

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 TINA MORRIS, Ph.D.
TAKEN ON BEHALF OF PETITIONER
JANUARY 28, 2026

Reported by Celena D. Davis, RPR, CSR

CRL Exhibit 1069
CRL v. Seikagaku
IPR2025-00440

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 2 BEFORE THE PATENT TRIAL AND APPEAL BOARD
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 4 CHARLES RIVER LABORATORIES,)
 INC.,)
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 Petitioner,)
 6)
 vs.) Case No. IPR2025-00440
 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 TINA MORRIS, 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 January 28,
 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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APPEARANCES

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CERTIFIED SHORTHAND REPORTER (TN)
CERTIFIED LIVENOTE REPORTER
MAGNA LEGAL SERVICES
Celena D. Davis

1 (The deposition began at 9:03 a.m. CST.)

2 TINA MORRIS, 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. Morris. How are you
8 today?

9 A. I'm well. Thank you. How about you?

10 Q. I'm okay. Yesterday was a tricky one, but
11 I appreciate everybody's flexibility and the ability to
12 pivot and do this deposition remotely so we can be
13 respectful of everybody's time. So thank you very much.
14 Could you please state and spell your name
15 for the record?

16 A. Tina S. Morris, Ph.D.

17 Q. And how do you spell your last name?

18 A. M-O-R-R-I-S.

19 Q. And where do you currently reside, Doctor?

20 A. Jupiter, Florida.

21 Q. And are you represented by counsel today?

22 A. Yes, I am.

23 Q. And who is that? I can't see the other
24 people in the room, but maybe you can verbally tell me
25 who is in the room with you today.

1 A. Maria Doukas.

2 Q. And she's a lawyer for Morgan Lewis;
3 correct?

4 A. Correct.

5 Q. Now, you understand that you're under oath
6 today; correct?

7 A. I understand, yes.

8 Q. And that means you must answer my questions
9 truthfully over the course of the day; understood?

10 A. Understood.

11 Q. Okay. Is there any reason why you can't
12 give truthful answers to my questions today, Doctor?

13 A. No.

14 Q. Thank you.

15 Have you ever given testimony in a
16 deposition before?

17 A. No.

18 Q. All right. So in view of that, I'll just
19 lay out a few rules that we can all operate by today to
20 make sure that this goes as smoothly as possible. So
21 during the deposition today, I'm just going to ask you
22 some questions. I'd just like that you answer each of
23 those questions to the best of your ability; okay?

24 A. Yes.

25 Q. If at any point you don't understand one of

1 my questions, just let me know and I'll repeat the
2 question or ask a better question. But if you don't say
3 anything, I will assume that you understood my question;
4 is that fair?

5 A. Fair.

6 Q. We'll take a break approximately every
7 hour, but if at any point you do need to take a break,
8 just let me know. The one rule on that front is if
9 there's a question pending, I will need you to answer
10 the question before we take a break; okay?

11 A. Okay.

12 Q. And you do have to answer all of my
13 questions today, unless your counsel, Ms. Doukas,
14 instructs you specifically not to answer. I'm going to
15 ask you several questions; Ms. Doukas may object to
16 those questions. But unless she specifically instructs
17 you not to answer, you still have to answer even if
18 there's an objection; do you understand?

19 A. Understood.

20 Q. And, obviously, you are joined by a court
21 reporter today. So their job is to write everything
22 down to provide a record of your testimony today. So I
23 will ask that you answer all of my questions verbally,
24 because the court reporter can't write down a head nod
25 or a shrug or something that you do physically; okay?

1 A. Okay.

2 Q. And then finally, Doctor, technology has
3 allowed us to have this deposition go forward today,
4 even though I'm halfway across the country, which is
5 fortunate for us. It does require a level of trust.

6 I'm going to assume that you are not able
7 to communicate with counsel today outside of my
8 questions, outside of what's verbally on the record.
9 That means I assume you are not text messaging or have
10 access to any communication platform while I'm asking
11 you questions.

12 Can you confirm that?

13 A. I can confirm that.

14 Q. Thank you.

15 Do you have any other questions about the
16 rules of this deposition before I proceed?

17 A. No, I don't think so.

18 Q. Excellent.

19 Doctor, how did you come to be involved in
20 the case of -- the PTAB case, Charles River versus
21 Seikagaku?

22 A. Because of my expertise in my field and my
23 background and publications that I have made in that
24 area. I was contacted for my expertise.

25 Q. Okay. And when, approximately, were you

1 contacted?

2 A. I would say about a year ago. I --

3 Q. And who contacted you?

4 A. Shon Lo, counsel from Morgan Lewis.

5 Q. And when you were contacted about this
6 case, had you ever heard of the company Seikagaku
7 before?

8 A. Yes.

9 Q. In what context did you have an awareness
10 of Seikagaku?

11 A. I think anybody working in the field of
12 recombinant protein manufacturing and who is familiar
13 with endotoxin testing and endotoxin testing
14 requirements knows the manufacturers and the providers
15 and the experts in that field. So the company and many
16 others were known to me through my experience.

17 Q. Had you ever had a role working for or
18 consulting with Seikagaku prior to your work in this
19 case?

20 A. No.

21 Q. And similar question with respect to
22 Charles River: Did you have an awareness of Charles
23 River prior to your involvement in this case?

24 A. Yes.

25 Q. And was that through your -- as you noted,

1 your experience in this field?

2 A. Yes.

3 Q. And had you ever -- before your involvement
4 in this case, had you ever worked for or consulted for
5 Charles River?

6 A. No.

7 Q. Prior to your involvement in this case, had
8 you ever had the occasion to work with, on a committee
9 or a working group or, you know, something of that
10 nature, with employees of Charles River related to
11 recombinant Factor C?

12 A. Over the course of my career, because of my
13 work both at PDA, at the Parenteral Drug Association and
14 at the United States Pharmacopeia, I have interacted
15 with many experts in that area. So I -- over the years,
16 I am sure I have had committee members or expert panel
17 members from those companies that I worked with, but not
18 specifically on this particular -- on the matter that we
19 will be discussing today.

20 Q. Did you have any involvement on a working
21 group that -- whose task it was to make a determination
22 about the introduction of recombinant Factor C as an
23 alternative to the LAL assay?

24 A. Would you clarify if you're asking about a
25 specific working group? Because there are -- there were

1 many different efforts in that area over time.

2 Q. Do you have awareness of the earliest
3 working group that was asked to assess that?

4 A. Which working -- who convened that working
5 group? Was it an industry group?

6 Q. So I don't have like all of the expertise
7 that you have, Doctor. It was an industry group in
8 which a woman by the name of Karen McCullough was
9 involved. Do you have a knowledge of that individual
10 and the working group she was a part of?

11 A. I have awareness of it because, if I recall
12 correctly, that was during the time when I was at the
13 United States Pharmacopeia.

14 And at that time, because of my role at the
15 United States Pharmacopeia, as a standard-setting
16 organization, the USP itself, or staff at the USP, would
17 not have been directly involved in an industry working
18 group. The working group would have come to the
19 standardization body with proposals to be evaluated.

20 Q. And do you have a recollection of what the
21 proposals in that group brought to the USP were?

22 A. Not specifically anymore. There were many
23 iterations.

24 Q. Do you -- during your time -- you know,
25 around that time that that working group was convened,

1 did you form any opinions about the positions of that
2 group and those recommendations?

3 A. I don't think I specifically formed any
4 opinions. I certainly followed the field and -- as it
5 was evolving. And if you give me a specific time frame
6 you are asking about, I can give you a more precise
7 answer, because I can align it with what I was working
8 on at the time.

9 Q. So -- and, again, you know, I don't have
10 all of the details related to these working groups. But
11 I'll just -- maybe I'll just ask: Did you have an
12 awareness with respect to the committee and the
13 recommendations that were being formed by the working
14 group of which Karen McCullough was a part, that there
15 was a resistance to the introduction of recombinant
16 Factor C as an alternative to the LAL assay?

17 A. I think everybody in the industry was aware
18 of that resistance and of the challenges and the
19 different opinions and scientific conversations that
20 were happening at the time.

21 Q. And at that time, did you have an opinion
22 yourself about whether the recombinant Factor C sort
23 of -- was a viable alternative to the LAL assay?

24 MS. DOUKAS: Objection, outside the scope
25 and vague.

1 THE WITNESS: Can I answer?

2 MS. DOUKAS: You can answer.

3 A. I would say as a general statement, I have
4 always been a proponent and supported the introduction
5 of recombinant alternatives to animal testing. And
6 during my entire career at the USP, I've worked and
7 followed many efforts in that area.

8 I am also aware of -- because of the
9 universal role of -- in this particular test,
10 especially, there are many different scientific
11 considerations, and also patient safety considerations
12 that go into the development and approval of such a
13 test. So it's a complex scientific issue that takes a
14 long time to resolve.

15 And I can honestly say that I cannot --
16 until we -- unless you give me a specific scientific
17 scenario, I cannot tell you what I thought at the time.
18 But in general terms, I would say supporting recombinant
19 replacements for animal-based assays is a good thing,
20 and I've always, as a scientist, supported that and been
21 a proponent of it at USP.

22 BY MS. LOUGHRAN:

23 Q. As a proponent of it, did that ever cause
24 you to be adverse to or in conflict with the
25 recommendations of Charles River on this issue,

1 specifically?

2 A. No.

3 MS. DOUKAS: Objection, outside the scope,
4 vague.

5 A. No.

6 BY MS. LOUGHRAN:

7 Q. Did you have an understanding of what
8 Charles River's position was with respect to the
9 introduction of recombinant Factor C? And, again,
10 specifically at the time frame when Karen McCullough was
11 on that working group.

12 A. I believe so.

13 Q. And what was your understanding of Charles
14 River's position?

15 A. Framing it generally and not specifically,
16 only to Charles River, I would say, scientifically, the
17 greatest concern in the replacement of an established
18 harmonized assay that has been around for a long time is
19 to assure that the replace- -- the performance of the
20 replacement assay is sufficient -- is equivalent or
21 better to the original test.

22 And, scientifically speaking, that was
23 always the main driver of -- of any, I would say
24 scientific concern, over the replacement.

25 Q. Okay. And was it your understanding that

1 Charles River or companies like Charles River were
2 interested in ensuring that there was enough data to
3 demonstrate that equivalence?

4 A. I would like to clarify something. The
5 standard-setting process that is involved in -- in the
6 compendial standard-setting process that is involved in
7 replacing an official assay relies on many -- on
8 established processes, of public notice and comment. It
9 has requirements for public review of the data, the
10 amount of data that's required. There is expert
11 deliberation. There is a lot of data analysis involved.

12 And to my knowledge, the USP not only had
13 an expert committee, but had dedicated expert panel
14 deliberations and sought opinions beyond Charles River
15 across the industry. So I would caution here that the
16 opinions that I'm giving are based on the scientific
17 data that I was aware of that came from a working group
18 and from industry and user experiences that go far
19 beyond Charles River.

20 So I want to clarify that I am not able to
21 speak specifically to Charles River's position, but more
22 what my experience is from the discussions in expert
23 panel, expert committee, and scientific deliberations at
24 conferences at the time.

25 Q. Okay. Understood. And with that

1 clarification, let me just rephrase my question.

2 Was it your understanding that the
3 stakeholders involved in that decision were interested
4 in ensuring that there was enough data to demonstrate
5 equivalence between the recombinant product and the
6 natural lysate LAL test?

7 A. It is my understanding and my experience
8 with this type of discussion that concerns comparability
9 and questions of equivalence, that it's a dynamic of
10 the -- obviously, the proponents, the scientific
11 proponents of replacement providing data to convince an
12 expert body that there is enough data, and the
13 proponents of retaining the current assay, bringing data
14 that challenged that opinion.

15 And that's appropriate. That is the
16 scientific process. We are talking about an assay that
17 is a very important impurity test that is important to
18 patient safety. So the bar, naturally, for replacement
19 is very high. So because -- and that is -- that's
20 appropriate.

21 So it's a dynamic that is not unique. And
22 it is the role of the standard-setting body and the
23 governance rules and procedures to assure that
24 science -- that scientific decisions are made and that
25 conflicts of any kind are managed.

1 Q. Okay. And so do you agree that a robust
2 amount of data should be -- strike that.

3 Do you agree that a robust amount of data
4 should be offered in making comparisons between the
5 recombinant product and the native?

6 MS. DOUKAS: Objection, form.

7 BY MS. LOUGHRAN:

8 Q. You still do have to answer that question.

9 A. The way I would answer that is that there
10 are established expectations that are assay-dependent
11 that should be met. And that is also, in this
12 particular case, where the regulator comes in; right?

13 We're talking about a compendial test, but
14 the compendial test is enforced and used by the
15 regulatory agency. And so the bar of what is good
16 enough for a test like this is not just up to the
17 standard-setting organization or the expert panel or the
18 expert committee, but it also requires regulatory
19 approval.

20 Q. Thank you. Are you aware that there are
21 other experts who have submitted testimony in this case,
22 in the PTAB case for which we're here today?

23 A. Yes.

24 Q. And are you aware that a separate expert in
25 this case was retained by Seikagaku and submitted some

1 testimony? His name is Brian Schaefer?

2 A. I am aware, but I have not reviewed his
3 material.

4 Q. Okay. Do you know Dr. Schaefer? Did you
5 know Dr. Schaefer prior to this case?

6 A. No.

7 Q. And are you aware that the petitioner had
8 submitted testimony by an expert by Dr. Siddhartha Jain?

9 A. Yes.

10 Q. And did you have an awareness of Dr. Jain
11 before this case?

12 A. No.

13 Q. Did you or -- did you have any
14 conversations with Dr. Schaefer?

15 A. No.

16 Q. And I believe we'll get to this, but I
17 believe you did review Dr. Jain's testimony in this
18 matter; correct?

19 A. Are you speaking about the testimony or the
20 declaration?

21 Q. His declaration, I believe, and his
22 deposition transcript.

23 A. The deposition transcript, I have not
24 reviewed in entirety, just, I would say, highlights.

25 Q. But you did review his declaration?

1 A. I did.

2 Q. I would like to turn you to your
3 declarations submitted in this case. So if you have
4 that box handy, a copy of it should be in a folder
5 marked tab 1. If you could grab that document and have
6 it in front of you, that would be wonderful.

7 A. Thank you. I have it.

8 (Exhibit 2042 was introduced to the
9 witness.)

10 BY MS. LOUGHRAN:

11 Q. And I will just note that this document has
12 been premarked as Exhibit 2042. Do you see that at the
13 bottom of the front page?

14 A. Yes.

15 Q. Okay. And this is a document marked
16 Exhibit 2042, entitled "Declaration of Tina Morris,
17 Ph.D. in association with Case No. IPR2025-00440."

18 Do you recognize this document, Doctor?

19 A. I do.

20 Q. Okay. And is this your declaration that
21 was submitted in support of patent owners' arguments in
22 the IPR related to Patent No. 11,236,318?

23 A. Yes.

24 Q. Is this the only declaration that you
25 submitted with respect to the IPR related to the '318

1 patent?

2 A. Yes.

3 Q. And you did not submit any declaration
4 related to the co-pending case, the PGR case, relating
5 to the '109 patent; is that correct?

6 A. Correct.

7 Q. Do you have any awareness of the issues
8 involved in that '109 patent post grant review?

9 A. Not really.

10 Q. Were you asked to provide any testimony
11 related to the '109 PGR?

12 A. No.

13 Q. So, Doctor, do you -- if you could just
14 turn to the last page of this declaration, it's page 24,
15 and you'll see there your signature.

16 Is that your signature, in fact?

17 A. That is my electronic signature, yes.

18 Q. Okay. And you did sign this document on
19 December 1, 2025?

20 A. Yes, I did.

21 Q. And you reviewed all of the contents of
22 this declaration to ensure that they were true
23 statements before you signed it; right?

24 A. Correct.

25 Q. And is there anything about this

1 declaration that you would like to change as we sit here
2 today?

3 A. No.

4 Q. Did you write this document, Doctor?

5 A. I wrote it with the assistance of counsel.

6 Q. Could you clarify what you mean by that?

7 A. I would say counsel wrote, and I provided
8 scientific input and reviewed the language.

9 Q. And did you make edits to what counsel
10 wrote?

11 A. I made edits on the scientific matters,
12 yes.

13 Q. Besides yourself, did you have anyone --
14 strike that.

15 Aside from counsel's involvement, so not
16 anyone that worked at Lewis, but besides yourself, did
17 you have any assistance or people helping you with your
18 editing or revising of this declaration?

19 A. No.

20 Q. Did you speak with any of the inventors on
21 the '318 patent during the process of forming your
22 opinions in this case?

23 A. No.

24 Q. Do you know an individual by the name of
25 Dr. Mizumura, the first named inventor on this patent?

1 A. No.

2 Q. Have you ever interacted with any of the
3 inventors on the patent prior to this case?

4 A. Not to my knowledge or recollection.

5 Q. Do you have any legal education, Doctor?

6 A. I do not.

7 Q. Have you ever had any involvement with the
8 United States Patent system?

9 A. Because of my work at the United States
10 Pharmacopeia, I have been exposed to the patents -- to
11 the patent system and -- yes, I have.

12 Q. Are you a named inventor on any patents?

13 A. Yes, I am. But they are --

14 Q. How many?

15 A. -- unrelated to the matter we are
16 discussing.

17 Q. And how many patents are you a named
18 inventor on?

19 A. Two.

20 Q. And so in the process of securing those
21 patents, did you have occasion to learn about any of the
22 legal standards that are involved in patentability in
23 the US patent system?

24 A. Not really.

25 Q. I believe in this declaration, you indicate

1 that counsel explained a few of the standards to you?

2 A. They did.

3 Q. We'll get to that.

4 Are there any other sources from which you
5 have an understanding of the legal standards involved in
6 this case?

7 A. No. Primarily from counsel.

8 Q. And I understand that you are testifying in
9 support of the patent owner in this case as an expert;
10 correct?

11 A. Correct.

12 Q. And for your time, you're being paid an
13 hourly rate; is that correct?

14 A. That is correct.

15 Q. And what is that rate?

16 A. \$700.

17 Q. All right. If you could turn to page 6,
18 let me see, yes, page 6 of your declaration, there is a
19 table here. You indicate you have reviewed the
20 materials cited here in the petition, the deposition
21 transcript of Dr. Jain, as well as the following list of
22 materials; is that an accurate statement?

23 A. Yes.

24 Q. And you did, in fact, review all of the
25 documents listed here; correct?

1 A. I did.

2 Q. Did you read every word or did you just
3 focus on particular portions?

4 A. I read every word of everything, I would
5 say, except for the transcript.

6 Q. Okay. So you read through the file history
7 of the prosecution for the '318 application which
8 matured into the '318 patent?

9 A. I would say I read a great amount of that.

10 Q. Did you review any case law in preparing
11 your declaration?

12 A. I am familiar with some of the case law
13 that was cited, but I did not review it.

14 Q. So did you actually read the cases or you
15 just have an awareness of the legal principles?

16 A. I have an awareness.

17 Q. Okay. Did you run any experiments in the
18 course of doing your analysis that led to the testimony
19 in this declaration?

20 A. No.

21 Q. And did you form any opinions about the
22 unexpected results, the alleged unexpected results of
23 the invention at Claim 21 that are not discussed in this
24 declaration?

25 A. No.

1 Q. Doctor, did you do anything to prepare for
2 the deposition today?

3 A. Document review.

4 Q. Anything else?

5 A. Conversation with counsel.

6 Q. So with respect to conversation with
7 counsel, so do you mean you had a meeting with counsel
8 to prepare?

9 A. Yes.

10 Q. Okay. And when was that meeting?

11 A. Yesterday.

12 Q. And how long was that meeting with counsel?

13 A. Approximately three hours.

14 Q. Did you have any other meetings with
15 counsel to prepare for today's deposition?

16 A. We had one teleconference.

17 Q. And how long was that?

18 A. One hour.

19 Q. And you said you reviewed some documents.
20 Are any of those documents documents that are not cited
21 in this declaration or listed in your list of materials
22 considered?

23 A. No.

24 Q. So all the documents that you reviewed to
25 prepare for today's deposition are referenced or cited

1 in your declaration; correct?

2 A. Yes.

3 Q. Did you speak with anybody, other than
4 counsel, in preparing for today's deposition?

5 A. No.

6 Q. Have you corresponded with anyone in
7 Seikagaku in forming the opinions that are found in your
8 declaration?

9 A. No.

10 Q. So I believe you referenced that you were
11 sort of writing down some Latin names. Through the
12 course of this deposition, I just want to establish a
13 little bit of nomenclature right now that hopefully will
14 help us through the course of this deposition.

15 So the petitioner in this case, obviously,
16 is Charles River Laboratories, Incorporated. During the
17 deposition, I'm going to refer to them as Charles River.
18 I just want you to confirm that you understand I'm
19 referring to the petitioner, Charles River Laboratories;
20 is that okay?

21 A. Yeah. Understood.

22 Q. Okay. And then, likewise, there is the
23 patent owner, which is a company named Seikagaku
24 Corporation. I will refer to them just as Seikagaku,
25 but I'll be referring to the patent owner; okay?

1 A. Yeah.

2 Q. In addition, the horseshoe crabs that we
3 refer to as *Limulus polyphemus* --

4 A. Uh-huh.

5 Q. -- during the deposition, I will refer to
6 *Limulus polyphemus* as *Limulus*. I realize that there's
7 some less-than-precise language that is often referred
8 to using the word *Limulus*, but if I use that word today,
9 I'm referring to the particular species *Limulus*
10 *polyphemus*; is that okay?

11 A. That's okay.

12 Q. Likewise, there is the horseshoe crab
13 species *Tachypleus tridentatus*. I'll refer to that as
14 *Tachypleus*, but I will be referring to the specific
15 species; is that okay?

16 A. Yes.

17 Q. Great. Finally, there is the species
18 *Carcinoscorpius rotundicauda*. I don't know if that's
19 exactly the pronunciation. But if I say the words
20 *Carcinoscorpius*, I'm referring to that species in
21 particular, the Singaporean species; is that okay?

22 A. Correct. That's okay.

23 Q. So we're on the same page for nomenclature.
24 Thank you.

25 If you turn to page 2 of your declaration,

1 you've set forth a series of paragraphs under the
2 heading "Education and Qualifications"; do you see that?

3 A. Yes.

4 Q. Okay. Now, in paragraph 6, you say you
5 earned a Ph.D. in molecular virology; do you see that?

6 A. Yes.

7 Q. Do you have a recollection of what
8 department you received your Ph.D. in molecular virology
9 under?

10 A. Yes, I do.

11 Q. What is that?

12 A. It's the department of medical
13 microbiology.

14 Q. Okay. Was there a particular institute
15 underneath that department in which Ph.D. students in
16 molecular virology were assigned or were part of?

17 A. Yes. The laboratory was housed in the
18 Institute For Molecular Virology. And that's where I
19 did my Ph.D. with Dr. Valena Garasmalda (phonetic).

20 Q. Now, at that time, was there a separate
21 Ph.D. program for someone who was pursuing an education
22 specifically in molecular biology?

23 A. It was the then-typical setup of a medical
24 school having Ph.D. programs in medically related
25 fields, in this particular case, infectious diseases.

1 And my studies were focused on the molecular biology and
2 chemistry of hepatitis A virus. And because the -- the
3 field has relevance to medical microbiology because
4 hepatitis A is a big medical problem. And the study of
5 it is -- was very heavily focused on molecular biology.
6 So that program was supported by both institutes.

7 Q. And when you say both institutes, which are
8 you speaking of?

9 A. Molecular biology, where it was housed, the
10 physical laboratory; but the degree was conferred by the
11 Institute of Medical Microbiology.

12 Q. Okay. And in the course of securing your
13 Ph.D. in molecular virology, did you take courses
14 outside the Institute For Molecular Biology?

15 A. No, I did not, come to think of it.
16 Actually, strike that.

17 Biochemistry. Yes, biochemistry.

18 Q. Did you take any classes in engineering or
19 biomedical engineering?

20 A. No, I did not. That field did not exist in
21 1994.

22 Q. Got it.

23 So I suppose that answers the question
24 about whether any biomedical engineering students took
25 courses in the Molecular Virology Institute.

1 A. Yes.

2 Q. No to that; correct?

3 A. Correct. It was mostly medical students
4 that we had.

5 Q. So in -- if you turn to the next page,
6 page 4, you talk about in 2003, you joined United States
7 Pharmacopeia; do you see that?

8 A. Yes.

9 Q. And you refer to -- you represented USP as
10 the WHO expert committee for biological standardization
11 for nearly a decade?

12 A. Correct.

13 Q. And did that biological standardization
14 involve this question about replacing or also using
15 recombinant Factor C in addition to the LAL assay?

16 A. The expert committee for biological
17 standardization at WHO sets the international reference
18 materials for biologics. One of those reference
19 materials is the International Standard For Endotoxins.

20 And I was involved with the -- one of the
21 replacement studies for this reference material, which
22 was made in collaboration between the USP, the European
23 Pharmacopeia, the National Institute For Biological
24 Standardization and Control in the United Kingdom, and
25 the Japanese Pharmacopeia.

1 And as part of that study, alternative
2 methods were -- were allowed into the study, but not for
3 the assignment of the value. That's -- is published.

4 Q. Okay. And just in terms of the people who
5 were on that committee, were they all molecular
6 biologists, or was it an interdisciplinary committee?

7 A. It's a very interdisciplinary committee
8 because the ECBS has an extremely wide scientific
9 agreement of biological standards.

10 Q. So that committee involved people with a
11 variety of different scientific and medical backgrounds?

12 A. Correct.

13 Q. Let me ask you: In terms of your
14 experience, starting in 2003 at US Pharmacopeia, were
15 you doing any sort of hands-on scientific lab work, like
16 bench work experiments, in your role there?

17 A. No. That was not part of my role. But I
18 evaluated data, laboratory data.

19 Q. Is it -- would you give the same answer
20 with respect to your professional experience since then,
21 in terms of whether you've been involved with sort of
22 hands-on laboratory experiments?

23 A. I would say yes. I have not worked
24 hands-on in the laboratory after leaving Human Genome
25 Sciences; although I did teach a couple of classes,

1 specialized classes at the Parenteral Drug Association
2 that had to do with laboratory quality. And they
3 involved hands-on teaching of how to do specific quality
4 studies; for example, a smoke study, so -- but that has
5 nothing to do with this case.

6 Q. Okay. So in terms of you actually doing
7 hands-on experiments in the technical area that this
8 case is involved, is it fair to say that you have not
9 done any of that work since your time at HGS, which you
10 started in 1998?

11 A. Yes.

12 Q. And if you look at paragraph 8 of your
13 declaration, you say -- just give me a moment. Are you
14 there?

15 A. Yes.

16 Q. Okay. You said, "Over the nearly six years
17 of my tenure at HGS," I'm reading the second sentence,
18 "my expertise focus deepened in the area of product
19 characterization and specification development for
20 clinical materials." And then you say, "Endotoxin
21 testing was routinely done on our clinical batches."

22 Did you do that endotoxin testing
23 personally, or was that other folks at HGS?

24 A. I did some of it personally in the
25 development laboratory at the time as part of batch

1 screening and development work on particular candidates.

2 Q. Okay. And then the next sentence, you say,
3 "Recombinant proteins from different expression systems,
4 including Sf9, yeast, CHO and other mammalian cell lines
5 were routinely analyzed for structure function
6 profiles."

7 Did you do that analysis yourself or was
8 that done by others at HGS?

9 A. I did some of it myself and I also analyzed
10 data from members of my department. But I did hands-on
11 work.

12 Q. And you left HGS sometime prior to 2003
13 when you joined US Pharmacopeia; correct?

14 A. October 2003.

15 Q. Okay. Now, your testimony in your
16 declaration refers to opinions that you formed about
17 what a person with skill in the art would think or
18 expect as of 2019; is that fair?

19 A. That's fair.

20 Q. Okay. And in terms of what you were doing
21 professionally in 2019, were you doing any hands-on lab
22 work?

23 A. No.

24 Q. In 2019, did you have any awareness of
25 about whether there was or was not a known cDNA sequence

1 for Factor C of Limulus polyphemus?

2 A. I would say no, that was not a concern
3 scientifically for me.

4 Q. In 2013, did you have any awareness about
5 whether there was or was not a known cDNA sequence for
6 Factor C of Limulus polyphemus?

7 MS. DOUKAS: Objection, outside the scope.

8 BY MS. LOUGHRAN:

9 Q. You can still answer, Doctor.

10 A. I did not. Same answer.

11 Q. Okay. In your professional experience,
12 have you had any exposure to efforts to sequence
13 horseshoe crab coagulation factors?

14 A. I have awareness because of the efforts
15 that were ongoing to establish replacement assays. And
16 it's clear that creating recombinant reagents as part of
17 that, that are based on the sequence of the original
18 animal protein.

19 Q. Okay. So you would agree that the creation
20 of the recombinant protein requires the underlying
21 sequence of, as you said, the original animal?

22 A. Of course.

23 Q. Have you ever, yourself, recombinantly
24 produced any horseshoe crab zymogen proteins?

25 A. No.

1 Q. Have you overseen other scientists in their
2 production -- of recombinant production of horseshoe
3 crab zymogen proteins?

4 A. I have not.

5 Q. Did you ever work with horseshoe crabs
6 directly?

7 A. I have not.

8 Q. And have you ever, yourself, run any
9 experiments in which you have compared an endo --
10 zymogen proteins, horseshoe zymogen proteins, with
11 recombinantly produced horseshoe crab proteins?

12 A. Not horseshoe crab. I have been involved
13 in many comparability and assay replacement studies but
14 not -- and I have evaluated data for those in many
15 cases. But I have not done this for the horseshoe crab,
16 hands-on.

17 Q. So you don't, yourself, have experience
18 with, for example, selecting the conditions of such a
19 comparison, i.e., temperature, concentration, et cetera?

20 A. No.

21 Q. Have you ever, yourself, used an endotoxin
22 detection assay?

23 A. Yes.

24 Q. In what context?

25 A. In the context of my work at HGS, I have

1 reviewed many data sets of endotoxin assays as part of
 2 my work at USP, because I oversaw the laboratory at USP
 3 that generated data. And so I have reviewed laboratory
 4 data for those assays, and also as part of the WHO
 5 studies that we already discussed.

6 Q. Have you ever, yourself, generated an
 7 endotoxin detection assay?

8 A. No.

9 Q. So if you turn to the first page of your
 10 declaration at paragraph 3 --

11 A. 3?

12 Q. Paragraph 3, yes.

13 You indicate that you have not been asked
 14 to comment on the priority date of Claim 21 of the '318
 15 patent; do you see that?

16 A. Yes, I do.

17 Q. Okay. And that's true?

18 A. Yes.

19 Q. So the scope of your opinion in this case
 20 is limited to whether unexpected results exist for the
 21 claimed invention as of April 30th, 2019; correct?

22 A. Correct.

23 Q. And when you say the claimed invention
 24 there, you're referring to Claim 21 of the '318 patent;
 25 yes?

1 A. Correct.

2 Q. Did you look at any other claims of the
3 '318 patent?

4 A. I've read the document.

5 Q. Did you form any opinions about unexpected
6 results with respect to any claim other than 21?

7 A. No, I did not.

8 Q. Would you turn to paragraph 41, please,
9 Doctor?

10 A. Yes.

11 Q. Okay. And I think here, you reiterate sort
12 of the scope, the limited scope of your opinion in this
13 case. But under that paragraph, you say, "I have not
14 been asked, nor do I offer an unexpected results opinion
15 based on a December 2013 priority date."

16 Do you see that?

17 A. Yes.

18 Q. Why would an opinion based on a
19 December 2013 priority date be any different than any of
20 the opinions that you offered here?

21 A. I honestly don't know, but I was asked to
22 render an opinion within the scope, and I rendered an
23 opinion within the scope.

24 Q. Okay. So you don't have an opinion as to
25 whether the analysis about unexpected results in 2013

1 would be the same or different from your conclusions
2 with respect to 2019?

3 A. I did not consider it.

4 Q. Do you know whether the data that you
5 looked at in forming the opinions in your declaration
6 would be relevant to an analysis of unexpected results
7 as of 2013?

8 MS. DOUKAS: Objection to form.

9 A. I think as a scientist, one always
10 considers the connectivity of data and progress and --
11 but beyond that, I also, as a scientist, and as a
12 standardization scientist, understand scope and what is
13 in scope, what is out of scope. So I -- I render an
14 opinion. I looked at the data I was asked to look at,
15 and I have an opinion.

16 BY MS. LOUGHRAN:

17 Q. But you agree that some of the data that
18 you looked at did not exist in 2013; right?

19 A. That is always the case. I would be
20 shocked if scientists did not continuously work on
21 improving assay systems, products, results. It's a --
22 science and scientific products are built on continual
23 progress. That is the case here as well.

24 Q. Right. I understand that. I'm just asking
25 the data that you looked at in forming your opinions in

1 this declaration that were generated at some point after
2 2013; right?

3 A. Understood. I -- as somebody knowledgeable
4 in this area and experienced in this space, you take
5 into consideration an entire body of information and
6 experience that always goes beyond the documents that
7 are the core scope of this conversation --

8 Q. That's fair.

9 A. -- including peer reviewed literature that
10 was published in that time frame, which is significant.

11 Q. But for a person with skill in the art in
12 2013, that person wouldn't have access to the data that
13 you considered in forming your opinions in this case;
14 right?

15 A. The advancement in recombinant protein
16 technology and analysis in a decade, or even within the
17 six years that you state is always -- is significant.
18 And so there is, of course, always progress in the
19 technology, in the assays, in all of it. So, of course,
20 you have more and better data six years down the road
21 from 2013.

22 And the way I think about it is what is the
23 particular state of the art at a given time. What is
24 sort of the -- and that's different every year. So, of
25 course, you always have more data and better data within

1 a year or two or three.

2 Q. Okay. So just so we're clear, you agree
3 that a person with skill in the art in 2013 would not
4 have access to the data that you considered in forming
5 your opinions in this case; right?

6 MS. DOUKAS: Objection, asked and answered.

7 A. If I may ask for clarification, what you're
8 specifically referring to.

9 BY MS. LOUGHRAN:

10 Q. Yes. So you -- in your declaration, you
11 point to, for example, data that was submitted in a 2021
12 declaration by Dr. Mizumura, and data that was submitted
13 during prosecution of the '318 patent that we sort of
14 referred to as Claim 19.

15 A. Uh-huh.

16 Q. The data that you looked at has -- is dated
17 at a date after 2013; correct?

18 A. Correct.

19 Q. Okay. So if I am a person with skill in
20 the art in 2013, I do not have access to that data; do
21 you agree with that?

22 A. Of course.

23 Q. All right. Were you asked to form an
24 opinion as to the ultimate question of the obviousness
25 of Claim 21?

1 A. I was not.

2 Q. Do you have an opinion?

3 A. I do not.

4 Q. Were you asked to form an opinion about the
5 novelty of Claim 21?

6 A. I was not.

7 Q. Did you consider or form an opinion about
8 whether Claim 21 has sufficient written description for
9 patentability?

10 A. I was not.

11 Q. Were you asked to consider or form an
12 opinion about whether Claim 21 has sufficient enabling
13 disclosure for patentability?

14 A. I was not.

15 Q. And with respect to these other legal
16 tests, do you have an opinion one way or the other?

17 A. I do not.

18 Q. Okay. Were you asked to form any opinion
19 about the applicability of prior art to Claim 21?

20 A. I was not.

21 Q. And you talk about unexpected results in
22 this declaration, which is one example of secondary
23 considerations of nonobviousness. Did you consider any
24 other examples of secondary considerations of
25 nonobviousness; for example, commercial success?

1 A. I did not.

2 Q. Do you believe Claim 21 to be obvious?

3 MS. DOUKAS: Objection, outside the scope.

4 A. I do not have an opinion on that.

5 BY MS. LOUGHRAN:

6 Q. In the course of putting together your
7 declaration, did counsel suggest any arguments that you
8 disagreed with?

9 A. No.

10 MS. DOUKAS: Objection, I'd just counsel
11 let's not reveal any attorney-client privilege.

12 BY MS. LOUGHRAN:

13 Q. Now, in this declaration, you refer to
14 Claim 21. Do you have an awareness of a proposed
15 amended substitute Claim 22?

16 A. I do not.

17 Q. Do you have an awareness that counsel for
18 Morgan Lewis cited your declaration here in support of
19 that proposed amended Claim 22?

20 A. I have not.

21 Q. Did you authorize the opinions in this
22 declaration to be used with respect to Claim 22?

23 A. I'm not aware.

24 Q. Do you have any understanding of what
25 proposed substitute Claim 22 is?

1 A. I do not.

2 MS. LOUGHRAN: We've been going about an
3 hour, so this is a good time for our first break. Let's
4 go off the record and come back by, my time, 11:15.
5 Does that work?

6 THE WITNESS: Sure.

7 MS. LOUGHRAN: Excellent. Thanks very
8 much.

9 (A break was taken.)

10 BY MS. LOUGHRAN:

11 Q. Hello again, Dr. Morris. How are you?

12 A. I'm fine.

13 Q. Did you -- during the break, did you
14 discuss the substance of your testimony with counsel?

15 A. I did not.

16 Q. Just to circle back briefly, I asked you
17 earlier if you had done any experiments in the course of
18 your engagement for patent owner in this case. I
19 believe you said no; is that correct?

20 A. Correct.

21 Q. Did you generate any data yourself, whether
22 from other data sets or from experiments in the course
23 of your engagement with patent --

24 A. I did not.

25 Q. All right. If you could turn to page 6 and

1 7 of your declaration, please, now, there's a section
2 here entitled "Person of Ordinary Skill in the Art"; do
3 you see that?

4 A. Yes, I do.

5 Q. And you say that you understand that
6 Dr. Jain has proposed the following definition of a
7 POSA, which you then lay out at the top of page 7; do
8 you see that?

9 A. Yes, I do.

10 Q. And then you say you understand from
11 counsel that patent owner proposes the following
12 definition of a POSA, which you lay out in the middle of
13 page 7; do you see that?

14 A. I see that.

15 Q. And then you conclude, "I would have been a
16 POSA under either party's proposed definition as of
17 December of 2013"; do you see that?

18 A. I do.

19 Q. Okay. Now, the patent owner's definition
20 under paragraph 20 is that "POSA has a Ph.D. in
21 molecular biology, biochemistry or enzymology"; do you
22 see that?

23 A. I see that.

24 Q. Now, just specifically with respect to the
25 language, your Ph.D. is in molecular virology, which is

1 not listed there; right?

2 A. Uh-huh.

3 Q. Is that a yes?

4 A. It is.

5 Q. And so your -- you say you would have been
6 a POSA. It is because you're interpreting one of these
7 fields to include the experience that you have; is that
8 fair?

9 A. I would like to say that if -- and if you
10 look at my publication record, the work, even though the
11 degree is inferred in molecular virology, my Ph.D.
12 studies included every single one of these fields.

13 And the subject matter of my degree, in
14 fact, is in an enzyme. And so the -- biochemistry and
15 enzymology are an integral part of the degree, even
16 though the degree, because it is on a virus and it's
17 virology -- is virology, it includes the expertise in
18 these disciplines, which you are welcome to verify with
19 my graduate school.

20 Q. Okay. So when you say you would have been
21 a POSA under patent owner's definition, it's not because
22 you have the specific degree or words matching the
23 degrees listed, but because of your experience, your
24 publications and the Ph.D. work that you did; is that
25 fair?

1 A. Correct, yes.

2 Q. And so you agree that somebody who doesn't
3 specifically have a Ph.D. in molecular biology,
4 biochemistry or enzymology, as those words are written
5 on the page, could still be a POSA depending on their
6 experience; right?

7 A. If their documented and published
8 experience supports that.

9 Q. Now, organic chemistry is not a degree
10 that's listed here as a Ph.D. that matches patent
11 owner's definition; correct?

12 A. Correct.

13 Q. And organic chemistry is not one that's
14 listed under Dr. Jain's proposal, either; right?

15 A. Right.

16 Q. So could an organic chemistry -- sorry -- a
17 person with a Ph.D. in organic chemistry be a POSA under
18 either of these definitions?

19 MS. DOUKAS: Objection to form.

20 BY MS. LOUGHRAN:

21 Q. You can answer, please.

22 A. Organic chemistry is a wide field, and
23 only -- that would only be applicable if that person --
24 if they have a degree in organic chemistry, their
25 scientific expertise is in large molecules and enzyme

1 reactions, because that is applicable here.

2 Q. So, again, it wouldn't matter if that
3 person's Ph.D. was, in name, organic chemistry; it would
4 matter what their actual experience is; right?

5 MS. DOUKAS: Objection to form.

6 A. The documented, published experience in the
7 relevant scientific subject matter is important.

8 BY MS. LOUGHRAN:

9 Q. And I think that you testified earlier that
10 you did some coursework in biochemistry, which was
11 outside the specific department of molecular biology
12 where you got your Ph.D.; correct?

13 A. Correct.

14 Q. And that experience was also relevant to
15 your analysis about why you're a POSA under either of
16 these definitions; correct?

17 A. It is.

18 Q. If you turn to page 8 of your declaration,
19 please, Doctor, and there's a heading there that says
20 "Obviousness"; do you see that?

21 A. Uh-huh.

22 Q. So in paragraphs 24 through 26, you discuss
23 your understanding of the legal tests associated with
24 obviousness; right?

25 A. Right.

1 Q. And you said this was based on your
2 understanding from counsel, not your reading of
3 particular cases; correct?

4 A. Correct.

5 Q. So in paragraph 25, you say that, "I
6 understand that secondary considerations of
7 nonobviousness can include unexpected results"; do you
8 see that?

9 A. I do.

10 Q. And you do understand there are other types
11 of secondary considerations of nonobviousness; right?

12 A. Right.

13 Q. Why is your testimony limited to unexpected
14 results?

15 MS. DOUKAS: Objection to form, and I'd
16 just counsel you not to reveal any attorney-client
17 privilege.

18 A. I was specifically asked to render an
19 opinion on this particular area, and I did.

20 BY MS. LOUGHRAN:

21 Q. So you did not form any opinions about
22 other types of secondary considerations of
23 nonobviousness because counsel did not ask you
24 specifically to do that; right?

25 A. Correct.

1 Q. Do you have any such opinions, separate and
2 independent from what counsel told you to do?

3 MS. DOUKAS: Objection.

4 A. That is immaterial.

5 BY MS. LOUGHRAN:

6 Q. Well, I'm just asking if you have any of
7 those opinions.

8 MS. DOUKAS: Objection, outside the scope.

9 A. I do not.

10 BY MS. LOUGHRAN:

11 Q. Now, earlier, you used the word "scope."
12 And in these paragraphs, for example, paragraph 25, the
13 second sentence, you say, "I understand that this
14 analysis includes looking at whether the claimed subject
15 matter exhibits superior properties or advantages that a
16 person with skill in the art would have found surprising
17 or unexpected, and that any such unexpected results must
18 be superior relative to the POSA's prior art"; do you
19 see that?

20 A. I see that.

21 Q. When you use the phrase "the claimed
22 subject matter" there, what are you referring to?

23 A. Claim 21.

24 Q. And that means the full scope of Claim 21;
25 correct?

1 A. This particular matter of the unexpected
2 results; that's really what my analysis focused on.

3 Q. Right. But is your analysis about whether
4 there are unexpected results with respect to the full
5 scope of Claim 21?

6 A. I really focused on this particular
7 scientific question and the information relevant to that
8 question, not any other issues.

9 Q. Okay. I'm not asking about any other
10 issues. What I'm asking is: Did you -- is your
11 analysis of unexpected results, is it with respect to
12 the full scope of Claim 21, or something narrower than
13 the full scope of Claim 21?

14 A. I don't think I understand your question.

15 Q. Okay. Let me -- let me ask you a different
16 question. Are you aware of, you know, the principle
17 that unexpected results, in order to be indicative of
18 nonobviousness, have to be commensurate with the full
19 scope of the claim that you're analyzing?

20 A. That, I understand.

21 Q. Okay. So with that understanding, was your
22 analysis in this declaration with respect to the full
23 scope of Claim 21?

24 A. In that context, yes.

25 Q. And in paragraph 26, you say, "I further

1 understand that to be considered, secondary

2 considerations of nonobviousness must have a nexus to

3 the claimed invention"; do you see that?

4 A. I see that.

5 Q. What is your understanding of what is meant

6 by a nexus to the claimed invention?

7 A. Can you clarify your question, please?

8 Q. Yep. You say in your declaration, "I

9 further understand that to be considered, secondary

10 considerations of nonobviousness must have a nexus to

11 the claimed invention."

12 You wrote or signed off on that statement;

13 right?

14 A. Yeah. A nexus is a connection.

15 Q. Okay. And so with respect to the data that

16 you considered, the evidence of unexpected results that

17 you considered in this declaration, what is the nexus

18 that you contend exists between that data and the

19 claimed invention?

20 A. The nexus, put most simply, is really

21 the -- how do I put this -- really, the scientific

22 context of the invention; so the -- the body of data and

23 the described scientific parts of the assay components

24 and the assay performance.

25 Q. And how does that body of data have a nexus

1 to Claim 21?

2 A. Scientifically speaking, one takes into
3 consideration -- when you look at a piece of data, as is
4 the case here, you view and review that data in the
5 context of what the invention does and the -- the
6 data -- the body of scientific data that's connected
7 with it. So how does it relate to that and what is it
8 built on. So I'm not sure how to describe that better.
9 I apologize.

10 Q. Okay. Maybe we'll try it a different way.
11 So some of the data that you point to in your
12 declaration is data about Factor C proteins expressed in
13 CHO cells; is that fair?

14 A. Yes.

15 Q. Now you understand that expression of
16 Factor C in CHO cells is not part of the claimed
17 invention of Claim 21; right?

18 A. I understand that, yes.

19 Q. Okay. So what is your contention as to why
20 that data has a nexus to Claim 21?

21 A. Because I look at -- my expertise, as you
22 know from my background, is in the endotoxin assay and
23 assay performance. And when I review data from -- and
24 some of the data that is in -- that we'll be talking
25 about, all has to do with the performance of the assay

1 based on where those reagents -- how those proteins were
2 generated.

3 So of course I am aware and I looked at
4 data from Factor C expressed in the different expression
5 systems. And you evaluate and study and form an
6 opinion, not just in this particular set of data based
7 on the experience and everything that has gone into the
8 development of this particular data set.

9 If you ask any scientist to evaluate a
10 single piece of data, as in this particular -- or a
11 particular scope of data, the scientist will evaluate,
12 based on the available data, but also based on a
13 scientific opinion or expectation that's formed by data
14 that you have reviewed and that's in the context of this
15 particular data set.

16 Q. Okay. But that did not answer my question.
17 So I just want to focus you back on the question, which
18 is I think we agreed that you looked at some data here
19 on expression of proteins in CHO cells, which are not
20 part of the claimed invention. They're not within the
21 scope of the claimed invention.

22 But my question is: How -- in your
23 opinion, how is that data, how does it have a nexus,
24 which is the word you use in your declaration, to Claim
25 21?

1 A. Do you want to talk about a specific data
2 set that we are looking at? You are asking me
3 specifically about CHO cells. So can you point me to a
4 particular figure or to better --

5 Q. We'll get there. I just wanted to probe
6 your understanding of nexus. But we'll get there and
7 I'll follow up on that. Let me ask a different
8 question.

9 Do you agree that the production of
10 horseshoe crab Factor C in CHO cells was already
11 disclosed in the prior art, as of 2019?

12 A. I agree, yes. Data that I have reviewed
13 and that I am aware of shows comparisons of recombinant
14 proteins that are expressed in different systems, not
15 just CHO, but others as well.

16 Q. Okay. So you agree that the production of
17 Limulus Factor C in CHO expression systems, CHO cells,
18 was already disclosed in the prior art by 2019?

19 A. Yes.

20 Q. And you agree that the expression of
21 zymogen proteins, Factor C, for example, was already
22 disclosed in HEK cells in the prior art by 2019; right?

23 MS. DOUKAS: Objection, outside the scope.

24 A. Yes.

25 BY MS. LOUGHRAN:

1 Q. By 2019, scientists had already
2 demonstrated expression of horseshoe crab Factor C in
3 mammalian cells; right?

4 A. Yes.

5 Q. If you turn to the next section, which is
6 pages 9 and 10 of your declaration, it's an overview of
7 the '318 patent. Are you there?

8 A. Specific page, please?

9 Q. So I want to actually look at Claim 21,
10 which is paragraph -- which is page 9210.

11 A. Uh-huh.

12 Q. You reviewed this claim in the course of
13 putting together your declaration; right?

14 A. Right.

15 Q. Okay. Now, do you agree that each of the
16 residual activity features are optional? And I'll
17 strike that. Let me ask it more clearly.

18 You agree that a particular claimed Factor
19 C could meet its claim if it meets either residual
20 activity test number 1 or residual activity test number
21 2; right?

22 A. Correct.

23 Q. So the scope of Claim 21 is broad enough to
24 encompass recombinant Factor C proteins that meet either
25 number 1 or number 2; correct?

1 A. Correct.

2 Q. And in order to be within the scope of this
3 Claim 21, the recombinant Factor C protein has to be
4 from the *Limulus polyphemus* horseshoe crab; right?

5 A. Correct.

6 Q. And it also has to be produced through
7 recombinant expression with a HEK 293 cell; right?

8 A. Correct.

9 Q. Now, in paragraphs 31 and 32, you talk
10 about the concept of -- and I guess paragraph 33, you
11 talk about the suppression of the endotoxin detection
12 reaction in the presence of ions.

13 Do you have an understanding of that
14 phenomenon, Doctor?

15 A. Yes.

16 Q. In your opinion, why does that suppression
17 occur?

18 MS. DOUKAS: Objection, outside the scope.

19 A. Generally speaking, there are multiple ways
20 that salt ions and other charged molecules in a test
21 solution can suppress the -- or mask the detection of
22 endotoxin. There are multiple mechanism -- ways this
23 can happen, in which that can happen that have been
24 published. So there's not a single way of this
25 happening.

1 The molecules we are talking about are
2 large molecules that have large charge-attracting
3 surfaces. Bacterial endotoxins are known to be actively
4 binding molecules themselves. So we are talking about
5 an assay environment where large molecules are
6 interacting with each other in an environment where a
7 lot of salt ions are available.

8 And in many different ways, those can
9 create what is called suppression, masking effects. And
10 that's what we are talking about here.

11 BY MS. LOUGHRAN:

12 Q. Thank you for that answer. You read the
13 '318 patent; correct?

14 A. Correct.

15 Q. And did you understand from the '318 patent
16 that the inventors had hypothesized that one of the
17 reasons had to do with the sialylation, the
18 post-expression terminal sialic acid that gets added in
19 the expression of mammalian cells; do you understand
20 that?

21 MS. DOUKAS: Objection to form.

22 A. I understand that.

23 BY MS. LOUGHRAN:

24 Q. And did you understand that at some point
25 in the prosecution of this patent, the inventors

1 abandoned that theory?

2 A. I understand that, yes.

3 Q. Do you agree with the conclusion that that
4 is not one of the reasons for ion inhibition of
5 endotoxin detection?

6 MS. DOUKAS: Objection, outside the scope.

7 A. In my scientific opinion, the interference
8 and interaction that occurs in such assays is
9 multifactorial and very difficult to attribute to a
10 single -- to a single origin.

11 The hypothesis of sialylation is one that
12 is scientifically understandable because sialic acid --
13 terminal sialic acids are charge carriers.

14 And terminal sialic acids have been, as
15 published in the peer reviewed literature, established
16 as key functional -- functionally important components
17 of a glycoprotein. But glycoprotein structure and
18 function and its interaction with other molecules in an
19 environment is much more complicated than that.

20 BY MS. LOUGHRAN:

21 Q. Okay. So is it fair to say that this ion
22 inhibition phenomenon is -- has potentially many causes
23 and is -- could not just be attributed to
24 posttranslation sialic acid addition?

25 MS. DOUKAS: Objection, outside the scope,

1 form.

2 A. Yes, it is multifactorial. And the
3 carbohydrate structure or terminal -- the carbohydrate
4 or glycosylation structure or function or relationship
5 is often much more complicated than the terminal sialic
6 acids.

7 BY MS. LOUGHRAN:

8 Q. And I believe you referenced a charge as a
9 potential factor in the multifactorial -- I think you
10 used the words "multifactorial explanation"; is that
11 correct?

12 A. That's correct.

13 Q. So proteins, Factor C proteins with
14 different charges may have different reactions to ions
15 because of their charge; is that fair?

16 A. It's incomplete. I would not -- the Factor
17 C proteins are large proteins, large glycoproteins. And
18 they're -- the structure function relationship in large
19 proteins like that is very complicated and is not easily
20 attributable to a single factor. So I would hesitate to
21 make that statement.

22 Q. Would you agree that charge could have an
23 impact on the ion inhibition of these large Factor C
24 proteins?

25 A. Yes, it could.

1 Q. Okay. Now, if we look at Claim 21, it uses
2 the phrase "residual activity." And in paragraph 34 of
3 your declaration, you also talk about the concept of
4 susceptibility to reaction inhibition and the term
5 "residual activity"; do you see that?

6 A. I do.

7 Q. Is residual activity -- was residual
8 activity a known concept, as such, prior to the
9 inventor's use and definition of it in this patent?

10 A. The concept of residual activity, and
11 several synonyms of it, has been discussed actively for
12 quite some time. And I hesitate to put a time frame
13 around it, but it is -- it's been known and discussed
14 for some time.

15 Q. But like do you have an awareness of
16 publications before 2013 that used residual activity in
17 the art as the inventors define it in this patent?

18 A. I can't ascertain the use of the term and
19 specific timing. But the concept -- anybody who was
20 scientifically concerned with endotoxin assay
21 performance has worried about -- scientifically, about
22 what the performance and the activity of any endotoxin
23 testing reagent is under any given conditions, under the
24 most adverse imaginable conditions in a biological
25 testing environment.

1 And I would say that over time, the
2 concept, as more data was collected and also published,
3 the concept of residual activity was formed.

4 Q. I'm just trying to understand if, before
5 2013, before this patent came about, whether the term
6 residual activity and the calculation that's provided in
7 this patent were things that were in the field, or
8 whether the inventors sort of articulated this newly in
9 their patent?

10 A. In my scientific opinion, and I think
11 generally, when you talk about what was discussed in the
12 field, everything was driven or is driven by the assay
13 performance and the performance criteria that --
14 established by the compendial tests. So --

15 And the compendial tests, the
16 specifications, the limits, the numbers, the maximum
17 derived solutions drive how the assay has to perform.
18 And so, to me, the concept of residual activity is
19 anchored in the compendial requirement and how well an
20 assay and all its associated reagents have to perform.

21 And that discussion has been going on, in
22 one shape or form or another, since the introduction of
23 recombinant alternatives. Because the benchmark is to
24 compend the performance equivalent or better to the
25 compendial test, the harmonized compendial tests.

1 That's the benchmark here.

2 And any studies, any experimentation, any
3 alternative reagent has to perform equivalent or better
4 to the compendial requirements under test article and
5 reference material circumstances that occur in a
6 pharmaceutical testing requirement -- or testing
7 environment. That's how this is framed for me
8 scientifically.

9 Q. Okay. So, then, is it fair to say the
10 concept of residual activity, even if maybe not used in
11 those specific words, the concept that this definition
12 captures was well known in the field prior to 2013?

13 A. Yes. And -- yes. In different -- in
14 different scientific iterations, I would say, yes.

15 Q. And a POSA, person of skill in the art, as
16 of 2013 would have been aware of this concept before,
17 you know, this patent was filed, the concept of residual
18 activity; right?

19 A. Yes.

20 Q. Okay. Did you personally study the concept
21 of ion inhibition on residual activity as part of your
22 scientific work prior to 2013?

23 A. Are you asking about experimental work or
24 are you asking about data review and analysis?

25 Q. Let's start with experimental work.

1 A. Experimental work, no.

2 Q. How about data review and analysis?

3 A. Yes.

4 Q. Are you aware of anyone defining this
5 concept using this specific definition, you know, a
6 relative reactivity observed for a measurement specimen
7 prepared by adding endotoxin to an ion-containing test
8 specimen with respect to the reactivity observed for
9 another measurement specimen by adding endotoxin to
10 injection water, had anybody defined it that way prior
11 to 2013, in your review of the data?

12 A. I'm not sure about the term. But the
13 concept and the -- the comparison and the numbers are,
14 again, based in the compendial tests. So when you
15 establish the validity of your assay as part of the
16 compendial test procedure, the negative control is
17 always endotoxin free or water for injection. And
18 you're looking for a particular number that falls within
19 the assay validity of the compendial test. So I can't
20 tell you about the specific term.

21 But the concept and getting valid data
22 within the compendial testing requirement is -- those
23 requirements have been the same for a very long time.
24 So the entire idea of having reagents that perform
25 within the same criteria that are universally met within

1 a compendial test requirement is what anchors this
2 definition.

3 So I can't honestly tell you when the term
4 started to be used. But I think everybody who was
5 involved in the scientific discussions around endotoxin
6 has accepted this concept for a long time. That's the
7 goalpost, so to speak. You want to -- that's where you
8 need to be with your assay.

9 Q. But just to be clear, you don't -- you
10 can't say one way or another whether this particular
11 definition had been articulated prior to 2013?

12 A. No. But I would not be -- yeah. No, I
13 can't.

14 Q. Okay. And just in terms of this
15 calculation, as I read it a minute ago, it's here at
16 paragraph 34. Does the math here, the calculation,
17 allow for residual activity values above 100 percent?

18 A. So the endotoxin test in this type of assay
19 is what is called a relative test, which means a test
20 article is compared to an -- a reference material of a
21 known concentration. In this particular case, that
22 should be an official standard or a material that's
23 calibrated to an official standard.

24 And in -- you would call this a relative
25 potency assay. And the range of results that you obtain

1 in that particular assay, and the quality of the data,
2 because it's called a like versus like test, so you get
3 percentage values, is dependent on the -- your test
4 article and your reference standard.

5 And so all of -- all relative assays have a
6 range. And within that range, yes, you can be -- you
7 can be above 100 percent. It depends on --

8 Q. And that would be -- go ahead. Sorry.

9 A. No. Go ahead. Ask your question.

10 Q. Well, I just wanted to say that would be a
11 scenario in which the test specimen actually is --
12 instead of being sort of inhibited, relative to the
13 control, actually does better than the control; correct?

14 A. Correct.

15 Q. And so that would, in theory, allow -- I
16 don't want to say infinite, but you could have scenarios
17 where the test specimen does much better than water and
18 you can get to values well above 100; correct?

19 A. No, it should not. Because for -- you
20 should have assay validity criteria that determine the
21 range of valid results. And so as your compendial tests
22 explain, you have -- you have -- each assay has criteria
23 that determine the valid -- the validity of your
24 results. So you cannot have infinite numbers if your --
25 if your assay has a given range. And all properly

1 validated assays do.

2 And, typically, you have -- and you see in
3 the data, you have error bars associated -- that give
4 some significance to the quality of, you know, what the
5 range is expected. But you have assay validity data --
6 criteria that limit, you know, what you should consider
7 a valid result in an assay.

8 Q. Okay. So 100 percent is not a ceiling;
9 correct?

10 A. No. The ceiling --

11 Q. And then it's -- go ahead.

12 A. The assay validity criteria and the range
13 that you establish for valid test results is --
14 establishes what falls within an appropriate result
15 range.

16 Q. So the ceiling would depend on the validity
17 criteria, the assay validity criteria for your
18 particular test?

19 A. Correct.

20 Q. In paragraph 33, you make a statement that,
21 "because pharmaceutical injections frequently contain a
22 variety of salt ions, the suppression of the cascade
23 reaction in the presence of ions as seen when expressing
24 Factor C, Factor B and pro-clotting enzyme cells as the
25 host cells is not desirable"; do you see that?

1 A. Uh-huh.

2 Q. Okay. And then you say, "The '318 patent
3 explains the problem to be solved by the invention is to
4 ensure that the cascade reaction, including Factor C, is
5 not susceptible to reaction inhibition in the presence
6 of these salt ions"; do you see that?

7 A. I do.

8 Q. And how did the inventors, their invention
9 solve -- or solve this problem that you refer to there?

10 A. By using a recombinant factor that is
11 not -- from a different expression system.

12 Q. You agree, however, that the inventors
13 expressed Factor B and pro-clotting enzyme in insects
14 providing their data; right?

15 A. Yes.

16 Q. So it's not that the expression of Factor B
17 in pro-clotting enzymes in insect cells is not
18 desirable; correct?

19 A. Correct.

20 Q. It's that, per the inventors, it's the
21 expression of Factor C in insect cells that's not
22 desirable; correct?

23 A. Correct.

24 Q. In fact, the inventors don't discuss the
25 production of Factor B and pro-clotting enzyme in any

1 expression system other than insect cells; right?

2 A. Right.

3 Q. Now, you have a figure on page 11, I think
4 it's Figure 1 from the patent. You agree, Doctor, that
5 activity of Factor C, which is a term that the claim
6 uses, it says, "A horseshoe crab Factor C protein having
7 activity of Factor C," you agree that that activity of
8 Factor C depends on this cascade shown in Figure 1,
9 including Factors B and pro-clotting enzyme; right?

10 A. It does not depend. The Factor C is the
11 first protein in a cascade reaction. So it's more that
12 Factor B activation depends on Factor C.

13 So if you look at Figure 1, the endotoxin
14 interacts with Factor C, and that activates the factor.
15 And the activated Factor C activates Factor B. And then
16 the activated Factor B activates the preclotting enzyme
17 to become clotting enzyme, which then triggers the color
18 reaction that we measure.

19 Q. I understand that. But my question is:
20 The way that the inventors use the phrase "activity of
21 Factor C" is in order to know that Factor C has the
22 activity of Factor C, the Factor C has to be mixed with
23 or put in an assay with Factors B and pro-clotting
24 enzyme to get some results; right?

25 A. You have to create -- every recombinant

1 assay constitution that involves a cascade requires you
2 to put the recombinant component in with the appropriate
3 reagent -- other reagents to work. So yes.

4 So you are reconstituting or you're
5 recreating a known -- a cascade that's -- that's known
6 to occur in the natural environment with the recombinant
7 reagent present.

8 Q. Okay. And so actually, if you could grab
9 the '318 patent out of the box, it should be, actually,
10 in tab 2, it would be helpful.

11 And in front of you, you have what's been
12 marked as Charles River Labs Exhibit 1001. Do you see
13 that on the page, it's the '318 patent?

14 A. Yes.

15 (Charles River Labs Exhibit 1001 was
16 presented to the witness.)

17 BY MS. LOUGHRAN:

18 Q. Okay. And if you look at -- right. If you
19 look at column 15 of the patent --

20 A. Yes.

21 Q. -- and you go down that column to
22 approximately line 35, and it says, "The activity of
23 Factor C refers to such an activity that the Factor C is
24 activated in the presence of endotoxin to convert Factor
25 B into activated Factor B"; do you see that?

1 A. Yes.

2 Q. And then it says, "Whether the Factor C of
3 the present invention has activity of Factor C can be
4 confirmed, for example, by combining the Factor C of the
5 present invention with a suitable Factor B and a
6 suitable pro-clotting enzyme in the presence of
7 endotoxin and detecting the progress of the cascade
8 reaction"; do you see that?

9 A. I do.

10 Q. Okay. So as far as the inventors use that
11 term, "activity of Factor C," you need to combine Factor
12 C with Factors B and pro-clotting enzyme to measure the
13 progress of that reaction; do you agree?

14 A. I agree.

15 Q. Okay. And so we're going to look at the
16 data that you cite in your declaration. It's data about
17 the residual activity of Factor C. But in those
18 experiments, they all involve the expression of Factors
19 B and pro-clotting enzyme, and then combining them with
20 Factor C as well; right?

21 A. Uh-huh, yes.

22 Q. Okay. Great. All right. You can turn to
23 paragraph 13 of your declaration. So going back to the
24 declaration, you summarize some of the prosecution
25 history of the '318 patent; right?

1 A. Which paragraph, please?

2 Q. So it starts on paragraph 37.

3 A. Oh, 37. Okay.

4 Q. And you said you reviewed the prosecution
5 history, or most of it; right?

6 A. Yes.

7 Q. You say, "During prosecution of the '318
8 patent, Claim 21 was added as a new point on
9 August 24th, 2021 as part of patent owner's amendments
10 and arguments"; do you see that?

11 A. I do.

12 Q. Do you know what date the inventors of
13 Claim 21 allege they invented the subject matter of that
14 claim?

15 A. It's dated here August 24th, 2021.

16 Q. And then you say, "As part of the
17 submission, patent owner included an affidavit from one
18 of the inventors"; do you see that?

19 A. I do.

20 Q. Do you have an understanding that the --
21 one of the inventors, Dr. Mizumura, submitted multiple
22 declarations during the prosecution history of the '318
23 patent?

24 A. I am aware.

25 Q. Okay. In your declaration, you cite one of

1 those declarations. Did you happen to review the other
2 two?

3 A. I did not.

4 Q. Did you review any of the file histories,
5 prosecution histories of any related patents, other than
6 the '318 patent?

7 A. I did not.

8 MS. LOUGHRAN: All right. We've been going
9 about another hour, so this would be a good time to take
10 a quick break. So let's come back on the record at
11 about, I guess, your time, 11:21, 22-ish.

12 (A break was taken.)

13 BY MS. LOUGHRAN:

14 Q. All right. Hello again, Dr. Morris.

15 A. Hello.

16 Q. During the -- hello.

17 Did you speak with your counsel about the
18 testimony that you gave during the break?

19 A. I did not.

20 Q. Okay. At paragraph 42 of your declaration,
21 if you could just take a look at that.

22 A. Uh-huh.

23 Q. You say, "In this assumption and
24 understanding, I assessed whether unexpected results
25 exist as compared to the closest prior art in

1 April 2019." And then you say, "Based on Dr. Jain's
2 invalidity grounds 1 and 2, the closest prior art
3 reference identified is US Publication No. 2015-0307864
4 to Mizumura Exhibit 1009"; do you see that?

5 A. Uh-huh.

6 Q. How did you decide that Mizumura was the
7 closest prior art to Claim 21 in April of 2019?

8 A. Can you clarify or scope your question a
9 little bit more specifically?

10 Q. Well, sure. So you write, "I assessed
11 whether unexpected results exist as compared to the
12 closest prior art in April 2019."

13 A. Uh-huh.

14 Q. So I understand that to mean you looked at
15 some data and you assessed whether that data showed
16 unexpected results compared to the closest prior art as
17 to Claim 21, which is one of the legal standards that we
18 looked at earlier.

19 A. Yes.

20 Q. And then you picked this Mizumura
21 reference, the 864 publication, as the closest prior art
22 reference?

23 A. Yes.

24 Q. My question is just: Why did you pick that
25 reference?

1 A. Scientifically speaking, because the
2 scientific data here is cumulative. And the results
3 from Dr. Mizumura, as an inventor, obviously, to me,
4 scientifically, it is obvious to look at the closest
5 data that was previous -- that this is built on.

6 And I think we've talked about this
7 previously: The overall development here is to create
8 or to have an assay, an assay component that performs in
9 the best possible way without -- the best assay
10 performance. And so the closest art or the closest
11 science here is from the same -- in my mind, is from the
12 same inventor.

13 Q. Did you consider other prior art to Claim
14 21, aside from the Mizumura publication?

15 A. I did not.

16 Q. So you did not say, there's all this prior
17 art to the '318 patent as of 2019, but I think that this
18 Mizumura reference, in particular, is closer to Claim 21
19 than all the other prior art? You didn't do that
20 analysis?

21 A. I didn't.

22 MS. DOUKAS: Objection, form.

23 A. I did not. I looked at -- I approached
24 this question based on the scientific principle that
25 the -- of evolving the assay based on prior data, and

1 what was previously done in the same experimental and
2 scientific context.

3 Because, scientifically, you also have to
4 consider what you can really -- what is considered
5 comparable or what you can really -- what you can --
6 which data you can relate to what.

7 BY MS. LOUGHRAN:

8 Q. Okay. So you say you looked at prior data
9 and what was previously done in the same experimental
10 and scientific context. So other than this Mizumura
11 publication, what other prior art data did you look at?

12 A. I looked at the scientific literature
13 available, and I was aware of that prior to my
14 involvement here, having followed the field. And I
15 reviewed the Mizumura work in the context of my
16 experience with the assay and the existing body of
17 knowledge in the field.

18 Q. Okay. When you say "scientific
19 literature," do you have a specific like article or
20 publication in mind?

21 A. I don't.

22 Q. You didn't cite any other prior art
23 scientific literature in your declaration; right?

24 A. I did not. As a scientist and as a person
25 working in this space, you read a lot of articles every

1 day, so -- which adds to your general knowledge and
2 experience.

3 Q. Right. But none of them warranted actually
4 citing in your declaration?

5 A. Correct.

6 Q. Are you aware that the Mizumura
7 publication, the closest prior art reference that you
8 analyze in your declaration, is actually the same
9 content, the same substantive content as what is in that
10 '318 patent that's right next to you?

11 A. I did not consider it from that point of
12 view.

13 Q. But did you know that they were the same
14 disclosures?

15 A. I did not consider that.

16 Q. Okay. Now, in the -- well, if you turn to
17 paragraph 46 of your declaration, which is on page 17,
18 you reference the declaration of Dr. Mizumura that was
19 submitted during prosecution; right?

20 A. Uh-huh, correct.

21 Q. And you reviewed that declaration; right?

22 A. Yes.

23 Q. Okay. And in that declaration,
24 Dr. Mizumura also provides an opinion about unexpected
25 results; right?

1 A. Correct.

2 Q. And he compares his claim, Claim 21, to the
3 prior art; do you recall that?

4 A. I do.

5 Q. Okay. He compares it to different prior
6 art than you compared it to, though; do you recall that?

7 A. I do not at the moment.

8 Q. Okay. If you could, please, there should
9 be a binder in the box. And it's actually the
10 prosecution history of the '318 patent. If we could
11 turn to that, please.

12 Obviously, it's a big document, but I
13 should be able to point you to page numbers pretty
14 easily.

15 Do you have it?

16 A. I do.

17 (Exhibit 1004 was presented to the
18 witness.)

19 BY MS. LOUGHRAN:

20 Q. Okay. What I would like you to do is turn
21 to page 82 -- before you do that, do you see that this
22 document has been marked as Exhibit 1004 on the front?

23 A. I see that.

24 Q. Okay. This is the prosecution history of
25 the '318 patent, which you indicate in your declaration

1 that you reviewed; correct?

2 A. Correct.

3 Q. Okay. If you could turn to page 82, that
4 should be the first page of the Mizumura declaration
5 that you reviewed; correct?

6 A. That is correct.

7 Q. And that's the declaration that you
8 discussed in your declaration; correct?

9 A. Correct.

10 Q. Okay. If you look at the bottom of page
11 82, Dr. Mizumura says, "This declaration is submitted to
12 further explain and demonstrate that our invention
13 provides unexpected superior results over Day, et al.,
14 in view of current protocols in molecular biology, and
15 Thomas, et al."; do you see that?

16 A. Uh-huh, I do.

17 Q. And then it goes on to the next page, page
18 83, "and as evidenced by Mizumura, et al. 2012-118226";
19 do you see that?

20 A. I see that.

21 Q. And that Mizumura, et al., is different
22 than the one that you looked at in your declaration;
23 right?

24 A. It is.

25 Q. Okay. Did you -- so the inventor himself

1 compared his unexpected results to these other four
2 references. Did you review any of those references?

3 A. I may have looked at -- no, I cannot
4 recall.

5 Q. Okay. Do you know why your comparison was
6 to the Mizumura publication and not to any of these four
7 prior art references?

8 A. I can -- scientifically, it makes sense to
9 me, but I cannot -- that's what I would say.

10 Q. In what way does it make scientific sense?

11 A. Because of the context of the results. I
12 look at what type of scientific results make sense to be
13 compared with each other. And I looked at it strictly
14 in that context, which is very narrow.

15 Q. And when you say what type of scientific
16 results make sense to be compared with each other, what
17 makes -- what is something that makes sense? What are
18 you referring to as making sense there?

19 A. Simply speaking, it's what I call the
20 apples to apples versus an apples to orange comparison.
21 So when you compare scientific data from different
22 laboratories, companies, inventors versus scientific
23 data from a -- the same laboratory, the same test
24 system, et cetera, it makes -- it's a more
25 straightforward comparison. So that is always

1 scientifically your first go-to.

2 And in a situation where you are looking
3 at -- and I'm speaking scientifically, you -- my
4 first -- the first comparison as a scientist as you look
5 at something, you look at your prior results. You look
6 at what have you done before in the same test system.
7 What have you -- what results have you gotten, and then
8 what is -- that is a direct comparison.

9 And the data that I have reviewed or the
10 history that I am aware of, the scientific -- I would
11 say the -- what you would call the scientific line that
12 goes through that data, that I would call the primary
13 line, is based on what the inventor has done.

14 If you draw comparisons to another data set
15 from another laboratory, another author, you have to
16 consider that data set in comparing -- like how was it
17 validated. Are you comparing the right things to each
18 other?

19 So the first conclusion you would always --
20 the first go-to would always be the prior -- the prior
21 data. And when you look at the figures that were chosen
22 in my declaration, scientifically, the comparison is
23 consistent in my view.

24 Q. Okay. So because you were looking at
25 unexpected results with respect to Claim 21, which is an

1 invention or a purported invention by Dr. Mizumura,
2 your -- your view of the closest prior art was impacted
3 by the fact that the Mizumura publication is by the same
4 person; right? Is that right?

5 A. Not just by the same person, but an
6 inventor, a scientist, anybody who applies a reasonable
7 scientific method builds their scientific progress on
8 prior results.

9 And an important consideration in this
10 overall, I would say scientific framework of what we're
11 talking about, is here -- is the experience with these
12 complicated molecules, the -- it's assuring that data
13 you compare -- I talk to you about validity criteria,
14 and making sure that conclusions you draw are based on
15 appropriate -- appropriate expectation -- scientific
16 expectations.

17 And those are most comfortably drawn when
18 you can assume that an inventor, a laboratory, a
19 scientist has built their next set of data with the same
20 scientific expectations, the same systems, the same
21 validation criteria. It's basically -- it's -- the data
22 is built on each other.

23 And from my understanding and reading of
24 the materials, as well as the peer reviewed
25 publications, the overall scientific picture here is

1 very systematic based on long experience with these
2 molecules and the assay system, and the performance
3 expectation that is the international compendial
4 requirement. So that is the scientific framework that I
5 applied to my analysis, understanding that that may be a
6 very narrow view.

7 Q. Okay. And so in this declaration in front
8 of you, which is from Dr. Mizumura himself, the
9 inventor, he cites to one of his own patent
10 publications, WO 2012-118226, as the prior art that he
11 compared his claim to for purposes of his unexpected
12 results analysis.

13 And so my question is: Did you consider
14 that publication in your analysis?

15 A. I may have looked at it. And I looked
16 at -- I am -- I have been aware and I have looked at a
17 lot of the work that was -- that was prior -- that
18 was -- that was published and was publicly available.
19 So it's part of the data that his lab generated. So I'm
20 certain I have looked at it at some point.

21 Q. Okay. But in your view, the Mizumura 864
22 publication, which you cite at paragraph 42, is the
23 closest prior art for purposes of assessing unexpected
24 results?

25 A. Yes.

1 Q. Closer than those publications that
2 Dr. Mizumura himself cited; right?

3 A. Yes.

4 Q. Okay. And that publication is, in fact,
5 identical to the '318 patent; right?

6 A. I did not look at it from that point of
7 view, to establish whether it's exactly the same. I
8 looked at -- I compared the data, and that is the limit
9 of my analysis.

10 Q. Okay. Since you have the '318 patent right
11 next to you, do you want to just pick it up, please?
12 It's right next to you. Yep. And you can just look at
13 Figure 7.

14 A. Could you point me to the page, please?

15 Q. Yes. It's page -- if you look at the top,
16 it should say "Sheet 5 of 10." It's one of the -- it's
17 probably the sixth or seventh page.

18 A. Yes.

19 Q. And you see Figure 7 there is, in fact, the
20 same Figure 7 that appears at paragraph 43 of your
21 declaration; right?

22 A. Yes.

23 Q. Okay. Now, Doctor, in paragraph 42, you
24 acknowledge that the Mizumura publication doesn't
25 disclose everything in Claim 21; right?

1 A. What language are you specifically
2 referring to in your question?

3 Q. So about halfway down that paragraph, you
4 say, "As described below, while Mizumura provides
5 residual activity data and various salt solution for
6 Tachypleus tridentatus Factor C, it does not provide
7 express residual activity data for the claim to Limulus
8 polyphemus Factor C"; do you see that?

9 A. I do.

10 Q. Okay. And so my question is: You agree
11 that the Mizumura publication did not disclose
12 everything in Claim 21; right?

13 A. That's correct.

14 Q. So I would like to ask you some questions
15 about the data that actually appears in Figure 7 of
16 Mizumura. So it's -- in that paragraph 43 of your
17 declaration is probably the best -- maybe the best place
18 to look.

19 Now, I think that your position is that
20 Figure 7 shows that recombinant Factor C has a greater
21 residual activity in CHO and HEK cells than the -- than
22 the native TAL, or as expressed in insect cells; right?

23 A. That's correct.

24 Q. Now, you recognize that the concentrations
25 of each of these samples, the concentrations of Factor C

1 in each sample are, in fact, different; right?

2 A. Are you referring to the dilution factors
3 that are given in -- in the column on the right?

4 Q. No. I'm referring to the concentrations of
5 each factor that were used for these experiments. And
6 it's not a memory test. So maybe we can just look at it
7 in Mizumura itself, if you want to grab the document
8 that's in tab 5. It's the 864 Mizumura publication.

9 And so you're looking at a document that
10 has been marked Charles River Labs Exhibit 1009?

11 A. Correct.

12 (Charles River Labs Exhibit 1009 was
13 presented to the witness.)

14 BY MS. LOUGHRAN:

15 Q. It's the Mizumura publication that you
16 allege to be the closest prior art; correct?

17 A. Uh-huh, correct.

18 Q. Okay. And if you'd turn to -- the page at
19 the top is 17. It's paragraph 305.

20 Okay. And it says, "In the above assay
21 system, the final concentration of each factor was as
22 follows." And then it lists out a bunch of
23 concentrations for each of the factors that were used in
24 those assays; do you see that?

25 A. Not yet.

1 Q. Okay. 305.

2 A. Oh, 305. Okay. Yes, I've read that.

3 Q. Okay. So you agree that the concentrations
4 of each factor were different for the factors used in
5 the assay that gave rise to Figure 7; right?

6 A. Yes.

7 Q. And the difference in concentration could
8 contribute, for example, to the difference in function
9 of those factors; right?

10 A. Not alone. It's not that simple.

11 Q. Okay. Well, let me maybe rephrase and
12 narrow my question.

13 Do you agree that the difference in
14 concentration could be a factor that would contribute to
15 the difference in function of each of those recombinant
16 factors?

17 A. Possibly. However, you see that there is
18 also language in there about the amount of the factor
19 being basically calibrated by activity. I explained to
20 you earlier that these are relative assays and relative
21 potency assays. It's also a -- as we discussed earlier,
22 a cascade reaction that you have going on in -- in that
23 mixture.

24 So you have your Factor C, you have your
25 Factor B, you have your pro-clotting enzyme, and you

1 have your substrates, and you have your -- your ions or
2 whatever is floating around in there. And to have
3 comparability in an assay like that in an assay system
4 is more complicated than just -- it doesn't work like
5 having the same concentration of everything in there.
6 That's a simple way of saying I wouldn't -- I wouldn't
7 draw that conclusion.

8 Q. Well, could you rule out that the
9 differences in concentrations would contribute to
10 differences in residual activity?

11 A. With the available information that I have,
12 I can't. So you would -- you would have to -- to make a
13 determination like that, you would have to have a lot
14 more -- you would have to have more information. But
15 with the information at hand, I cannot.

16 Q. Okay. You agree that the concentration of
17 Factor C, recombinant Factor C and HEK cells, is about
18 200 times that of native TAL?

19 A. I do not think I put a number like that on
20 it.

21 Q. Well, at paragraph 305, it says,
22 "Recombinant Factor C is 51.5 micrograms per mL. And
23 Factor C TAL is 0.25 micrograms per mL."

24 A. The system -- I refer you to paragraph 306,
25 where the inventor explains that the assay system was

1 based on -- was calibrated based on activity
2 equivalence. And with that in mind, the consideration
3 of actual protein amounts is secondary. The -- I
4 explained to you previously that we're talking about
5 relative assays and relative activity measurement.

6 And in the world of relative activity
7 measurement, to achieve comparability and driving the
8 results into the same range, to put it simply and
9 generally, requires that you calibrate your reagent
10 amounts accordingly so the actual amount of protein
11 is -- is not as important as it might seem.

12 Q. Okay. I appreciate that. But my question
13 was really just: Is it true that the amount of protein
14 for Factor C expressed in HEK is 200 times that for
15 native TAL?

16 A. It is.

17 Q. Okay.

18 A. If I calculated that correctly quickly.
19 But I wanted to put that into the context of that --
20 that I would put it into as I read -- as I understand
21 and interpret the assay. Because it's important --

22 Q. And so -- go ahead.

23 A. Because it's important to understand the
24 difference between relative activity determinations and
25 absolute protein amounts. And I would always caution to

1 not take the difference in amount of protein out of
2 context.

3 Q. Understood. But my understanding of this,
4 and I am not the expert, you are far more suited to
5 explain these things, is there's a lot more protein that
6 was recombinantly produced with HEK cells than the
7 native protein that was purified from the horseshoe crab
8 lysate itself, even though, as the inventors show you in
9 Figure 6, that that larger amount of protein still gives
10 you the same level of activity; am I understanding that
11 correctly?

12 A. I will reiterate that it's not that simple.
13 It's not -- you cannot draw that conclusion. I would
14 not draw that same conclusion with my understanding of
15 the assay system.

16 Q. Would you be able to -- do you have an
17 opinion as to why 51.5 micrograms per mL of
18 recombinantly produced Factor C and HEK gives
19 approximately the same amount of activity as
20 0.25 micrograms per mL of TAL?

21 A. There could be a variety of reasons for
22 that and -- there could be a variety of reasons.

23 Q. Could one be the lower specific activity of
24 the recombinantly produced protein?

25 A. It could be a number of different things.

1 Q. Okay. Is that one of them, though? Could
2 that be a possibility?

3 A. It could be.

4 Q. Okay. Could it also be that a lot of the
5 HEK-produced protein is just nonfunctional?

6 A. It could be a number of different things.

7 Q. Okay. Could it also just be impurities?

8 A. You have a -- it could be. You have a
9 complicated test system, as we discussed earlier. You
10 have multiple proteins in solution, you have different
11 salts that have charges that have complexing capability.
12 You have multiple reactions going on at the same time
13 that have different reaction kinetics.

14 The proteins, as Dr. Mizumura describes
15 himself, have undergone -- they undergo different types
16 of preparation as they go into the assay, which all
17 could have an impact. So speculating about which of
18 those factors has -- you know, I can't make any
19 speculations there. I can only render an opinion based
20 on what I read in this paragraph.

21 And I understand the intent -- the
22 scientific intent of calibrating the assay into the same
23 range by activity so you can get a valid assay. Because
24 like I said, it's a relative potency assay. And if you
25 review the compendia, these are relative activity tests

1 that are driven by the allowed dilutions of the test
2 articles.

3 Q. Okay. So it's fair to say, then, that
4 there could be many different things that are actually
5 driving the resulting function, not just, for example,
6 concentration?

7 A. That's always the case, especially for
8 proteins of that nature.

9 Q. Okay. Now, each of these -- each of these
10 samples that we see in Figure 7, Sf9 being the very dark
11 color, CHO being in white, HEK being in dark gray and
12 TAL being in light gray, these all represent Tachypleus
13 tridentatus-based results; right?

14 A. Yes.

15 Q. And the actual expressions in, for example,
16 Sf9, come about with different protocols than
17 expression, for example, with CHO; right?

18 A. What do you mean by protocol?

19 Q. Yeah. So for expression of Sf9, the
20 inventors used Sf9 0003 medium; right?

21 A. Yes.

22 Q. Which is different -- a different
23 supernatant than was used for CHO; right?

24 A. Of course.

25 Q. CHO, I think, was serum-free complete

1 media; right?

2 A. They're completely different cell lines so
3 they have completely different expression media.

4 Q. Okay. And the differences in the
5 expression media could also contribute to differences in
6 function; right?

7 A. Well, you have cell lines from completely
8 different species that have completely different media
9 requirements for protein expression that are well
10 described. Insect cells, HEK cells, and CHO cells have
11 very different cultivation requirements and protocols
12 that are well described for optimal protein expression.

13 So the media that is used for the
14 expression of the host cells making any assumptions
15 about those or inferring any differences from the
16 expression media I think is scientifically challenging,
17 because you expressed the protein and the protein
18 afterwards is purified and isolated. There are many
19 different steps.

20 But it's expected that different expression
21 cell lines use completely different media and
22 cultivation conditions.

23 Q. Okay. I'm not -- I'm not suggesting that
24 you would draw a conclusion from those differences. I'm
25 more asking because of those, you couldn't rule out that

1 those differences between the media used for expression
2 of those cell lines couldn't potentially have an impact
3 on the resulting function. You couldn't rule it out;
4 right?

5 A. You could not rule it out.

6 MS. DOUKAS: Objection, form.

7 BY MS. LOUGHRAN:

8 Q. And just to be clear, the -- I think you
9 used the words purified, but I think the only -- the
10 only protein that was purified is the native protein;
11 right?

12 A. Yes.

13 Q. CHO and HEK are not purified proteins;
14 right?

15 A. Yes.

16 Q. Okay. And just to confirm my
17 understanding, so we talked about the CHO cells being
18 expressed in serum-free complete media; right?

19 A. Uh-huh.

20 Q. Is that chemically defined?

21 A. Does it say which -- typically, these are
22 very well defined at this point.

23 Q. Yeah. Okay. You can look at paragraph 287
24 of Mizumura. It says, "CHO DG44 cell line highly
25 expressing Factor C with condition in the serum-free

1 complete medium."

2 A. Yeah. Then it's chemically defined.

3 Q. Does that still have components like amino
4 acids and buffers?

5 A. It is a -- yeah, it has quite -- it has
6 different components, of course, as the name complete
7 implies.

8 Q. And you can't rule out that those
9 components could have a role in salt inhibition; right?

10 MS. DOUKAS: Objection, form.

11 A. You would have to consider the dilution
12 factor within the assay; and if, you know, when you look
13 at the different salt concentrations that are applied in
14 the assay to evaluate the residual activity or overall
15 inhibition, the impact -- my general opinion would be
16 that the impact of the individual assay components, in
17 terms of contributing additional salts or other
18 impurities, is -- I would consider that minor in
19 comparison to the fairly high salt concentrations that
20 are being tested here to establish residual activity.

21 BY MS. LOUGHRAN:

22 Q. Okay. So the impact would be minor, but
23 you can't rule it out; right?

24 MS. DOUKAS: Objection to form.

25 A. I would consider it or assume it to be

1 minor. I would not rule it out.

2 BY MS. LOUGHRAN:

3 Q. And then a different supernatant was used
4 for expression with HEK cells as well; right?

5 A. Yes.

6 Q. Okay. And that was DMEM medium, statically
7 cultured in a DMEM medium. I'm looking at paragraph
8 290. Do you see that?

9 A. Yes.

10 Q. Which contains fetal bovine serum?

11 A. Yes, FBS.

12 Q. And that contains growth factors and other
13 proteins; right?

14 A. It does.

15 Q. And, again, while potentially minor, you
16 couldn't rule out that those additional proteins would
17 have an impact on salt inhibition; right?

18 MS. DOUKAS: Objection to form.

19 A. I would -- my educated estimate --
20 estimation would be that the impact is negligible, but
21 you can't rule it out.

22 BY MS. LOUGHRAN:

23 Q. Well, I just have a few more questions
24 before a lunch break.

25 A. That's okay.

1 Q. The vectors that were used for each of the
2 recombinant systems to generate the data in Figure 7
3 were also different; right?

4 A. Are you talking about the expression
5 vectors, i.e., and what was used to clone the sequence?

6 Q. Yes. So my understanding is that for --
7 for example, for HEK, the vector was PCA 7 and for CHO,
8 it was pCI-neo. Those are two different vectors for
9 expressions; right?

10 A. Yes.

11 Q. And could the difference in vectors also
12 have an impact on functionality of the resulting
13 proteins?

14 MS. DOUKAS: Objection to form.

15 A. I very much doubt that.

16 BY MS. LOUGHRAN:

17 Q. Okay. Well, do certain vectors drive
18 higher levels of expression?

19 MS. DOUKAS: Objection to form.

20 A. Protein expression in sophisticated
21 recombinant systems is, again, a multifactorial system.
22 And different cell lines require different expression
23 vectors. And the choice of expression vector is usually
24 driven by the cell line and by many other factors. I --
25 I would not want to attribute this to a single factor.

1 BY MS. LOUGHRAN:

2 Q. Understood. And, again, I think we're on
3 the same page, that this is a multifactorial question,
4 what is actually driving the function here. My question
5 to you is these were different vectors used to express
6 these proteins.

7 So it's true that you can't rule out that
8 that difference also had some impact on the resulting
9 function; right?

10 MS. DOUKAS: Objection to form.

11 A. You can't use certain vectors across
12 expression systems. You have to use different vectors.
13 So can you rule it out? No. But I -- scientifically,
14 yeah, I -- the choice of vector is driven by the
15 expression system you're working in, i.e., you can't use
16 a particular vector in insect -- for insect cells, yeast
17 cells, HEK cells. It just doesn't work.

18 BY MS. LOUGHRAN:

19 Q. Right. I understand that a scientist
20 can't -- well, let me just ask it this way: A scientist
21 who is running this test can't control for the vector
22 used; right?

23 A. No. And he or she wouldn't want to,
24 because I think they would consider it -- I wouldn't say
25 immaterial, but as one of the very minor vectors, if at

1 all, that could impact the assay.

2 Q. Okay. And to get the results shown in
3 Figure 7 of Mizumura, I think we discussed this, but the
4 other factors in the cascade, those being Factor B and
5 pro-clotting enzyme, also had to be expressed and used
6 in this assay; right?

7 A. Yes.

8 Q. Okay. And Mizumura tells us that those
9 were expressed in Sf9 insect cells; right?

10 A. Yes.

11 Q. And that is just to confirm, that is at
12 paragraphs 293 through 295. Do you agree that's what is
13 discussed at paragraphs 293 to 295?

14 A. Yes.

15 Q. Do you know why or do you have a -- any
16 opinion as to why those factors were not also expressed
17 in mammalian cells?

18 MS. DOUKAS: Objection, form, outside the
19 scope.

20 A. So I have an informed opinion. Sf9 insect
21 cells are high protein expressors. They're known for
22 that. They've been used extensively. And they're a
23 very well established, reliable expression system. If
24 it works for your protein, you go ahead and do that. It
25 creates stable clones. Clonal selection is easy.

1 So if they got good protein out of Sf9,
2 they would have never looked any further. It's an
3 obvious choice.

4 BY MS. LOUGHRAN:

5 Q. And do Factor B and pro-clotting enzyme,
6 did not -- when expressed in Sf9 -- well, let me strike
7 that question.

8 Are you aware of anyone having expressed
9 Factors B and pro-clotting enzyme in any mammalian cells
10 by 2013?

11 MS. DOUKAS: Objection to form, outside the
12 scope.

13 A. I am not.

14 MS. LOUGHRAN: It looks like it's about
15 12:20 in Chicago. Can we take a lunch break? We'll
16 come back maybe around like 1:00 your time, if that's
17 enough time.

18 THE WITNESS: Yeah.

19 (A lunch break was taken.)

20 BY MS. LOUGHRAN:

21 Q. Hello again, Dr. Morris. How are you?

22 A. I'm fine. How are you?

23 Q. Good. Thanks.

24 Did you speak with counsel about the
25 substance of your testimony over the lunch break?

1 A. I did not.

2 Q. Okay. Great.

3 Just to wrap up a train of thought that I
4 had before the break, if you could look back at
5 paragraph 305 in the Mizumura publication, the document
6 you allege to be the closest prior art, it's the
7 paragraph with all the concentrations of the factors; do
8 you see that?

9 A. 305?

10 Q. Yes.

11 A. Yep.

12 Q. Okay. Mizumura states here, "The above
13 exemplified concentrations, except for the case of TAL,
14 were calculated on the assumption that all the protein
15 species present in the sample, i.e. filtrate, prepared
16 from an expression of factor of interest consisted of
17 the factor of interest"; do you see that?

18 A. I do.

19 Q. Okay. So the -- Dr. Mizumura, the inventor
20 of this publication, made that assumption; right?

21 A. Uh-huh, yes.

22 Q. As a scientist, you acknowledge, however,
23 that that assumption could be false; right?

24 MS. DOUKAS: Objection to form.

25 A. It could be. But my expectation is that

1 his -- the assumption is based on verifying tests and
2 knowledge from those tests, i.e., you would not go into
3 an activity assay like this with a filtrate that you
4 haven't previously shown in some other appropriate
5 manner to contain the reagent that you intended to
6 contain.

7 BY MS. LOUGHRAN:

8 Q. Okay. But I'm just going off of what the
9 inventors here are telling us.

10 A. Yes.

11 Q. And they are saying that they made this
12 assumption.

13 A. Yes.

14 Q. Is there anything -- I mean, other than
15 them indicating that they made that assumption, is there
16 any -- did you see anything or is there anything else
17 that indicates a verification of that assumption? Or is
18 it just an assumption?

19 MS. DOUKAS: Objection to form.

20 A. When you take the -- no. There are other
21 tests described in this very same document, you know,
22 SDS page, and other analytical results that precede or
23 complement the characterization of the protein. You
24 would use those -- you would use that data in its
25 totality to make that assumption.

1 So I am not reading paragraph 305 in
2 isolation; I am reading it in the context of the other
3 parts of this document; for example, in just the column
4 across, they're talking about the comparison of the
5 molecular weight of Factor C proteins.

6 When you express a protein in a recombinant
7 system and you follow all the steps involved with that
8 type of an exercise, a very typical and expected and
9 appropriate set of experiments that follows that is that
10 you characterize that expression product with a variety
11 of different analytical approaches that are also
12 included in here.

13 BY MS. LOUGHRAN:

14 Q. But when I read this, the inventors don't
15 say we verified or we confirmed or we made certain that
16 all protein species present in the sample consisted of
17 the factor of interest. They say we proceeded on the
18 assumption that that was true.

19 And all I'm asking is, if possible, that
20 that is not -- that that assumption is not 100 percent
21 true; right?

22 MS. DOUKAS: Objection to form.

23 A. Possible, but very highly unlikely.

24 BY MS. LOUGHRAN:

25 Q. But possible; correct? It is an

1 assumption?

2 MS. DOUKAS: Objection to form.

3 A. Based on the context of this document, it's
4 a very well grounded and supported assumption.

5 BY MS. LOUGHRAN:

6 Q. But, again, there is no data in this
7 document that says the assumption is factually true;
8 correct?

9 MS. DOUKAS: Objection to form.

10 A. If you look at Figure 2, which is right on
11 page 2 of the document, you will have some of the data
12 that the inventors used to characterize the expression
13 products. And you can see here that it's not just a
14 molecular weight, but it's an anti-Factor C monoclonal
15 antibody.

16 So from an identification point of view,
17 they are using a test that is typical and accepted to
18 verify that the material that you're working with is, in
19 fact, the material, even though they chose a different
20 word here.

21 BY MS. LOUGHRAN:

22 Q. Right. So, again, they don't point to
23 Figure 2 to say, we verify that all species present in
24 the sample consisted of the factor at interest. I mean,
25 I didn't write this. The inventors themselves made an

1 assumption; right?

2 MS. DOUKAS: Objection to form.

3 A. And I'm --

4 BY MS. LOUGHRAN:

5 Q. Sorry. I think you just nodded, so I need
6 an answer to that question.

7 A. I am telling you, as a scientist, that in
8 reading this document, and following what the inventors
9 are doing, they are following a typical path of what one
10 would do when they express a recombinant protein. They
11 do a typical set of characterization tests. And by the
12 time they get to activity, they have a very good
13 assessment of what is in their vial that they're putting
14 in the assay.

15 Q. And all I'm saying is, based on this
16 language, it is possible that that there are protein
17 species present in the sample that are not the factor at
18 issue; right?

19 MS. DOUKAS: Object to form, asked and
20 answered.

21 A. You can't exclude that there's -- if you're
22 referring to that there's other proteins in there. But
23 I would say that the context of the document establishes
24 very thoroughly that the inventors characterize the
25 material they expressed and that there's a high

1 likelihood that that's what's in the assay.

2 BY MS. LOUGHRAN:

3 Q. Okay. I just want you to confirm, you
4 can't exclude that there could be other proteins in
5 that --

6 A. That I can't exclude.

7 Q. -- assay.

8 Okay. Just to go back to Figure 2, all of
9 these molecular weights are actually different; right?

10 A. Yes.

11 Q. Okay. And do you have an understanding of
12 what the standard Factor C molecular weight is?

13 A. There is no standard Factor C molecular
14 weight.

15 Q. And why is that?

16 A. Because Factor C is a glycosylated protein,
17 and it has posttranslational modifications. And
18 depending on the expression, and depending on a lot of
19 different things, you have variations in molecular
20 weight, as you can see in that gel, and which is
21 scientifically expected.

22 Q. So those differences in molecular weight
23 could also have an impact on the resulting functions of
24 the proteins; right?

25 MS. DOUKAS: Objection to form.

1 A. Could, but don't have to, necessarily.

2 Could, yes.

3 BY MS. LOUGHRAN:

4 Q. And just -- I'm not sure that the court
5 reporter got it, specifically. But just to rephrase my
6 question, the differences in molecular weight could have
7 an impact on the function of the resulting proteins;
8 right?

9 MS. DOUKAS: Objection.

10 A. They could.

11 BY MS. LOUGHRAN:

12 Q. Okay. As a scientist, you could not rule
13 it out; right?

14 A. I could not.

15 Q. If you could just turn back to your
16 declaration, please, which is Exhibit 2042, now, you
17 used the words or the phrase "unexpected results"
18 throughout this declaration.

19 Could you tell me what your understanding
20 of unexpected results is in the context of your opinions
21 here?

22 A. My opinion is based from an -- especially
23 from an assay performance point of view, on the
24 assumption of functional equivalence and equivalence
25 between the enzymes from the different species. And

1 when you see results that indicate a surprising
2 superiority of one over the other, that is, to me,
3 surprising, as it was to Dr. Mizumura.

4 Q. What about as a person who is skilled in
5 the art, did you consider the POSA's position in forming
6 your opinion?

7 A. I did. And especially if we considered a
8 definition that is proposed by the inventors, I think
9 the POSA would also be surprised.

10 Q. Do you believe that Dr. Mizumura is,
11 himself, a person of skill in the art --

12 A. Absolutely.

13 Q. -- as of 2019?

14 A. Absolutely. I would consider him one of
15 the experts in the field.

16 Q. So at least a person of skill in the art --

17 A. Yes.

18 Q. -- as of --

19 And is that true for 2013 and 2019?

20 A. I would say since the 1980s.

21 Q. Got it. Okay. You do have an awareness of
22 Dr. Mizumura's background and experience, et cetera?

23 A. Yes.

24 Q. Now, I believe we talked about scope
25 before. But do you understand that unexpected results,

1 in the context of the inquiry of nonobviousness, have to
2 be commensurate with the full scope of a claim to defeat
3 a finding of obviousness?

4 A. Yes.

5 Q. And if you would just turn back to the
6 claim itself, which I believe is on page 9 and 10 of
7 your declaration, so you -- do you understand that a
8 recombinantly produced Limulus Factor C using HEK
9 protein -- or using a HEK expression system, where the
10 Factor C protein has a residual activity of, let's say,
11 11 percent in the presence of 21 mls sodium citrate,
12 that would be within the scope of this claim; right?

13 A. Yes.

14 Q. Regardless of what the ion residual
15 activity is for magnesium sulphate; right?

16 A. Yes. Because of the ways it's framed is of
17 at least one of the two.

18 Q. Right.

19 A. We talked about that before lunch.

20 Q. Yeah, exactly. And then similar
21 recombinant Factor C protein from Limulus polyphemus
22 expressed in HEK cells that has a residual reactivity
23 of, let's say, 99 percent, in the presence of 21
24 millimolar sodium citrate would also be within the scope
25 of this claim; right?

1 A. Yes.

2 Q. And all the factors and proteins in between
3 are also in the scope of this claim, between 11 percent
4 and let's say 99 percent; right?

5 A. Yes.

6 Q. Okay. This claim would cover all of those
7 proteins; right?

8 A. Yes.

9 Q. Okay. So I understand your contention in
10 your declaration relative to the Mizumura declaration
11 that we've been looking at is that -- and that was data
12 on the Tachypleus species of horseshoe crabs.

13 Your contention is that the residual
14 activity of Limulus polyphemus Factor C that was
15 produced in CHO cells was known by 2019, was
16 unexpectedly good based on Dr. Mizumura's data in his
17 declaration. Is that a fair characterization of your
18 opinion?

19 A. Yes.

20 Q. All right. So I think it would be helpful
21 if you could look at the same time at both Figure 7,
22 which is at paragraph 43 of your -- of your declaration,
23 and then you also reproduced Figure 1 from the Mizumura
24 declaration at paragraph 47. It's on like the next
25 page.

1 And my understanding is that you looked
2 at -- let's look at what's in, I guess, Box 2 for both
3 of those things. You look at Figure 1 from the Mizumura
4 declaration as having a residual activity of like, let's
5 say 50 to 55 percent; do you see that?

6 A. Uh-huh.

7 Q. Okay. And this is in 16 millimolar
8 magnesium sulphate?

9 A. Yeah.

10 Q. And you compare that to Figure 7, again, in
11 Box 2, again, in 16 millimolar magnesium sulphate, which
12 I guess you say is around 40 percent; do you see that?

13 A. Uh-huh, yep.

14 Q. All right. And your -- and just to be
15 clear, this data is expressed in CHO DG44 expression
16 system; right?

17 A. Correct.

18 Q. So none of this data is actually Factor C
19 proteins within the scope of Claim 21; right?

20 A. Are you referring to the fact that Claim 21
21 covers just Limulus?

22 Q. Oh, no. I'm referring to the fact that
23 Claim 21 requires that the Factor C be expressed in HEK
24 cells.

25 A. Oh, just --

1 Q. The data we're looking at is expressed in
2 CHO cells.

3 A. I looked at -- I look at this data and I
4 look at the assay data overall across these different
5 expression systems; right? And I look at it -- I guess
6 I look at it from the point of view of a scientist
7 looking at the -- both the activity levels and the
8 activity profiles, looking for the most robust and
9 reliable expression source that gives consistent
10 activity. And so from that, I'm looking at that from --
11 I'm looking at it from that point of view.

12 So the different expression system products
13 in the -- that are reproduced here are consistently used
14 by the inventors. They've -- as you see here, they use
15 Sf9, CHO, HEK and then the original TAL to, basically,
16 like I said earlier, create an apples to apples
17 comparison. And so that allows you to actually compare
18 the performance of the expression product in a like
19 versus like manner. That is the scientific approach
20 that I use to analyze the data.

21 Q. Okay. But your opinion here, as you write
22 it in -- again, in, for example, your last paragraph,
23 paragraph 55, is that you have found unexpectedly
24 superior residual activity values supporting a finding
25 that Claim 21 of the '318 patent is not obvious. You

1 see that; right?

2 A. I see that, yes.

3 Q. Okay. So your opinion is that the -- what
4 the inventors invented, right, Claim 21 --

5 A. Uh-huh.

6 Q. -- generates unexpectedly good results
7 relative to the closest prior art; right?

8 A. Yes.

9 Q. Okay. And you understand that the
10 invention, Claim 21, the invention, requires expression
11 in HEK cells; right?

12 A. Yes.

13 Q. Okay. So you agree that when you're
14 referring to Figure 1 from the Mizumura declaration, and
15 you're making comparisons about that data to Figure 7,
16 and the Mizumura prior art, you're looking at expression
17 in CHO cells. That has nothing to do with the claimed
18 invention; right?

19 A. You are -- I am comparing the results in
20 Figure 7 to the results in Figure 1, where the HEK
21 cells, the results -- it's -- so your point is that
22 there is no HEK -- there's no HEK cells in a
23 side-by-side comparison. Is that what you're getting
24 at?

25 Q. Well, my point is that, for example, in

1 paragraph 48, right, you say the residual activity in 16
2 millimolar magnesium sulphate is unexpectedly superior
3 for Limulus polyphemus Factor C.

4 A. Yes.

5 Q. And you say 55 percent, as compared to
6 Tachypleus tridentatus?

7 A. Yes.

8 Q. Now, that 50 and 40 are taken from
9 expression in CHO cells; right?

10 A. Yes.

11 Q. And CHO cells is not in the scope of the
12 Claim 21; right?

13 A. But there is -- you can make from this
14 comparison, which, again, is across different expression
15 systems, under the same conditions, I am drawing the
16 conclusion that the Limulus-derived material is
17 surprisingly more active or has higher residual
18 activity. That's one assumption right there.

19 So they are separate points. There is the
20 cell line expression system point, and then there is
21 where is that expression product coming from, which
22 species.

23 Now, you can look at what is your -- what
24 is -- the inventors look at two different aspects of
25 optimizing or improving their invention or what they're

1 looking at. One is through the expression system, which
2 is why we are looking at these different expression
3 systems, and the other one is -- it's a combinatorial
4 scientific question.

5 And the key here is that you're looking at
6 like versus like systems. And the assumption that the
7 scientific approach they have taken has been the same
8 across -- across their entire evolution of science.

9 And so I am looking at CHO versus CHO,
10 within the CHO expression system, you compare the
11 different species. And then you look at the further
12 optimization. You look at that within HEK versus CHO.
13 Those are two separate things. And taken together, you
14 have a significant performance improvement. That is
15 surprising --

16 Q. Okay.

17 A. -- scientifically.

18 Q. I don't know that that answers my question,
19 though, which is I understand when you look at CHO
20 versus CHO, that is -- those are results from an
21 expression system that is not part of the inventors'
22 claimed invention; do you agree?

23 A. I agree. But it's part of the scientific
24 basis that's taken into -- that I took into
25 consideration.

1 Q. Okay. But I just -- again, you're saying
2 that these show unexpectedly good results with respect
3 to this invention. The data that you point to in CHO
4 cells does not fall within the scope of that invention.
5 I just want to be clear about that. You agree with
6 that?

7 MS. DOUKAS: Objection to form.

8 A. Yes. Framed like that, yes.

9 BY MS. LOUGHRAN:

10 Q. Now, the difference that you see is
11 approximately 40 percent, compared with approximately 50
12 to 55 percent; do you see that?

13 A. I see that.

14 Q. Okay. Is that a difference as a matter of
15 degree or a difference as a matter of kind?

16 A. I don't understand your question.

17 Q. Is it a difference of degree along the same
18 spectrum, right, like a percent difference? Or is it
19 something completely -- or it is something that's
20 completely different as a matter of, you know,
21 scientific -- it is like at 50 to 55 percent, you're
22 talking about a completely different protein, for
23 example?

24 A. You can't make a determination like that
25 based on one assay figure.

1 Q. Okay. So do you agree that the difference
2 here between 40 percent and 50 to 55 percent is a
3 difference that's a matter of degree?

4 A. It would always be if your assay system is
5 valid. Otherwise, the data wouldn't make any sense.

6 Q. Well, right. And sometimes when the data
7 doesn't make any sense, that's when you think that
8 something is surprising. But I'm asking you --

9 A. No. Or you could have bogus science, to be
10 blunt. If you have -- there's two different kinds of
11 surprising data, and not all of it is good. But you
12 have to have a valid assay system. And in a valid assay
13 system, you would expect your data to be within an
14 acceptable range. We talked about that earlier. So
15 that range is established by your assay validity
16 criteria. And that's what we're working with -- that's
17 what you would work within.

18 Q. Okay. So, I mean, just so I'm clear and I
19 understand your opinion about that, the difference
20 between 40 and 50 to 55 percent, you and I may differ on
21 how significant that difference is, but you agree that
22 it is a matter of degree, a percent difference along a
23 continuum; right?

24 A. Yes.

25 Q. Okay. If you look at -- so you focused

1 here on the Box 2. Now, Box 5, the relative Box 5 is
2 also within the scope of the claim, right, the
3 10 percent sodium citrate; do you see that?

4 A. Yes.

5 Q. Okay. Now, for the results for Box 5,
6 Tachypleus expressed in CHO was, I think you said
7 approximately 25 percent, around 25 percent?

8 A. Yes.

9 Q. Okay. And then when you looked at Limulus
10 expressed in CHO, the DG44, the results I think you said
11 was I think you said approximately 20 to 30 percent. It
12 looks like, you know, maybe somewhere south of
13 25 percent; right?

14 A. Yep.

15 Q. Okay. Would you consider those to be
16 relatively equivalent?

17 A. I -- again, a determination of equivalence
18 can only be made if you know what the validity criteria
19 of the assay are. I would never use equivalents without
20 knowing those.

21 Q. Okay. Let me phrase it differently.

22 Do you -- with respect to the data on
23 sodium citrate, would you say that those -- that
24 comparative data is not unexpectedly surprising or
25 unexpectedly different?

1 A. I would not look at that in isolation. And
2 the difference is less than in the other salt medium.
3 But I would, again, I would look at the data in its
4 totality, but I would say the difference is not as
5 great.

6 Q. Well, then, I'm just going by the numbers
7 that you put in your declaration. So just under
8 25 percent and approximately 20 to 30 percent. Do you
9 have an opinion as to whether, comparatively, the
10 Limulus produced unexpectedly good results relative to
11 the Tachypleus?

12 A. For that specific medium, test medium?

13 Q. Correct.

14 A. I would still say yes. Again, I look at
15 the -- I look at the data in its totality and take the
16 scientific context into consideration as well.

17 Q. Okay. So when we were looking at magnesium
18 sulphate, you were focused on the difference between
19 40 percent and 50 to 55 percent. And you said that was
20 indicative with unexpectedly good results.

21 Now we're looking at sodium citrate, and
22 there is -- you were talking about just under 25 percent
23 and just under 25 percent, based on these figures. So
24 is it fair to say that, at least with respect to that
25 aspect of the claim, these results are not unexpectedly

1 good?

2 A. I would not want to isolate a statement
3 like that, no.

4 Q. Okay. Doctor, could you look at the white
5 bar for Figure 7 and the white bar for Figure 1 and
6 explain to me how you conclude that, with respect to
7 that ion, one is unexpectedly good over the other?

8 A. So you're talking about 5 versus 5 in --

9 Q. Yes.

10 A. Which would you like me to compare?

11 Q. Well, it's the comparison that you are
12 making. You are comparing Tachypleus, expressed in CHO
13 DG44 in Figure 7, so that's the white box in 5, to
14 Limulus, expressed in CHO DG44, which is the white box
15 in Figure 1.

16 A. I would concur that, for this particular
17 data point, they are close.

18 Q. So one is not unexpectedly good over the
19 other?

20 A. For this particular data point.

21 Q. Okay. And residual activity in 10 percent
22 sodium citrate is one of the aspects of Claim 21; right?

23 A. It is one, yes.

24 Q. So the Factor Cs that are studied in Claim
25 5 between these two figures fall within the scope of

1 Claim 21?

2 A. They do.

3 Q. Now, just looking at Figure 7, this is your
4 data on your closest prior art; right? This is from
5 Mizumura, the closest prior art that you allege to be
6 relative to Claim 21; right? Yes, this is the data from
7 the closest prior art; right?

8 A. Yeah.

9 Q. Okay. Now, if we take this and we say, all
10 right, this is Tachypleus data, but let's look at HEK
11 293, right, because the claim specifies HEK 293; okay?
12 So we're looking at the darker gray box. For magnesium
13 sulphate, the claim requires 10 percent -- or 15 percent
14 or higher in the presence of 16 millimolar magnesium
15 sulphate; do you see that?

16 A. Uh-huh.

17 Q. Okay. This prior art falls within the
18 scope of that claim; right?

19 MS. DOUKAS: Objection to form and
20 objection, outside the scope.

21 BY MS. LOUGHRAN:

22 Q. And I'd just direct you to your own
23 statement at the top of page 17. You say that the
24 expression in HEK cells is about 20 to 25 percent, which
25 is above 15 percent; correct?

1 A. Yes.

2 Q. And then for sodium citrate, which is in
3 lane 5, and that's the next bullet point down, residual
4 activity is about 20 to 30 percent in HEK 293 cells; do
5 you see that?

6 A. I do.

7 Q. And that falls within the scope of Claim 21
8 as well, because 20 to 30 percent is higher than
9 10 percent; right?

10 A. Yes.

11 Q. Okay. So you agree with me that this prior
12 art, the residual activities demonstrated in this prior
13 art also fall within the scope of the residual
14 activities set forth in the claim?

15 MS. DOUKAS: Objection, outside the scope.

16 A. To my understanding, it falls within -- as
17 far as the numbers are concerned, yes.

18 BY MS. LOUGHRAN:

19 Q. Okay. Doctor, your declaration involves
20 making two comparisons, I think, between some
21 experimental data that you reviewed and you -- from that
22 data, you draw a conclusion about unexpected results;
23 right?

24 A. Yes.

25 Q. Okay. And as we were looking at, you

1 compared the Mizumura declaration, the data in Figure 1
2 to Figure 7, and then you also compared some data in a
3 document called D19 to Figure 7; is that fair?

4 A. That's fair.

5 Q. Okay. In your career, have you had
6 occasion to compare different experimental results to
7 try and draw a conclusion about the impact of certain
8 factors in those experiments?

9 A. In many different contexts.

10 Q. Okay. And are you familiar with the
11 concept of like an experimental control holding a
12 feature -- you know, as a control -- I believe you
13 referred to it as like apples to apples.

14 Can you explain that?

15 A. I worked in standardization for 15 years,
16 so I'm very familiar with the term of controls and
17 reference materials, but I'm also very precise and
18 careful about the use of those terms.

19 Q. Okay.

20 A. So I would like to understand very
21 carefully where we're going with this.

22 Q. Okay. Let's just -- maybe we'll just look
23 at one of your publications and we can talk about it
24 that way.

25 So this is going to involve pulling up a

1 document that's not in the box. We're going to have to
2 look at it on the computer screen. I don't know if we
3 can put that up in front of the witness.

4 (A discussion was held off the record.)

5 (Exhibit 2062 was presented to the
6 witness.)

7 BY MS. LOUGHRAN:

8 Q. So this is an exhibit that was marked 2062.
9 It says "PDA Journal" at the top. Do you see that
10 Dr. Morris?

11 A. I do.

12 Q. And are you familiar with this document?

13 A. I am.

14 Q. Okay. So this is a document that's been
15 marked Exhibit 2062. It is an article in the PDA
16 Journal of Pharmaceutical Science and Technology.

17 A. Yeah.

18 Q. What is your understanding of what this
19 document is, Dr. Morris?

20 A. It is a publication that was drafted -- or
21 that was put together by a group of endotoxin scientists
22 during the time -- and experts during the time when I
23 was at the Parenteral Drug Association. And we had --
24 the PDA had a group of experts in the area that looked
25 at recombinant alternatives for endotoxin testing.

1 Q. Okay. So you are a named author on this
2 publication; right?

3 A. Yes, I am.

4 Q. And so you would have reviewed it and
5 agreed with the contents in the publication; correct?

6 A. Yes.

7 Q. Okay. And Jack Levin is also a named
8 author. He is the -- is he the founder or co-founder of
9 the assay?

10 A. He is one of the original scientists
11 involved in the LAL assays, yes.

12 Q. And in your words, what was the -- what was
13 the point of the research that went into this
14 publication? What were you trying to demonstrate?

15 A. In brief terms, it is a -- what I would
16 call a review of the current, at the time, available
17 recombinant alternative assays, and to the horseshoe
18 crab assay.

19 Q. Okay. And did this involve doing any
20 experiments? Or were you just reviewing data and
21 literature that already existed?

22 A. As you can see in the article, it's
23 really -- it's a literature review.

24 Q. Okay.

25 A. And a review of the compendial -- the state

1 of compendial discussions and the regulatory -- the
2 regulatory opinion at the time.

3 Q. Okay. Now, as far as the literature review
4 piece, if you want to, if you could scroll to page 605.
5 There is a heading called "Literature Review."

6 A. Yeah, I see that.

7 Q. If you can describe what you --

8 A. Yeah.

9 Q. Now, in the second paragraph of that first
10 column, you talk about, "Several published peer review
11 studies support the claim that RFC is comparable or
12 superior to LAL, including the lack of sensitivity to
13 beta glucans."

14 Do you see that last paragraph?

15 A. Yes.

16 Q. You say, "Comparing the results with RFC
17 and LAL requires careful study design to reach accurate
18 conclusions"; do you see that?

19 A. I see that.

20 Q. Do you agree with that statement?

21 A. Yeah.

22 Q. And then you say, "Studies of this nature
23 are inherently difficult to conduct, because the
24 variation and results of any type of endotoxin testing
25 is relatively high because of the very low subpicogram

1 level tested and the tremendous sensitivity of the
2 assay"; do you see that?

3 A. I do.

4 Q. Okay. And you agree with that statement?

5 A. I do.

6 Q. Okay. And then you go on to say, "As a
7 consequence, large dilutions of standards and samples
8 are necessary to obtain results in range." And you say,
9 "Minor differences in procedure (temperature, mixing
10 time and operators) result in significant variation,
11 even when the same LAL method is used on the same
12 samples at the same time in the same laboratory"; do you
13 see that?

14 A. Yes.

15 Q. So are you describing here the idea that
16 slight variations in procedure can lead to different
17 results in how particular Factor C assays behave or give
18 endotoxin detection readouts?

19 A. I would not phrase it that way. And I
20 think it's more -- it's more complex than that. I would
21 not simplify it that way.

22 Q. Okay. Well, do you agree with the
23 statement, "minor differences in procedure, such as
24 temperature, mixing time and operators, result in
25 significant variation even when the same LAL method is

1 used on the same samples at the same time in the same
2 laboratory"?

3 A. Differences have always had an impact. But
4 that's why the assay validity criteria are important,
5 and the reference materials and the controls. And
6 that's why it's also important to understand the assay
7 parameters that were used. That's -- every assay is
8 that way.

9 Q. Okay. I'm just trying to understand if you
10 stand by this statement that minor differences in
11 procedure result in significant variation, even when the
12 same LAL method is used on the same samples at the same
13 time in the same laboratory. Is that an accurate
14 statement?

15 A. I -- I would say it's still an accurate
16 statement.

17 Q. Okay. So if you were doing a comparison of
18 different endotoxin detection assays, you would want
19 information about these procedural details, for example,
20 temperature, mixing time, operators; correct?

21 A. Correct. And these are usually -- these
22 are standard -- these are standard -- part of an
23 analytical operating procedure that's captured as part
24 of the assay.

25 Q. And, in fact, when we were talking about

1 the closest prior art, you said that you believed the
2 Mizumura publication to be the closest prior art,
3 because it was by Mizumura, the same inventor, again,
4 probably in the same lab, et cetera; right?

5 A. The same assay systems, the same lab, the
6 same -- the same experience with the assay, yes.

7 Q. Okay. And then I think at the -- so then
8 at the end of this paragraph, you say, "For our review,
9 we evaluated comparative studies, LAL versus RFC in peer
10 review journals and put more weight on those that
11 controlled for these well-known variables"; do you see
12 that?

13 A. Yes.

14 Q. And you agree that that was appropriate for
15 purposes of this study at that time?

16 A. I would like to put that into context, that
17 this is a literature review. And when you do a
18 literature review, you frame appropriately what you can
19 and cannot conclude from a comparative peer review
20 literature review.

21 So -- and as I would say as a -- as an
22 expected standard in scientific literature, the reader
23 of a review like that puts the conclusions from a review
24 into that context, that the authors have taken prior
25 literature, looked at the results, looked at the body of

1 data that is in each of the articles that they
2 considered, what the controls were around the data, and
3 you qualify your conclusions and -- around that. That's
4 the context.

5 Q. Okay. Thank you.

6 But just to be clear, it is true that
7 you -- in the context of this study, you put more weight
8 on, you know, articles or literature in which you could
9 determine that the authors controlled for --

10 A. Absolutely.

11 Q. -- variables such as --

12 A. Yeah.

13 Q. Okay. And you put more weight on that
14 because you could -- is it because you could draw more
15 reliable conclusions if you knew that the authors held
16 certain variables controlled?

17 A. Of course. The more you control an assay
18 and the more you understand how the author of the study
19 controlled both the procedure, the standards, and the
20 assay parameters, you would always put more weight on
21 that.

22 (Exhibit 1004 was presented to the
23 witness.)

24 BY MS. LOUGHRAN:

25 Q. Okay. So I would like you to have in front

1 of you the Mizumura declaration from the file history.

2 So that is page 82 of Exhibit 1004.

3 A. Yeah.

4 Q. So now, your understanding of this
5 declaration -- well, I won't put words in your mouth.

6 What is your understanding of why
7 Dr. Mizumura submitted this declaration during
8 prosecution of the '318 patent?

9 A. I'm not sure -- I'm not sure what you're
10 asking or --

11 Q. Well, you reviewed this declaration and you
12 cite to Dr. Mizumura's data in here --

13 A. Yes.

14 Q. -- to draw your conclusions regarding
15 unexpected results.

16 So I'm just asking you: What is your
17 understanding of what Dr. Mizumura was arguing or
18 conveying through this declaration?

19 A. I have to think about that for a minute.

20 Q. Okay. You can take your time and review
21 the declaration itself. And there's no rush.

22 A. I would say in summary, that the data that
23 is submitted as part of this -- and that's the intent of
24 his declaration, supports the nature of the unexpected
25 results.

1 Q. Okay. And Dr. Mizumura here points to the
2 expression of recombinant Limulus Factor C to make that
3 argument regarding unexpected results; right?

4 A. Yes.

5 Q. Okay. So if you look on page 2 of the
6 declaration, the -- under heading 1, he describes
7 "recombinant L. Polyphemus Factor C produced by using
8 Sf9 cell." And he says, "cDNA coding L. Polyphemus
9 Factor C (SEQ ID Number:1 in US2019/0241629A1) was
10 inserted between EcoR1 recognition site and Xho1
11 recognition site of the P1Z-V5 vector"; do you see that?

12 A. Yeah.

13 Q. And then he says a similar thing with
14 respect to "cDNA encoding, L. Polyphemus Factor C
15 optimized for expression in CHO cells" in heading 2; do
16 you see that?

17 A. Uh-huh.

18 Q. Do you have an understanding of what
19 document Mr. Mizumura is citing there, to get to item
20 number 1?

21 A. No, I don't.

22 Q. There are several variants of Limulus
23 polyphemus Factor C sequence. Do you know what variant
24 Dr. Mizumura used?

25 A. I don't.

1 Q. The experiments that he ran here were
2 conducted at different times than those that were run to
3 generate Figure 7; correct?

4 MS. DOUKAS: Objection to form.

5 A. I am not sure.

6 BY MS. LOUGHRAN:

7 Q. Well, this declaration is dated 2021;
8 right?

9 A. Yes.

10 Q. And Figure 7 -- the data that was submitted
11 in Figure 7 was part of the original application as
12 filed in 2013. So do you agree that the results in
13 Dr. Mizumura's declaration were generated at a different
14 time --

15 A. Yes.

16 Q. -- than those in Figure 7?

17 Okay. Were they generated in the same
18 laboratory, the results in Mizumura's declaration?

19 A. I can't know that.

20 Q. Okay. Do you know if the same operators
21 who generated the results in Figure 7 were the operators
22 to generate the results in Dr. Mizumura's 2021
23 declaration?

24 A. I can't know that.

25 Q. Okay. Do you know if the temperature under

1 which the assay was run to generate Figure 7 was the
2 same temperature that the assay run for Figure 1 was
3 used?

4 MS. DOUKAS: Objection to form.

5 A. Good laboratory procedures, GLPs, and all
6 other common requirements would make that assumption
7 very likely.

8 BY MS. LOUGHRAN:

9 Q. But you can't know for sure?

10 A. I can't know.

11 Q. Right. Dr. Mizumura didn't specify, either
12 in his declaration or in the Mizumura publication, what
13 the temperature was; correct?

14 A. He does not.

15 Q. Now, to get the data in -- that was
16 generated in the Mizumura declaration, I'll say Figure 1
17 in particular, I think we agreed that Dr. Mizumura would
18 have had to express Factor B and pro-clotting enzyme as
19 well; correct?

20 A. Yes.

21 Q. Do you know what expression system he used
22 for Factor B and pro-clotting enzyme expression to get
23 the data in Figure 1?

24 A. My -- if my recollection is correct, it was
25 Sf9.

1 Q. Where does he say that?

2 A. In the 2015 patent document that's authored
3 by Mizumura, et al., under "Activity Measurement," in
4 that section, he describes under 293 the Factor B.

5 Q. So we know that for Figure 7, Dr. Mizumura
6 used Sf9 to generate recombinant Factor B and
7 pro-clotting enzyme. My question is: For the data that
8 he created with respect to Figure 1 in his declaration,
9 what expression system did he use to generate Factor B
10 in pro-clotting enzyme?

11 A. That is not captured in the declaration, I
12 believe.

13 Q. Okay. So is it fair to say we don't know
14 what expression system he used?

15 A. Not based on this document.

16 Q. Do you know what expression system he used
17 based on any other document?

18 A. Looking at it from the assay
19 standardization control perspective, and looking at
20 the -- I would assume that he -- I assume that the
21 Factor B reagent is the same, because it's been
22 previously shown to perform well, and has been
23 well-characterized.

24 And as part of your assay control, you
25 would use the same reagents -- we just discussed that --

1 the same reagents, the same experimental conditions and
2 the same overall assay parameters.

3 And a typical approach to this is
4 iterative, obviously. So if you are looking at a new
5 variable, which in this case is the Factor C, and the
6 Factor C under different -- from different -- if you are
7 evaluating Factor C, you are not also creating other
8 variables in your assay. That's just good assay
9 practice.

10 Q. Okay. But if you look at recombinant
11 L. Polyphemus Factor C produced by using CHO's DG44
12 cell, which is spanning page 2 and 3, Mr. Mizumura
13 specifically says that those were produced as described
14 in paragraphs 109 to 112 of the specification as filed;
15 do you see that?

16 A. On page 3?

17 Q. Uh-huh. Yes. And --

18 A. Yes.

19 Q. Okay. And so it refers to his prior -- his
20 prior -- he explains that in this declaration, Factor C
21 was recombinantly produced as described in paragraphs in
22 the specification as filed. But there's nothing in here
23 that describes how Factor B or pro-clotting enzyme were
24 expressed; correct?

25 A. The -- it is not described, but he refers

1 back to the previous data, which implies that it's the
2 same assay system.

3 Q. It implies that, but we don't know for sure
4 whether Factors B and pro-clotting enzyme were similarly
5 produced in Sf9; right?

6 A. It's not spelled out here.

7 Q. So we can't know for sure; correct?

8 A. Yes.

9 Q. And, similarly, do we know whether
10 Mizumura -- Dr. Mizumura expressed Limulus Factor B and
11 pro-clotting enzyme or Tachypleus Factor B and
12 pro-clotting enzyme?

13 A. That is not spelled out.

14 Q. So we don't know; correct?

15 A. Correct.

16 Q. And those differences could have an impact
17 on the resulting function of the proteins; correct?

18 A. Could. Again, it depends on the assay
19 controls.

20 Q. Okay. Now, Dr. Mizumura submitted this
21 declaration in support of the patentability of Claim 21;
22 do you understand that?

23 A. I do.

24 Q. Okay. And as we discussed, Claim 21
25 requires expression in the HEK expression system; right?

1 A. Yes.

2 Q. But in this -- in this declaration,
3 Dr. Mizumura only provides experimental evidence with
4 respect to Limulus expressed in CHO cells. You agree;
5 correct?

6 A. Yes.

7 Q. Okay. Do you have an opinion as to why
8 Dr. Mizumura did not just do the experiments in HEK
9 cells?

10 MS. DOUKAS: Objection to form.

11 A. I have an educated guess why one would do
12 that, but I know -- I know what I would do first. And,
13 I mean, there's -- from CHO cells is a better expression
14 system, because it's a permanent -- the expression
15 construct retention is better. And HEK cells, for a
16 long period of time, were considered transient
17 expressors.

18 So if you're making a product and you are
19 planning on consistently making a product the same way,
20 you would always go with CHO first before you went to
21 HEK. So from a protein manufacturing strategy point of
22 view, it makes complete sense that you would go to CHO
23 first.

24 And you would look at a bunch of cell lines
25 and then you would make your -- would make your choices

1 based on a number of factors and -- that are very --
 2 that have variants that cover all different aspects of
 3 product manufacturing, and you would make your choice.
 4 HEK has advantages, but it also has downsides. And I
 5 can understand why you would go with CHO first, but I
 6 have no way of knowing what Dr. Mizumura thought.

7 BY MS. LOUGHRAN:

8 Q. Right. My question -- well, thank you for
 9 that. That's helpful.

10 Dr. Mizumura is going to the patent office
 11 and asking to be granted a patent claim for the
 12 expression of Limulus polyphemus in HEK cells, and
 13 trying to convince the patent office that he has
 14 invented that.

15 A. Uh-huh.

16 Q. However, the data that he presents that he
 17 ran himself is not in HEK cells.

18 So let me ask you: Are you aware of any
 19 contradictory data, any data that would have suggested
 20 that HEK cells were not better, were not good, to
 21 produce Limulus polyphemus Factor C?

22 A. I am not aware of that data, but I can -- I
 23 am not aware of that data.

24 Q. Would you -- could you think of a reason
 25 why -- well, strike that.

1 Would you be surprised if such data
2 existed?

3 MS. DOUKAS: Objection to form.

4 A. As a scientist with over 30 years of data
5 review, I can imagine almost anything. But no, of
6 course, every scientific choice has upsides and
7 downsides. And as a manufacturer of a particular
8 product, you make choices. And all of those choices
9 have scientific, production, manufacturing, availability
10 reasons.

11 And I view the choices somebody would make
12 from my scientific lens, which is the assay lens and the
13 compendial requirement lens, which I understand best. I
14 have no way of knowing what -- what Dr. Mizumura would
15 consider critical quality attributes.

16 BY MS. LOUGHRAN:

17 Q. By 2019 -- or actually -- yeah, by 2019,
18 when he has filed the application for this patent, it
19 was -- was it possible to express Limulus polyphemus
20 Factor C in HEK cells?

21 A. From a technology state of the art point of
22 view, absolutely.

23 Q. Does Dr. Mizumura specify which
24 concentrations of each factor he used for the data that
25 resulted in Figure 1 of his declaration?

1 A. It is not covered in the declaration beyond
2 a reference to Figure 7. So the educated assumption
3 would be that the same approach was used, which would be
4 to calibrate based on relative activity to get the
5 enzymes into the same range.

6 Q. But he did not specify, so we can't know
7 for sure; right?

8 A. Beyond what he says on page 3, where he
9 refers back to the salt experiments.

10 Q. Yep. Paragraphs 134 to 136?

11 A. Uh-huh.

12 Q. Is that what you're referring to?

13 A. Yes.

14 Q. Okay. So if you look at -- if you're still
15 in this big document, if you look at -- if you go to
16 page 606, and you'll see there's paragraph numbers on
17 606, they start with 133, and then it goes to 134, 135,
18 136. Just to confirm, these are not the paragraphs that
19 talk about the concentrations of the proteins in each
20 assay; correct?

21 A. Yes.

22 Q. And just to be very clear, if you turn back
23 to page 604, those are found in paragraph 130; correct?

24 A. Yeah. But he's using the same approach, as
25 described. He's calibrating them based on relative

1 activity. That's what I was talking about.

2 Q. Well, but in his declaration, he doesn't
3 cite to paragraph 130. He only cites to paragraphs 134
4 to 136.

5 A. Yeah.

6 Q. So we don't know if he did the same thing
7 in creating Figure 1 as described in 130. He doesn't
8 say; correct?

9 A. That is correct. But as you read here,
10 it's the same approach, which scientifically makes
11 sense.

12 Q. Well, just so that we understand, when
13 you're looking at pages 604, 605 of Exhibit 1004, that
14 is Dr. Mizumura's application as filed. So it's the
15 application of the '318 patent as filed. It's the same
16 substantive content as what's in his Mizumura
17 publication that you rely on as the closest prior art.
18 It's the same as what's in the '318 patent. You
19 understand that; right?

20 A. Yes.

21 Q. In his declaration, when he's talking about
22 how he created this new data, Figure 1, he never
23 references paragraph 130, which has the concentration
24 data; right?

25 A. Understood.

1 Q. Okay. So we don't know what concentrations
2 he used to generate Figure 1; correct?

3 A. Correct.

4 Q. So, Dr. Morris, when we look at the data in
5 Figure 1 of the Mizumura declaration, we've talked about
6 some things that were -- are different and things that
7 are unknown; for example, the temperature at which the
8 experiments were conducted; what factors B and
9 pro-clotting enzyme expression systems were used.

10 You can't rule out that those differences
11 would have some impact on the resulting function of the
12 proteins; right?

13 MS. DOUKAS: Objection to form.

14 A. You can't rule it out.

15 MS. LOUGHRAN: Okay. We can take a break.

16 (A break was taken.)

17 BY MS. LOUGHRAN:

18 Q. Hello again, Dr. Morris. How are you?

19 A. I'm fine.

20 Q. Great.

21 If you could look at paragraph 49 of your
22 declaration.

23 A. Yes.

24 (Exhibit 1022 was presented to the
25 witness.)

1 BY MS. LOUGHRAN:

2 Q. And I'll just -- okay. You cite to a
3 document, Exhibit 1022. And that is tab 9 in the box,
4 if someone could be so kind as to hand Dr. Morris
5 Exhibit 1022.

6 You have been handed a document that's been
7 marked as 1022. Do you have that in front of you?

8 A. I do.

9 Q. And do you -- have you seen this document
10 before?

11 A. Yes.

12 Q. Okay. This is the document you cited in
13 your declaration; right?

14 A. Not for -- I'm not sure how you're linking
15 that to point 49.

16 Q. Well, on page 19, you have a sentence. And
17 then you say, "CEG Exhibit 1022 at 153, stating these
18 findings also lead to the idea that the hemocytes of
19 L. Polyphemus probably contain a coagulation system
20 similar to that" --

21 A. Okay. I got ya.

22 Q. So you cite to this Tokunaga reference,
23 Exhibit 1022, to support the idea or your contention
24 that the two species have been consistently considered
25 functionally equivalent in terms of activity; do you see

1 that?

2 A. Yes.

3 Q. Now, you have an awareness -- or I'll ask:
4 Are you aware that this Tokunaga reference contains some
5 partial amino acid sequence comparisons between
6 Tachypleus and Limulus?

7 A. Yes.

8 Q. Okay. And that is at the very end of the
9 document?

10 A. Yes.

11 Q. On page 157, you agree that there are some
12 amino acid sequence differences between Tachypleus and
13 Limulus, at least for this partial sequence of Factor C;
14 right?

15 A. Yes.

16 Q. And I believe Tokunaga shows those
17 differences exist in the -- let's see -- the heavy
18 chain; correct?

19 A. Yes.

20 Q. And in the light chain; is that right?

21 A. Yes.

22 Q. And then, also, there is an amino acid
23 difference at the carbohydrate attachment site where the
24 black dot is located; right?

25 A. Yes.

1 Q. All right. So these differences in amino
2 acids could lead to different structures as between
3 these two proteins; right?

4 MS. DOUKAS: Objection to form.

5 A. I would never make structural assumptions
6 based on individual amino acid exchanges. Those are
7 very, very, very large proteins that are glycosylated.
8 And in every protein family and every enzyme family that
9 has -- you find amino acid exchanges. And so that is,
10 from a biochemical and structural function point of
11 view, nothing unusual.

12 BY MS. LOUGHRAN:

13 Q. Okay. So when you say you would never make
14 structural assumptions, does that work both ways?

15 A. Based on individual amino acid exchanges.
16 Again, you wouldn't --

17 Q. So you wouldn't assume that the amino acid
18 differences lead to differences in structure or
19 similarities in structure?

20 A. No, not -- and especially not in -- viewing
21 in isolation. There's different types of exchanges. It
22 depends on where is it. There are a lot of factors that
23 impact whether there's a structural or functional
24 difference or not.

25 Q. Okay. So you just wouldn't know if there's

1 going to be some structural difference based on a
2 difference in amino acid; right?

3 A. On that piece of data alone, no. And as I
4 point out, I'm looking at functional equivalents in
5 my -- focusing on functional equivalents in my
6 statement.

7 Q. Okay. But your conclusion in your
8 declaration is actually that there's not functional
9 equivalents; right?

10 A. What are you -- they have -- I'm saying
11 they have been considered functionally equivalent for a
12 very long time, based on -- they weighed -- in the
13 published and documented history of international ring
14 studies that include lysates derived from those species,
15 they have been consistently considered functionally
16 equivalent in terms of activity. That's what I'm
17 talking about.

18 Q. I understand that. But you are also, in
19 your declaration, arguing that Limulus and Tachypleus
20 are not functionally equivalent; in fact, one, in your
21 view, gives better results than the other; right?

22 A. One gives better results, but they still --
23 from a functional point of view, they have been
24 considered equivalent. That's why it's surprising that
25 one would have a higher activity.

1 Q. But the conclusion that you draw that one
2 has better residual activity than the other could be
3 because of some of these differences in amino acids;
4 right?

5 A. There's a number of different reasons that
6 could apply.

7 Q. And differences in amino acid sequence is
8 at least one possibility; right?

9 A. It is one possibility.

10 Q. Now, Tokunaga, this reference Exhibit 1022
11 doesn't actually talk about residual activity; right?

12 A. Right.

13 Q. So when you use the word "functional
14 equivalence," you're using it in a broader sense than
15 the residual activity metric in the claim; is that fair?

16 A. I am describing exactly the context -- I'm
17 using it in the context of the LAL -- the use in the LAL
18 assay in international ring studies.

19 So the endotoxin reference material that's
20 established by the WHO and that the pharmacopeias use is
21 established in large international ring trials in which
22 many laboratories from around the world participate.

23 In those studies -- and those are publicly
24 available from the WHO and published. In those studies,
25 the laboratories that participate in those studies and

1 execute the LAL test with lysates come from around the
2 world. And those lysates that are admitted to those
3 studies come from the three different -- from those
4 different species, which underpins the assumption that
5 they're functionally equivalent, or close enough to be
6 used in a large standardization ring trial. That is the
7 context of my point.

8 And the ring trials are based on the
9 harmonized compendial assay, which is the same in the
10 USP, the EP, and the Japanese Pharmacopeia, and the
11 International Pharmacopeia. So that is the context for
12 that statement for functional equivalents.

13 Q. In neither the Tokunaga or the WHO study,
14 which we'll get to, was there a specific measurement of
15 residual activity; right?

16 A. No. No.

17 Q. Okay. So when you say "functional
18 equivalence," you're talking about something else?

19 A. I am talking about the performance of the
20 horseshoe crab lysates in the compendial endotoxin test,
21 which is what we're talking about here.

22 Q. When you say "what we're talking about
23 here," what do you mean?

24 A. The residual activity -- the lysate is used
25 to clot, for a clotting test. And the original clotting

1 test is the -- I would say, the benchmark to which a
2 recombinant test has to perform.

3 And so the functional equivalence statement
4 refers to the ability of the lysate or the reagents to
5 perform in this test. And that is what -- that's what I
6 mean. And the residual activity is a sub-aspect of this
7 type of testing, from my point of view, scientifically.

8 Q. Right. So my original question is: When
9 you use the word "functional equivalence," you're using
10 it in a broader sense than the residual activity metric
11 in the claim; that's right?

12 A. That's fair.

13 Q. All right. That is fair. Thank you.

14 All right. The ring study is actually at
15 tab 10, if we want to hand that to Dr. Morris, please.
16 And so you've been handed an exhibit that's been marked
17 Seikagaku Corporation Exhibit 2107.

18 Is that the document you have in front of
19 you?

20 A. It is.

21 (Seikagaku Corporation Exhibit 2107 was
22 presented to the witness.)

23 BY MS. LOUGHRAN:

24 Q. And this is the WHO study that you cite and
25 discuss at paragraph 49 of your declaration; correct?

1 A. Correct.

2 Q. Now, you say in your declaration that "35
3 participating global laboratories use lysates from three
4 different regional species." And then you go on to
5 describe the analysis that was done.

6 Where, in this document, does it specify
7 what species those were?

8 A. I believe this is not in the document, but
9 it's -- let me check. You have the participating
10 laboratories in -- on page 83 of the document. And the
11 participating laboratories, especially the regulatory
12 laboratories, would be testing to their national assays.
13 And for the Asia-Pacific region, for example, Japan, and
14 those countries, their referenced lysates are based on
15 the specific species.

16 Q. Okay. So it's not specified in this
17 document, but -- so what three species; do you know?
18 What three species are tested here?

19 A. I do not know it from this document.

20 Q. Okay.

21 A. It's captured in the regulatory and
22 compendial requirement for these countries. And there
23 is supplementary WHO documentation that has all of that
24 information --

25 Q. But the document --

1 A. -- which is also -- this document does not
2 have it.

3 Q. This document doesn't specify what those
4 species are; correct?

5 A. Correct.

6 Q. If you look at Table 10, which -- or
7 actually, no, Figure 1, what is being shown in here?
8 It's on page 92.

9 A. May I ask why you're asking this so I can
10 better focus my response?

11 Q. Well, sure. I guess where I'm going is
12 your -- you know, in your opinion or your review of this
13 data, is it fair to say that there is a significant
14 variation in the sample readings across laboratories?

15 A. I would qualify my answer by saying that,
16 again, the assay context here is the establishment of a
17 reference standard. And the assay requirements and the
18 validity criteria are based on the compendial and the
19 regulatory requirements.

20 And the -- what you're seeing is the
21 histogram of the values, the spread of values, unit
22 values across the laboratory in a gelation assay. And
23 that's -- which is one of the tests. So that is a
24 typical data representation for this type of assay.

25 Q. Okay. So for Sample D, for example, you

1 could have one lab where the results come in at 8500,
2 and what they're showing here is a different lab, lab
3 number 5, and the results come in at 17,500; is that
4 fair? Is that what's being shown?

5 A. Yes. You see the laboratory spread over
6 the different samples.

7 Q. So that's like about a two-fold difference
8 between those two laboratories; correct?

9 A. Correct.

10 Q. And, again, that has to do with, as we were
11 talking about with respect to your other article,
12 differences in procedure, like temperature, operators,
13 et cetera, in the labs; right?

14 A. This is also a study where -- it has to do
15 with a lot of different, yes, factors. That could be
16 the reason. I would not guess beyond that.

17 Q. Okay.

18 A. Which is why, for a large international
19 ring trial, you have statisticians, several
20 statisticians analyzing the results.

21 Q. Yeah.

22 On paragraph 51 of your declaration, after
23 looking at the data in Figure 1 and talking about the
24 Tokunaga reference in this ring study, you say, "Based
25 on this data, a POSA would have recognized that

1 recombinantly producing Factor C from Limulus polyphemus
2 exhibits unexpectedly superior results in the Claim 16
3 millimolar magnesium sulphate solution, as compared to
4 the closest prior art of Tachypleus Factor C in the same
5 claimed 16 millimolar magnesium sulphate solution"; do
6 you see that?

7 A. I do.

8 Q. So just to confirm, the data that you're
9 relying on here was produced in CHO cells, not HEK
10 cells; correct?

11 A. Correct.

12 Q. And you only have an opinion with respect
13 to the unexpectedly superior results on the magnesium
14 sulphate ion data; correct?

15 A. Correct.

16 MS. DOUKAS: Objection to form.

17 A. Yeah.

18 BY MS. LOUGHRAN:

19 Q. You don't believe that these two species of
20 Factor C demonstrated unexpectedly superior results as
21 to sodium citrate; right?

22 MS. DOUKAS: Objection to form.

23 BY MS. LOUGHRAN:

24 Q. Let me strike that.

25 As we've discussed, you have not opined --

1 A. I have not.

2 Q. -- that Limulus polyphemus expressed in CHO
3 cells demonstrates unexpectedly superior results
4 relative to Tachypleus expressed in CHO cells; correct?

5 A. Correct.

6 Q. And, in fact, your review of the data shows
7 that they are -- I know you don't want to use the word
8 equivalent --

9 A. No.

10 Q. -- but they are very similar; correct?

11 A. They are closer, yes.

12 Q. All right. So let's move on to the final
13 piece of data here, which is the data marked D19. So
14 how did you come about -- how did you come to consider
15 D19?

16 A. Would you explain?

17 Q. Yeah. Did you find this yourself or was it
18 provided to you by counsel?

19 A. It was provided to me by counsel.

20 Q. Did you locate or look for any other
21 instances of data showing the expression of Limulus
22 polyphemus Factor C in HEK cells as of 2019?

23 A. I did not do a literature or an -- beyond
24 what I have read in the peer reviewed literature, no.

25 Q. So there were no other Limulus polyphemus

1 data of expression of Factor C in HEK cells that
2 informed your conclusion here regarding unexpected
3 results; right?

4 A. Correct.

5 Q. Okay. So you reproduced the table that you
6 described, D19, at paragraphs 52 through 54. I will
7 also ask that you be handed the actual D19 reference,
8 which is Tab 6, Exhibit 2033, please.

9 (Exhibit 2033 was presented to the
10 witness.)

11 BY MS. LOUGHRAN:

12 Q. You've been handed a document that's marked
13 Exhibit 2033. It's titled "D19. A comparison of
14 Limulus polyphemus Factor C expressed with and without
15 terminal sialic acid glycosylation."

16 Is that the document you have in front of
17 you?

18 A. Yes.

19 Q. And did you review this document in
20 preparing your declaration?

21 A. Yes.

22 Q. Who carried out the experiments that
23 generated the data in D19?

24 A. I believe that the experiments were carried
25 out by scientists at Charles River Laboratories.

1 Q. And how do you come to believe that?

2 A. Based on the information I received from
3 counsel.

4 Q. Did counsel just tell you that, or what
5 information are you referring to?

6 MS. DOUKAS: Objection. I would caution
7 the witness not to reveal any attorney-client privilege.
8 But you can answer to the extent you don't delve into
9 privileged information.

10 A. Based on my knowledge, this is part of a --
11 of another patent proceeding.

12 BY MS. LOUGHRAN:

13 Q. Okay. A patent proceeding in Europe?

14 A. Yes, to my understanding.

15 Q. Okay. And is it -- does it say on the
16 document somewhere that this was created by scientists
17 at Charles River?

18 A. It does not.

19 Q. Did you see another document that indicated
20 that the D19 was created by scientists at Charles River?

21 A. I did not.

22 Q. Okay. So are you scientifically certain
23 that this document -- the data in this document was
24 created by scientists at Charles River?

25 MS. DOUKAS: Objection to form.

1 A. It didn't make any -- it did not make a
2 difference to me. I looked at the -- I looked at the
3 information just like I look -- I would look at any
4 other scientific information.

5 BY MS. LOUGHRAN:

6 Q. Okay. Well, let's assume that it was
7 created by the scientists at Charles River. That's a
8 different laboratory than Dr. Mizumura's laboratory;
9 correct?

10 A. It is, yes.

11 Q. And so the fact that this data was created
12 in a different laboratory could have an impact on the
13 results and the measurements of endotoxin detection as
14 between the two experiments; right?

15 MS. DOUKAS: Objection to form.

16 A. It could.

17 BY MS. LOUGHRAN:

18 Q. Do you know where, geographically, the
19 experiments were conducted that led to this data?

20 A. No.

21 Q. Do you know what dates the experiments were
22 conducted that led to this date?

23 A. No.

24 Q. Do you know anything about the
25 qualifications of the scientists who conducted the tests

1 that led to this data?

2 A. No.

3 Q. Did you speak with anybody who you know
4 were the individuals who created this data?

5 A. No.

6 Q. Okay. Did you get any other information or
7 details about the experiments that gave rise to this
8 summary, other than what's in the summary itself?

9 A. No.

10 Q. Now, in your professional capacity, I
11 believe you are the executive director of the American
12 Association of Pharmaceutical Scientists. Would you
13 just accept the results of a document like this without
14 any indication of an author or credentials or
15 affiliation or laboratory location?

16 MS. DOUKAS: Objection to form.

17 A. It always depends on the context of what
18 a -- I -- this type of data review has nothing to do
19 with my current role, honestly. So...

20 BY MS. LOUGHRAN:

21 Q. Okay. Well, did you question the
22 reliability of this data at all in view of the fact that
23 you have no information about who did it or where it was
24 done or when?

25 A. I always would question the context of data

1 as -- yes, you look at a piece of data and you always
2 have those questions, yes. There's always caveats.

3 Q. Relatively speaking, would this data be
4 less reliable than the data that you looked at directly
5 from Mizumura?

6 MS. DOUKAS: Objection to form.

7 A. There are -- there's a totally different
8 data context for both of them; right? I -- because of
9 the -- naturally, I have more data context for the
10 Mizumura data.

11 BY MS. LOUGHRAN:

12 Q. And would that additional data context lead
13 you to believe that the results are more reliable than
14 those in this document?

15 A. Experience and data history always plays a
16 role.

17 Q. So your answer is yes?

18 A. Yes. A qualified yes, yeah.

19 Q. Did you ask anyone for more information
20 about the data in D19 before you did your analysis?

21 A. A scientist always asks for more
22 information.

23 Q. So you did ask?

24 A. I -- I evaluated this information and I --

25 Q. And gave it the appropriate weight?

1 A. Sorry.

2 Q. Did you give it the appropriate weight in
3 view of not having that information?

4 A. I evaluated the data in its -- yes, in its
5 existing context.

6 Q. Okay. So for purposes of the experiments
7 that were conducted in D19, you agree that many of the
8 conditions that were used to generate the results in D19
9 were different from those that Dr. Mizumura used in
10 generating the data in Figure 7; right?

11 A. I agree.

12 Q. Okay. So, for example -- well, for
13 example, they use different substrates; correct?

14 A. Yes.

15 Q. Okay. And use of different substrates
16 could have an impact on the resulting functional values
17 of the proteins; right?

18 A. Not if appropriately controlled in the
19 assay.

20 Q. And is there anything in D19 that discusses
21 whether the comparatively different substrates between
22 the experiments done by the authors of D19 and
23 Dr. Mizumura in creating Figure 7 were experimentally
24 controlled?

25 A. No. I would --

1 Q. So the -- well, go ahead.

2 A. No. Go ahead.

3 Q. So the difference in substrate could impact
4 the resulting difference in function; right?

5 A. It could.

6 Q. Do we know what the temperature was that
7 was used for carrying out the experiments in D19?

8 A. Temperature is not indicated.

9 Q. Okay. So it could have been different than
10 the temperature Dr. Mizumura used, which was also not
11 indicated by him; right?

12 A. Yes.

13 Q. Okay. Do we know what variant sequence of
14 *Limulus polyphemus* was used for the experiment in D19?

15 A. No.

16 Q. Okay. It could have been a different
17 *Limulus polyphemus* variant than the one Dr. Mizumura
18 used in creating his -- his data shown in Figure 1 of
19 his declaration; right?

20 A. Could have been.

21 Q. What was the molecular weight of *Limulus*
22 Factor C reported in D19?

23 A. That's captured in Figure 1.

24 Q. Uh-huh.

25 A. Again, I -- it's based on a -- let me see

1 if this is -- it's a western blot, so it's both
2 molecular weight and antibody identification.

3 Q. So can we tell what the molecular weight is
4 from the information provided in D19?

5 A. Only approximate for this type of assay.

6 Q. Okay. So, approximately, what is the
7 weight?

8 A. It's around 100 kilodalton, based on this
9 figure.

10 Q. Okay. And that is different than the
11 molecular weight -- that is different than the molecular
12 weight that is discussed in the Mizumura publication;
13 right?

14 A. Based on that gel, yes. I will add that
15 anybody who has been trained and run their own fair
16 share of SDS page gels can tell you that unless you run
17 these proteins side by side in the same gel, you should
18 never make that kind of conclusion from two separate
19 experiments, because a skilled biochemist can make it
20 look like almost any molecular weight you want.

21 Q. Okay. Fair enough. So we don't have
22 appropriate data on the molecular weight for which to
23 make a comparison between these two datasets; right?

24 A. No. That would be completely
25 inappropriate.

1 Q. Okay. So we can't say that the molecular
2 weights were similar; right?

3 A. Right.

4 Q. And differences in molecular weight could
5 have impacts on resulting protein function; right?

6 A. Potentially.

7 Q. What concentration for Limulus Factor C
8 expressed in HEK cells in D19 was used?

9 A. The description does not indicate microgram
10 amounts for the proteins.

11 Q. So we don't know what concentration was
12 used; right?

13 A. The endotoxin concentration, the -- are the
14 same. The -- the paper indicates just common mixtures
15 of functional -- no. No, we don't.

16 Q. Now, again, if there were differences in
17 concentrations used in the experiments in D19, those
18 could be a factor in the difference in function; right?

19 MS. DOUKAS: Objection to form.

20 A. Again, this being a -- this being the same
21 type of assay as we discussed previously, a relative
22 activity assay, the assumption is that the colleagues
23 who ran this assay would calibrate -- and there's a
24 mention of a standard curve -- calibrate the assay into
25 the range where they can achieve comparable results.

1 And that is from an approach -- from a
2 scientific approach point of view, is the same. While
3 we don't know the actual numbers, it's -- the assay is
4 calibrated via a standard curve with the reagents to be
5 in a -- in an acceptable range based on the validity
6 criteria for the assay.

7 BY MS. LOUGHRAN:

8 Q. Okay. But when we were looking at
9 Mizumura's data, I think you pointed to Figure 6 as
10 being sort of a calibration where he was producing in --
11 he was producing Factor C in insect cells and CHO cells
12 and HEK cells, all at different concentrations. But my
13 understanding is, you know, he sort of figured out that
14 at these different concentrations, those Factor Cs were
15 giving somewhat similar activity as the native; right?
16 That was his calibration internally with respect to that
17 experiment; right?

18 A. Not quite like that. And you basically --
19 I don't think that's -- that's correct, that way.

20 Q. Okay.

21 A. We have no way of knowing what the
22 scientists for the D19 data did. But the fact that
23 they -- the comparison, when you look at the Figure 4 in
24 there, in my declaration, the -- my scientific
25 assumption was that they used the same approach to

1 calibrate the activity into a comparable range.

2 Q. Okay. But is there anything in D19 that
3 suggests that the people who were carrying this out were
4 trying to make a comparison between this and Mizumura?

5 A. No. No. This --

6 Q. Okay.

7 A. The data was created for a different
8 purpose. Let's be clear about that; right?

9 Q. Right. So there's nothing to suggest that
10 the scientists who created D19 were trying to make their
11 experiment give data that's comparable to what
12 Dr. Mizumura did in creating his data in his
13 declaration; right?

14 A. But we are talking about a particular type
15 of assay for which -- whether written down in the
16 description or not, I would say accepted approaches
17 exist. And those approaches, how you calibrate, how you
18 do a standard curve, how you -- how you get results
19 within that dataset that means something, those are
20 accepted for a type of assay.

21 We're still talking about the same type of
22 assay. We are talking about different assay settings,
23 different operators, but we're still talking about the
24 same type of relative activity assay.

25 Q. Okay. So you're assuming that the

1 scientists for -- that created the data for D19
2 calibrated their data in some way that was similar to
3 Mizumura's data, just by virtue of them being the same
4 type of endotoxin detection assay?

5 A. Yes. Because, ultimately, again, I'm
6 bringing it back to what all these assays do and how
7 they are used and how, in the end, the results of these
8 assays have to be used, which is they have to pass the
9 compendial or the regulatory bar. And once they do
10 that, the assay validity criteria around these assays
11 are very well established.

12 And so the assumption -- I think the
13 educated assumption that's underlying here is that an
14 assay developer or an assay reagent developer, who
15 ultimately has the goal to have assay reagents that are
16 used in a regulatory or compendial context, would apply
17 the principles that are required for that type of assay
18 to pass that -- those validity criteria as they develop
19 the assay. Otherwise, there wouldn't be scientific or
20 business sense in doing that, quite frankly.

21 Q. Okay. And I appreciate that that's the
22 assumption that you're working on. But you acknowledge
23 that that assumption is not necessarily true. There's
24 nothing in this document that says that's true?

25 A. That's correct.

1 Q. So it could be that these scientists used
2 different concentrations; right?

3 A. Yes.

4 Q. Okay. Second, in the WHO documents that we
5 just looked at, all of those laboratories were using
6 what you have suggested or what you had called, you
7 know, sort of regulatory or compendial context; right?

8 A. Yeah.

9 Q. And even in that study, you saw that at
10 least two laboratories got at least two full different
11 results in their endotoxin detection studies; right?

12 A. There's always laboratories -- there's
13 always test results that fall outside of range.

14 Q. Okay. And so it is possible that these
15 results in D19 fall outside of a range, or are different
16 than the results shown by Mizumura for reasons other
17 than the fact that the scientists in D19 were expressing
18 Limulus and HEK cells; right?

19 MS. DOUKAS: Objection to form.

20 A. It's possible.

21 BY MS. LOUGHRAN:

22 Q. Do we know how the scientists who created
23 D19 expressed Factors B and pro-clotting enzyme?

24 A. I do not believe we do.

25 Q. And in D19, the scientists actually say --

1 so on the first page under "Methods," scientists say
 2 that they -- under "Preparation of Limulus Factor C,"
 3 that "expressed Factor C from both lines were collected
 4 from the medium and concentrated by tangential flow
 5 filtration for use in all experiments"; do you see that?

6 A. Yes.

7 Q. Okay. Dr. Mizumura, when he described his
 8 experiments, he didn't say anything about using -- about
 9 concentrating the protein by tangential flow filtration;
 10 right?

11 A. He did a concentrated -- they filtrated,
 12 they just used a different filtration method. They used
 13 a 20-micron filter consistently in all the experiments.

14 Q. Right. Which was not used by the
 15 scientists in D19; right?

16 A. Right. Same purpose, though.

17 Q. And we don't know what the concentrations
 18 of Factor B or pro-clotting enzyme were used by the
 19 scientists to generate the data in D19; right?

20 A. No.

21 Q. Okay. Can you rule out that differences in
 22 concentration of Factors B or pro-clotting enzyme would
 23 impact the resulting residual activities?

24 MS. DOUKAS: Objection to form.

25 A. I can't rule it out.

1 BY MS. LOUGHRAN:

2 Q. And how did they actually measure residual
3 activity in the data that -- that was reported in D19?

4 A. Are you asking which substrates they used?

5 Q. Well, is it the same? I mean, they talk
6 about residual activity being calculated by dividing the
7 average absorbance change measured in the salt solution
8 versus absorbance change --

9 A. Yeah, that's the same.

10 Q. It is the same combination as --

11 A. Same control, yes.

12 Q. Okay. And --

13 A. And they used a -- yeah.

14 Q. Well, they talk about the reference
15 endotoxin without salts.

16 A. Yes.

17 Q. Is that the same as water?

18 A. Yeah. That's the standard way of doing it.
19 Also, they used the conditions in the compendial assay,
20 which is control against the standard in what is either
21 called water for injection or endotoxin-free water.

22 The positive control in that assay is
23 always -- so that the concentration is always 0.05
24 EU/mL. That's also in the compendial test. And the
25 salt-free control is always water for injection or

1 specifically specified endotoxin-free water.

2 Q. Uh-huh.

3 A. That's standard for this type of assay.

4 Q. Right. I'm just asking: In Mizumura, the
5 residual activity was calculated by using a measurement
6 specimen 0.5 EU/mL prepared by adding endotoxin to
7 injection water?

8 A. Yeah, that's water for injection.

9 Q. Yeah. And the D19 scientists say they used
10 0.05 EU/mL endotoxin without salt. Those two things are
11 different; yes?

12 A. Could be, but --

13 Q. Okay. And if different, that could also
14 impact the resulting residual activity measurements;
15 right?

16 A. Could.

17 Q. The HEK cells were also -- the expression
18 in HEK cells were also different; correct?

19 MS. DOUKAS: Objection to form.

20 A. Yes, they would have been different.

21 BY MS. LOUGHRAN:

22 Q. In D19, I believe they used Thermo Fisher
23 Freestyle 293 medium, which is different from the fetal
24 bovine serum that Mizumura used; correct?

25 A. Yes. Well, the Thermo Fisher is, I

1 believe, a proprietary medium.

2 Q. But the 10 percent fetal bovine serum would
3 have different proteins, et cetera, than the Thermo
4 Fisher Freestyle; correct?

5 A. Yes.

6 Q. And the elements of the media used to
7 generate the proteins could also impact the function;
8 correct?

9 A. Could.

10 Q. So just one other question before I get to
11 my final line.

12 When you look at the data, for example, in
13 Figure 1 or Figure 7, in your declaration that you
14 reproduced, you know, there's seven lanes. Are those
15 individual specimens that each contain the ions noted
16 and no other ion?

17 A. Are you asking if I know if there's nothing
18 else other in there other than the ion specified?

19 Q. Well, I guess what I'm asking is when you
20 look at, for example, lane 1, that is -- what they're
21 trying to show there is the activity of Factor C in
22 10 percent sodium chloride --

23 A. Yes.

24 Q. -- on its own; right?

25 A. Yeah.

1 Q. Okay. Is there any data -- did you see any
2 data that was -- that gave a result for what the
3 residual activity for Factor C would be in a sample that
4 contained both magnesium sulphate and sodium citrate?

5 A. From a context of use for this type of
6 assay, that would make absolutely no sense. The salt
7 solutions and the concentrations that are chosen by the
8 inventors were chosen, in my opinion, based on the
9 context of use of the assay.

10 Endotoxin testing is used to assure that
11 patients who get injectables do not have sepsis based on
12 endotoxin. The types of salt solutions are
13 representative, I believe, of the types of formulations
14 that are expected to be put into patients in the
15 marketplace.

16 So an assay developer for this type of
17 assay would choose salt solutions and salt combinations
18 that are encountered in the pharmaceutical marketplace.
19 So my educated guess and assumption was, when I saw the
20 choices of those ions and those combinations, that those
21 are a representative spectrum of the context of use for
22 this assay. Because, again, the ultimate goal for a
23 recombinant test like this is to be equivalent or better
24 to the compendial test.

25 So I would have not expected the inventor,

1 or anybody who designs an assay like this, to go out and
2 try all these different kinds of combinations of ions
3 just because they exist. But because -- these are based
4 on a deliberate assay design to challenge the reagents
5 in an anticipated context of use for the assay.

6 Q. And I appreciate that. I don't know what
7 the appropriate use of commercial concentrations would
8 be. All I'm asking is: Is there anything in the '318
9 patent, in Mizumura's patent, that discloses what a
10 residual activity would be for a -- in a solution that
11 contains both 21 millimolar sodium citrate and 16
12 millimolar magnesium sulphate.

13 Is there any data that shows what that
14 result would be?

15 A. I believe not.

16 Q. You did not see any; correct?

17 A. I do not recall.

18 Q. So just wrapping up on D19, we talked about
19 the difference in substrates, the unknowns related to
20 concentration, the difference in expression systems
21 between -- for HEK between the D19 data and Mizumura.

22 Those differences and those unknowns could
23 contribute to the differences that we see in the
24 resulting residual activities; correct?

25 A. Could, yes.

1 Q. Okay. Couldn't rule out that those
2 differences were contributing to the different residual
3 activities; right?

4 A. Yes. Could not.

5 MS. LOUGHRAN: Let's just take a break. I
6 think I'm pretty much done, but I just want to review my
7 notes and come back. Let's take a 10-minute break.
8 Come back at 3:45 and wrap up.

9 (A break was taken.)

10 BY MS. LOUGHRAN:

11 Q. Hello again, Dr. Morris. How are you?

12 A. I'm fine. How are you?

13 Q. Good. Thanks.

14 A couple final questions. I appreciate
15 your patience.

16 If you could just turn to your declaration
17 again, to paragraphs 49 and 50, and in these paragraphs,
18 you argue that the lysates derived from polyphemus and
19 Tachypleus have been consistently considered
20 functionally equivalent in terms of activities.

21 Do you see that at the bottom of page 18
22 and top of page 19?

23 A. Yes.

24 Q. Okay. And that's a statement you believe
25 to be true?

1 A. Based on the context that I provide around
2 the statement, yes.

3 Q. Okay. And then in paragraph 50, you said,
4 "A POSA would have expected this equivalence to carry
5 forward into the recombinant expression systems and not
6 find one species being unexpectedly superior over the
7 other"; do you see that?

8 A. Yes.

9 Q. Did you see any data or any results from
10 the inventors or anyone else that would contradict that
11 assertion that these two species of Factor C would be
12 functionally equivalent?

13 A. As we discussed earlier today, the results
14 with the -- that Dr. Mizumura found surprising, I found
15 surprising as well.

16 Q. Okay. Do you have an awareness that the
17 inventors actually had already demonstrated by 2019 that
18 recombinant Factor C from Limulus had a different and a
19 higher activity than recombinant Factor C from
20 Tachypleus?

21 MS. DOUKAS: Objection to form.

22 A. I believe we talked about -- I literally --
23 let me put this differently.

24 As we discussed, the CHO-based results that
25 are -- would indicate that as well. But I --

1 BY MS. LOUGHRAN:

2 Q. That the --

3 A. Go ahead.

4 Q. Go ahead. Sorry. Finish your statement,
5 of course.

6 A. As we discussed earlier, the CHO data in
7 Figure 7 and the HEK data, taken in totality, led me to
8 that conclusion of surprising results. That's what I
9 based my assessment on.

10 Q. Okay. But I'm asking, you know, you're
11 talking about what a POSA would have expected by 2019.
12 And I'm asking you: Were you aware that there was
13 already information out in the field that demonstrated
14 the recombinant Limulus did not have functional
15 equivalence with Tachypleus, recombinant Tachypleus,
16 such that a POSA would not find the results of the D19
17 or Mizumura's Figure 1 to be surprising?

18 MS. DOUKAS: Objection.

19 BY MS. LOUGHRAN:

20 Q. Are you aware of that?

21 MS. DOUKAS: Objection to form.

22 A. I was not.

23 BY MS. LOUGHRAN:

24 Q. Okay. Could I just direct you to one more
25 document, please? Could we hand Dr. Morris

1 Exhibit 1005? It's tab 13. And this has been marked
2 Charles River Labs Exhibit 1005. It is the 498 PCT from
3 Inventor Mizumura.

4 Do you have that in front of you, Doctor?

5 A. I do.

6 (Charles River Laboratories Exhibit 1005
7 was presented to the witness.)

8 BY MS. LOUGHRAN:

9 Q. Okay. Do you have an awareness of what
10 this document is?

11 A. I'm looking at it right now. I understand
12 what the document is, in looking for it --

13 Q. Okay. So this is the document in which the
14 inventors disclose the Limulus sequence. So when
15 Dr. Mizumura talks about using the Limulus sequence to
16 express Factor C in CHO cells and he cites to a
17 document, it is the related case to this PCT; do you
18 understand that?

19 MS. DOUKAS: Objection to form and
20 objection as outside the scope.

21 BY MS. LOUGHRAN:

22 Q. You reviewed Dr. Jain's declaration; right?

23 A. I did.

24 Q. And he talked about this 498 PCT at length;
25 right?

1 A. Yes. But I did not review it.

2 Q. Do you see that on the top of this
3 document, on basically the third page, there's an
4 international publication date? I think you have to go
5 back a couple more. It's like the third physical page,
6 not --

7 A. Oh, okay.

8 Q. Yeah, there at the top.

9 A. Yeah.

10 Q. It says "43 International Publication Date
11 April 26th, 2018"; do you see that?

12 A. Okay. Yes, I do.

13 Q. All right. So this was published by 2018,
14 which is before the 2019 date that you were looking at;
15 okay?

16 A. Uh-huh.

17 Q. All right. If you turn to page 44 of this
18 document -- and you can look at the page numbers at the
19 top.

20 A. Yeah.

21 Q. Paragraph 186 has a heading, "Activity
22 Comparison With Recombinant Factor C From Tachypleus";
23 do you see that?

24 A. I do.

25 Q. It says, "The activity of recombinant

1 Factor C herein referred to as L. Factor C derived from
2 Limulus polyphemus, was compared with that of
3 recombinant Factor C, hereinafter referred to as TFC,
4 derived from the genus Tachypleus"; do you see that?

5 MS. DOUKAS: I'm going to object as outside
6 the scope and have a standing objection. But objection
7 as outside the scope.

8 BY MS. LOUGHRAN:

9 Q. Okay. You can answer. Is that a fair
10 characterization of what this document says?

11 A. I have not looked at this document in a
12 while, so I -- but --

13 Q. Did I read it correctly?

14 A. You read back correctly what is in 0186,
15 yes.

16 Q. Okay. And if you'll look at paragraph 191,
17 which is on page 45 --

18 A. Yeah.

19 Q. Okay. It provides some results. And in
20 the second sentence, they say, "In this system," and
21 this is Mizumura himself, "LFC showed approximately 1.6
22 times the activity of TFC, approximately 2.2 times when
23 the difference in protein amount mentioned above is
24 taken into consideration"; do you see that?

25 A. I do.

1 MS. DOUKAS: Same objection, outside the
2 scope.

3 BY MS. LOUGHRAN:

4 Q. My question to you is a person of skill in
5 the art would have known of this data; right?

6 MS. DOUKAS: Objection, outside the scope.

7 A. Not necessarily.

8 BY MS. LOUGHRAN:

9 Q. Why not necessarily?

10 A. Because a person skilled in the art and
11 working in this area would still not be looking at, you
12 know, international patent documents on a daily basis
13 and looking for specification in their spare time.

14 Q. Okay. But we sort of suspend -- that may
15 be practically true. We sort of suspend the
16 practicalities of that, and it is sort of understood
17 that a person with skill in the art is aware of all of
18 the relevant prior art, of which international patent
19 publications are included.

20 So I'm just asking: By 2019, this was
21 publicly available. A person with skill in the art
22 could have picked this up and read the difference in
23 activity of 1.6 times difference in activity between
24 Limulus recombinant Factor C and Tachyplesus recombinant
25 Factor C; right?

1 A. They could have. But, again, I'm bringing
2 this back to the context of the scientific reality and
3 use of these assays, which is typically in a, you
4 know -- in a pharmaceutical regulated environment. And
5 until an assay -- a new assay reagent is actively tested
6 in the field, published, you know, it takes a while for
7 the -- and presented at meetings and conferences, it
8 takes a while for these things to get into the
9 scientific community discussion.

10 Q. Okay. But, again, this is the inventor,
11 Mizumura himself, providing this data showing that
12 Limulus polyphemus recombinant Factor C has a 1.6 times
13 activity --

14 A. Understood.

15 Q. -- compared to Tachypleus.

16 So my question is: If a person with skill
17 in the art saw that, read that, which we presume that
18 they would have, wouldn't they have found the results of
19 Figure 1 in D19 to be consistent with and not surprising
20 in view of Dr. Mizumura's data here in the 498 PCT?

21 MS. DOUKAS: Objection to form, objection
22 as outside the scope.

23 BY MS. LOUGHRAN:

24 Q. They could; correct?

25 MS. DOUKAS: Same objections.

1 A. I don't -- I don't know if they could. I
2 don't -- I'm not -- no, I would say not necessarily.

3 BY MS. LOUGHRAN:

4 Q. Okay. Would you agree that this data, this
5 activity data demonstrating that Limulus recombinant
6 Factor C has a 1.6 times activity of Tachypleus Factor
7 C, recombinant Factor C, as consistent with the data
8 that is shown in D19 and in Dr. Mizumura's Figure 1?

9 MS. DOUKAS: Objection to form, objection
10 as outside the scope.

11 A. I would still want to see additional
12 information.

13 BY MS. LOUGHRAN:

14 Q. It demonstrates that there is a difference,
15 however; correct?

16 MS. DOUKAS: Objection to form and
17 objection as outside the scope.

18 A. It points in that direction.

19 BY MS. LOUGHRAN:

20 Q. Okay.

21 A. That's all I --

22 MS. LOUGHRAN: Okay. I have no other
23 questions for you, Doctor. Thank you.

24 MS. DOUKAS: I have a few questions on
25 redirect.

1 EXAMINATION

2 QUESTIONS BY MS. DOUKAS:

3 Q. Dr. Morris, if you could pull up again the
4 file history, it's Exhibit 1004, and Mizumura's
5 declaration that we were talking about.

6 A. Yes.

7 Q. It would be page 82 of the file history
8 documents, the larger one.

9 A. This one?

10 Q. Yes.

11 A. Okay.

12 Q. I just want to direct your attention to
13 page 82 of Exhibit 1004, which is a part of
14 Dr. Mizumura's declaration.

15 A. Hold on. I have a lot of documents open
16 here. I have 83. I know we were just there.

17 Q. If you have 83, it should be on the back of
18 it.

19 A. There we go.

20 Q. So you're looking at page 84 of
21 Exhibit 1004?

22 A. Yes, I am.

23 Q. Do you recall counsel asking you questions
24 about the testing protocols used in Dr. Mizumura's
25 declaration to generate Figure 1 in his declaration?

1 A. I do.

2 Q. Okay. And do you recall counsel asking you
3 whether Dr. Mizumura states in his declaration how
4 Factor B and pro-clotting enzyme were expressed?

5 A. Yes, I believe so.

6 Q. Okay. So if you just look at that page 84
7 of Exhibit 1004, and at the bottom, there is -- I lost
8 my place. It says -- the last paragraph, full paragraph
9 at the bottom.

10 A. Uh-huh.

11 Q. "The above L. polyphemus Factor Cs were
12 used for endotoxin assay in the presence of salts. The
13 assay was conducted under the same condition and
14 materials in Figure 7 and paragraphs 134 to 136 of the
15 specification as filed, except that L. polyphemus Factor
16 Cs were used instead of T. tridentatus Factor Cs"; do
17 you see that?

18 A. I do.

19 Q. So in that paragraph, Dr. Mizumura
20 identified where he made a change in the conditions and
21 materials and stated he used a different Factor C; is
22 that correct?

23 A. That is correct.

24 Q. And in that paragraph, he doesn't say
25 anything about making a change to the Factor B or the

1 pro-clotting enzyme expression that was used in this
2 testing, does he?

3 A. He doesn't.

4 MS. LOUGHRAN: Objection, leading.

5 BY MS. DOUKAS:

6 Q. Does he identify any other changes in this
7 paragraph, besides changing Factor C?

8 A. No.

9 Q. And if you could just go now to your
10 declaration, please, and it's Exhibit 2042. And if
11 you'd turn to paragraph 51 of your declaration, please.

12 A. Yes.

13 Q. Do you recall counsel asking you about your
14 opinion as you have it stated in paragraph 51 of your
15 declaration?

16 A. Yes.

17 Q. Are you withdrawing your opinion, as you've
18 stated it in paragraph 51 of your declaration?

19 A. No.

20 Q. Are you withdrawing any of your opinions
21 stated in your declaration?

22 A. No.

23 MS. DOUKAS: That's all I have.

24 MS. LOUGHRAN: No further questions for me.

25 Thank you.

1 (The deposition concluded at 4:04.)

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