention, the discovery, is the
4 expression, hey, let's use the human cells or the Chinese hamster cells
5 instead of the green monkey kidney cells. If that's the invention, the
6 discovery, how do we get to recite *Limulus* in particular?

7 MS. LO: Well, the specification does say that Factor C is from
8 each of the four species of crab are part of the present invention. I think that
9 you would be able to extrapolate to the other species of crab. The claim here
10 just focuses on -- the dispute here focuses on the *Limulus* Factor C. I will
11 -- yeah.

12 JUDGE FITZPATRICK: Okay. Is there any reason why the
13 Patent Owner was aware of it? Why in both patents the targets seem to be
14 either *Limulus* exclusively or *Limulus* and one of the other four species?

15 MS. LO: Well, if I may speculate, I would say that it's because the
16 *Carcinoscorpius rotundicauda* Factor C is already a commercial product. It
17 was already well known, well described in the prior art, and so there was no
18 mystery, there was no really extremely inventive aspect there. Whereas
19 *Limulus* was relatively unexplored. We're not conceding that there were
20 difficulties obtaining *Limulus* genes or expressing them after the disclosures
21 of the '767 application. However, that was -- and of course, *T. tridentatus* is
22 SKK's native species of crab, which they have conducted extensive research
23 on.

24 JUDGE FITZPATRICK: Thank you.

25 JUDGE MITCHELL: And I think you all are about the same time

1 as far as your full rebuttal times.

2 MS. LOUGHRAN: Okay.

3 JUDGE MITCHELL: But you can feel free to not use at all if you
4 would -- if you'd like to, feel free there.

5 MS. LOUGHRAN: Maybe that will depend on your question.

6 Okay. I think perhaps easiest to start where we left off in terms of rebuttal
7 and I'll answer any questions that Your Honors have. Just to rebut the last
8 point on *Teva*. As we explained in our responsive brief, the key difference
9 between *Teva* and these claims is that in *Teva*, there was -- they did have the
10 humanized protein. They had it. There was one example that was
11 described. Therefore, they had the protein. So in *Teva*, they said, well, you
12 could get the sequence because we know you have the protein.

13 And we know that when you make that protein, you're always
14 going to get the claimed function. So for the PGR, as my opposing counsel
15 just made the point, they say *Teva* is on point here, but again, for purposes
16 of, do you have an example of this method? Have you described an example
17 of this method? Not all of them, but one example? No, they haven't.

18 They don't have the *Limulus* protein by their own admission and
19 they have -- the patent and the claims talk about the challenge, as Your
20 Honors have recognized, is expressing in certain mammalian cells, right?
21 Why were they able to get active Factor C by secreting in CHO and HEK
22 cells when they couldn't get it in the COS-1 cell? What is the link there?
23 Like in *Teva* where they said, well, we know that these antagonists are all
24 going to treat headache. There is no link there.

25 If you look at opposing counsel's slide, the timeline, the thing that

1 is missing from that timeline, there's plenty of information about these
2 proteins, but the thing that is missing from that timeline is mammalian
3 expression of these other species of crab. And I think she pointed to some
4 cross-reactivity data in 2012 that Seikagaku had put in the record. That was
5 expression of Factor B in pro-clotting enzyme in insect cells. So there's a lot
6 of information that they'd like to import into this specification.

7 The key information and the information that the inventors were
8 actually grappling with is how do you do this? How do you make these
9 proteins in a functional form, as Your Honor has recognized, the claims
10 require them all to have their activity when all we know about recombinant
11 production in mammalian cells at this point is does it work in COS-1?
12 Okay, we've solved that problem for Factor C, but there's no other
13 information with respect to Factor B and pro-clotting enzyme.

14 Now, they say Dr. Jain didn't provide any explanation as to why
15 that would be a challenge, and that is not true. So Dr. Jain's declaration talks
16 about why there's no explanation. Again, they didn't include that greater
17 sialic acid limitation in any of these claims. He talks about the difficulties at
18 the time with recombinant production in mammalian cells. He talks -- and
19 I'm at Jain Declaration 121, 124, 130, 132. He talks about, well, we know in
20 mammalian cells you're going to get glycosylation, and he cites articles,
21 including the Haussler paper.

22 Now, they've disparaged that paper, but that paper is cited in the
23 patent itself, right? So he's looking at what the Patent Owners, what the
24 inventors would have been looking at and knowing about glycosylation and
25 the challenges with glycosylation, and the fact that even if you have small

1 variances in amino acid sequence, you might get different -- you know, a
2 person of skill in the art would understand you could get different
3 glycosylation profiles.

4 He talks about recombinant technology being unpredictable, and
5 he talks about the fact that it was known that it was a challenge to get these
6 proteins to secrete, right? And that's sort of where we get up to with respect
7 to the inventors putting that in the application. This was a secretion -- this
8 presented a secretion problem, which they solved for Factor C, but not for
9 the other claimed proteins.

10 So, I mean, I understand they want to import a lot of background
11 information, but it's not the key information that would allow a person of
12 skill in the art to understand that they had possessed everything, the full
13 scope of what they claimed in that application, and *Teva* does not dictate
14 otherwise.

15 JUDGE CHANG: So a question for you in terms of the written
16 description. There's a fairly old case law that says it's not the function of the
17 claim to specifically call out what's not going to work in terms of written
18 description. I've got to say that if it becomes too -- there's too many things
19 that don't work, too many combinations don't work, then you have to, if
20 there's undue experimentation, then you may need to -- there might be an
21 enablement issue.

22 So given that, is it required or is it inadequate written description if
23 the combination, they have claimed this combination of different species and
24 host cells, but if the majority of that will work and it's not undue
25 experimentation, it's discovered which one will not work, is that sufficient

1 for written description, putting aside that enablement issue?

2 MS. LOUGHRAN: So I agree with Your Honor that you can have
3 some -- I guess maybe you're getting at some inoperable embodiment and
4 still have adequately described your invention. Is that sought of the line --

5 JUDGE CHANG: Yes, right.

6 MS. LOUGHRAN: Yes. Right, so exactly. So that -- I don't think
7 that that line of cases undermines the written description point here because
8 it's, again, it's not that their claim doesn't encompass an inoperable
9 embodiment and therefore there's no written description. It's that there has
10 been no explanation on how to overcome what was inoperable about that
11 expression of that cell, right? And that fact is not -- does not then appear in
12 the scope of their claims.

13 So they look out in the field and their experiments show that you
14 can't do it for COS-1 and therefore our invention is something different than
15 that. And then, you know, but then they're saying, well, we're going to add
16 all these limitations, all these additional limitations about proteins having not
17 actually tested or described or offered any theory as to why those proteins
18 would not run into that problem as well.

19 So, you know, I don't think that the mere fact that Factor B and
20 pro-clotting enzyme, those limitations encompass COS-1 is what doesn't
21 create written description here. It's that there is absolutely no description of
22 how they overcome or knew to overcome that problem. And not just
23 -- again to underscore Dr. Jain's point, not just to express these proteins,
24 right? It is not an expression problem here for them because what they went
25 ahead and said is they have to actually go and have their function. And

1 that's a step even further removed from what they've described here.

2 And, you know, there's a question of, well, is it capable of? Yes. I
3 mean, I think if you look at Factor B, pro-clotting enzyme, and Factor C,
4 each one has to have its activity. So they all work in a chain. There's no -- I
5 don't think we've alleged and Dr. Jain certainly didn't say that, oh, you know,
6 that they have to ultimately detect endotoxin at the end. But the result of
7 putting all of those proteins together as the claim requires, you know,
8 producing, you know, Factor B, Factor C, Factor C with their activity, if all
9 of those elements are met, you would get, as Your Honor says, an endotoxin
10 detection assay that's capable of detecting endotoxin.

11 And that was Dr. Jain's point, is that in expressing these proteins in
12 mammalian cells, you don't just have to express them. There was a problem
13 with getting them actually functional, and the inventors did not describe or
14 enable how to do that for the vast majority of this claim.

15 Okay. I'd like to -- just one more, just to go back now, unless -- do
16 Your Honors have any more questions on the PGR?

17 JUDGE CHANG: No.

18 MS. LOUGHRAN: Okay, then I'll go back to the IPR. So I think
19 Your Honors ended on reasonable expectation of success. And I do just
20 want to emphasize, again, I think that my opposing counsel said that Dr. Jain
21 didn't put on any evidence about comparing those sequences from which he
22 could then conclude that you would get -- a POSA would have a reasonable
23 expectation of getting something within, again, within the goal posts of the
24 claim range. But he cited the inventors' own sequencing and their own
25 statements of the comparability.

1 So I don't think that he would have needed to go and do that
2 sequence himself, because by 2019, I think to Your Honors' point, the
3 inventors themselves in the 498 PCT and in their declaration of prosecution
4 had put that sequence in the public domain. A POSA would have had that.
5 So he didn't need to go and do that process.

6 He references that to say, oh, at this point now, we see that there is
7 some level of similarity between these sequences. And so a person of skill
8 in the art would have reasonably expected to get an example, a species
9 within the scope of the claim, thus rendering it obvious in view of
10 everything that was known by 2019.

11 Let me just go back, Your Honor. I think you had a question for
12 my opponent about, you know, if all of this stuff was so routine, what is
13 patentable about this claim? And I think that the suggestion there, the
14 instinct there is correct. And let me see if I can maybe square that for you. I
15 mean, I think the idea here is we have species of horseshoe crab. As I
16 started with in our discussion earlier, different groups were moving along at
17 different paces to sequence and express these proteins.

18 I think by 2016, the idea of doing this was most likely obvious.
19 Obviously, that's what's being argued in Europe. And when I say this, I
20 mean get the sequence and recombinantly express it. I think that informs the
21 obviousness arguments there.

22 And I think, again, in 2013, probably also an obvious thing to do.
23 But what I think was patentable or what the inventors were maybe driving
24 for was not that the recombinant production of *Limulus polyphemus* was the
25 patentable thing. They link it up to the function, right? They link it up to

1 the residual activity. I think that is how they say in 2013, or as of 2013, or
2 as of their actual application date, that this was a new thing.

3 And so, in order to do that, they have to put the public on notice of
4 the full scope of what it is that they believe to have contributed to the public
5 knowledge on this topic. And I think where they have come up short, both
6 on written description and enablement, is they have provided an example
7 from a different species that you would see a residual activity value. And
8 they sort of put that data in the application and then claim much broader than
9 that.

10 But if they really wanted to commit to the idea that *Limulus* and
11 *Tachypleus* were so similar, you could envision a claim that says within 5
12 percent of the residual activity of this other species, or something like that.
13 But because that metric is so variable and unpredictable, which I think is
14 undisputed on this record, they claim everything above it. Everything above
15 these very low thresholds.

16 In the parlance of *Magsil* and others, to the enablement point, they
17 seek to dominate all Factor C proteins that have this characteristic, whether
18 the person who made them was trying to get them or not, regardless of
19 whether they knew how to achieve any particular value. I think it's very
20 clear from the case law that that is impermissible because it takes a lot out of
21 the scope of the public domain when the Patent Owner did not teach how to
22 do that. Leaves it to the POSA to engage in trial and error to do that.

23 And if you look at one of the cases that was pretty well cited,
24 *Boston Scientific*, there's an interesting -- I mean, we talk about what's well
25 known in the art and whether or not that can be imported into a specification.

1 But if you look at that case -- let me see if I can -- the Patent
2 Owner, there's the main claims that are discussed there, but then there's the
3 claim -- there's a claim that has a limitation much like this one which is, you
4 know, it's not just that it requires the rapamycin or those analogs that were
5 found to be not described or enabled, but also it required them to use those
6 in a way where the in diameter -- in-stent late loss in diameter following
7 implantation in a human was less than about half a millimeter.

8 And the Court looks and says, well, there's nothing in the
9 specification that suggests how a person of skill in the art would select these
10 particular analogs or these proteins and get something within that function
11 that they're claiming that they have invented. There's no indication of which
12 structural features of those analogs are necessary to achieve these results.

13 And Judge Fitzpatrick, you used the word achieve. I think maybe
14 that's where this is coming from. It's possible that one could use trial and
15 error, but that is insufficient both for written description, frankly, and
16 enablement under this case law.

17 So I do think that when we talk about what's inventive about this
18 claim, if it's anything, it is this functional metric which has been
19 demonstrated to be highly unpredictable. And the Patent Owner just did not
20 put enough information into that '767 application to describe and enable it.
21 And the attempt to import things that a POSA could have done, things that a
22 POSA could have envisioned.

23 There was some other -- I think the word was contemplated. That
24 is, under all of this case law, where you don't have an example of something,
25 and you don't have a direct line between that composition and the broadly

IPR2025-00440 (Patent 11,236,318)

PGR2025-00023 (Patent 11,959,109)

1 claimed function that you've put in your claim, you can't import all of that
2 into the specification to say, oh, this was my invention. Patent law does not
3 allow that, either through the written description or the enablement process.
4 Do Your Honors have any questions on that?

5 JUDGE CHANG: I do have a very generic question on the burden
6 of proof issue.

7 MS. LOUGHRAN: Yeah.

8 JUDGE CHANG: So I think I had asked both you, opposing
9 counsel and you, about the same issue in terms of the burden of production
10 versus the burden of proof or persuasion, I should say, under *Tech Licensing*.
11 And I think -- I thought you had said that you understood both of those, that
12 it is also the Patent Owner's burden to show that the claims were not
13 described or enabled, or were described and enabled by the prior application.

14 And I understand the Patent Owner's point is that they have the
15 burden of production, but that Petitioner ultimately has a burden of showing
16 that the '767 spec does not support the claims. So do you guys actually
17 disagree on that, or am I misunderstanding your position?

18 MS. LOUGHRAN: I don't -- I mean, when I heard my opponent
19 answer your question, I didn't detect a disagreement on that. I mean, just for
20 the record, I'll restate our position, which is, you know, Petitioner comes
21 forward with evidence, some preliminary evidence and argument of a lack of
22 description. It is Patent Owner, or that essentially identifies the priority
23 dispute, right? That this is a requirement that they are claiming a 2013 date.

24 Patent Owner then comes forward with evidence demonstrating, I
25 think the language in *Tech Licensing* is evidence sufficient to demonstrate

1 that they are entitled to that date, which our position here is that that has
2 been insufficient, that evidence has been insufficient. And then it is, you
3 know, and then, and so they are not entitled to that date from which now we
4 have the burden to show, well, how is the claim invalid or unpatentable in
5 some other.

6 JUDGE CHANG: Okay. So your position is that they have not
7 yet satisfied their burden of production even to show the priority date, and
8 therefore the ultimate question of whether or not the patent is entitled to that
9 priority date is still -- I guess the Patent Owner has not shown that, their
10 burden on that issue. Is that right?

11 MS. LOUGHRAN: Yes. I mean, to take it as an example, because
12 I do have some time left, and I don't have too many other points to get to,
13 but for example, on this issue of enablement of claim 21, we have argued, I
14 think -- well, not I think. We have absolutely argued that that claim requires
15 enablement of the full scope of the claimed open-ended ranges, and have put
16 forward the allegation that the specification does not teach a person of skill
17 in the art to practice the full scope of that claim.

18 They have not come back and pointed to anything in that
19 specification, like said, here's where it is, here's how you get a residual
20 activity with 50 percent, or here's how you get a residual activity with 75
21 percent. It's not there, and they have not pointed to it or demonstrated their
22 entitlement to import well-known or routine -- there's obviously a difference
23 between well-known and routine, but known information that would tell a
24 POSA how to do that.

25 And therefore, they are not entitled to that priority date under the

1 appropriate priority date, the '629 publication or the 490 public PCT and Ms.
2 Amora invalidate that claim.

3 JUDGE CHANG: Okay. I think that -- I would just say that I do
4 think Petitioner has the ultimate burden of showing invalidity. And so under
5 your position, though, it seems that -- okay, I think I understand just in terms
6 of I think you and Patent Owner may have a difference of opinion in terms
7 of what the threshold is to show that they have met the burden of production.
8 I think I understand your position. Thank you.

9 MS. LOUGHRAN: Okay.

10 JUDGE MITCHELL: Can I ask one? Sort of -- this is not, a little
11 bit troubling, but a little bit -- not troubling. But trying to parse through the
12 patent here, there seems to be statements on both sides from Patent Owner
13 and Petitioner that are really, you know, to be considered statements against
14 interest could be considered. Admission is kind of you're saying the patent
15 does contain something that now you're saying does not and then Patent
16 Owner is saying, oh, this is all new and a new application, when they're
17 trying to say, no, we really had possession at the time.

18 So if I'm weighing those, would it not be fair to say, look,
19 Petitioner has a burden. We know you have the burden all the way through
20 to prove unpatentability of any of the claims. So would it be fair for me to
21 then say, should I weigh more heavily against you? Those statements that
22 really show, hey, you've said two different things.

23 Now, I know you have, you know, and we have to first be like
24 what were you really saying in opposition, and that is a different standard,
25 different thing. You're not necessarily addressing a certain written

1 description here not in the patent. So that all comes into it. But that's sort
2 of, you know, who do we hold more accountable, I guess, when we're
3 talking about the burden or should we?

4 MS. LOUGHRAN: So that's a good question. And, you know, I
5 mean, I would say you should take the evidence, maybe there's an
6 evidentiary hierarchy is the way I would think about it. So let's say that
7 there was no E.P. opposition and we were not making these statements,
8 right? Then we would be looking at the evidence that existed. And I think
9 what's very probative is the admissions of the inventors themselves three
10 years later, as Judge Fitzpatrick said, that this was very hard to do and that
11 they were not able to do it until now.

12 And the fact that they got -- they did get a patent off of those
13 statements and those allegations. Okay, so that's one grouping of things that
14 we've been arguing about inconsistency, but that did not come about because
15 of any dispute in Europe. That was just their inventors going ahead three
16 years later in an unrelated case trying to get claims for recombinant *Limulus*
17 *polyphemus*.

18 JUDGE MITCHELL: So essentially an unforced error.

19 MS. LOUGHRAN: Exactly. That is just -- and we say that's great
20 evidence. We can't prove that the, you know, it's hard to -- we can't reach
21 into the inventor's brain in 2013 and say, did you have this idea? Nobody
22 can really do that. But we can say, well, they told everyone, including, you
23 know, in the public and the patent offices, that they had invented it later. So
24 that's great probative evidence of what was in their head. And that is, as you
25 say, an unforced error. That did not come about because of any dispute.

1 That was their affirmative choice and we will hold them to those statements.

2 Then when you get, okay, well, now there's a dispute about, like,
3 whether that was really patentable in Europe. You know, I think you take
4 those pieces of evidence in sort of an equivalent form. But what I would say
5 is, you know, is I would take into account that as I started with this
6 presentation, you know, something can be obvious and not described.

7 And so it is not inconsistent to say, well, making recombinant
8 Factor C from *Limulus Polyphemus* was obvious in 2016, 2015, 2014, 2013,
9 and all of the arguments that went to that argument, right? All of the
10 evidence that went to that argument. Not inconsistent with saying, okay,
11 fine, but you haven't described and enabled the full scope of that thing plus
12 the function that you have attributed to it, to Judge Fitzpatrick's point, to get
13 this claim in the first place.

14 So there is not an inconsistency, and I know we're both saying that
15 there is an inconsistency and Your Honors are entitled to weigh that as you
16 would. I don't think that it counts, you know, more heavily against Patent
17 Owner or Petitioner. We are trying to demonstrate that these two, when
18 these two legal principles are applied, there is no inconsistency. Your
19 honors are entitled to make that determination or not.

20 But I do think you would separate out the inventor's own
21 statements against their, you know, essentially statements against interest is
22 different in kind than, you know, the things that have happened, you know,
23 with respect to the opposition. And take that as a, you know, sort of a
24 different bucket of admissions. As Your Honor has said, sort of an unforced
25 error.

1 JUDGE MITCHELL: So are you saying too with just taking
2 statements that Petitioner made in opposition, you're saying, well, what we
3 said doesn't go far enough to say they were in possession of the full claim?

4 MS. LOUGHRAN: Yeah.

5 JUDGE MITCHELL: Okay.

6 MS. LOUGHRAN: Right. We're saying, all we said is -- and just
7 to cabin this off, the Frohman Declaration was only about Factor C. It has
8 nothing to do with residual activity, nothing to do with Factor B, nothing to
9 do with pro-clotting enzyme, okay? The claim in Europe is just to
10 recombinant *Limulus* Factor C, which we're saying, if you look at everything
11 that's in the art, including the '767 specification read by that time in 2016,
12 yeah, a person of skill in the arts is going to say, that's an obvious thing to
13 do.

14 But, and legally speaking, that is not inconsistent with backing up
15 three years, reaching into the inventor's minds and, you know, sort of what
16 was known by a person of skill in the art at the time and saying, did they
17 invent the full scope of that thing in the functional form that allowed them to
18 get that claim in the first place? Those are not inconsistent arguments. I
19 realize that, you know, my opponent has put the statements up and has said,
20 they've admitted that this thing was known, but that was -- we're saying that
21 it was known. That was known as an obvious thing as of 2016.

22 JUDGE CHANG: Well, I mean -- okay, I'm sorry. I just wanted
23 to mention that I understand your argument. It's obviously a different legal
24 standard. It's a different, you know, issue, obviousness versus enablement
25 and written description. But I think what we're concerned about is the

1 factual statement that's made in support of the arguments, which could be
2 seen as inconsistent. For instance, that it would be routine or it would be
3 easily, well, I forgot the exact term, but it would be routine to be able to
4 accomplish something.

5 Because I think one of the major arguments in this case is whether
6 or not -- I think it's a little different for written description, but just
7 enablement, whether it's, you know, enabling to express Factor C, let's say.
8 And I think that some of the factual statements in support of obviousness
9 does go to that. Although I understand, I guess, in the IPR case, at least
10 most of your enablement argument is with respect to the functional
11 limitation. So that may not be as inconsistent.

12 MS. LOUGHRAN: Correct.

13 JUDGE CHANG: Okay.

14 MS. LOUGHRAN: Correct, exactly. That is why there's not an
15 inconsistency there. Your Honor is exactly correct there. And then with
16 respect to the PGR, just to close the loop on that, you know, those arguments
17 about getting the sequence for Factor C and expressing Factor C, you know,
18 again may have been obvious by 2016. That's what Professor Frohman's
19 declaration was in support of.

20 But those statements don't get at Factor B. Those statements don't
21 get at the challenges with Factor B, Factor C, expressing them in
22 mammalian cells, expressing them in the same or different cells. So the
23 insufficiencies of written description and enablement with respect to claim
24 109 go well beyond the statements regarding the EP '670 patent.

25 Do Your Honors have any other questions? I will, since I have a

1 few minutes left, I will just briefly rebut on the point about unexpected
2 results, because, you know, my opponent did raise it. The data that you saw
3 on unexpected results for the inhibition data, if anything, shows that the
4 prior art and the D19 data show that, like, that Patent Owner essentially
5 claimed what was in the prior art, right? So for unexpected results, the idea
6 is that you would need to compare what was the closest prior art with your
7 unexpected results to show that the claim was non-obvious.

8 Patent Owner points to figure 7, the Mizumura figure, as closest
9 prior art, but the values in figure 7 are within the claimed ranges. So it's
10 hard to say, because this claim is so broad, it is hard to say, oh, they
11 demonstrated unexpected results as compared with the closest prior art.
12 Well, the closest prior art is within the scope of the claim anyways. They
13 haven't come forward with any evidence of unexpected results
14 commensurate with the breadth of that claim.

15 And, you know, I'll just direct Your Honors to our reply at page 24
16 through 26, because Dr. Morris relied on that inhibition data, but there were
17 an enormous number of inconsistencies between how that data was gathered
18 and the comparison that she made. And so, you know, we cited to her
19 testimony over and over and over, I said, well, was the temperature the
20 same? I don't know. Were the concentrations the same? I don't know.
21 Could that have impacted the results? It could have.

22 So the evidence of unexpected results in this case is legally
23 insufficient to save this claim from obviousness. It is not commensurate
24 with the scope of the claim. It's based on data that was, you know, that the
25 expert had not verified, was subject to a whole host of differences that

1 couldn't be compared with the Mizumura data. And, you know, the claim is
2 so broad that it encompassed the comparative prior art in any case.

3 So for that reason, claim 21 is obvious. There's no unexpected
4 results that would compel a finding otherwise. And Your Honors, Petitioner
5 requests that an order enter for unpatentability as to the challenge claims in
6 the '318 patent and the '109 patent.

7 JUDGE MITCHELL: Thank you.

8 MS. LOUGHRAN: Thank you.

9 MS. LO: Your Honors, Shon Lo again for Patent Owner. So first,
10 with respect to the '629 publication, I just want to emphasize that no U.S.
11 patent issued from that publication. The claims were rejected as obvious and
12 that application was abandoned. Now, if we're going to talk about the '629
13 publication, we should talk about the entire publication and the evidence
14 concerning it. Since Petitioner is relying on it so heavily as a purported
15 statement against interest, we dispute that it is a statement against interest.

16 But regardless, what the '629 publication reflects is that routine
17 techniques, such as RACE PCR, were used to clone the *Limulus* proteins,
18 Factor C, Factor B, and pro-clotting enzyme. And then the same techniques
19 described in the '767 application were used to express those three proteins in
20 mammalian cells. So that is actually entirely consistent with our arguments
21 to the Board in these two proceedings. Only routine techniques were
22 required.

23 Professor Froman looked at the 498 PCT and drew the same
24 conclusions. He said in his declaration that, aside from a few surprisingties
25 (sic), I don't see any evidence of difficulties in doing this work. So if the

1 Board is going to weigh the evidence of the '629 publication, it should weigh
2 it in the context, in its full context. Petitioner should not be allowed to pick
3 and choose how it wants to rely on the '629 publication.

4 Judge Chang, with respect to your questions about burden, I think
5 the law is clear. Petitioner raised a question about 112 support, entitlement
6 to the priority date. It's fairly ludicrous to say that Patent Owner has not met
7 its burden of production. It's a burden of production of evidence, and we
8 have submitted expert declarations and voluminous prior art references
9 illustrating and proving that this genus of proteins, Factor C, as well as the
10 other two proteins, were well-known in the art and well-characterized.

11 Therefore, a POSA would have expectations and knowledge
12 concerning these proteins. They're not starting from a blank slate, and I
13 think that that is entirely permissible and indeed required in the written
14 description analysis. It is not importing knowledge from outside the
15 specification. It is part of the general knowledge and skill of a person of
16 ordinary art, and that is something that we'll submit that Petitioner's expert
17 did not fully consider. He did not have the right perspective because he only
18 considered 22 references as opposed to everything that a POSA would know
19 about these proteins.

20 So Patent Owner has come forward and met its burden of
21 production, and the ultimate burden of persuasion of unpatentability is
22 always on the challenger. The presumption of validity stands here, and we
23 submit that when you weigh that evidence, the evidence that Petitioner's
24 come forward with against the evidence that Patent Owner has come forward
25 with, that that evidence weighs in favor of Patent Owner.

1 With respect to the differences between the opposition and
2 -- Petitioner's position and statements in the opposition and here, Petitioner's
3 emphasized the difference in date. 2013 priority date for the claims in
4 question here versus 2016 at issue in the opposition. However, when we
5 challenged them to say, hey, identify some change in the art that would
6 affect Professor Frohman's factual statements and testimony in a sworn
7 declaration that would explain these inconsistencies, they didn't.

8 And in fact, there was no change in the art between 2013 and 2016
9 other than perhaps the publication of genomic data that Patent Owner later
10 showed was already available as of the priority date. So really, those
11 intervening three years, there's nothing new, nothing changed. Petitioner's
12 testimony, arguments, and evidence in the opposition concerning *Limulus*
13 Factor C should apply equally to Factor B and pro-clotting enzyme. That
14 was another point that we made that they never responded to.

15 They never said, no, these are reasons why a POSA would not
16 apply those statements to Factor B and pro-clotting enzyme, and they never
17 responded to that. So in terms of burden, I think that it is Petitioner that has
18 failed to meet its burden and Patent Owner's satisfy that burden.

19 With respect to the case law here, so the *Teva v. Lilly* case, as well
20 as the earlier Federal Circuit opinion in *Ajinomoto*, both of those cases stand
21 for the proposition that background knowledge and routine techniques can
22 supply representative species for a well-known genus. And the claims here,
23 I think the overwhelming preponderance of the evidence shows that the
24 genus of proteins in both proceedings is small, well-known, and expressly
25 identified in the specification. So --

1 JUDGE CHANG: I do want to talk about *Teva* a little bit, because
2 I actually sort of logged on it so that I can pull it up and kind of ask you
3 questions about it, because I did think there were some differences, right?
4 So especially for the IPR case, right? For example, I think in *Teva*, the
5 Court explicitly said the claims are to the method of treating headaches, not
6 to the antibodies themselves. And here, at least in IPR, it is actually to a
7 biological molecule. It is to the recombinant Factor C of that particular
8 species. That's the first issue.

9 And the second issue, I think, in the spec, I believe they also said
10 in the spec, they discussed in the spec the method of humanization. So I
11 don't think there's any discussion in the specification of the '767 application
12 about how you would determine the sequence of the Factor C protein. So
13 how does that apply to the IPR case first? And do you think there's a
14 difference between the IPR case and the PGR case, given that the latter is a
15 method claim?

16 MS. LO: Yes, Your Honor. So yes, we agree that *Teva* is more on
17 all squares with the PGR claims, because the PGR claims are method claims
18 versus the claim to the protein in the '318 patent.

19 However, for the IPR, *Teva* is still relevant because it stands for
20 the proposition that examples outside of the claim genus can support written
21 description, and that sequences, given Petitioner's focus on sequences, that
22 sequences that are a routine step away from proteins that were known or
23 accessible to persons of ordinary skill, the POSA -- the inventors were
24 deemed to be in possession of those sequences, constructive possession in
25 the specification of the sequences of known proteins. That is how *Teva*

1 supports the claims of the IPR.

2 With respect to your second question which -- sorry, can you
3 remind me what your second question is?

4 JUDGE CHANG: Yeah, I just think in the specification of the
5 *Teva* patents, there was also a lot more description of how you would
6 accomplish, for example, a humanization, and I don't know that that similar
7 type of disclosure was in the '767 application.

8 MS. LO: Yes, I think that actually was in the '767 application, and
9 one of the references that were incorporated by reference, Patent Owner's
10 own prior patent publication concerning the cloning of pro-clotting enzyme
11 -- of recombinant pro-clotting enzyme that was incorporated by reference in
12 that specification, earlier specification, describes the cloning of the enzyme
13 and says that these regular routine molecular biology techniques could be
14 used to clone pro-clotting enzyme from any species of crab. They used the
15 *T. tridentatus* as an example in that earlier application. And so
16 incorporation by reference is one way of doing it. I admit it's a little
17 attenuated.

18 However, again these were well-known and routine techniques, the
19 techniques that the inventors described in the '629 publication in which they
20 provided a specific example of cloning *Limulus* Factor B and pro-clotting
21 enzyme. They used the RACE technique that Professor Frohman invented
22 or first published in 1988. And he said in his declaration, it's been cited
23 thousands and thousands of times since then. That was part of the routine
24 bucket of skills that a POSA would have.

25 A POSA doesn't need to be told that this is how you clone a gene

IPR2025-00440 (Patent 11,236,318)

PGR2025-00023 (Patent 11,959,109)

1 in 2013. They would have known that based on the high sequence
2 homology of the *T. tridentatus* proteins that they could design primers and
3 make that protein.

4 And with respect to an earlier question about whether or not you
5 need to know the nucleotide-by-nucleotide sequence of a gene in order to
6 express the protein, the answer is no, you don't. All you need to know is one
7 end of the protein -- I mean, one end of the gene, design a primer for one
8 end, a generic primer for the other end, and then PCR and plug that into an
9 expression vector. That evidence is found in Professor Schaefer's
10 declaration. It's in Professor Frohman's declaration as well.

11 JUDGE CHANG: But is that described for the cloned species in
12 the spec, that procedure?

13 MS. LO: That specific technique is not described in the '767
14 application. However, it was a routine and well-known technique which
15 Petitioner's evidence itself establishes, as well as Patent Owner's.

16 JUDGE CHANG: Okay, thank you.

17 JUDGE FITZPATRICK: Let me ask you, this is as it relates to
18 *Teva*, and let's just focus on the '318 patent, the IPR patent. What is the
19 known genus?

20 MS. LO: Well, I'm actually not sure that it's --

21 JUDGE FITZPATRICK: Or the well-known genus. Somebody
22 said, *Teva* says well-known genus. What is the -- like you're applying *Teva*
23 to this case, you say it applies, so what's the well-known genus here?

24 MS. LO: Well, I think that really the '318 patent is directed to a
25 specific protein with some normal degree of variation. It's not recited in the

1 claims, but the specifications does talk about percentages of homology. So
2 to the extent that that claim is considered a genus claim, it's a very small
3 genus based on the well-known *Limulus polyphemus* Factor C protein.

4 JUDGE FITZPATRICK: But that protein, I mean, that's what
5 you're claiming. You're claiming Factor C, just only when it has been, you
6 know, recombinantly expressed. I guess, well, I mean, it's your analogy that
7 *Teva* applies to this situation. So I'm just wondering if you can articulate
8 what the well-known genus is.

9 MS. LO: I believe the well-known genus is *Limulus polyphemus*
10 Factor C. That's the protein that's claimed -- that's recited in the claim.

11 JUDGE FITZPATRICK: Okay.

12 MS. LO: Yeah.

13 JUDGE FITZPATRICK: You mean the native one? Because it
14 can't be the one that's recited in the claim, because then it's not --

15 MS. LO: I see your point. Yes, the native protein. But again,
16 recombinant versions of other Factor C proteins are known and one was
17 commercialized, in fact, from one of the Asian species as well. So --

18 JUDGE FITZPATRICK: So you take the well-known genus. I
19 mean, I read the briefs, but I was scratching my head, okay, how do we
20 think, again, the *Teva* court, the Fed Circuit panel, to tell us about that
21 situation, you know, how do we apply it here? And I didn't see a definitive
22 articulation of what the well-known genus is. But if it's the native, you
23 know, *Limulus* Factor C, and then is it just your position that we would only
24 take routine, you know, routine -- I don't know how you want to articulate it.
25 If native *Limulus* Factor C is the well-known genus, then I guess what would

1 be the invention if everything else is routine?

2 MS. LO: The invention is the inventor's discovery that this protein
3 could be, the Factor C protein, could be recombinantly expressed by
4 mammalian cells. The known problem in the art was this 1997 publication
5 that said, oh, we tried to express Factor C in the monkey cells, but it was not
6 secreted and it was insoluble and then inactive. And so the inventors
7 thought, well, let's take another crack at this problem. Let's try it in CHO,
8 the Chinese Hamster Ovary and HEK293 cells. And they found that it
9 worked and that it not only was secreted, it was functional. And so that is
10 really --

11 JUDGE FITZPATRICK: Yeah.

12 MS. LO: -- and then, you know, they went on to test its residual
13 activity and the claims were ultimately granted because of unexpected
14 superiority, because everyone expected that the *Limulus* and the T.
15 *tridentatus* Factor C proteins would have similar functional properties, right?
16 That was the prevailing wisdom in the art. That's what a POSA would have
17 believed.

18 And so, if you observed a slightly improved quality or resistance to
19 ion solutions, this was unexpected, and that was the basis of part of the
20 disclosure as well as the issues in the claims. Well, so the thing, and they --

21 JUDGE FITZPATRICK: But it's fair to say that discovery that
22 you were just paraphrasing, that discovery is with respect to the *Tachypleus*
23 *tridentatus* and whereas the claim is targeting a different species.

24 MS. LO: Yes.

25 JUDGE FITZPATRICK: And so is it -- there's an additional leap,

1 I think, when we're trying to square the *Teva* case on to this claim.

2 MS. LO: For the '109 patent, I agree that the applicability of *Teva*,
3 it's less on all squares. I think there's provisions from *Teva* that apply.

4 JUDGE FITZPATRICK: I guess, but there's -- I don't know if it
5 was just, yeah, the '318 patent. Yeah, yeah, it's just claiming the Factor C,
6 right? So you take the -- you take *Limulus*, native *Limulus* Factor C. If
7 that's your well-known genus, then I said, okay, well, what's the invention
8 that everyone wants to claim? And you said, it was the discovery that you
9 could express it in a human kidney cell line, a HEK293 cell line, and it
10 would work.

11 But their discovery was with respect to a different species. So that
12 part was routine. And then, so there's a routine jump, and then there's also
13 this extrapolation. It's like it's two steps removed. But we want to also say,
14 okay, since it works for *T. tridentatus*, we're going to assume it works for *L.*
15 *polyphemus*.

16 MS. LO: Yes, and I think that that's not just an assumption. It's an
17 informed assumption based on the public disclosures of the high percentage
18 of sequence identity between the three Factor C proteins that were -- so, you
19 know, the *rotundicauda* and *Limulus* Factor C were reported to be at least 90
20 percent sequence identity. And then the *rotundicauda* and the *T. tridentatus*
21 proteins were 97.7 percent identity with most of the differences in some non-
22 translated region, untranslated region.

23 So these were known to be very, very highly similar, nearly
24 identical proteins. And so that extrapolation is actually well supported by
25 the knowledge and the evidence of those -- the knowledge of those of

1 ordinary skill in the art.

2 JUDGE FITZPATRICK: Thank you.

3 MS. LO: I believe I'm out of time, if that's what the flashing red
4 light means. So unless the Board has any other questions, thank you for
5 your time and attention.

6 JUDGE MITCHELL: Thank you. And thank you all so much.
7 This was incredibly helpful, and I know, exhausting. So I hope you all have
8 a nice evening. If you all could stay just for a few minutes to make sure
9 with the court reporter -- give her any spellings that she needs. And
10 otherwise we're adjourned. Thank you so much.

11 (Whereupon, the above-entitled matter went off the record.)

IPR2025-00440 (Patent 11,236,318)
PGR2025-00023 (Patent 11,959,109)

PETITIONER:

Scott McKeown
Flora Luo
WOLF, GREENFIELD & SACKS, P.C.
smckeown-ptab@wolfgreenfield.com
fluo-ptab@wolfgreenfield.com

PATENT OWNER:

Alexander Stein
Christopher Betti
Alison Slaughter
Maria E. Doukas
MORGAN, LEWIS & BOCKIUS LLP
alexander.stein@morganlewis.com
christopher.betti@morganlewis.com
alison.patitucci@morganlewis.com
maria.doukas@morganlewis.com