

UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD

CHARLES RIVER LABORATORIES,)
INC.,)
)
Petitioner,)
)
vs.) Case No. IPR2025-00440
) Patent No. 11,236,318
SEIKAGAKU CORPORATION,)
)
Patent Owner.)

DEPOSITION OF BRIAN SCHAEFER, Ph.D.

TAKEN ON BEHALF OF PETITIONER

FEBRUARY 13, 2026

VOLUME 2

Reported by Celena D. Davis, RPR, CSR

CRL Exhibit 1068
CRL v. Seikagaku
IPR2025-00440

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EXHIBITS

Exhibit 2094262
 (Clustal O (1.2.4) sequence alignment)
 Exhibit 2074290
 (International Patent Application
 2008/004674)

(The exhibits are attached.)

1 UNITED STATES PATENT AND TRADEMARK OFFICE
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4 CHARLES RIVER LABORATORIES,)
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7) Patent No. 11,236,318
SEIKAGAKU CORPORATION,)
8)
Patent Owner.)
9

10 IT IS STIPULATED AND AGREED by and between
11 counsel for Petitioner and counsel for Patent Owner that
12 the deposition of BRIAN SCHAEFER, Ph.D. may be taken for
13 Discovery purposes by and on behalf of the Petitioner,
14 pursuant to the provisions of the rules pertaining to
15 depositions taken for the Petitioner on February 13,
16 2026, at the law offices of Morgan, Lewis & Bockius, 110
17 N. Wacker Drive, in the City of Chicago, State of
18 Illinois, before CELENA D. DAVIS, Registered
19 Professional Reporter and Certified Shorthand Reporter
20 within and for the State of Illinois.

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21 REGISTERED PROFESSIONAL REPORTER

22 CERTIFIED COURT REPORTER (MO)

23 CERTIFIED SHORTHAND REPORTER (IL)

24 CERTIFIED SHORTHAND REPORTER (KS)

25 CERTIFIED SHORTHAND REPORTER (CA)

CERTIFIED SHORTHAND REPORTER (TN)

CERTIFIED LIVENOTE REPORTER

MAGNA LEGAL SERVICES

Celena D. Davis

1 (The deposition began at 9:04 a.m. CST.)

2 BRIAN SCHAEFER, Ph.D.,

3 duly sworn to tell the truth, the whole truth, and

4 nothing but the truth, testified as follows:

5 EXAMINATION

6 QUESTIONS BY MS. LOUGHRAN:

7 Q. Good morning, Dr. Schaefer. How are you?

8 A. I'm good.

9 Q. All right. So again, my name is Chelsea
10 Loughran from the law firm Wolf, Greenfield & Sacks.
11 I'm here asking questions on behalf of the petitioner,
12 Charles River Labs. Again, I have my colleague, Flora
13 Luo, also from Wolf, Greenfield.

14 Thank you for your time and answering these
15 questions today.

16 Let's -- we're going to talk today about
17 your declaration in the PGR. I realize there's a lot in
18 the PGR declaration that overlaps with the stuff we
19 talked about yesterday, so I'm going to try not to
20 retread ground that we already covered.

21 A. Okay.

22 Q. If you can pull out your declaration in the
23 PGR, it is Exhibit 2062. We did refer to it yesterday,
24 so you should have it in your pile of documents there.
25 Take a moment to find it there.

1 A. It might take a minute. Am I looking for
2 something thick?

3 MS. LO: Yeah. Is that it sitting to your
4 left? Yeah.

5 THE WITNESS: Okay.

6 BY MS. LOUGHRAN:

7 Q. Does it say 2062?

8 A. It sure does.

9 Q. Great. Wonderful.

10 So we have the declaration of Brian C.
11 Schaefer, Ph.D., in Case Number PGR23, relative to
12 Patent No. 11,959,109. And is this the -- your
13 declaration in the PGR about the '109 patent; right?

14 A. Yes.

15 Q. If you could turn to page 12 of your
16 declaration here, it is the section that starts "Legal
17 Principles."

18 Do you see that?

19 A. Which pagination are we looking at here?

20 Q. So it's page 12, the paragraph is 9, the
21 section is "Legal Principles."

22 A. These page numbers or these page numbers?

23 Q. I'm looking at the actual page numbers of
24 the document, which is just a matter of habit. Sorry.

25 A. Got it.

1 Q. Are we there?

2 A. Yeah.

3 Q. So I just want to ask you very simply your
4 understanding of the legal principles of written
5 description and enablement. We talked about those
6 yesterday relative to the IPR.

7 Do you remember that?

8 A. I do.

9 Q. The legal principles that you're applying
10 in this PGR relative to the '109 patent, are those the
11 same legal principles as you were using with respect to
12 the IPR?

13 A. I do believe the same text is written in
14 both documents. If that is not the case, let me know.
15 But I believe the same text is written in both.

16 Q. And so if there were text that was
17 different, is it just a matter of drafting, or in your
18 brain, are you applying it differently to test, is my
19 question?

20 A. I don't think there's any difference in the
21 description of the legal principles.

22 Q. Okay. So, I mean, there are some minor
23 discrepancies. But I guess my question is just those
24 are not substantively different in terms of the legal
25 principles that you're applying between the PGR and the

1 IPR?

2 A. I do not believe so.

3 Q. Okay. Okay. I would like to hand you
4 the -- it's been marked as Exhibit 1001, which is the --
5 Exhibit 1001 in the PGR, which is the '109 patent.

6 Do you see that?

7 A. I do.

8 Q. And you reviewed this document in preparing
9 your declaration; is that correct?

10 A. That is correct.

11 Q. Great.

12 And if you turn to the second-to-last page
13 of the document, you will see the claims.

14 Do you see that?

15 A. Yes.

16 Q. Okay. And are you aware that patent owner
17 disclaimed Claim 10, so we are only talking about in
18 this PGR Claims 1 through 9?

19 A. I'm aware that we're talking about Claims 1
20 through 9, yes.

21 Q. Okay. If you look at paragraph 61 of your
22 declaration -- and you can just hold the patents with
23 the claim next to you.

24 A. Yes.

25 Q. Do you see where that is?

1 A. Uh-huh.

2 Q. You provide some testimony about why the
3 challenged claims don't require any particular function.
4 I think there's a dispute between yourself and Dr. Jain
5 on that point.

6 Are you aware of the dispute?

7 A. I am aware of the fact that Dr. Jain was
8 repeatedly speaking as though you had to conduct an
9 entire assay. So, yes, there are some discrepancies
10 between how we view the claims and how he views the
11 claims.

12 Q. Okay. So I just want to talk about that
13 discrepancy for a bit. So if we look at Claim 1 of the
14 '109 patent -- I just want to get to where the
15 discrepancy actually lies.

16 A. Yes.

17 Q. So the claim requires -- basically, it says
18 a method for producing an endotoxin assay agent.

19 Do you see that?

20 A. Yes.

21 Q. Okay. So the claim does require an
22 endotoxin detection assay agent, whatever that may be
23 defined as; right?

24 MS. LO: Objection to form.

25 A. An agent is what you need to perform an

1 assay, but it -- there's nothing in the language that
2 says at the end of the day you have to perform that
3 assay. The claim said it's an assay agent.

4 BY MS. LOUGHRAN:

5 Q. Okay. I understand that your position is
6 you don't have to actually do the assay. But the agent
7 has to be capable of working as an endotoxin detection
8 assay agent; is that fair?

9 A. I would not word it quite that way. It is
10 an agent that has activity consistent with it being
11 used -- I don't even want to say that.

12 The claim says "endotoxin agent," so that
13 is something that could be used in an endotoxin assay.

14 Q. Could be used in an endotoxin assay. Okay.

15 And that agent has to have, at least per
16 this claim, at least three things in it; right?

17 A. Yes. One is specified as Factor C,
18 Factor B and proclotting enzyme from the horseshoe crab.

19 Q. Okay. Great.

20 Now, the claim also provides some
21 requirements for what each of those components have
22 to -- characteristics that they have to have; is that
23 your understanding of the claim?

24 A. The claim outlines characteristics for each
25 one of those proteins; correct.

1 Q. Okay. So the endotoxin assay agent has to
2 have, as the claim says here -- well, in making this
3 endotoxin assay agent, you have to express horseshoe
4 crab Factor C in Chinese hamster ovary cells or human
5 embryonic kidney cells; right?

6 A. Uh-huh.

7 Q. Okay. So you have to do that.

8 And then those -- that horseshoe crab
9 Factor C has to be secreted into an extracellular
10 culture supernatant; right?

11 A. That is what is written there, yes.

12 Q. It has to be recovered?

13 A. Also written there.

14 Q. And it has to have what the claim says is
15 Factor C -- is activity of Factor C?

16 A. Activity of Factor C, yes. That's also
17 written there.

18 Q. And we discussed that yesterday.

19 So the Factor C has to have the ability to
20 function as Factor C; right?

21 A. Yes. It has to have a function that you
22 could measure in an assay that is accepted as a Factor C
23 assay; in other words, cleaving an appropriate substrate
24 such as a chromogenic substrate that's known as a Factor
25 C substrate.

1 Q. Okay. But not just cleaving; right? It
2 has to actually bind to something; right?

3 A. It also has to bind to LPS. So it has to
4 bind to LPS in order to be activated; and upon that
5 activation, it has to cleave a substrate that is a known
6 Factor C substrate.

7 Q. Okay. So that has to be part of the
8 endotoxin assay agent, is Factor C that has that
9 ability; right?

10 A. Yes.

11 Q. Okay.

12 A. That's what's understood as Factor C
13 activity, yes.

14 Q. Okay. And then that Factor C, the claim
15 says, has to come from one of two species of crabs,
16 either Tachypleus or Limulus; right?

17 A. Yes.

18 Q. Okay. Now, also, this agent has to include
19 Factor B from a horseshoe crab; right?

20 A. Yes.

21 Q. Which also has activity of Factor B; right?

22 A. Yes.

23 Q. Okay. So activity of Factor B, what is
24 your understanding of what activity of Factor B means?

25 A. In Factor B, when cleaved by an appropriate

1 upstream protease, will cleave an appropriate substrate,
2 a substrate that's known as a Factor B substrate.

3 Q. Okay. And so the upstream protease, are
4 you thinking of that as broadly could be anything that
5 would activate Factor B, or is it activated Factor C?

6 A. Any protease that is activated in a public
7 disclosure as being capable of activating Factor B.

8 Q. So other than activated Factor C, what are
9 you thinking of there?

10 A. I would have to look again at some of the
11 references that we cite that describe the initial
12 characterization of Factor B.

13 Q. Okay. So sitting here today, other than
14 activated Factor C, you're not aware of something that's
15 going to activate Factor B?

16 MS. LO: Objection, mischaracterizes.

17 A. There is a lot of literature in association
18 with these patents. I don't recall every single detail
19 of every single paper. But I know there were extensive
20 characterizations of each of these protease zymogens --

21 Q. Okay.

22 A. -- and what could activate them.

23 Q. Could you grab the '767 application, which
24 is -- you should probably be able to find it. It's a
25 big document.

1 A. Yeah.

2 Q. Do you have it?

3 A. I believe so.

4 Q. It should say "Exhibit 1006" --

5 A. Yes.

6 Q. -- at the bottom. And just for the record,
7 in the PGR, it's Exhibit 1017.

8 So this is the '767 application that you
9 contend provides adequate written description enablement
10 support for the challenged claims of the '109 patent;
11 right?

12 A. Correct.

13 Q. Okay. Could you turn to paragraph 28,
14 which is on page -- Exhibit 106 -- 1006, page 46.

15 A. Okay.

16 Q. Do you see it says, "The activity of
17 Factor C refers to such an activity that the Factor C is
18 activated in the presence of endotoxin to convert
19 Factor B into activated Factor B"?

20 A. I see that.

21 Q. Okay. So we were just talking about
22 activity of Factor C.

23 Is your understanding of what activity of
24 Factor C means the same as this section of the '767, or
25 is it different in some way?

1 MS. LO: Objection to form.

2 A. What's written here is an example of how
3 you might determine the activity of Factor C. This is
4 the canonical activity of Factor C in the cascade. A
5 POSA would understand that there are other ways to
6 measure Factor C activity.

7 BY MS. LOUGHRAN:

8 Q. Okay. So when you see the phrase "activity
9 of Factor C" in the claim, you are interpreting that
10 term to include what's here, but it could include other
11 things; is that right?

12 A. Certainly.

13 Q. Okay. So like this says "activate in the
14 presence of endotoxin," but in your view, it could be
15 any LPS protein; right?

16 MS. LO: Objection to form.

17 A. Endotoxin is an even broader term than LPS.
18 It's quite -- it's the broadest term that they could
19 use.

20 BY MS. LOUGHRAN:

21 Q. Okay. And in your view, when it says
22 "activate in the presence of endotoxin to convert
23 Factor B into activated Factor B," when you think about
24 activity of Factor C, it could also be just a substrate,
25 right --

1 A. Yes.

2 Q. -- instead of activated Factor B?

3 A. A known substrate of Factor C.

4 Q. Okay. And then if you look at -- if you
5 turn to paragraph 49, which is now on page 59 of the
6 exhibit, okay, it says, "The activity of Factor B refers
7 to such an activity that the Factor B is activated in
8 the presence of activated Factor C to convert
9 proclotting enzyme into the activated form thereof,
10 i.e., the corresponding clotting enzyme."

11 Do you see that?

12 A. I see that.

13 Q. Now, when we were talking about Claim 1 of
14 the '109 patent and activity of Factor B, I believe your
15 interpretation of that phrase is that it doesn't have to
16 be activated Factor C. It can be any protease known to
17 activate Factor B?

18 A. Correct.

19 Q. Okay. And then, likewise, you know, sort
20 of for the downstream portion, in your view, activity of
21 Factor B could also be converting -- well, doing
22 something to -- doing something to a substrate as
23 opposed to converting proclotting enzyme into its
24 activated form; is that fair?

25 A. Correct.

1 Q. Okay. And what are the possible substrates
2 that could be cleaved or acted on by activated Factor B?

3 MS. LO: Objection to form.

4 A. Each of the different proteases in this
5 cascade has a series of known peptides that are
6 coupled -- they're blocked on one end. On the other
7 end, they're coupled to a chromogenic substrate or
8 chlorogenic substrate. So when that substrate gets
9 cleaved off, there's a color reaction that can be
10 detected either by a spectrophotometer or by a
11 fluorogenic substrate.

12 And the peptides are three amino acids
13 long. There's different ones that have been described
14 for the different proteases in this cascade.

15 BY MS. LOUGHRAN:

16 Q. So Factor B that -- do you use the word
17 "triggers" or "activates" this substrate? What's the --

18 A. Cleaves the substrate.

19 Q. Okay. So activated Factor B that cleaves
20 the substrate would also be considered activity of
21 Factor B as used in the claim --

22 A. Yes.

23 Q. -- is that your understanding?

24 A. Yes.

25 Q. Okay. And then -- and I know we're working

1 with a couple of documents, but if you look back to
2 Claim 1 of the '109 patent, it then says "expressing the
3 horseshoe crab proclotting enzyme in a mammalian cell as
4 a host cell."

5 Do you see that?

6 A. Yes.

7 Q. Okay. But if you -- I think this is a
8 little bit of patent legalese. The last page, there's a
9 certificate of correction, and the patentee specified
10 that that phrase actually should be "proclotting enzyme
11 having activity of proclotting enzyme" in that section
12 of the claim.

13 Do you see that?

14 A. I do.

15 Q. Okay. So proclotting enzyme also has to
16 have some activity and capability to do something;
17 correct?

18 A. Yes.

19 Q. Okay. And then what's your understanding
20 of what the activity of proclotting enzyme is?

21 A. It's analogous to the activity of Factor B.
22 So all of these are serine proteases, right: Factor B,
23 Factor C, proclotting enzyme. And they're all measured
24 in the same way.

25 So Factor C is the only one that needs to

1 bind to endotoxin to be activated. Then Factor B needs
2 to be cleaved to be activated. It then cleaves a
3 substrate. Same with the proclotting enzyme; it needs
4 to be cleaved to be activated, and then it cleaves an
5 appropriate substrate. Again, this would be a
6 chromogenic substrate.

7 Q. Okay. So then when the patent -- if you
8 look at paragraph 51 on the next page in the '767
9 application, it says, "The activity of proclotting
10 enzyme is such an activity that the proclotting enzyme
11 is converted into the activated form thereof" --

12 Do you see that?

13 A. I see that.

14 Q. -- "i.e., the corresponding clotting enzyme
15 in the presence of activated Factor B to react with the
16 below mentioned substrate for detection."

17 Do you see that?

18 A. I see that.

19 Q. So that is a possible definition or an
20 example definition of activity of proclotting enzyme.
21 But in your view, that term is broader; right?

22 MS. LO: Objection to form.

23 A. Yes. And to be precise, I would say that
24 term includes the cleavage of chromogenic substrates.

25 BY MS. LOUGHRAN:

1 Q. Okay. In addition to converting the -- or
2 yeah -- sorry. Strike that. Okay. Just strike that.

3 And just to be clear, in your view,
4 proclotting enzyme can be activated by something other
5 than activated Factor B?

6 A. Any protease that cleaves it in the
7 cleavage sites that are required for activation will
8 activate the enzyme, any other protease.

9 Q. And sitting here today, can you provide an
10 example of such a protease?

11 A. Again, I would have to look at the cited
12 literature. You know, in the case of Factor C, they
13 showed that Factor C was activated by chymotrypsin and
14 not trypsin.

15 My not-100-percent recollection is that the
16 same is true of each of the other enzymes in the
17 cascade. But, again, I would have to refer back to
18 those specific papers.

19 Q. Okay. And so if the protein does not -- is
20 not able to have the downstream reaction, for example,
21 if Factor C, or let's take Factor B, is not able to
22 cleave a substrate or activate that proclotting enzyme,
23 does that mean it does not have activity of Factor B?

24 MS. LO: Objection, incomplete
25 hypothetical.

1 A. Yeah. It's a very difficult question to
2 answer, because you haven't -- you haven't provided any
3 reason why Factor B wouldn't be activated.

4 BY MS. LOUGHRAN:

5 Q. So does the reason why it doesn't do its
6 downstream -- perform its downstream function matter for
7 whether or not you are practicing the claim, Claim 1 of
8 the '109 patent?

9 MS. LO: Objection, incomplete
10 hypothetical, outside the scope.

11 A. Yeah. I don't understand what that
12 question means, and I can't think of a scenario that
13 would clarify what you're asking me.

14 BY MS. LOUGHRAN:

15 Q. Well, I guess my question is: If you have
16 Factor B, activated Factor B, and it is not able -- it
17 does not cleave proclotting enzyme, does that Factor B
18 have activity of Factor B?

19 MS. LO: Same objections and incomplete
20 hypothetical, outside the scope.

21 A. You haven't provided me enough information
22 to answer that question. If Factor B is activated,
23 unless you give me a specific reason why it's not going
24 to cleave its known substrates, it's going to cleave its
25 known substrates because it's activated Factor B, so

1 it's a property of the activated enzyme.

2 If it doesn't cleave its substrate, then
3 you've done something to destroy the activity of the
4 enzyme, in which case, you know, that's an artificial
5 construct or you're not actually working with Factor B.
6 BY MS. LOUGHRAN:

7 Q. If you have activated Factor B but there's
8 no substrate provided, that Factor B does not have
9 activity of Factor B; right?

10 MS. LO: Objection, mischaracterizes,
11 incomplete hypothetical.

12 A. Yeah. I -- that seems like an absurd
13 conclusion.

14 BY MS. LOUGHRAN:

15 Q. Well, I'm just trying to understand whether
16 your interpretation of activity of Factor B requires,
17 you know, sort of -- is sufficient for the thing to be
18 able to do it or whether it needs to -- we have to
19 actually confirm that it does do it.

20 MS. LO: Objection to form.

21 A. The way the claims are laid out, they state
22 that each factor has a known activity of that factor.
23 And these activities were very well characterized, very
24 well known in the literature. And so the only way to
25 confirm an activity is to measure the activity by its

1 ability to cleave a substrate.

2 And, you know, the most quantitative way to
3 do that, actually, is with some sort of chromogenic
4 substrate.

5 BY MS. LOUGHRAN:

6 Q. Okay. Now, I think your opinion in
7 paragraph 61 is that these things don't have to all sort
8 of happen in cascade in order for them to satisfy Claim
9 1; is that correct?

10 A. What I'm saying is that, yes, you can
11 measure each one individually. For example, you can mix
12 Factor C with endotoxin and a substrate, and you can
13 measure the activity of Factor C that way.

14 You can mix proclotting enzyme with an
15 appropriate activated protease, perhaps activated Factor
16 B, and again measure its activity by the cleavage of a
17 chromogenic substrate.

18 You don't have to assemble all of them
19 together to measure the activity. In fact, that's
20 probably not the best way to do it because then you have
21 them all together and you can't say how much activity
22 each enzyme in a cascade has, only that you were able to
23 complete the cascade.

24 Q. Okay. But do you agree that the claim
25 encompasses the scenario in which you use them all in a

1 cascade?

2 A. I don't see that stated in the claim.

3 Q. Well, you say in paragraph 61 that there is
4 nothing in the challenged claim that requires a cascade
5 reaction or detection of endotoxin via such a reaction;
6 right?

7 A. Correct. That's what is stated there.

8 Q. It's not required. But is it your position
9 that the claim excludes that possible embodiment?

10 A. I'm not sure what you mean by "exclude."
11 Is there a legal definition that we're talking about?

12 Q. I'm not using a legal definition. I'm just
13 trying to understand, in your view of this claim, if I
14 did have Factor C, Factor B and proclotting enzyme
15 proceeding in a cascade, that would be an example of
16 what this -- and it may not be the only example of what
17 this claim requires, but it would be an example. Is
18 that true, from your perspective?

19 A. Again, I'll go back to the fact that the
20 language of the claim does not describe that cascade.
21 And it does not require that that cascade be performed
22 in order for the claims to be valid.

23 Q. Okay. Again, I'm just trying to
24 understand -- I understand your point that it's not
25 required. It doesn't have to always be that way. But

1 in an instance, it is possible that you can have it that
2 way; right?

3 A. That's a very vague question. What do you
4 mean "can have it that way"?

5 Q. Okay. Let's just -- give me one moment.

6 So if you turn to -- well, let me just
7 first ask you, if you look at Figure 1, which is on page
8 118...

9 Do you see that?

10 A. I see that.

11 Q. Okay. So this is the cascade we've been
12 talking about; correct?

13 A. It is.

14 Q. Okay. That is an example of how Claim 1
15 could work; right?

16 A. What does the legend for Figure 1 state?

17 Q. Well, Figure 1 states -- is a chart showing
18 a cascade reaction of the Limulus test.

19 MS. LO: I'm sorry. Counsel, where are we?

20 MS. LOUGHRAN: Oh, it's on page 38.

21 A. In the interest of supplying some
22 background information -- and, you know, this is a
23 figure that I've seen in many publications in the field.
24 It simply outlines how a complete Limulus assay might be
25 performed that contains all of the enzymes.

1 BY MS. LOUGHRAN:

2 Q. Okay. So is it an example of how Claim 1
3 could work?

4 A. I would not characterize it that way.

5 Q. Okay. Well, how about let's look at
6 Figure 4. So if you look at the -- the legend for
7 Figure 4 on page 38, it says "a scheme of measuring the
8 activity of Factor C."

9 Do you see that?

10 A. Yeah.

11 Q. Okay. And Factor 4 is a protocol including
12 all of those: Factor B, Factor C and proclotting
13 enzyme; right?

14 A. Yes. I would associate Figure 4 with Claim
15 10.

16 Q. Okay. But Figure 4 says "the scheme of
17 measuring the activity of Factor C."

18 And we just talked about how Claim 1
19 includes the phrase "activity of Factor C."

20 A. Still, based on what is shown there, I
21 would associate that figure with Claim 10.

22 Q. Is it your position that Claim 1 excludes
23 what is shown in Figure 4?

24 MS. LO: Objection, form.

25 A. I would only say that Claim 1 leaves a POSA

1 with many options for determining how Factor C would be
2 measured; but the most straightforward way would be
3 cleavage of a substrate directly by Factor C.

4 BY MS. LOUGHRAN:

5 Q. Okay. But an alternate way is shown in
6 Figure 4; right?

7 A. What is shown in Figure 4 is not described
8 in Claim 1. It is described in Claim 10.

9 Q. Okay. What about Claim 1 would tell a POSA
10 that the embodiment of Figure 4 is not part of Claim 1?

11 MS. LO: Objection, outside the scope.

12 A. Claim 1 does not direct a POSA to perform
13 what is shown in Figure 4.

14 BY MS. LOUGHRAN:

15 Q. Okay. But does Claim 1 tell a POSA do not
16 put all of those factors together?

17 MS. LO: Objection to form.

18 A. To my knowledge, claims don't
19 particularly -- they don't characteristically tell
20 someone what not to do.

21 BY MS. LOUGHRAN:

22 Q. Right. So if they don't tell someone what
23 not to do, then they're permissive in that respect;
24 right?

25 A. There are plenty of things that are not

1 stated in that claim that have nothing to do with the
2 claim. So I don't think you can be so open-ended to say
3 that if something is not specifically included in the
4 claim, then we can do it as part of the claim. The
5 language in the claim is simply not connected to what is
6 shown in Figure 4.

7 Q. Okay. But you're not pointing to anything
8 in the claim that says you cannot do it this way, the
9 way shown in Figure 4?

10 MS. LO: Objection, argumentative and
11 outside the scope.

12 A. Again, but you can make an infinite list of
13 things that the claim does not say not to do.

14 BY MS. LOUGHRAN:

15 Q. Could you turn to paragraph 44 of the '767
16 application, which is on page 57.

17 A. Okay.

18 Q. Could you just read the first sentence in
19 that paragraph.

20 A. "For example, the Factor C of the present
21 invention may be used in combination with Factor B and
22 proclotting enzyme for endotoxin assay."

23 MS. LO: And I'll just interject that,
24 Dr. Schaefer, feel free to read the rest of paragraph 44
25 to yourself, if that would be helpful.

1 A. Again, you can connect this --

2 MS. LO: Wait for a question.

3 BY MS. LOUGHRAN:

4 Q. So thank you for reading that.

5 The next sentence says, "In other words, an
6 embodiment of the endotoxin assay agent of the present
7 invention is an endotoxin assay agent containing the
8 Factor C of the present invention, Factor B and
9 proclotting enzyme."

10 Do you read that?

11 A. I read that.

12 Q. Okay. Now we've looked at Figure 1, we've
13 looked at Figure 4, and we've looked at paragraph 44 of
14 the '767 application.

15 A. Yes.

16 Q. All of which indicate that you can have
17 Factor C of the present invention in combination with
18 proclotting enzyme and Factor B; do you agree?

19 A. Again, I would point out that both Figure 4
20 and paragraph 44 are consistent with what was described
21 in Claim 10.

22 Q. And what about Claim 1 that's different
23 than Claim 10 signals to you that those embodiments are
24 excluded from Claim 1?

25 MS. LO: Objection, mischaracterizes; also

1 outside the scope.

2 A. Yeah. I don't think I said those words.
3 All I said was paragraph 44 and Figure 4 are consistent
4 with what is written in Claim 10, and they are not
5 particularly consistent with what is written in Claim 1.
6 What is written in Claim 1 is more simple, and it does
7 not describe anything about the complete cascade.

8 BY MS. LOUGHRAN:

9 Q. Is it your position that what is in Figures
10 1, 4 and paragraph 44 is inconsistent with Claim 1?

11 MS. LO: Objection, mischaracterizes.

12 A. Again, I don't think I use those words, you
13 know. You've asked me the same question a number of
14 different ways. And these -- in the figure and in the
15 paragraph that describes the complete cascade, that
16 information is consistent with Claim 10 and inconsistent
17 with what is written in Claim 1.

18 What is written in Claim 1 is very simple
19 and just describes each of the assay agents individually
20 and says that each agent must have its own activity
21 individually.

22 BY MS. LOUGHRAN:

23 Q. Where in Claim 1 does it say that each
24 agent must have its own activity individually?

25 A. So we have separate paragraphs here. One

1 describes "expressing the horseshoe crab Factor C in two
2 types of cells, secreting Factor C into the
3 extracellular supernatant, recovering the Factor C,
4 wherein the recovered Factor C has activity of
5 Factor C."

6 Then we have a different paragraph that
7 says "horseshoe crab Factor B, having activity of
8 Factor B."

9 Then we have a different paragraph that
10 says "expressing proclotting enzyme in a mammalian
11 cell."

12 And then we have a different paragraph that
13 says "producing an endotoxin assay agent, comprising
14 horseshoe crab Factor C, Factor B, horseshoe crab
15 proclotting enzyme, wherein the host cell for expressing
16 horseshoe crab Factor C, Factor B, proclotting enzyme
17 may be the same or different."

18 There's nothing in there that says that the
19 activities have to be measured together. Just each
20 enzyme has to have the activity consistent with its
21 known activity.

22 Q. Okay. Can you look at Claim 10, please.

23 A. Yes.

24 Q. Claim 10 has those paragraphs as well that
25 you just read; right?

1 A. Yes.

2 Q. So what about Figures 1, 4 and paragraph 44
3 of the '767 application is consistent with Claim 10 that
4 you contend is not consistent with Claim 1?

5 MS. LO: Objection, mischaracterizes.

6 A. I don't recall saying those words. The
7 difference in the language of Claim 10 is the part where
8 it says "mixing the endotoxin assay agent and test
9 specimen and measuring the progress of a cascade
10 reaction." That part is not in Claim 1, and that
11 distinguishes Claim 10 from Claim 1.

12 BY MS. LOUGHRAN:

13 Q. So Claim 10 requires that mixing; right?

14 A. Yes. Claim 10 requires -- specifies
15 mixing.

16 Q. And Claim 1 says nothing about mixing or
17 not mixing; right?

18 A. Claim 1 does not specify mixing.

19 Q. Okay.

20 A. And does not specify measuring a cascade
21 reaction --

22 Q. Okay.

23 A. -- which Claim 10 does.

24 Q. But Claim 1 doesn't say don't mix; right?

25 A. Again, there is an entire universe of

1 things that Claim 1 doesn't say. I am focused on what
2 Claim 1 does say.

3 Q. I just want to be clear that the mixing
4 limitation of Claim 10 is what you believe to be
5 consistent with the cascade reaction; right?

6 A. Both mixing of the endotoxin agent and a
7 test specimen and measuring the progress of a cascade
8 reaction, both of those things. Those are two very
9 specific things.

10 Q. Okay. So Claim 10 is more specific than
11 Claim 1?

12 MS. LO: Objection, outside the scope.

13 A. I did not use those words. Claim 10 has
14 additional steps that are not included in Claim 1.

15 BY MS. LOUGHRAN:

16 Q. Okay. If a POSA were to do what is
17 specified in paragraph 44 of the '767 application, would
18 that combination of factors satisfy Claim 1?

19 MS. LO: Objection to form, outside the
20 scope.

21 A. I don't really know how to answer that
22 question. It sounds like a question more for a lawyer
23 than for me.

24 BY MS. LOUGHRAN:

25 Q. If you were to run the cascade that we have

1 been looking at, we looked at in Figure 1, and we looked
2 at several times yesterday, and you got, you know,
3 cleavage of the final product or activation of the final
4 product -- I think it's coagulin is one example, for
5 example -- would the Factors C, B and proclotting enzyme
6 in that cascade each have their activity, their activity
7 of Factor C, Factor B and proclotting enzyme?

8 A. If you're performing the cascade reaction
9 where you activate the cascade using endotoxin, and each
10 of the enzymes in the cascade has their characteristic
11 activity; that is, Factor C binds endotoxin, cleaves
12 Factor B, cleaves Factor B, which is then activated,
13 cleaves proclotting enzyme, becoming activated
14 proclotting enzyme, and proclotting enzyme cleaves a
15 suitable substrate, then -- I forget -- your question
16 was what again?

17 Q. Well, each of those components would have
18 their activity. So Factor C would have its activity of
19 Factor C; same with Factor B; same with proclotting
20 enzyme.

21 You agree with that?

22 A. Yes. That's the nature of the cascade.
23 Each enzyme cascade, when it's been properly activated,
24 has its characteristic activity.

25 Q. Okay. Fair enough.

1 Okay. Dr. Schaefer, if you could turn to
2 page -- or paragraph 38 of your declaration. Now, I
3 think we established that claims -- the challenged
4 claims of the '109 patent require Factors B and
5 proclotting enzyme; right?

6 A. Sorry. Can you repeat the question?

7 Q. Yeah. The challenged claims, Claim 1 that
8 we were just referring to and its dependent claims,
9 require Factors B and proclotting enzyme; right?

10 A. Both Factor B and proclotting enzyme are
11 contained within the claim.

12 Q. Okay. And you talk about the fact that
13 the -- for Tachypleus, those proteins were sequenced in
14 1993 for Factor B and 1990 for proclotting enzyme;
15 correct?

16 A. Correct.

17 Q. And by 2013, had there been any publication
18 of the Factors B or proclotting enzyme for Limulus
19 polyphemus?

20 A. I don't believe so.

21 Q. And by 2013, had there been a publication
22 of Factors B or proclotting enzyme for Carcinoscorpius?

23 A. I do not recall for that one.

24 Going back to Limulus, however, I will say
25 the same thing that I said for Factor C, which is that

1 the sequences were available in a database, the
2 BioProjects, which had the entire cDNA sequence and the
3 entire genome for Limulus.

4 And also, those could have been obtained by
5 RACE PCR or selective cloning. There's RACE PCR
6 selective cloning could have been used for
7 Carcinoscorpius -- Carcinoscorpius enzymes as well.

8 Q. Okay. My question was by 2013, had there
9 been publication of the sequences for Factors B or
10 proclotting enzyme for Carcinoscorpius?

11 A. I do not recall for that particular species
12 whether those two had been cloned and sequenced and
13 reported. But, again, they could be obtained easily by
14 RACE PCR or by blotting with appropriate probes using
15 Tachypleus, using a lambda gt11 library.

16 Q. Do you know if Factor B and proclotting
17 enzyme sequences for Carcinoscorpius have been published
18 even as of today?

19 A. I would have to look again at my list of
20 references that's listed in here. I do not recall
21 specifically for that species whether it has been
22 published or not.

23 Q. You definitely -- strike that.

24 At least here where you're talking about
25 the publication of Tachypleus, you don't include any

1 corresponding information for the publications of
2 Limulus or Carcinoscorpius; right?

3 A. It's not listed.

4 Q. And to my knowledge, it's not in your
5 declaration.

6 Do you have any other or inconsistent view
7 on that point?

8 A. If it's not in the declaration, it's not
9 there.

10 Q. Okay.

11 A. I just don't recall off the top of my head.
12 But given that it's not in this paragraph, I think it is
13 probably not out there.

14 Q. Okay. Now, we talked about the fact that
15 there was some partial sequencing in the reference
16 Tokunaga for Factor C --

17 A. Yes.

18 Q. -- of Tachypleus and Limulus; correct?

19 A. Yes.

20 Q. Was there any partial sequencing published
21 for Factors B or proclotting enzyme for Limulus
22 polyphemus by 2013?

23 A. I don't recall that. But, again, you don't
24 need that. Certainly, for cloning from a lambda phage
25 library, all you would need is a probe made from

1 Tachypleus, which we have the entire sequence for. You
2 could easily identify it that way.

3 And you could make degenerate primers using
4 the sequence from Tachypleus to perform RACE PCR to both
5 the N-terminal and C-terminal ends, and then do standard
6 PCR after that.

7 So the fact that there wasn't published
8 sequence information is not really an impediment to
9 obtaining those sequences quite quickly.

10 Q. Was there any partial sequencing of
11 Factors B or proclotting enzyme for Carcinoscorpius by
12 2013?

13 A. I believe you had just asked that, but --

14 Q. I just asked about Limulus.

15 A. Sorry. I'm not aware of any for
16 Carcinoscorpius.

17 But my answer is the same for Limulus. You
18 could use a lambda gt11 library using a Tachypleus probe
19 to identify it, or you could use a combination of RACE
20 PCR and standard PCR to easily get the sequence.

21 We have the advantage here that the
22 sequences between species are highly homologous which
23 makes the cloning of the individual factors from the
24 other species quite straightforward, whether they're
25 known or not.

1 (Exhibit 2094 was introduced to the
2 witness.)

3 BY MS. LOUGHRAN:

4 Q. I'm going to hand you what's been marked as
5 Exhibit 2094 in the PGR. So this is Exhibit 2094 in the
6 PGR.

7 Do you recognize this document?

8 A. I do.

9 Q. Okay. So we looked at a similar one
10 yesterday, but is it fair to say this is the Clustal
11 sequence alignment that includes Factor C, B and
12 proclotting enzyme?

13 A. Yes. All three are present in the exhibit
14 that you handed me.

15 Q. Okay. Now, for Factor C, is this the
16 same -- essentially the same algorithmic output that we
17 looked at yesterday with respect to the IPR?

18 A. It should be identical to what we looked at
19 yesterday, yes.

20 Q. Okay. And the Limulus sequence here is the
21 sequence taken from the 629 publication; right?

22 A. Correct.

23 Q. Okay. And then for -- if you look at
24 pages -- page 4, this is the -- a similar alignment for
25 Factor B; correct?

1 A. Correct.

2 Q. Okay. Now, it only has Limulus and
3 Tachypleus. Why is that?

4 A. Those were the only two that were available
5 in the database in complete form.

6 Q. Okay. So the Connecticut researchers that
7 we talked about yesterday deposited information about
8 Limulus polyphemus, but there's no analogous database
9 for Carcinoscorpius; right?

10 MS. LO: Objection, outside the scope.

11 A. I did not check specifically to see if
12 there's an analogous database for the other Asian
13 species.

14 BY MS. LOUGHRAN:

15 Q. So to your knowledge, you don't know if
16 there is or is not?

17 A. I do not know if there is or is not.

18 Q. And then the same thing for proclotting
19 factor, there's only Limulus and Tachypleus here;
20 correct?

21 A. Correct.

22 Q. Okay. And you don't know one way or the
23 other whether there is analogous sequencing information
24 regarding the genome of Carcinoscorpius analogous to the
25 Yukon deposits; right?

1 A. Correct. I don't know one way or another.
2 I didn't consider it terribly important for this
3 analysis.

4 Q. And for all of these sequences, the Limulus
5 sequence that is used to do the comparison is based off
6 of what the inventors of the '629 patent disclosed in
7 2016; right?

8 A. Correct.

9 Q. Okay. And again, I asked you this
10 yesterday with respect to Factor C, but with respect to
11 Factors B and proclotting enzyme, did you actually
12 assemble the cDNA or amino acid sequences of those
13 proteins?

14 A. Can you ask your question more
15 specifically?

16 Q. Sure. So you looked at the deposits from
17 the Yukon researchers regarding the genome of Limulus
18 polyphemus?

19 A. Yes.

20 Q. And you did some analysis of the short
21 reads in that database?

22 A. Yes.

23 Q. Yesterday, I think you indicated that you
24 did not actually assemble the Factor C sequence from
25 those short reads; is that fair?

1 A. Correct. I did not assemble a complete
2 sequence from the short reads because that's -- there's
3 no point in doing that. That's not what a POSA would do
4 with those sequences.

5 A POSA would merely blast the library, see
6 that there were many short reads that align, make a --
7 make a composite alignment using Clustal or something
8 like that to come up with a consensus sequence, compare
9 that consensus sequence back to Tachypleus, actually,
10 and look and see where the closest agreement was; and
11 then use those sequences to create primers for beginning
12 to PCR the Limulus sequence.

13 We never simply assemble a sequence from
14 the short reads and go with that. It all has to be
15 confirmed by PCR. Then you clone those PCR products,
16 sequence them, and then if you've done at least a couple
17 independent PCRs and assemblies that cover the entire
18 genome, then you would assemble that in your PCR.

19 So the assembly of the short reads is a
20 tool that gets you to the final validated product.

21 Q. Okay. And so I just want to confirm that
22 your answer is the same for proclotting enzyme and
23 Factor Bs.

24 A. Yes.

25 Q. Your position is it would be unnecessary

1 for a POSA to actually assemble the sequence of those
2 proteins from the short reads deposited by the Yukon
3 researchers?

4 A. Yes. The answer is the same. It would be
5 unnecessary to assemble all of those. You just wouldn't
6 use the information that way. What the short reads show
7 is that the entire sequence was covered. It was a very
8 thorough sequencing effort. All the sequences there
9 show you can easily derive the complete validated
10 sequence from that information.

11 Q. Now, I think as we discussed yesterday,
12 there were some variants for Factor C; right?

13 A. The language you're using is not very
14 precise.

15 Q. Okay.

16 A. Can you rephrase what you're saying?

17 Q. Sure.

18 Just yesterday we discussed that there were
19 two variants of Factor C protein; right?

20 A. We're talking about splicing variants now?

21 Q. Now, well, how were you understanding it
22 when we discussed it yesterday?

23 A. When we were talking yesterday, my
24 understanding of what you were saying was that there
25 were different -- different transcript isoforms known,

1 different mRNA transcript isoforms.

2 Q. And those were reflected in the
3 different -- in the multiple sequences provided by the
4 '629 publication inventors; is that -- are we talking
5 about the same thing?

6 A. I don't believe we referenced the '629
7 yesterday when we were discussing that.

8 Can you point me to where you're talking
9 about?

10 Q. Sure. Did I already -- well, I guess we
11 can look at the sequences that were included in the '498
12 PCT, which was Exhibit 1005. So you can look at page 45
13 of that document. You can look at -- well, we can start
14 at paragraph 175.

15 So paragraph 174 has the heading "Obtaining
16 cDNA of a Protein Having Limulus Polyphemus B Factor
17 Activity."

18 A. Uh-huh.

19 Q. And then 17 [sic] talks about using the
20 cDNA and methods to get that cDNA sequence. And it says
21 in paragraph 175, "This resulted in the elucidation of
22 the full-length cDNA sequences and coding proteins that
23 may have Limulus polyphemus Factor B activity." And
24 there's a number of sequences there.

25 Do you see that?

1 A. I see that, yes.

2 Q. Okay. So do you consider those alternate
3 sequences to be variants of Factor B?

4 MS. LO: Objection, form.

5 A. I would not describe it that way. The
6 inventors are being very thorough here, and they're
7 trying to take into account any possible variation that
8 somebody else might say, Oh, hey, here's a Factor B
9 that's possibly produced by alternative splicing or
10 whatever that not covered by your patent.

11 So they're taking every possible sequence,
12 translated sequence that can be derived from the known
13 mRNAs, and they're including that in their patent.

14 BY MS. LOUGHRAN:

15 Q. Okay. And then if you look at paragraph
16 177, is it your position that they did a similar thing
17 for a proclotting enzyme?

18 A. Yes.

19 Q. Okay. So which of these different
20 sequences did you use when you did your Clustal
21 alignment that we just looked at in Exhibit 2094?

22 A. I used the sequences that are considered
23 the canonical sequences, the ones that I believe are
24 also in the NCBI database as the canonical sequences.

25 Q. So did you -- so did you compare the

1 alternate sequences in this publication with the NCI
2 database and then choose one?

3 A. I don't recall the exact series of steps.
4 But whenever there are variants of a known transcript,
5 there will always be one in the NCBI database that is
6 considered the canonical transcript. It's the one
7 that's the most validated. It's the one that was first
8 identified in the publication.

9 So, yes, the one we used is whatever was
10 first identified in a publication as being the
11 full-length Factor B, the full-length PC.

12 Q. Okay. And do you recall what that first
13 publication was that was cited in the NCBI database?

14 A. Presumably, one of the Muta publications.
15 I believe both of those were in Muta, et al., in the
16 1990s.

17 Q. But that would have been Tachypleus; right?

18 A. Yes, Tachypleus.

19 Q. But we're talking about Limulus.

20 A. Oh, we're talking about Limulus.

21 So the Limulus would be the one that was
22 most homologous to the known Tachypleus.

23 Q. All right. So just backing up, how did
24 you -- for Factor B, how did you decide which one of
25 these sequences to use in your Clustal alignment?

1 A. It's the one that's homologous to the
2 canonical sequence from Tachypleus.

3 Q. So you selected the sequence that's
4 provided in this '498 PCT that is most similar to the
5 Factor B sequence for Tachypleus?

6 A. Yes. That's the one that is most likely to
7 be the predominant isoform.

8 Q. Okay. Now, in terms of expressing
9 Factor B, as required by the claim that we looked at
10 earlier, the claim doesn't limit which variant of
11 Factor B you express; right?

12 A. It would not be a good decision by the
13 patentholders to limit it, again, for the same reason.
14 They don't want somebody else making some variant of
15 Factor B that may not even be actually produced then
16 saying, we didn't claim this.

17 So, yes, they've been very thorough in what
18 they've said, that any of these that have the activity
19 in Factor B are also considered Factor B --

20 Q. Okay.

21 A. -- for the purpose of their intention. And
22 they did the same thing for describing engineered
23 variants, like putting an on epitome tag or making other
24 minor modifications to the sequence. They have written
25 the patents in such a way that somebody cannot make

1 trivial alterations that don't change the activity of
2 the enzyme and claim that the patent doesn't cover that.

3 Q. Well, what if an alteration does change the
4 activity of the enzyme? Would that still be covered by
5 the claim?

6 MS. LO: Objection, incomplete
7 hypothetical.

8 A. Yeah, the way you have stated that is very
9 open-ended. What do you mean by "change the activity of
10 the enzyme"? If you change it in such a way that it no
11 longer cleaves known substrates, then it's not Factor B
12 anymore, and it's not useful to anybody else for
13 measuring endotoxin.

14 BY MS. LOUGHRAN:

15 Q. Did you look at any of the other variants
16 of Factor B or proclotting enzyme to assess how similar
17 or different they were from the ones that you used in
18 your Clustal alignment?

19 A. I did not consider the other variants. It
20 did not seem particularly relevant because the inventors
21 say that in order for something to be Factor B, it has
22 to have the activity of Factor B.

23 In order for something to be proclotting
24 enzyme, it has to have the activity of proclotting
25 enzyme.

1 So I didn't see the utility in doing those
2 comparisons to protein sequences that may not actually
3 exist. And we just have slight variances with regard to
4 the canonical sequence anyway.

5 MS. LOUGHRAN: We've been going about an
6 hour and 15. Do you want to take a break?

7 (A break was taken.)

8 BY MS. LOUGHRAN:

9 Q. Hi again, Dr. Schaefer. How are you?

10 A. I'm good.

11 Q. Just with respect to the sequencing
12 information that we were just talking about, when you
13 performed your analysis of the sequences for Factors B
14 and proclotting enzyme, did you note any differences in
15 the end glycosylation sites for those -- between those
16 proteins, between species?

17 A. I didn't mark any on the sequence. In my
18 quick scan, I didn't see it. But I presume you're about
19 to tell me there's at least one.

20 Q. I'm just asking if you did the
21 investigation.

22 A. I don't recall whether I did at the time.
23 And again, in scanning the sequence right now, none jump
24 out at me.

25 Q. Okay. But you certainly didn't identify

1 any in your testimony; right?

2 A. There's nothing indicated for glycosylation
3 sites specifically on these sequences.

4 Q. Okay. You agree that the claims, the
5 challenged claim of the '109 patent, require the
6 expression of Factors B and proclotting enzyme in
7 mammalian cells; right?

8 A. That is what is stated, correct.

9 Q. Okay. Prior to 2013, had anybody described
10 the expression of those proteins in mammalian cells?

11 A. To my knowledge, expression of those
12 proteins in mammalian cells had not been publicly
13 reported.

14 Q. Okay. And so to your knowledge, is the
15 description -- what is the first public report of
16 expression of Factors B and proclotting enzyme in
17 mammalian cells?

18 MS. LO: Objection, outside the scope.

19 A. Yeah, I don't believe that there is a
20 citation to any public disclosure in any -- in any of
21 the patents that we are discussing.

22 BY MS. LOUGHRAN:

23 Q. Okay. Have you seen any description of it
24 in any journal article or any other publication?

25 MS. LO: Same objection, outside the scope.

1 A. I didn't look at that because it's not part
2 of this patent claim discussion, so I don't specifically
3 recall whether or not I did one way or the other.

4 BY MS. LOUGHRAN:

5 Q. Well, the claim requires expression of
6 these proteins in mammalian cells. We agree on that;
7 right?

8 A. We do agree on that.

9 Q. Okay. So I'm just asking: What is your
10 position on when that was first described in a printed
11 publication or a patent?

12 MS. LO: Objection, outside the scope.

13 A. I do not know when it was described
14 publicly. My position is that these proteins are serine
15 proteases that are quite closely related to the Factor C
16 serine protease. It was shown not only that the
17 Factor C serine protease can be expressed in the
18 mammalian cells, but that certain properties actually
19 get better in mammalian cells, the residual activity
20 that is referred to by the inventors multiple times.

21 Factor B and proclotting enzyme are
22 smaller, more simpler proteins. They do have that same
23 conserved serine protease domain, and the POSA would
24 understand that there is no reason to expect difficulty
25 in expressing those in mammalian cells.

1 BY MS. LOUGHRAN:

2 Q. Okay. If you turn to page 14 of the '767
3 application, so your big document there.

4 A. 14?

5 Q. Yes. Now, you agree that the claim
6 requires not only expression in the mammalian cells, but
7 that the resulting protein have its activity; right?

8 A. That is correct.

9 Q. And the inventors here in paragraph 11,
10 they're describing -- and you can sort of look at the
11 heading of the section, which is shown on page 11, but
12 the background art in the field at the time.

13 A. Okay.

14 Q. The inventors say there's a known case of
15 using mammalian cells as host cells where Factor C
16 derived from the Singaporean horseshoe crab was
17 expressed in COS-1, which is a cell line derived from
18 African green monkey kidney cells as host cells.

19 "However, it's been reported that when
20 COS-1 was used as a host, the expressed Factor C was
21 insoluble; that is, there's never been known a case
22 where functional Factor C is produced using mammalian
23 cells as host cells."

24 Do you see that?

25 A. I do see that.

1 Q. Okay. So do you agree that a POSA would
2 acknowledge that there were some mammalian cells that
3 did not express functional zymogen proteins?

4 MS. LO: Objection, vague.

5 A. A POSA -- sorry. A POSA considering both
6 the entirety of what is in the '767 and the entirety of
7 what have been published, would look at the data between
8 those sources.

9 So this one published example in COS-1
10 cells where the protein was insoluble, and then the
11 patentholders demonstrate here what then becomes a
12 surprising observation that, look, if you actually use
13 these other cell lines, HEK cells and CHO, or CHO-DG44,
14 they actually express quite well and they're soluble,
15 and you can recover them and they are functional.

16 So a POSA can extrapolate from that and
17 say, okay, we're not going to use COS-1 cells because,
18 for whatever reason, they don't appear to be good for
19 the enzymes. Let's stick with HEK cells and CHO cells
20 for expression of enzymes in the cascade.

21 BY MS. LOUGHRAN:

22 Q. So the claim requires you to stick with CHO
23 cells and HEK cells for Factor C. But expression of
24 Factors B and proclotting enzyme are not so limited in
25 the claims; right?

1 A. That is my recollection.

2 Q. The claim -- or the claims allow for
3 expressing those proteins in any mammalian cell; right?

4 A. I believe that's what is stated.

5 Q. Okay. And does the '767 application
6 describe expression of Factors B and proclotting enzyme
7 in any mammalian cell?

8 MS. LO: Objection to form.

9 A. I believe -- can you point to the data that
10 are in the '767 where expression is shown?

11 BY MS. LOUGHRAN:

12 Q. Well, I cannot. But my question is: Can
13 you point me to data in the '767 application where the
14 inventors showed expression of Factor B or proclotting
15 enzyme in any mammalian cell?

16 A. Those data are not in this document.
17 Again, a POSA would reasonably conclude that the
18 expression of Factor B and proclotting enzyme would
19 follow closely with what is shown for Factor C, because
20 the inventors actually state that the expression can be
21 performed -- I forget the Latin phrase, rotundus
22 something, the MM phrase, which means with the necessary
23 modifications.

24 So they don't show the data, but they state
25 that it is not only possible, it's trivial. Follow

1 these instructions for Factor C; we show you we can
2 produce Factor C; do the same thing for Factor B and for
3 proclotting enzyme; and that's how you do it.

4 Q. And the instructions that the inventors
5 give for Factor C, again, are limited to particular
6 mammalian cells; right?

7 MS. LO: Objection to form.

8 A. They are. The inventors show data for
9 expression in CHO cells and for HEK cells. And to my
10 recollection, those are the cell lines that they call
11 out in their claims.

12 BY MS. LOUGHRAN:

13 Q. So beyond those two cell lines that are
14 called out for Factor C, where are the mutatis mutandis
15 instructions for Factors B and proclotting enzymes as to
16 mammalian cells that are not CHO or HEK?

17 A. I guess it really comes down to how you
18 interpret the mutandis mutatis phrasing. Does -- would
19 the necessary modifications also include other mammalian
20 cells? I think it reasonably can. Because, again, I
21 don't think -- I don't think they specified super
22 specifically that you have to use those two cell lines
23 with the other two factors.

24 Q. Right. They don't specify using HEK or CHO
25 for Factors B or proclotting enzyme; right?

1 A. Not to my recollection. They say mammalian
2 cells, as you stated before.

3 Q. And so there are many examples of other
4 mammalian cells that you can express those proteins in
5 other than HEK and CHO; right?

6 A. That's a pretty open-ended question. I
7 don't think a POSA would look at it that way. There is
8 a relatively small subset of cells that investigators
9 tend to rely on for expression of proteins that get
10 secreted at useful levels.

11 HEK, CHO, COS-1 are the big ones. And we
12 already have data showing here that COS-1 is not
13 suitable. So a POSA would exclude that from the list
14 simply based on that.

15 There are other mammalian cell lines that
16 are occasionally used, but these are not really the ones
17 that a POSA would generally consider. But the claims do
18 specify mammalian cell lines, and so that is what is
19 stated.

20 Q. So a POSA would know that of the three
21 mammalian cell lines that are discussed in the
22 specification, one, COS-1, doesn't work, at least for
23 Factor C; is that fair?

24 A. The inventors show that Factor C -- or they
25 report the data that Factor C is not soluble when

1 produced in COS-1 cells. And that would lead a POSA to
2 tend not to try the other enzymes in that cell line.

3 Q. But the claim allows for expression in
4 COS-1. So how would a POSA figure out how to do that to
5 satisfy the claim?

6 A. Again, there's a relatively small
7 collection of mammalian cell lines that are used for
8 expression. It would be rather trivial for a POSA to
9 test those cell lines to find the one that gives the
10 best production of the protein.

11 Q. When you say "relatively small," what are
12 you talking about quantitatively? How many?

13 A. Again, I would say that the workhorse cell
14 lines are all listed here: HEK, CHO and its
15 derivatives, and COS-1. Sometimes people will use a
16 cell line like HeLa because it grows very quickly, but
17 it's not a typical workhorse for these types of
18 production experiments.

19 So three cell lines. I would start with
20 three as a POSA, and I would have a reasonable
21 expectation of success based on what is described in
22 this document.

23 Q. Okay. But you acknowledge that the claims
24 of the '109 patent don't say, "express in mammalian
25 cells that are the typical workhorse cells"; right?

1 A. There is no statement worded like that;
2 correct.

3 Q. So the claim could include lesser-known and
4 more -- well, I'll just say could include lesser-known
5 and less-used mammalian cell expression systems; right?

6 MS. LO: Objection, calls for a legal
7 conclusion.

8 A. I'm not a lawyer, so I can't tell you if
9 that's what it means or not.

10 BY MS. LOUGHRAN:

11 Q. Okay. Is there anything in the claim that
12 you look at when you look at that claim that says "I
13 would exclude lesser-known mammalian cell expressions"?

14 A. I'm working from the point of view of a
15 POSA. So I would not phrase it that way. From the
16 point of view of a POSA, there are specific cell lines
17 that you would attempt to use based on both the
18 literature and what is written in the '767.

19 Q. Okay. I understand from that -- from your
20 view of a POSA, that's your perspective. But the claim
21 has a scope, and you understand the written description
22 has to be present for the full scope of the claim;
23 right?

24 A. Yes.

25 Q. And the full scope of the claim, with

1 respect to expression of Factors B and proclotting
2 enzyme, will include some lesser-known expression --
3 mammalian expression systems that are not explicitly
4 described in the specification.

5 Do you understand that?

6 A. Potentially, yes.

7 Q. And there's no description in the
8 specification of how to express those proteins in those
9 lesser-known mammalian cells; right?

10 MS. LO: Objection to form.

11 A. Again, the inventors have stated that the
12 proteins for Factor B and proclotting enzyme can be
13 expressed in mammalian cells in the same way that they
14 were expressed for Factor C with necessary
15 modifications.

16 And from my perspective, necessary
17 modifications would include whatever mammalian cell line
18 ends up being most optimal, given that the inventors
19 have not called out specific cell lines for Factor B and
20 proclotting enzyme.

21 And the inventors state that you can follow
22 their instructions for expression of Factors B and
23 proclotting enzyme with the detailed instructions that
24 are included in the setup.

25 BY MS. LOUGHRAN:

1 Q. How would a POSA know which necessary
2 modifications, to use your words -- and I think you're
3 citing the specification -- to ensure that the
4 expression of Factors B and proclotting enzyme each have
5 their respective activities of Factors B and proclotting
6 enzyme?

7 A. Well, again, with -- I'm using with
8 necessary modifications to paraphrase the Latin *mutandis*
9 *mutatis* phrasing. But they give very detailed
10 instructions for how to produce Factor C. And a POSA
11 should follow those same instructions, simply changing
12 the cell line to produce Factor B and proclotting
13 enzyme.

14 Anything else, any other modification
15 needed, would be considered, you know, within the
16 boilerplate optimization steps that a POSA would know
17 how to perform. Again, it's not required for a patent
18 to teach things that are considered well known in the
19 art.

20 Q. So -- well, let me just ask you: Have you
21 ever used the phrase "*mutatis mutandis*" in any of your
22 scientific publications?

23 A. It's not one that I use, no.

24 Q. Okay. If you're -- as a POSA, if you are
25 modifying a variable such as an expression system and

1 you're writing a publication about that, don't you have
2 to describe the methods that you use to carry that out?

3 MS. LO: Objection, outside the scope,
4 incomplete hypothetical.

5 A. When you're writing a method section, you
6 report your final conditions. You don't report
7 everything you did to optimize. You report the final
8 conditions, and then you expect that somebody reading
9 what you wrote will start with those final conditions
10 and they'll make whatever modifications are necessary to
11 adapt what you've written to their system.

12 Even moving from lab to lab with the same
13 cell lines, the same culture media, the same this, the
14 same that, there's always little modifications that need
15 to be made, because things you can't account for are
16 always different, you know. Maybe -- I don't even want
17 to get into it.

18 But there are always small things that are
19 different. Every protocol that you look at is going to
20 require some sort of modification. A POSA knows how to
21 perform those modifications.

22 BY MS. LOUGHRAN:

23 Q. So if you look at Claim 1 of the ''109
24 patent, in your view -- you have testified about a whole
25 lot of routine and trivial things that are involved in

1 this claim. What is the inventive aspect of this claim?

2 MS. LO: Objection to form, outside the
3 scope.

4 A. I guess I am not really sure what you're
5 trying to get at. What are you really asking me here?

6 BY MS. LOUGHRAN:

7 Q. Well, you -- in your declaration and your
8 testimony, you rely heavily on the fact that a lot of
9 things were known in the art and that a POSA would find
10 there to be a lot of boilerplate modifications, trivial
11 things to do to -- you know, we talked about the
12 expression of Factor B and proclotting enzyme had never
13 been demonstrated before in mammalian cells. But your
14 position is it would have been routine.

15 I'm asking you: What in this claim do you
16 find to be inventive?

17 MS. LO: Objection, outside the scope.

18 A. Yeah, I am not a patent lawyer, and
19 "inventive" is a legal term that I don't feel qualified
20 to assess.

21 BY MS. LOUGHRAN:

22 Q. Okay. Let's take "inventive" out of it.

23 Is there anything in this claim that was
24 new as of 2013?

25 MS. LO: Objection, outside the scope.

1 BY MS. LOUGHRAN:

2 Q. Just from a scientific perspective.

3 MS. LO: Same objection.

4 A. I don't really know how to answer that
5 because this -- this is not a scientific publication.
6 This is a patent. And the way you evaluate a patent is
7 based on legal terms. The way you evaluate a
8 publication is completely different.

9 So I don't feel like the question that
10 you're asking me translates to a patent in the way that
11 you're asking it.

12 BY MS. LOUGHRAN:

13 Q. So from a scientific perspective, as a
14 technical expert in this case, you can't tell me what in
15 that claim was new as of 2013?

16 MS. LO: Objection, outside the scope.
17 That's not at issue in this proceeding.

18 MS. LOUGHRAN: His testimony is that --

19 MS. LO: Asked and answered.

20 MS. LOUGHRAN: -- all of this stuff is
21 routine and trivial and boilerplate. So I'm just asking
22 him what in this claim is new.

23 MS. LO: But the issues that Charles River
24 has raised in this proceeding have to do with written
25 description and enablement. So, you know, that's what

1 his declaration addresses. We're not talking about
2 obviousness.

3 MS. LOUGHRAN: Are you instructing him not
4 to answer the question?

5 MS. LO: I am stating my objection for the
6 record and the basis for the objection. Outside the
7 scope.

8 You can keep asking him, I suppose.

9 A. Yeah. Again, I hear you asking me a
10 question to evaluate what's in Claim 1 as though it was
11 a peer-reviewed publication, and it's not a
12 peer-reviewed publication. There are no callouts to
13 figures, there's no references, so I really have no
14 means to answer your question in the way that you're
15 asking it.

16 BY MS. LOUGHRAN:

17 Q. Well, is it your position, Dr. Schaefer,
18 that the expression of Factors B and proclotting enzyme
19 in mammalian cells was new in 2013?

20 MS. LO: Same objection, outside the scope.

21 A. I don't know what you mean by "new."

22 BY MS. LOUGHRAN:

23 Q. Had anybody disclosed how to do that before
24 2013?

25 MS. LO: Same objection, outside the scope,

1 asked and answered.

2 A. I think we've discussed previously that I
3 agree that there were no peer-reviewed publications that
4 showed Factor B or proclotting enzyme expression in
5 mammalian cells.

6 BY MS. LOUGHRAN:

7 Q. Were there any publications, peer-reviewed
8 or patent publications, describing the expression of
9 these zymogen factors in different species and combining
10 them into a cascade to detect endotoxin?

11 A. Among these patent documents, there are
12 data showing expression of Factor B and proclotting
13 enzyme in insect cells and combining the products,
14 Factor C, Factor B and proclotting enzyme, in a cascade
15 to measure endotoxin.

16 Q. And do you understand that data, those
17 disclosures to be relevant to how a POSA would
18 understand Claim 1?

19 A. A POSA would understand that expression of
20 those -- of Factor B and proclotting enzyme in insect
21 cells show that they can indeed be expressed. And this
22 was similar to Factor C in insect cells.

23 Furthermore, Factor C expressed in
24 mammalian cells had superior properties, again, coming
25 back to residual activity, compared to Factor C from

1 both the purified enzyme and from the enzyme produced in
2 insect cells.

3 So a POSA would reasonably conclude that
4 since these serine proteases are closely related to
5 Factor C and, in fact, smaller proteins, which are
6 easier to express, that, again, given that we know they
7 can be expressed in insect cells, they would also be
8 successfully expressed in mammalian cells.

9 Q. Okay. So just to be clear, you agree that
10 no one in this field had described a scenario in which
11 these zymogen proteins could be expressed through
12 different species combined -- sorry, strike that.

13 Let me be clearer. You agree that no one
14 in this field had described a scenario in which the
15 zymogen proteins could be expressed in mammalian cells
16 where the zymogen proteins are from different species
17 and would be combined in a cascade to detect endotoxin?
18 We agree on that; right?

19 A. By a "different species," do you mean a
20 species that is not insects? Do you mean mammalian
21 cells? Can you be more clear?

22 Q. Well, I said "expressed in mammalian
23 cells," yeah.

24 MS. LO: Object to the form of the
25 question.

1 A. I agree that there were no peer-reviewed
2 publications showing expression of Factor B or
3 proclotting factor in mammalian cells. But the
4 teachings provided by the inventors in their patent
5 applications, including the '767, tell a POSA how to do
6 it.

7 So just because it hadn't been published in
8 peer-reviewed literature doesn't mean it's not possible,
9 doesn't mean a POSA would not understand that they could
10 be successful, given that the inventors described that
11 it could be done with necessary modifications as
12 compared to what was done for Factor C.

13 (Exhibit 2074 was introduced to the
14 witness.)

15 BY MS. LOUGHRAN:

16 Q. This is -- this is Exhibit 2050 in the PGR.
17 This one says 2074 because it's from the IPR.

18 I believe you -- you cite this document in
19 your declaration. Do you recognize it?

20 A. I do.

21 Q. Now, you understand that this document does
22 not describe expression of Factors B or proclotting
23 enzyme --

24 A. Correct.

25 Q. -- in --

1 A. Oh, sorry.

2 Q. -- in mammalian cells?

3 A. Yes.

4 Sorry. I anticipated the end of that
5 sentence.

6 Q. Okay. Just give me one more minute.

7 Okay. What species of crab were used for
8 each component in the cascade experiment that you refer
9 to in your declaration?

10 MS. LO: Can you direct us to where in
11 this -- either declaration or in this publication?

12 MS. LOUGHRAN: I would love to.

13 BY MS. LOUGHRAN:

14 Q. So at paragraph 47 of your declaration, you
15 write, "Coagulation cascade proteins from different
16 horseshoe crab species have successfully been used to
17 reconstruct the endotoxin detection cascade." And then
18 you cite Exhibit 2050, which is the document you have in
19 front of you, at 35 to 38.

20 Do you see that?

21 A. Yes.

22 Q. So what species are being used here?

23 MS. LO: Take the time you need to review.

24 A. Yes. I need some time to review.

25 BY MS. LOUGHRAN:

1 Q. Or I can ask you a different question,
2 which is the next one. So I'll withdraw that question.

3 Are any of the species that are being used
4 in this cascade from *Limulus polyphemus*?

5 A. Given the date on the application, no,
6 nothing in this document specifically uses *Limulus*. I
7 would, again -- I'll leave at it that.

8 Q. Okay. So there's no example or publication
9 of expressing proclotting enzyme or Factor B in
10 mammalian cells or in *Limulus*; right?

11 A. Can you rephrase that question?

12 Q. Sure.

13 The fields in which we're talking had not
14 described expressing proclotting enzyme or Factor B from
15 *Limulus polyphemus* horseshoe crabs, right, as of 2013?

16 A. As of 2013, the field -- there was no
17 peer-reviewed publication or other publicly available
18 publication that I'm aware of that had a completely
19 assembled proclotting factor or Factor B.

20 But, again, a POSA could use the tools at
21 their disposal, including the BioProjects deposited by
22 the University of Connecticut, including lambda phage
23 cloning using sequences derived from *Tachypleus* and
24 including a combination of RACE PCR and standard PCR, as
25 I've described several times now.

1 Q. Okay. Do you agree, Dr. Schaefer, that
2 simply because you can express a zymogen protein in one
3 mammalian cell does not mean you'll be successful in
4 expressing it in a different mammalian cell?

5 MS. LO: Objection, vague.

6 A. Yeah, your question is very vague and
7 hypothetical.

8 So if we are talking about a hypothetical
9 protein that is not well-characterized and that we have
10 essentially no information on, the scenario you lay out
11 is -- yes, certainly that is possible. That is a
12 possible outcome in the vague scenario -- the vague
13 hypothetical scenario that you've laid out.

14 BY MS. LOUGHRAN:

15 Q. Okay. And indeed, here, it was shown that
16 for the same proteins, right, Factor C protein being
17 expressed in HEK cells worked, but Factor C protein
18 expressed in COS-1 cells did not work. You agree with
19 that; right?

20 A. Yes. That is consistent with the
21 literature and with the information that was conveyed by
22 the patentholders.

23 Q. Okay. And that's even though the Factor C
24 that was being used in each of those cells was very
25 similar; right?

1 A. Yes. In the case of Factor C, it was known
2 that COS-1 was not a good cell line and that HEK and CHO
3 were both good cell lines for producing soluble Factor C
4 that is functional.

5 Q. So even where you have information about
6 the protein you want to express, you've characterized
7 it, as we've discussed, biochemically, you understand
8 how it works. It may still be that that protein doesn't
9 express in certain mammalian cell lines; right?

10 MS. LO: Objection, vague.

11 A. Again, if we're talking hypotheticals, we
12 can pretty much lay out any kind of hypothetical
13 scenario and say, Is this possible? And as a scientist,
14 I would say, yes, that's possible, unless you were
15 describing something that would break the laws of
16 physics.

17 So for a hypothetical like that, I'm not
18 going to say it's not possible.

19 BY MS. LOUGHRAN:

20 Q. Okay. Would you agree that a POSA would
21 take into account the fact that Factor C did not express
22 in COS-1 cells in considering whether it would express
23 in other mammalian cells?

24 A. Considering whether what would express in
25 other mammalian cells?

1 Q. Well, let me ask it a little more clearer.

2 Would you agree that a POSA would take into
3 account the facts that the inventors laid out in their
4 publication, that Factor C did not express in a
5 functional form from COS-1 cells, it would take into
6 account that fact in thinking about whether Factor C
7 would express in other mammalian cells?

8 A. Factor C?

9 Q. Yeah.

10 A. If a POSA -- so what's the scenario here?
11 Are we talking about a POSA that is looking to express
12 Factor C in other mammalian cells besides the ones that
13 have been described already?

14 Q. Yes.

15 A. So not COS-1, not DG44, not HEK?

16 Q. Yeah. So I just want to understand, like,
17 you are taking into account a whole lot of information
18 that you are saying a POSA would know and be familiar
19 with.

20 What I'm trying to understand is: You
21 agree that they would also take into account that in
22 COS-1 cells, Factor C did not express in a functional
23 manner. They would take that information into account;
24 correct?

25 A. A POSA is going to take all known relevant,

1 published or publicly accessible information into
2 account. Yes, I think we can agree on that.

3 Q. Okay. And at paragraph 47, where we were
4 just looking, that cites Exhibit 2050 --

5 A. Yes.

6 Q. -- you also cite Exhibit 2023.
7 Do you see that?

8 A. Yes.

9 Q. Okay. And you're aware that that
10 Exhibit 2023 at 4 just cites back to the same reference,
11 Exhibit 2050.

12 Are you aware of that?

13 A. I have not memorized the exhibits and what
14 they say. So I will take you at your word that that's
15 what it says, or you can show me.

16 Q. Okay. We'll -- I mean, the document will
17 speak for itself.

18 You also talk about a post-priority date
19 publication in this paragraph.

20 Do you see that?

21 A. Yes.

22 Q. Okay. And you agree that a POSA, as of
23 2013, is not going to have -- or would not take into
24 account information in post-priority date publications;
25 right?

1 A. That's what I understand post-priority date
2 publication to mean, yes.

3 Q. Okay. So why did you include that in your
4 declaration?

5 A. Simply because it's a confirmation of what
6 a POSA would have reasonably understood at the time of
7 publication.

8 Q. Okay. A POSA wouldn't take it into
9 account --

10 A. I'm not saying a POSA wouldn't have taken
11 it into account.

12 MS. LOUGHRAN: Okay. Let's take a quick
13 break. I'm getting close to the end here. I just want
14 to gather some files.

15 (A break was taken.)

16 BY MS. LOUGHRAN:

17 Q. Hello, again, Dr. Schaefer. How are you?

18 A. I'm good.

19 Q. Did you speak with your counsel, Ms. Lo,
20 about the substance of your testimony during any of the
21 breaks?

22 A. Not at all.

23 MS. LOUGHRAN: Okay. I have no other
24 questions for you in the IPR or PGR cases. I thank you
25 for your time.

1 MS. LO: I have just a couple of questions,
2 Dr. Schaefer.

3 EXAMINATION

4 QUESTIONS BY MS. LO:

5 Q. Do you recall yesterday Ms. Loughran asking
6 you questions about paragraph 87 in your IPR
7 declaration?

8 It would be helpful to pull that out.

9 A. I'll go back there.

10 MS. LOUGHRAN: Which paragraph, Shon?

11 MS. LO: 87.

12 THE WITNESS: Yes.

13 BY MS. LO:

14 Q. And she was asking you to identify where in
15 the three references cited that discuss the
16 characterization of the cleavage/activation site and
17 catalytic triad and substrate binding sites of Factor C
18 in the two species?

19 A. Yes.

20 Q. You mentioned yesterday in your answer that
21 there was additional literature beyond those three
22 references available to a POSA as of the priority date.

23 Does that sound right?

24 MS. LOUGHRAN: Objection, leading.

25 MS. LO: It's foundational.

1 A. Yes.

2 BY MS. LO:

3 Q. And if I can direct your attention in your
4 IPR declaration to the section starting on -- at
5 paragraph 24, which is on page 13. And this is the
6 subsection titled "Isolation and characterization of
7 Factor C."

8 Are you there?

9 A. Maybe I'm not at the right place.

10 Q. Paragraph 24?

11 A. Oh, paragraph 24. Sorry, I was on page 24.
12 Okay.

13 Q. Okay. And then in this section, you
14 discuss some of the references that were cited in
15 paragraph 87. I'll just represent that to you. You
16 don't need to confirm it for me.

17 A. Okay.

18 Q. But you also discuss in paragraph 32 and 33
19 a 1995 publication. Sorry. I will give you a moment.

20 You discuss on Exhibit 2008, which is 1995
21 publication concerning the characterization of
22 Carcinoscorpis Factor C; correct?

23 A. Yes.

24 Q. Okay. And would you like to see that
25 reference or -- I was going to ask you, would a POSA

1 view the results reported in this 1995 publication as
2 informative of the cleavage/activation site and
3 catalytic triad and substrate binding sites of Limulus
4 polyphemus Factor C?

5 MS. LOUGHRAN: Objection, leading.

6 MS. LO: So I understand if you want to see
7 the reference. I have it for you if you'd like.

8 A. Based on what is described in that
9 paragraph, that would be one more piece of evidence that
10 homology between the species was very high.

11 So now if you have Factor C from two
12 different species, both Carcinoscorpius and Tachyplesus,
13 and those have highly homologous serine protease
14 domains, including the catalytic triad that is very well
15 conserved between the serine proteases, the aspartic
16 acid, the serine triad, which is mechanistically
17 essential for proteolytic activity, that would lead a
18 POSA to conclude that -- very, very likely that Limulus
19 would also be very similar in sequence and extremely
20 likely to include that same catalytic triad.

21 BY MS. LOU:

22 Q. Thank you.

23 And if you can look at paragraph 34 of your
24 IPR declaration. And do you recall counsel asking you
25 yesterday about the different sequence identity

1 percentages reported between Carcinoscorpius Factor C
2 compared to Limulus Factor C?

3 A. Yes. We had a lengthy back-and-forth on
4 that.

5 Q. Yeah. Did any of your opinions depend on
6 the exact percentage of identity between those two
7 proteins?

8 A. No. None of my -- nothing I said depended
9 on the exact percentages. And, in fact, I think I
10 pointed out several times that the percentages are
11 extremely close, which would give, you know, a POSA
12 great confidence that they were all talking about the
13 same thing.

14 Q. And does the reason behind why there may
15 have been some small variation in the percentage
16 sequence identify affect your opinions at all, like the
17 explanation, the actual explanation for it?

18 MS. LOUGHRAN: Objection, leading.

19 A. The differences that are shown, I think, as
20 I remarked several times, are very small and trivial
21 and, no, did not impact my opinions.

22 MS. LO: Thank you. That's all.

23 MS. LOUGHRAN: Nothing further.

24 (The deposition concluded at 11:35.)

25 (Total time on record: 8 hours, 5 minutes.)

CERTIFICATE OF REPORTER

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2
3
4 I, Celena D. Davis, Registered Professional
5 Reporter and Certified Shorthand Reporter within and for
6 the State of Illinois do hereby certify that the witness
7 whose testimony appears in the foregoing deposition was
8 duly sworn by me; that the testimony of said witness was
9 taken by me to the best of my ability and thereafter
10 reduced to typewriting under my direction; that I am
11 neither counsel for, related to, nor employed by any of
12 the parties of the action in which this deposition was
13 taken, and further, that I am not a relative or employee
14 of any attorney or counsel employed by the parties
15 thereto, nor financially or otherwise interested in the
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DEPOSITION ERRATA SHEET

DECLARATION UNDER PENALTY OF PERJURY

I declare under penalty of perjury that I have read the entire transcript of my Deposition taken in the captioned matter or the same has been read to me, and the same is true and accurate, save and except for changes and/or corrections, if any, as indicated by me on the DEPOSITION ERRATA SHEET hereof, with the understanding that I offer these changes as if still under oath.

Signed on the _____ day of _____, 20____.

BRIAN SCHAEFER, Ph.D.

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3	_____
4	Reason for change: _____
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