UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Merck Sharp & Dohme LLC,
Petitioner,

v.

Halozyme, Inc.
Patent Owner.

Case PGR2025-00003
U.S. Patent No. 11,952,600

Case PGR2025-00004
U.S. Patent No. 12,018,298

Case PGR2025-00006
U.S. Patent No. 12,152,262

Case PGR2025-00009
U.S. Patent No. 12,123,035

VIDEO DEPOSITION OF GARY N. CHERR, Ph.D.,
San Francisco, California

Wednesday, November 12, 2025

STENOGRAPHICALLY REPORTED BY:
REBECCA L. ROMANO, RPR, CSR, CCR
California CSR No. 12546
Nevada CCR No. 827
Oregon CSR No. 20-0466
Washington CCR No. 3491

JOB NO. 7005263-001

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Case PGR2025-00009
16 U.S. Patent No. 12,123,035

17 _____

18 VIDEO DEPOSITION OF GARY N. CHERR, Ph.D.,

19 taken on behalf of the Petitioner, at Quinn Emanuel

20 Urquhart & Sullivan, LLP, 50 California Street,

21 22nd Floor, San Francisco, California, commencing

22 at 9:03 a.m., Wednesday, November 12, 2025 before

23 REBECCA L. ROMANO, a Registered Professional

24 Reporter, Certified Shorthand Reporter, Certified

25 Court Reporter.

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20 Inc.(via Web videoconference)
21 Josh Mack, Executive Director, Patent
22 Litigation Counsel at Halozyme, Inc.
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24
25 ///// U.S. Legal Support | www.uslegalsupport.com 5

1 I N D E X

2 DEPONENT EXAMINATION

3 GARY N. CHERR, PH.D. PAGE

4

5 BY MS. WANG 10

6

7 E X H I B I T S

8 (Exhibits Premarked)

9 NUMBER PAGE

10 Exhibit 1019

11 Exhibit 1020

12 Exhibit 1026

13 Exhibit 1061

14 Exhibit 2072

15 Exhibit 2103

16

17

18 COURT REPORTER'S NOTE: All quotations

19 from exhibits are reflected in the manner in which

20 they were read into the record and do not

21 necessarily indicate an exact quote

22 from the document.

23

24

25 ///// U.S. Legal Support | www.uslegalsupport.com 6

1 San Francisco, California;
2 Wednesday, November 12, 2025
3 9:03 a.m.
4 ---o0o---
5
6 THE VIDEOGRAPHER: We are on the record
7 at 9:03 a.m. Pacific time on November 12th, 2025.
8 Audio and video recording will continue to take
9 place until all parties agree to go off the record.
10 Please note that microphones are
11 sensitive and may pick up whispering and private
12 conversations.
13 This is the video-recorded proceedings of
14 Gary N. Cherr, Ph.D., taken by counsel for
15 Plaintiff, Merck Sharp & Dohme LLC, v.
16 Halozyme Inc., filed before the Patent Trial and
17 Appeal Board.
18 This proceeding is being held at
19 Quinn Emanuel Urquhart & Sullivan, LLP, located at
20 50 California Street, 22nd Floor,
21 San Francisco, California 94111.
22 My name is Zachariah Fuson. I am the
23 videographer on behalf of U.S. Legal Support,
24 located at 16825 North Chase Drive, Suite 900,
25 Houston, Texas 77060. I am not related to any

1 party in this action, nor am I financially
2 interested in the outcome.
3 The court reporter today is
4 Rebecca Romano on behalf of U.S. Legal Support.
5 Counsel will state their appearances for
6 the record, after which the court reporter will
7 enter the statement for remote proceedings into the
8 record and swear in the witness.
9 MS. WANG: Good morning.
10 My name is Sue Wang. Also with me is
11 Chelsea Himes. We are both from the Sidley Austin
12 firm, here for Petitioner Merck Sharp & Dohme.
13 I believe we also have in remote
14 attendance Mr. Jeff Kushan, also from the Sidley
15 firm, as well as Brian Goldberg from the Dechert
16 firm, both also for Petitioner.
17 MR. POWERS: Good morning.
18 My name is Ralph Powers, III, from
19 Sterne Kessler Goldstein & Fox, on behalf of Patent
20 Owner Halozyme Inc.
21 Also in the room for Halozyme we have
22 Nancy Zhang from Quinn Emanuel and Josh Mack from
23 Halozyme.
24 Attending on the line for Halozyme are
25 Eldora Ellison from Sterne Kessler,

1 Pratibha Khanduri from Sterne Kessler, and
2 Aubrey Haddach from Halozyme.
3 THE COURT REPORTER: My name is
4 Rebecca Romano. I am a California-licensed
5 Stenographic Court Reporter, No. 12546. I will be
6 producing a transcript that is automatically
7 admissible in court.
8 If you could raise your right hand for
9 me, please.
10 THE DEPONENT: (Complies.)
11 THE COURT REPORTER: You do solemnly
12 state, under penalty of perjury, that the testimony
13 you are about to give in this deposition shall be
14 the truth, the whole truth and nothing but the
15 truth?
16 THE DEPONENT: I do.
17
18
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25

GARY N. CHERR, Ph.D.,
having been administered an oath, was examined and testified as follows:

EXAMINATION

BY MS. WANG:

Q. Good morning.

Can you please state your full name for the record.

A. Yes, Gary Neil Cherr.

Q. Have you been deposed before, Dr. Cherr?

A. Yes, I have.

Q. How many times?

A. Twice.

Q. Were both in connection with patent proceedings?

A. No, not related at all.

Q. So you've never been deposed before in connection with a patent proceeding?

A. No.

Q. I'll go over a few ground rules for this deposition.

So the first one is that we shouldn't talk over one another. That allows the court reporter to create a clear record.

If you don't understand one of my

1 questions, please ask me to clarify. Otherwise, I
2 will assume that you understand it when you answer;
3 is that fair?
4 A. Yes.
5 Q. Okay. I'll try to take a break every
6 hour or so, but definitely, if you need a break,
7 please let me know.
8 A. I will.
9 Q. The only time we can't take a break if
10 there's -- is if there's a question pending.
11 And in this deposition format, you have
12 to answer my questions unless counsel instructs you
13 not to answer.
14 Do you understand that?
15 A. Yes.
16 Q. Do you understand you're here having your
17 deposition taken regarding declarations that you
18 submitted in four post-grant review proceedings?
19 A. Yes, I do.
20 Q. Okay. And those four post-grant review
21 proceedings are PGR2025-00003, -00004, -00006 and
22 -00009.
23 A. Yes.
24 Q. Do you understand that?
25 Okay. I see you have binder in front of

you. What is that that you have in front of you?
A. This is the -- the four declarations put together.
That's all.
Q. Okay. So it's your four declarations in the four PGR proceedings?
A. Yes, correct.
Q. And each of them is marked Exhibit 2072?
A. Yes, that's correct.
Q. Thank you.
And what, if anything, did you do to prepare for today's deposition?
A. Primarily, review my -- my declaration and -- and all the references that were in my declaration. And then I had some preparation with the attorneys that are in the room.
Q. And that would be Mr. Powers, Ms. Zhang and Mr. Mack?
A. Yes, correct.
Q. Did you meet with anyone else besides the attorneys in the room?
A. No, there -- well, with several people remotely. But in person, just these three.
Q. And who did you meet with remotely?
A. Lauren Martin and Fraser -- pronouncing

1 her last name -- Khandu -- sorry.
2 MR. POWERS: "Khanduri."
3 THE DEPONENT: Yeah.
4 Q. (By Ms. Wang) And approximately how long
5 did you meet with all of the attorneys?
6 A. For probably about six hours total.
7 Q. And when was that?
8 A. Over -- over two days, yeah.
9 Q. Which two days?
10 A. Monday and Tuesday of this week.
11 Q. And besides your declaration and the
12 references cited in your declaration, did you
13 review anything else?
14 A. Not -- not for today. I was primarily
15 focused on that.
16 And I did review Dr. Moon's -- or where
17 I -- which is a citation in my declaration. But
18 Dr. Moon's declaration, one portion of it.
19 Q. Did you review any of the references
20 cited in the portion of Dr. Moon's declaration that
21 you reviewed?
22 A. No, I did not.
23 Q. And let me make sure I have that -- ask a
24 better question.
25 Before today's deposition, had you

1 reviewed any of the exhibits cited in Dr. Moon's
2 declaration?
3 A. Well, I did, because some of them were
4 ones that I also cited in my declaration.
5 Q. Did you review any exhibits cited in
6 Dr. Moon's declaration that were not the ones cited
7 in your declaration?
8 A. No, I did not.
9 Q. When were you retained for this matter?
10 A. Let's see, I guess it would have been in
11 2023, which would have been, I believe,
12 January 2023.
13 Q. And approximately how long did it take
14 for you to prepare your declarations?
15 A. Altogether, probably three months.
16 Q. Is that three months of daily work?
17 A. Well, not daily work, but yes, three --
18 three months' time. But it was over an extended
19 period because of a lot of literature review,
20 et cetera.
21 Q. Do you have a rough estimate of how many
22 hours you spent?
23 A. Probably about -- I want to say about
24 36 hours, 40 hours, roughly.
25 Q. And did you write your declaration

1 yourself?
2 A. It was a collaborative effort with
3 counsel. But the science -- the substance of it
4 was mine.
5 Q. And did you type it yourself?
6 A. Yes.
7 Q. Okay. So I'd like you to turn to the --
8 your declaration in the -003 proceeding.
9 A. Okay.
10 Q. That's Exhibit 2072.
11 And in paragraph 3 of your declaration --
12 A. Yes.
13 Q. Are you there?
14 You understand you submitted this
15 declaration in a post-grant review proceeding
16 involving U.S. Patent No. 11,952,600?
17 A. Yes.
18 Q. Is it okay if I call it the '600 patent?
19 And I just want to confirm, the
20 '600 patent is not listed in your exhibits
21 referenced, correct?
22 A. No, I did not review the patent.
23 Q. You did not review the '600 patent --
24 A. No.
25 Q. Was before you signed your declaration?

1 A. No, I did not.
2 Q. Have you reviewed it since?
3 A. No, I have not.
4 Q. Okay. So your opinion is not based on
5 any disclosure --
6 A. No.
7 Q. -- in the '600 patent?
8 And is it fair to say the same is true of
9 the other three patents involved in the other three
10 proceedings?
11 A. Correct.
12 Q. So your opinions in the other three
13 proceedings, also not based on what's disclosed in
14 those patents?
15 A. Correct.
16 Q. Did you review any materials not cited in
17 your declaration?
18 MR. POWERS: Objection. Form.
19 THE DEPONENT: I -- could you be a little
20 bit more clear on what you mean by "materials."
21 Q. (By Ms. Wang) Did you review any
22 literature other than what is cited in your
23 declaration?
24 MR. POWERS: Objection. Form.
25 THE DEPONENT: I did -- I did review

other papers that were relevant or potentially relevant to my opinion. But if it's not included -- it's really the important papers were the ones that I included in my declaration.

Q. (By Ms. Wang) So there are papers that you thought were potentially relevant that are not cited in your declaration?

A. I didn't know --

MR. POWERS: Objection -- just a second.

THE DEPONENT: Excuse me.

MR. POWERS: Let me interpose my objection.

Objection. Form.

THE DEPONENT: So at -- I did literature searching. So I didn't -- to determine which ones would be relevant and which ones wouldn't be.

Q. (By Ms. Wang) Are there papers that you determined to be relevant that are not cited in your declaration?

A. No.

Q. So I'm handing to you Exhibit 1026. It's --

MR. POWERS: Do you have a copy, please?

Thank you, Counsel.

Q. (By Ms. Wang) And I'm present to you

1 that Exhibit 1026 is U.S. Application No. 13/694731
2 filed December 28th, 2012.
3 A. Okay.
4 Q. Have you seen Exhibit 1026 before today?
5 A. No, I have not.
6 Q. So you didn't review it in connection
7 with your declaration or --
8 A. Well, of course --
9 Q. Let me restate.
10 You did not review this exhibit in
11 connection with preparing your declaration?
12 A. Well, I can't offer a complete opinion
13 because I would have to look through this. I don't
14 know if there's sections -- you handed me a very
15 large stack, so I don't know what's in here. But
16 I -- it doesn't look familiar.
17 Q. It doesn't look...
18 A. Yeah.
19 Q. And Exhibit 1026 is not listed as a
20 reference in your declaration?
21 A. Correct.
22 Q. Okay. Do you recall reviewing any patent
23 applications?
24 A. No.
25 MR. POWERS: Objection to form.

1 THE DEPONENT: No, I did not.
2 Q. (By Ms. Wang) You did not review any
3 patent applications in connection with preparing
4 your declaration?
5 A. I did not.
6 Q. So you have no opinion on whether there
7 are any differences between the patent applications
8 that led to the '600 patent?
9 MR. POWERS: Objection. Form.
10 THE DEPONENT: No, because I did not
11 review them, so I can't talk about the...
12 Q. (By Ms. Wang) So your opinion doesn't
13 depend on any differences between the patent
14 applications that led to the '600 application?
15 MR. POWERS: Objection. Form.
16 THE DEPONENT: That is correct.
17 Q. (By Ms. Wang) Did you review any patent
18 or patent applications after you signed your
19 declarations in these proceedings?
20 A. No.
21 MR. POWERS: Objection.
22 Okay.
23 Q. (By Ms. Wang) So for the rest of today,
24 I'm going to use your declaration in the -003
25 proceeding for the '600 patent.

1 If your answer to one of my questions
2 would be different for a different patent, please
3 let me know, and we can go over to that
4 declaration. Otherwise, I'm going to assume that
5 your answer is going to be the same in all four
6 proceedings.
7 Understood?
8 A. Yes, I understand.
9 Q. Dr. Cherr, were you instructed on any
10 legal principles in developing your opinion?
11 A. No, I was not.
12 Q. Do you understand for what purpose your
13 opinion is being offered?
14 A. I do.
15 Q. And what is that?
16 A. Well, it's to support, fairly narrow, the
17 idea that the PH20 polyamino acid sequences,
18 polypeptides, could be used for
19 immunocontraception.
20 Q. And do you know what purpose your opinion
21 is being offered in connection with the
22 '600 patent?
23 MR. POWERS: Objection. Form.
24 THE DEPONENT: I don't know the specifics
25 relating to the patent, no.

1 Q. (By Ms. Wang) You were not -- you were
2 not instructed on what is legally required for an
3 invention to be useful?
4 A. No, I was not.
5 Q. And you were not instructed on the legal
6 standard for utility?
7 A. No.
8 Q. I'd like you to turn to paragraph 12 of
9 your declaration.
10 A. Okay.
11 Q. It states, "I have been asked to consider
12 whether a person of ordinary skill in the art," or
13 a POSA, "would have expected any of the 'modified
14 PH20 polypeptides' to be useful as contraceptive
15 vaccines in female mammals."
16 Do you see that?
17 A. Yes, I see that.
18 Q. Where did this question come from?
19 A. I'm sorry, the question?
20 MR. POWERS: Object to form.
21 Q. (By Ms. Wang) Yes.
22 Where did this question that you were
23 asked to answer come from?
24 MR. POWERS: Same objection.
25 THE DEPONENT: It was provided by

1 counsel.
2 Q. (By Ms. Wang) So you did not formulate
3 the question?
4 A. No, I did not.
5 Q. The paragraph continues, "I have read
6 Dr. James J. Moon's declaration as presented by
7 counsel."
8 Do you see that?
9 A. Yes.
10 Q. What does "as presented by counsel" mean?
11 A. I was presented to me or it was given to
12 me to read by counsel.
13 Q. Were you given a signed declaration from
14 Dr. Moon?
15 A. Oh, his -- I received -- what was termed
16 a near-final declaration just prior to his
17 signature.
18 Q. And is that the only version of
19 Dr. Moon's declaration that you reviewed?
20 A. I -- I reviewed his signed version, which
21 was a few weeks later.
22 Q. Did you review any earlier versions
23 before the near-final version of the declaration?
24 A. No, I did not.
25 Q. Around when did you review -- let me

1 rephrase.
2 How long before you signed your
3 declaration was it before you reviewed Dr. Moon's
4 near-final declaration?
5 A. Just to -- yeah.
6 MR. POWERS: Objection. Form.
7 THE DEPONENT: Approximately one week.
8 Q. (By Ms. Wang) So you reviewed Dr. Moon's
9 near-final declaration approximately one week
10 before signing your own declaration?
11 A. Yes.
12 Q. Did you speak to Dr. Moon before signing
13 your declaration?
14 A. Never spoken with him.
15 Q. Did you speak to Dr. Gregory Petsko
16 before signing your declaration?
17 A. No.
18 Q. Did you speak to Dr. Melanie Simpson
19 before signing your declaration?
20 A. No.
21 Q. Did you speak to Dr. Barbara Triggs-Raine
22 before signing your declaration?
23 A. No.
24 Q. Did you review Dr. Petsko's declaration
25 at any point?

1 A. I did not.
2 Q. Did you review Dr. Simpson's declaration?
3 A. I did not.
4 Q. Did you review Dr. Triggs-Raine's
5 declaration?
6 A. No, I didn't.
7 Q. And have you spoken to any of them since
8 signing your declaration?
9 A. No.
10 Q. Have you reviewed any of their
11 declarations since signing yours?
12 A. No, I have not.
13 Q. Did you speak to any Halozyme employee
14 before signing your declaration?
15 A. No, I did not.
16 Q. Have you spoken to any Halozyme employee
17 after signing your declaration?
18 A. No, I have not.
19 Q. And I should ask you a better question,
20 because I understand Mr. Mack might be a Halozyme
21 employee.
22 A. Yeah, when you -- yeah.
23 Q. Yes.
24 Other than Halozyme's lawyers, have you
25 spoken to any Halozyme

1 A. No, I have not.
2 Q. Thank you.
3 (Discussion off the stenographic record.)
4 MR. POWERS: Yeah, please slow down.
5 Q. (By Ms. Wang) I'd like to direct your
6 attention to paragraph 30 of your declaration.
7 A. Yes.
8 Q. The paragraph 30 begins, "In light of
9 Dr. Moon's declaration, I have been asked to
10 opine..."
11 Do you see that?
12 A. Yes, I see that.
13 Q. And what do you mean by, "In light of
14 Dr. Moon's declaration"?
15 A. I mean that in -- in that context that
16 his expertise in -- as an immunologist in opining
17 on immune responses that -- and regarding his --
18 his words regarding modified PH20 polypeptides.
19 So I -- you know, I was asked,
20 essentially, to opine on what was in his
21 declaration within mine.
22 Q. You said in the context of Dr. Moon's
23 expertise as an immunologist in opining on immune
24 responses.
25 Do you have an independent opinion on

1 immune responses?
2 A. Yes, and -- and in my declaration, my --
3 the opinion I gave in terms of immune responses as
4 related to contraception were all my views.
5 Q. You also said, in regards to Dr. Moon,
6 you were opining on his words regarding modified
7 PH20 polypeptides.
8 Do I understand that correctly?
9 MR. POWERS: Object to form.
10 THE DEPONENT: So could you -- I'm sorry,
11 could you repeat the question.
12 Q. (By Ms. Wang) Sure, let me try to ask a
13 better question.
14 Does your opinion depend on something
15 Dr. Moon has opined on?
16 A. No, absolutely not.
17 Q. So your opinions are completely
18 independent of Dr. Moon's opinions?
19 A. Yes, correct.
20 Q. Okay. Do you have opinions on Dr. Moon's
21 opinions?
22 THE DEPONENT: I'm sorry, could you
23 repeat that.
24 Q. (By Ms. Wang) Sure.
25 Do you have opinions

1 A. Yes.
2 Q. -- on the opinions in Dr. Moon's
3 declaration?
4 MR. POWERS: Object to form.
5 THE DEPONENT: I -- don't -- yeah.
6 So I -- I don't have opinions on -- on
7 his opinions except there's a few areas that
8 independently we agree on. So in paragraph 30 of
9 your declaration, you would say, "I have been asked
10 to opine on whether, by December 28th, 2012 POSAs
11 would have expected any of the modified PH20
12 polypeptides (defined in paragraph 12) to be useful
13 as contraceptive vaccines in female mammals, such
14 as human, chimpanzee, Cynomolgus monkey, rhesus
15 monkey, marmoset, orangutan, gibbon, cow, mouse,
16 rat, rabbit, guinea pig, and red fox."
17 Do you see that?
18 A. Yes.
19 Q. So this opinion includes a list of
20 mammals.
21 Who gave you this --
22 MR. POWERS: Objection. Form.
23 Q. (By Ms. Wang) Who gave you list of
24 assorted female mammals?
25 A. That's -- that's that list of mammals

are -- are mammals are well known to -- where PH20 sequence and expression has been studied. So that's information that I was well aware of.

Q. So you generated this list?

A. Well, so I -- no, actually I did not generate the full list, but part of the list.

Q. And where did the rest of the list come from?

A. And --

MR. POWERS: Objection. Form.

THE DEPONENT: So that was -- as a collaborative effort with counsel in terms of the -- the other species added in.

Q. (By Ms. Wang) The other species added in came from counsel?

A. Yes.

Q. Do you recall which species came from counsel?

A. I'm -- I believe it was marmoset and red fox.

Q. Any others?

MR. POWERS: Object to form.

THE DEPONENT: No. I think that's it.

Q. (By Ms. Wang) So Dr. Cherr, is it your opinion that all of the modified PH20 polypeptides

would display multiple epitopes to the host immune system and stimulate anti-PH20 polyclonal antibodies against these different epitopes?

A. Yes, it is.

Q. It's your opinion that all of the modified PH20 polypeptides would do so?

A. Yes.

Q. Is it your opinion that the polyclonal antibodies generated against any of the modified PH20 polypeptides would bind to the PH20 polypeptide of sperm in the reproductive tract of the female mammal?

A. Yes, if antibodies were of sufficient titer in the reproductive tract.

Q. Any of the PH20 polypeptide would cause polyclonal antibodies, any of those polyclonal antibodies would cause reproduction?

MR. POWERS: Objection. Form.

Q. (By Ms. Wang) Would cause contraception?

MR. POWERS: Same objection.

THE DEPONENT: So -- yeah. So -- could you ask that one more time.

Q. (By Ms. Wang) Sure. It's your opinion that any of the modified PH20 polypeptides would cause polyclonal antibodies that bind to PH20 on

1 sperm and that would then cause contraception?
2 MR. POWERS: Objection. Form.
3 THE DEPONENT: Could you -- that's a
4 pretty broad question. So are you -- because we
5 were just talking about all these different
6 species. Could you more specific about what
7 species you are referring to or -- or group of
8 species?
9 Q. (By Ms. Wang) Does the species matter?
10 A. It shouldn't matter, but I'm just trying
11 to understand -- I want to make sure I give you the
12 most accurate answer possible.
13 Q. I would like to direct your attention to
14 paragraph 32 of your declaration.
15 A. Okay.
16 Q. The last sentence you state, "Thus, POSAs
17 would have known that the binding of antibodies to
18 sperm PH20 polypeptide in the female reproductive
19 tract would cause contraception irrespective where
20 the antibodies bind on the PH20 polypeptides."
21 Do you see that?
22 A. Yes, I see that.
23 Q. And that statement is not qualified by
24 species.
25 Is it?

1 A. No, it is not.
2 Q. So your opinion would apply all female
3 mammals?
4 A. Yes, of the ones listed there, yes.
5 Q. Of the ones listed of paragraph 30 in
6 your declaration?
7 A. Yes, because -- because to say all
8 mammals regardless of the class, you know, or the
9 phylum or...
10 Yeah, I mean, I don't know. And it
11 hasn't been studied in all of them. So in that
12 list, yes.
13 Q. So your opinion is limited only to the
14 female mammals listed in paragraph 30 of your
15 declaration?
16 A. Yes.
17 Q. And you don't know if the female mammals
18 outside of those listed in paragraph 30 of your
19 declaration, if the PH20 would work as
20 contraception?
21 MR. POWERS: Objection. Scope.
22 THE DEPONENT: Yeah, I -- I -- I opined
23 on animal groups where PH20 had been identified in
24 the males in the sperm or in testes. So beyond
25 that, I would -- I wait to offer an opinion.

1 Q. (By Ms. Wang) Are there any species not
2 listed in paragraph 30 in which you believe PH20
3 would not work as a contraception?
4 MR. POWERS: Objection. Scope.
5 THE DEPONENT: I really -- I can't really
6 give you an opinion on that because it would -- it
7 would need to have -- I would need to have
8 information regarding expression of PH20 in the
9 males of those species, and it may not be
10 available, that -- that kind of scientific
11 information.
12 Q. (By Ms. Wang) And you did not
13 independently investigate other species to
14 determine if the PH20 would work as a
15 contraception?
16 MR. POWERS: Objection. Form.
17 THE DEPONENT: When you say --
18 MR. POWERS: Scope.
19 THE DEPONENT: -- "investigate other
20 species," if you could define that.
21 Q. (By Ms. Wang) You did not investigate
22 species outside of the list in paragraph 30 to
23 determine if additional -- if there are additional
24 species in which modified PH20 polypeptides would
25 work as contraception?

MR. POWERS: Objection. Form. Scope.
THE DEPONENT: No, I did not.
Q. (By Ms. Wang) So your opinion is that the binding of any antibodies to sperm PH20 polypeptide in the female reproductive tract would cause contraception, right?
MR. POWERS: Objection. Form.
THE DEPONENT: Sorry. One more time.
Q. (By Ms. Wang) Your opinion is that the binding of any antibodies to sperm PH20 polypeptide in the female reproductive tract would cause contraception --
MR. POWERS: Same objection.
Q. (By Ms. Wang) -- correct?
A. Yes, it has the potential to do that.
Q. Does the amount of antibodies that bind to sperm matter?
MR. POWERS: Objection. Form.
THE DEPONENT: Conceptually, yes. But quantitatively, I think that's unknown.
Q. (By Ms. Wang) So you don't know quantitatively how much antibody would have to bind to sperm PH20 in order to cause contraception?
MR. POWERS: Objection. Form.
THE DEPONENT: So are you -- are you

1 speaking in vivo, in the reproductive tract?
2 Q. (By Ms. Wang) Yes.
3 A. Yes, that's not known.
4 Q. Is it your opinion that all modified PH20
5 polypeptide would be effective as contraception
6 vaccines in female mammals?
7 MR. POWERS: Objection. Form.
8 THE DEPONENT: Yes.
9 Q. (By Ms. Wang) All of them would cause
10 contraception in female humans?
11 MR. POWERS: Objection. Form.
12 THE DEPONENT: They would if they were
13 administered in the proper way and elicited the
14 proper immune response.
15 Q. (By Ms. Wang) So just having modified
16 PH20 polypeptide is not sufficient?
17 MR. POWERS: Objection. Form.
18 THE DEPONENT: They would have to be
19 administered in an appropriate way so that there
20 would be mucosal response in the reproductive
21 tract.
22 Q. (By Ms. Wang) So in your opinion, you
23 need not only modified PH20 polypeptide, but also
24 an appropriate administration of it in order for
25 there to be contraception?

A. Yes, that's correct.
Q. You have only opined on whether the modified PH20 polypeptides would have been useful as contraception vaccines in female mammals, correct?
A. Yes, that is correct.
Q. The studies you cited demonstrating contraception from PH20 in guinea pigs was done in both male and female guinea pigs, correct?
A. Yes, that's correct.
Q. But you have no opinion on whether modified PH20 polypeptides would be effective contraception vaccine in male mammals?
A. I -- I did not opine on males in here because typically the response to immunization in males with PH20 polypeptides create pathogenic situation, and so there may be infertility, but may not be mechanistically related to what would occur in a female, and it maybe be certainly problematic for human use.
Q. Modified PH20 polypeptides would be problematic for human male use as a contraception?
MR. POWERS: Objection. Form. Scope.
MS. WANG: Counsel, scope is not a proper objection. Please keep your objections to scope --

1 MR. POWERS: I disagree, Counsel.
2 THE DEPONENT: Could you ask -- could you
3 ask it another way or ask it again?
4 Q. (By Ms. Wang) Modified PH20 polypeptides
5 would be problematic as a contraception vaccine for
6 human males?
7 MR. POWERS: Objection. Form. Scope.
8 MS. WANG: Again, Counsel, scope is not a
9 proper objection here.
10 MR. POWERS: I disagree, Counsel.
11 MS. WANG: Well, okay.
12 MR. POWERS: Go ahead.
13 MS. WANG: We take it --
14 MR. POWERS: I'm saying it one word or
15 term, just like in the trial practice.
16 MS. WANG: You are instructing -- you are
17 coaching your witness --
18 MR. POWERS: I am not.
19 MS. WANG: -- on -- it's not a proper
20 objection.
21 MR. POWERS: I disagree.
22 Q. (By Ms. Wang) Do you need me to repeat
23 the question?
24 A. Yes, please.
25 Q. Yes.

1 Modified PH20 polypeptides would be
2 problematic as a contraception vaccine for human
3 males?
4 MR. POWERS: Objection. Form. Scope.
5 THE DEPONENT: So that's a statement.
6 Are you -- is that a question you're
7 asking or...
8 Q. (By Ms. Wang) I'm asking you if that is
9 a correct statement --
10 A. Oh.
11 Q. -- of what you have told me.
12 A. Yes, it is.
13 Q. Would the POSA have expected PH20 -- let
14 me rephrase.
15 Would the POSA have expected modified
16 PH20 polypeptides to not be useful as contraceptive
17 vaccines in human males?
18 MS. WANG: Objection. Form. Scope.
19 THE DEPONENT: No, I think it would be
20 useful. But in human males, you would not want to
21 create a pathogenic situation.
22 Q. (By Ms. Wang) So the POSA would think it
23 would useful but also problematic in human males;
24 is that right?
25 MR. POWERS: Same objections.

1 THE DEPONENT: In humans, yes.
2 Q. (By Ms. Wang) And what is the pathogenic
3 issue you are referring to with respect to human
4 males?
5 MR. POWERS: Objection. Form. Scope.
6 THE DEPONENT: So in -- you referred to
7 the guinea pig males that were injected with PH20.
8 And there was epididymitis and orchitis in the
9 testes with massive inflammation. And that was
10 what was deemed to be responsible for the
11 contraceptive effect rather than any sort of
12 antibody binding to cells, per se.
13 Q. (By Ms. Wang) And you wouldn't want to
14 cause epididymitis or orchitis in humans?
15 MR. POWERS: Objection. Form.
16 THE DEPONENT: I would not.
17 Q. (By Ms. Wang) So the POSA would not
18 think that modified PH20 polypeptides would be a
19 viable contraceptive vaccine in humans?
20 MR. POWERS: Objection.
21 Q. (By Ms. Wang) Human males?
22 MR. POWERS: Form.
23 THE DEPONENT: I -- that is correct.
24 Q. (By Ms. Wang) I would like to direct
25 your attention to paragraph 12 of your declaration.

1 And you state here that you "use the
2 phrase 'modified PH20 polypeptides' to refer to
3 polypeptides comprising an amino acid sequence that
4 is at least 95 percent identical to the amino acid
5 sequence of any one of Sequence ID No.: 3 and 32
6 through 66, and includes a modification at
7 position 320 such that D is replaced with H, K, R,
8 or S."
9 Do you see that?
10 A. Yes, I do.
11 Q. Would you agree that modified PH20
12 polypeptides can contain more than one amino acid
13 modification?
14 A. Yes, I'm aware of that.
15 Q. Do you agree that modified PH20
16 polypeptides can contain between 70 -- 17 to 23
17 amino acid modifications?
18 MR. POWERS: Objection. Form.
19 THE DEPONENT: Yes, but the percent
20 identity is what's important for the immune
21 response.
22 Q. (By Ms. Wang) Did you calculate the
23 number of different possible modified PH20
24 polypeptides?
25 A. No, I did not.

1 Q. Do you know the number of possible
2 different PH20 polypeptides?
3 MR. POWERS: Objection. Form.
4 Q. (By Ms. Wang) Let me rephrase.
5 Do you know the number of different
6 possible modified PH20 polypeptides?
7 A. No, I do not know the number.
8 Q. Do you think it's a large number?
9 A. Yes, I do.
10 Q. Do you know what differences there are
11 between the four patents that are at issue in each
12 of the PGR proceedings that you provided a
13 declaration in?
14 MR. POWERS: Objection. Form.
15 THE DEPONENT: So I'm aware that there's,
16 at -- at several sites, replacement amino acids
17 that are -- that are different.
18 Q. (By Ms. Wang) Is it your understanding
19 that each of the four patents requires a different
20 amino acid modification at a different site?
21 A. I can't opine on that because I did not
22 look at the patent.
23 Q. But you understand that the four patents
24 have differences at the sites of replacement amino
25 acids?

1 MR. POWERS: Objection. Form.
2 THE DEPONENT: Yes, in terms of what was
3 provided to me by counsel.
4 Q. (By Ms. Wang) Is it fair to say that
5 these differences at the sites of replacement amino
6 acids didn't matter to your opinion?
7 MR. POWERS: My opinion, it did not
8 matter, because of their high -- very high percent
9 identity.
10 Q. (By Ms. Wang) So your opinion doesn't
11 change as between a required modification at
12 position 30 versus a required modification at
13 position 313?
14 A. Right.
15 MR. POWERS: Objection. Form.
16 Just give me a minute.
17 Q. (By Ms. Wang) If a modified PH20
18 polypeptide had 95 percent sequence identity to
19 Sequence ID No. 3 and 32 through 66 but did not
20 have a mutation at position 320, your opinion would
21 still be the same, correct?
22 MR. POWERS: Objection. Form.
23 THE DEPONENT: You're -- I'm -- could
24 you -- you're referring to my opinion.
25 What -- what opinion were you referring

1 to?
2 Q. (By Ms. Wang) The opinions in your
3 declaration --
4 A. Yeah.
5 Q. -- are all about modified PH20
6 polypeptides, correct?
7 A. Correct.
8 Q. And if a modified PH20 polypeptide had
9 95 percent sequence similarity to Sequence ID No. 3
10 or 32 through 66, but did not have a mutation at
11 position 320, the opinions in your declaration
12 would not change, would they?
13 MR. POWERS: Objection. Form.
14 THE DEPONENT: Yes, that's correct.
15 Q. (By Ms. Wang) And your opinions in your
16 declaration don't depend where on the PH20
17 polypeptide there are modifications; is that right?
18 MR. POWERS: Objection. Form.
19 THE DEPONENT: That is correct.
20 Q. (By Ms. Wang) And you would agree that
21 modified PH20 polypeptides can have amino acid
22 modifications anywhere along the sequence?
23 A. Yes, as long as that high percent
24 identity is maintained.
25 Q. You did not independently evaluate the

structure of PH20 in developing your opinions?
A. I did not.
Q. You did not identify the number of surface-successful residues on human PH20?
A. I did not.
Q. You did not identify the number of surface-successful residues on modified PH20 polypeptides?
A. I did not.
Q. You did not identify any particular epitopes on human PH20 that would be relevant to the contraceptive effect?
A. No, I did not.
Q. You did not identify any epitopes on modified PH20 polypeptides that would be relevant to contraception?
A. No, I did not.
Q. Would you have been able to identify such epitopes in 2012?
MR. POWERS: Objection. Form.
THE DEPONENT: I'm sorry, could you ask that again, or maybe in a slightly different way.
Q. (By Ms. Wang) Would you have been able to identify epitopes on PH20 relevant to conception? Let me rephrase.

1 A. Okay.
2 Q. Would you have been able to identify
3 epitopes on PH20 necessary for contraception in
4 2012?
5 MR. POWERS: Objection. Foundation.
6 Form.
7 THE DEPONENT: I think it would be --
8 generally, it would be essentially any of the
9 epitopes as long as there was an immune response,
10 as long as antibodies were binding to PH20 on
11 sperm.
12 Q. (By Ms. Wang) In your opinion, are you
13 assuming that the modified PH20 polypeptides are
14 folded?
15 MR. POWERS: Objection. Form.
16 THE DEPONENT: I don't know; I can't
17 opine on that.
18 But that doesn't necessarily matter for
19 triggering an immune response.
20 Q. (By Ms. Wang) So in your opinion,
21 unfolded modified PH20 polypeptides would still
22 trigger an immune responses?
23 A. Yes.
24 Q. And unfolded modified PH20 polypeptides
25 would cause polyclonal antibodies that could bind

1 to the native PH20?
2 A. Yes.
3 Q. Is it also your opinion that misfolded
4 modified PH20 polypeptides would trigger an immune
5 response?
6 A. Yes, misfolded, and denatured, actually,
7 as well.
8 Q. And it's your opinion that misfolded and
9 denatured modified PH20 polypeptides would trigger
10 an immune responses that would cause polyclonal
11 antibodies that could bind to the native PH20?
12 MR. POWERS: Object to form.
13 THE DEPONENT: Yes.
14 Q. (By Ms. Wang) It's your opinion that
15 these misfolded and denatured modified PH20
16 polypeptides would cause contraception?
17 A. Yes, if -- as long as the antibodies
18 bound to sperm in the reproductive tract and there
19 were sufficient antibodies in the reproductive
20 tract.
21 Q. Is it your opinion that misfolded and
22 aggregated modified PH20 polypeptides would still
23 cause contraception in a female?
24 MR. POWERS: Objection. Form.
25 Foundation.

1 THE DEPONENT: I can't really offer an
2 opinion on the aggregation. It -- it depends on
3 solubility, et cetera.
4 Q. (By Ms. Wang) Would you agree that
5 misfolded proteins can aggregate?
6 A. Yes, I'm aware of that.
7 Q. And aggregated proteins are not soluble?
8 MR. POWERS: Objection. Form.
9 THE DEPONENT: May -- may not be, yes,
10 that's correct.
11 Q. (By Ms. Wang) And aggregated misfolded
12 PH20 polypeptides that are not soluble would not
13 cause contraception in a female, would they?
14 MR. POWERS: Objection. Form.
15 THE DEPONENT: They could be solubilized,
16 though, and -- with denaturation. So aggregates
17 can still be useful, potentially, just not as an
18 aggregate.
19 Q. (By Ms. Wang) And aggregated misfolded
20 modified PH20 polypeptide, without further
21 processing, would not be useful as a contraceptive
22 in females?
23 MR. POWERS: Objection. Form.
24 THE DEPONENT: May not be because of the
25 form it's in and how it would be administered.

Q. (By Ms. Wang) Do you know how many amino acid modifications to an epitope in a modified PH20 polypeptide can be made in order for an antibody against that modified epitope to still bind to the corresponding epitope in a native PH20?

MR. POWERS: Objection. Form.

THE DEPONENT: Sorry, just need some clarification from you.

Are -- you're talking -- I mean, it sounds like you're talking about monoclonal antibodies to specific epitopes, not polyclonals to multiple epitopes?

Q. (By Ms. Wang) Well, I'm asking just about one epitope to another.

An epitope on a modified PH20 polypeptide, do you know how different that epitope can be before the antibody to that epitope doesn't bind to PH20?

MR. POWERS: Objection. Form.

THE DEPONENT: No, I don't know that number exactly.

MR. POWERS: Counsel, it's been about an hour.

Ready for a break?

MS. WANG: One more question, please.

1 MR. POWERS: Okay.
2 Q. (By Ms. Wang) Is it a fair understanding
3 that an epitope on modified PH20 polypeptide can be
4 so different that an antibody to that epitope would
5 not bind to the native PH20?
6 MR. POWERS: Objection. Form.
7 THE DEPONENT: I think, similar to what I
8 answered before, that if you have that 95 percent
9 identity, regardless of individual epitopes being
10 altered, but if overall there's that 95 percent
11 identity, there's going to be a consistent --
12 should be a consistent polyclonal response when
13 injected into a female, and it should react with
14 sperm surface PH20.
15 MR. POWERS: Are you ready for that
16 break?
17 MS. WANG: Yes.
18 MR. POWERS: Thank you very much.
19 THE VIDEOGRAPHER: Okay. The time is
20 10:00 o'clock -- 10:01 a.m. Pacific time. We are
21 off the record.
22 (Recess taken.)
23 THE VIDEOGRAPHER: The time is 10:15 a.m.
24 Pacific time. We are on record.
25 Q. (By Ms. Wang) Dr. Cherr, during the

1 break just now, did you speak with counsel?
2 A. No, I did not.
3 Q. Earlier this morning, I asked you about
4 the number of possible modified PH20 polypeptides.
5 And you agreed that it's a large number?
6 A. It's a large number.
7 Q. Do you know how many modified PH20
8 polypeptides within that large number would
9 aggregate?
10 A. No, I do not.
11 Q. Do you know how many modified PH20
12 polypeptides within that large number could be
13 made?
14 MR. POWERS: Objection. Form.
15 Foundation.
16 THE DEPONENT: Could you please define
17 what you mean by "could be made."
18 Q. (By Ms. Wang) Do you know if any
19 modified PH20 polypeptide could not be made?
20 MR. POWERS: Objection. Form.
21 THE DEPONENT: No, I can't offer an
22 opinion on that because I haven't done any sort of
23 analysis on that.
24 Q. (By Ms. Wang) I'd like to turn to
25 paragraph 31 of your declaration.

1 A. Okay.
2 Q. I apologize, I sent you to the wrong part
3 of your declaration.
4 It's paragraph 19.
5 A. Okay.
6 Q. Okay. And you here you state that "PH20
7 is a multi functional protein," correct?
8 A. Yes, correct.
9 Q. And that means PH20 has more than one
10 function?
11 A. Yes.
12 Q. It has a hyaluronidase function?
13 A. Correct.
14 Q. It has a hyaluronic acid, HA, binding
15 function to simulate sperm signaling activity?
16 A. Yes.
17 Q. And PH20 also acts as a sperm receptor
18 for an egg's zona pellucida on acrosome-reacted
19 sperm?
20 A. Yes.
21 Q. And all of these PH20 functions are
22 involved in fertilization, correct?
23 A. Yes, they are.
24 Q. In order for fertilization to occur, the
25 PH20 needs to have all of these functions?

A. No.

So they're all involved in fertilization, but from the standpoint of antibody binding to PH20, not all of them need to be inhibited.

Q. So my question was, in order for fertilization to occur, the PH20 needs to have all three of these functions; is that correct?

MR. POWERS: Object to form.

THE DEPONENT: So there -- all three of those functions are involved in the process of fertilization. I don't know if inhibition of any one of them alone would inhibit that fertilization.

Q. (By Ms. Wang) So PH20 has three functions involved in fertilization?

A. Correct.

Q. And you don't know if inhibiting just one of those three functions would be sufficient to inhibit fertilization?

MR. POWERS: Objection. Form.

THE DEPONENT: It doesn't matter, because if antibodies are bound to PH20 when it's on the sperm at the time of fertilization, the presence of antibodies bound pretty much anywhere to the PH20 protein and sperm, there would be an effect on fertilization, most likely a complete inhibition,

1 or contraception.
2 Q. (By Ms. Wang) So I appreciate that's
3 your opinion.
4 But the question I asked was, you don't
5 know if inhibiting just one of the three PH20
6 functions would be sufficient to inhibit
7 fertilization --
8 MR. POWERS: Objection. Form.
9 Q. (By Ms. Wang) -- correct?
10 THE DEPONENT: I think what I was
11 referring to is, when antibodies bind to PH20, and
12 it may or may not bind to regions of the
13 polypeptide that are responsible for that -- for
14 those different functions, just having antibodies
15 present on the entire PH20 will directly or
16 indirectly have an effect on fertilization.
17 Q. (By Ms. Wang) Dr. Cherr, my question
18 was, you don't know if inhibiting just one of the
19 three PH20 functions would be sufficient to inhibit
20 fertilization.
21 Do you have that question in mind?
22 A. It would -- it would --
23 MR. POWERS: Objection. Form.
24 THE DEPONENT: So inhibition of one of
25 those functions would have, potentially, an effect

on fertility.

Q. (By Ms. Wang) But you don't know if inhibition of just one of those functions would cause contraception?

MR. POWERS: Objection. Form.

THE DEPONENT: Correct.

I -- again, having an antibody bound anywhere along the PH20 polypeptide on sperm should have an impact on contraception or fertility.

Q. (By Ms. Wang) Am I correct in understanding that you think it would have an impact but not cause infertility?

MR. POWERS: Objection. Form.

THE DEPONENT: Sorry, can you -- when you say "it," could you please explain that.

Q. (By Ms. Wang) So I asked, you don't know if inhibition of just one of the functions of PH20 would cause contraception.

And your answer was?

A. So --

MR. POWERS: Objection. Form.

THE DEPONENT: So in my opinion in my declaration, I'm referring to antibodies that would bind -- polyclonal antibodies that would bind --

Q. (By Ms. Wang) Dr. Cherr, I understand --

1 MR. POWERS: Whoa, whoa, whoa, please let
2 him finish his answer.
3 MS. WANG: I --
4 MR. POWERS: Were you finished?
5 THE DEPONENT: No.
6 MR. POWERS: Okay. Please continue.
7 Yeah, Counsel, don't interrupt the
8 witness.
9 MS. WANG: I understand, and we'll get
10 to -- no, we'll get to your opinion, Dr. Cherr, but
11 I need my question --
12 MR. POWERS: You're not going to let the
13 witness finish his answer?
14 MS. WANG: I'm going to --
15 MR. POWERS: Please don't interrupt the
16 witness.
17 MS. WANG: The witness is not answering
18 my question, so I'd like the witness to --
19 MR. POWERS: He's --
20 MS. WANG: -- answer my question.
21 MR. POWERS: -- answering your question.
22 You may not like the answers, but he's answering.
23 Please continue with your answer.
24 THE DEPONENT: So the idea is that if you
25 have polyclonal antibodies that are bound to the

1 PH20 polypeptide on sperm, regardless of what
2 domain or what function they may or may not be
3 inhibiting, they're still going to affect
4 successful fertilization by just hav- -- by --
5 simply by the presence of immunoglobulin molecules
6 bound to the sperm surface.
7 Is that --
8 Q. (By Ms. Wang) My question, Dr. Cherr --
9 yeah, just could listen to my question, please.
10 A. Yeah.
11 Q. My question is, if you inhibit just one
12 of the functions of PH20 -- I'm not asking about
13 antibodies.
14 If you inhibit just one of the functions
15 of PH20, do you know if that inhibition alone will
16 cause contraception?
17 MR. POWERS: Objection. Form. Asked and
18 answered.
19 THE DEPONENT: I don't know about
20 contraception, but it would probably reduce the
21 efficiency of fertilization.
22 Q. (By Ms. Wang) It would reduce the
23 efficiency of fertilization but not cause
24 infertility?
25 A. I don't know, but

1 MR. POWERS: Objection. Form.
2 THE DEPONENT: -- yes, that would be my
3 opinion, that it would reduce efficiency of
4 fertilization.
5 Q. (By Ms. Wang) On the PH20 protein, the
6 HA binding domain is separate from the
7 hyaluronidase domain, correct?
8 MR. POWERS: Objection. Form.
9 THE DEPONENT: That is correct.
10 Q. (By Ms. Wang) The HA binding domain is
11 in a separate part of the protein from the
12 hyaluronidase domain?
13 A. Yes.
14 Q. In your opinion, for a modified PH20
15 polypeptide to be useful as a contraceptive, does
16 it have to cause infertility?
17 MR. POWERS: Objection. Form.
18 THE DEPONENT: So I -- I think your
19 question is, is contraception and infertility the
20 same thing? Is that what you are asking?
21 Q. (By Ms. Wang) In your mind, are
22 contraception and infertility the same thing?
23 A. Yes, although there's -- there are other
24 methods of contraception that are -- are quite a
25 distance from the process of fertilization.

1 Q. In your opinion, for a modified PH20
2 polypeptide to be useful as a contraception, is
3 there a certain level of reduction in infertility
4 that would need to be achieved?
5 A. So are you asking whether something would
6 be all or nothing versus varying degrees; is
7 that -- I am not clear on exactly what you are
8 getting at.
9 Q. I'm trying to understand your opinion
10 that a modified PH20 polypeptide would be useful as
11 a contraceptive vaccine.
12 A. Yes, I believe it would. Again, that's
13 with the understanding that it would be an
14 appropriate immune response in the reproductive
15 tract that combined the sperm.
16 Q. And I am trying to understand how do you
17 define "useful"?
18 A. Yes, so -- I define "useful" -- I mean,
19 there's -- in the literature with experimental
20 animals reducing litter size, people still use the
21 term as an effective contraception. But in my
22 mind, when it comes to human biology, it needs to
23 be close to 100 percent.
24 Q. So from modified PH20 polypeptide to be a
25 useful contraceptive in humans, it would need to

1 cause 100 percent infertility?
2 MR. POWERS: Object to form.
3 THE DEPONENT: Or close to 100 percent,
4 yes.
5 Q. (By Ms. Wang) For a modified PH20
6 polypeptide to be a useful contraceptive in
7 nonhuman mammals, how much or what percentage of
8 reduction in fertility would need to be achieved?
9 MR. POWERS: Objection. Form.
10 THE DEPONENT: It would be similar
11 ideally.
12 Q. (By Ms. Wang) It would need to be 100
13 percent or close to it?
14 A. Similar to what hormone contraceptives
15 are.
16 Q. PH20 structure changes depending on the
17 stage of sperm maturation, correct?
18 A. Yes.
19 Q. Native PH20 is proteolytically cleaved
20 late in sperm maturation?
21 A. I believe that's correct.
22 Q. PH20 can also take on different
23 glycosylation during maturation?
24 A. Right.
25 Q. PH20 structure also changes depending on

1 the stage of fertilization, correct?
2 MR. POWERS: Objection. Form.
3 THE DEPONENT: Sorry. Could I -- I just
4 want to make sure your question -- I understand
5 your question. Can you repeat it or reword it?
6 Q. (By Ms. Wang) PH20 structure changes
7 depending on where it is in the female reproductive
8 tract, correct?
9 MR. POWERS: Objection. Form.
10 THE DEPONENT: Well, it's associated with
11 sperm. So do you mean in terms of the -- where the
12 sperm are or --
13 Q. (By Ms. Wang) Yes.
14 A. Okay. So yes, it can, is the answer.
15 Q. PH20 structure can be different depending
16 on where the sperm is in the -- in the female
17 reproductive tract?
18 A. Yeah. Maybe it's more the physiology of
19 the sperm at those locations, not just its location
20 in the female tract.
21 Q. Sperm has a different physiology
22 depending on where it is in the female reproductive
23 tract?
24 A. Correct.
25 Q. And the PH20 on the sperm can have a

1 different structure depending on the different
2 sperm physiology?
3 A. I would say sperm -- sorry, I would say
4 PH20 that -- that's either on or in the sperm just
5 to be precise because it's in several places, the
6 sperm.
7 Q. PH20 on or in the sperm can have a
8 different structure depending on the sperm's
9 physiology?
10 A. It could be -- yes, it can be
11 asthmatically processed.
12 Q. PH20 is endoproteolytically cleaved at
13 the time of the acrosome reaction?
14 A. Yes, that's correct.
15 Q. And this endoproteolysis may alter the
16 three-dimensional structure of PH20?
17 A. Yes.
18 Q. Which form of the native PH20 must be
19 engaged by antibodies in order for to be effective
20 contraception?
21 MR. POWERS: Objection. Form.
22 Foundation.
23 THE DEPONENT: So polyclonal antibodies
24 react similarly with all forms of PH20, whether
25 it's cleaved or endoproteolytically cleaved or not

1 cleaved, so there is -- again, with polyclonal
2 antibodies, there isn't an issue in terms of
3 recognition of any -- any of the PH, whether it's
4 interact or some other membrane or plasma membrane
5 PH20.
6 Q. (By Ms. Wang) Is it your opinion that
7 polyclonal antibodies against any of the modified
8 PH20 polypeptides would be able to bind all forms
9 of PH20 regardless of sperm physiology?
10 A. Yes, that is my opinion.
11 Q. I would like to direct your attention to
12 paragraph 24 of your declaration.
13 It's actually the figure --
14 A. Oh, okay.
15 Q. -- on page 17 of your declaration.
16 A. Yes.
17 Q. And that is a reproduction of Figure 3 of
18 Exhibit 2103, correct?
19 A. Yes, correct.
20 Q. And the figures shows the reproductive
21 tract of female primates, right?
22 A. Yes, correct.
23 Q. Would this graphic look different for
24 nonprimate mammals?
25 A. Yes, it would.

1 Q. In what ways?
2 A. Depending on where the sperm are
3 processed, different mammals -- some sperm are
4 deposited in the vagina, but others, most of the
5 rodents' sperm, are deposited in the uterus so that
6 there's not cervical mucus.
7 Q. Cervical mucus identified at step B of
8 Figure 3 would not be in rodents?
9 A. Right.
10 Q. Would steps C, D, E, and F of Figure 3
11 look different in nonprimate mammals?
12 A. It might --
13 MR. POWERS: Object to form.
14 Go ahead.
15 THE DEPONENT: Yes, it might. In some
16 species -- many species have that binding of sperm
17 to the oviduct epithelium shown in the figure, but
18 that's to varying degrees depending on the species
19 or the mammal.
20 Q. (By Ms. Wang) So sperm of all mammals
21 has a glycocalyx, correct?
22 A. Of most. We don't know about some
23 mammals.
24 Q. The sperm of all of the mammals that you
25 have opined on in this declaration has a

1 glycocalyx?
2 A. It's unclear about the guinea pig.
3 Guinea pig is one that may not have that.
4 Nobody -- nobody has looked at that.
5 Q. So in 2012, no one knew if the guinea pig
6 sperm add a glycocalyx?
7 A. Right.
8 Q. Is it fair to say that in 2012 they also
9 didn't know that the guinea pig sperm didn't have a
10 glycocalyx?
11 MR. POWERS: Object to form.
12 THE DEPONENT: It was known -- it was
13 known in 2012 that guinea pig were -- sperm were a
14 little bit different than other mammals in that
15 they're capable of undergoing an acrosome reaction
16 very rapidly after insemination. For other
17 mammals, there has to be a residence time in the
18 female tract. So guinea pigs were known to be --
19 for some decades known to be different than
20 other -- other mammals.
21 Q. (By Ms. Wang) So in 2012 guinea pig
22 reproduction was known to be different from other
23 mammals?
24 A. Potentially.
25 MR. POWERS: Objection. Form.

1 Go ahead.
2 Q. (By Ms. Wang) In 2012 guinea pig sperm
3 was known to be different from other mammals?
4 MR. POWERS: Objection. Form.
5 THE DEPONENT: It -- it was hypothesized
6 that they're different, not known for a fact.
7 Q. (By Ms. Wang) There was an expectation
8 that it could be different?
9 MR. POWERS: Objection. Form.
10 THE DEPONENT: Potentially, yes.
11 Q. (By Ms. Wang) Looking back at the figure
12 of page 17 of your declaration, the PH20 in steps A
13 through D would all be protected by glycocalyx, and
14 the PH20 on the sperm would be inaccessible, right?
15 MR. POWERS: Objection. Form.
16 THE DEPONENT: I'm sorry, inaccessible
17 to -- or you said "inaccessible"?
18 Q. (By Ms. Wang) Yes.
19 A. Inaccessible to -- to what? Sorry.
20 Q. Sure.
21 The PH20 in steps A through D are
22 protected by a glycocalyx, right?
23 A. Yes, correct.
24 Q. So they're not accessible outside of the
25 glycocalyx?

1 MR. POWERS: Objection. Form.
2 THE DEPONENT: Yes. They're not exposed,
3 right.
4 Q. (By Ms. Wang) So because they are not
5 exposed, you would not expect antibodies to be able
6 to bind to PH20 while the glycocalyx is intact?
7 A. Yes, that's correct.
8 Q. And in Figure 3, the glycocalyx is
9 removed at step E?
10 A. Yes.
11 Q. So at that point in step E, PH20 is
12 exposed on the sperm surface?
13 A. Yes.
14 Q. Is PH20 endoproteolitically cleaved at
15 step F at Figure 3?
16 A. Step F in endoproteolitically cleaved at
17 the time of the acrosome reaction, which would be
18 at step -- within step F.
19 Q. So within step F, there would be a
20 endoproteolysis and the PH20 structure could
21 change?
22 A. Yes, when at the zona pellucida.
23 Q. And the steps where antibodies could
24 access PH20 to impede fertilization would be at
25 steps E and F?

1 A. Yes, at steps E and F.
2 Q. At step F some PH20 is also released from
3 the sperm surface as soluble PH20, correct?
4 A. From the acrosome; soluble PH20 come from
5 the acrosome.
6 Q. So at step F -- let me rephrase.
7 The acrosome reaction occurs during
8 step F?
9 A. Yes -- yes.
10 Q. And then releases soluble PH20?
11 A. Correct.
12 Q. Do antibodies need to bind these soluble
13 PH20 in order to prevent fertilization?
14 MR. POWERS: Object to form.
15 THE DEPONENT: No, but the antibodies,
16 polyclonal antibodies, should bind equally well to
17 soluble PH20 or to membrane associated PH20.
18 Q. (By Ms. Wang) Is your opinion that
19 polyclonal antibodies would bind to both the
20 soluble PH20 and sperm PH20?
21 A. Yes.
22 Q. The site of fertilization is an oviduct?
23 A. Correct.
24 Q. Polyclonal antibodies against PH20 would
25 have to engage sperm in the oviduct to prevent

1 fertilization, right?
2 A. Yes, as -- as stage E there throughout
3 the oviduct. But -- but yes, in the oviduct.
4 Q. So there has to be polyclonal antibody
5 against PH20 in the oviduct to prevent
6 fertilization?
7 A. Yes.
8 Q. How much anti-PH20 antibody would need to
9 be able in the oviduct for fertilization to be
10 prevented?
11 A. I can't offer an opinion on that, because
12 that's -- that's unknown.
13 Q. Because you don't have an opinion because
14 you don't know?
15 A. I don't know.
16 Q. Do you know how much sperm would need to
17 be bound by antibodies in order to prevent
18 fertilization?
19 MR. POWERS: Objection. Form.
20 THE DEPONENT: I'm sorry. Could you
21 repeat that? I'm -- I don't know if that was
22 turned around. Go ahead.
23 Q. (By Ms. Wang) Do you know how much sperm
24 would need to be bound by antibodies to prevent
25 fertilization?

1 MR. POWERS: Same objection.
2 THE DEPONENT: So at the stage E -- E
3 there, there's very few sperm that are present on
4 the oviduct on the order of 100 or 200. So any --
5 any sort of significant antibody titer throughout
6 that -- the fluids there would have an immediate
7 impact or binding to the sperm at that low sperm
8 density.
9 Q. (By Ms. Wang) Did you say there are
10 about 100 or 200 sperm?
11 A. Yes.
12 Q. Would all of that 100 or 200 sperm need
13 to be bound by antibody in order for there to be --
14 in order to prevent fertilization?
15 A. Well --
16 MR. POWERS: Objection. Form.
17 THE DEPONENT: Out of that handful of
18 relatively small proportion of the total sperm that
19 were introduced into the reproductive tract at
20 insemination, perhaps only one to three sperm
21 actually get to stage F there. So very few migrate
22 and actually interact with the oocyte cumulus
23 complex.
24 Q. (By Ms. Wang) What trying to understand,
25 Doctor, is what amount of the sperm that's there in

the oviduct needs to be bound by antibody in order to prevent fertilization?

A. Again, I can't opine on that because I -- I don't know. But if there was an antibody -- adequate antibody response in the reproductive tract and an antibody -- and present antibodies with that low sperm density, the assumption would be all of them would be coated with antibody.

Q. But you don't know?

A. I don't know.

Q. What antibody titer would be needed in order to engage all of the sperm available in the oviduct?

A. Yeah, I -- I don't -- I can't opine on that because I don't have -- I don't know those quantitative data. I'm not sure anybody does.

Q. Would the quantity differ by species?

MR. POWERS: Objection. Form.

THE DEPONENT: Sure, it may depending on the response.

Q. (By Ms. Wang) And would it differ by individual?

MR. POWERS: Objection. Form.

THE DEPONENT: It would always be some variability, individual variability, unless you are

1 dealing with a genetically inbred line of some
2 sort.
3 Q. (By Ms. Wang) And it would be fair to
4 say you wouldn't know until you do the test to
5 quantify it?
6 MR. POWERS: Objection. Form.
7 THE DEPONENT: No, I think if you had
8 sufficient antibody titers in the reproductive
9 tract fluids or in the oviduct, I think one could
10 be fairly certainly that that's going to have a
11 contraception effect and certainly a POSA would
12 have expected that.
13 Q. (By Ms. Wang) Would a POSA have known in
14 2012 how much antibody titer would be needed?
15 MR. POWERS: Objection. Relevance.
16 THE DEPONENT: Probably not, but it
17 didn't -- wouldn't matter as long as there was a
18 response in the reproductive tract.
19 Q. (By Ms. Wang) It is your opinion that
20 you would need a sufficient antibody titer in order
21 to cause contraception, correct?
22 A. Yes.
23 Q. I am trying to understand what the POSA
24 would have expected a sufficient antibody titer to
25 be?

1 A. Well, I -- I -- I can't opine on that in
2 vivo because that's not known. But there -- one
3 could look in vitro at antibody titers that might
4 affect sperm function and fertilization in vitro.
5 But other than that, I don't believe there's any
6 studies that have been in vivo with sperm
7 and antibodies.
8 Q. So in 2012 the POSA so would not have
9 known in vivo what antibody titer was needed
10 against sperm --
11 MR. POWERS: Objection.
12 Q. (By Ms. Wang) -- to cause contraception?
13 MR. POWERS: Form.
14 THE DEPONENT: Right. I don't believe
15 that information for in vivo studies would be
16 available at the time or -- or now.
17 Q. (By Ms. Wang) It was your testimony
18 earlier that in your opinion polyclonal antibodies
19 against PH20 raised in reaction to modified PH20
20 polypeptides would bind both soluble and
21 sperm-bound PH20?
22 A. Yes, correct.
23 Q. Would you expect there to be some
24 antibodies that only bind the soluble PH20 but not
25 the sperm-bound PH20?

1 A. Not in the polyclonal response, no.
2 Q. All of the antibodies in the polyclonal
3 response in your opinion would bind both the
4 soluble and the sperm bound PH20?
5 A. Yes.
6 Q. Antibody that binds the soluble PH20
7 would not impair the sperm's ability to fertilize
8 the egg, correct?
9 A. No, it would.
10 Q. In what way?
11 A. So soluble PH20 at the time of the
12 acrosome reaction is an acid-active form, and it
13 digest the cumulus extracellular matrix immediately
14 surrounding the sperm. So prior to that, the tail
15 of the sperm is -- is beating at a high frequency
16 but not a whiplike -- whiplash-like fashion. And
17 as the immediate -- there's an immediate clearing
18 right around the sperm of the extracellular matrix
19 in this acid-active form, which then of course, as
20 it becomes exposed to neutral conditions in the
21 cumulus, it loses its activity so the soluble
22 activity declines, but it clears a region around
23 the sperm. So the tail can beat at a very high
24 amplitude, and that's what help thrust -- helps to
25 thrust the sperm forward through the zona

1 pellucida.
2 Q. So it your opinion that soluble PH20
3 would also have to be bound by antibodies in order
4 for there to be a reduction of fertilization?
5 A. Well, as -- as stated earlier, it would
6 be bound by antibodies similar as to the
7 membrane-bound form.
8 Q. The amount of sperm in the vaginal cavity
9 is significantly higher than it would be in the
10 oviduct, correct?
11 A. Yes.
12 Q. So you would need substantially more
13 antibody in the vaginal cavity to bind sperm if you
14 were trying to achieve contraception in the vaginal
15 cavity?
16 MR. POWERS: Objection. Form.
17 THE DEPONENT: Potentially, yes.
18 Q. (By Ms. Wang) Are you saying
19 "potentially" because you don't know?
20 A. No. I'm just saying that you would need
21 more. Again, but PH20 would need to be exposed,
22 so...
23 Q. And PH20 is not exposed --
24 A. Normally, no --
25 Q. -- in the vaginal cavity.

1 A. -- but it could be.
2 MS. WANG: Okay to take a break?
3 MR. POWERS: Sure.
4 THE VIDEOGRAPHER: The time is
5 11:00 o'clock a.m. Pacific time. We are off the
6 record.
7 (Recess taken.)
8 THE VIDEOGRAPHER: The time is 11:15 a.m.
9 Pacific time. We are on record.
10 Q. (By Ms. Wang) Dr. Cherr, on the break,
11 did you speak with counsel?
12 A. No, I did not.
13 Q. Okay. And just to confirm, the answers
14 that you gave in the earlier sessions, would any of
15 those have differed for any of the four different
16 patents at issue?
17 A. No.
18 Q. So you state in paragraph 35 of your
19 declaration that by December 28th, 2012, PH20
20 polypeptide vaccines have been successfully used
21 for contraception in female guinea pigs?
22 A. Yes, yes.
23 Q. And as we discussed earlier, the studies
24 you cite also indicated successful contraception in
25 male guinea pigs?

1 A. Yes, correct.
2 Q. And in these studies with guinea pigs,
3 the scientists used unmodified guinea pig PH20
4 purified from sperm, correct?
5 A. Yes, that's correct.
6 Q. And the PH20 was injected subcutaneously
7 into guinea pigs.
8 A. Correct.
9 Q. Do you know how similar the guinea pig
10 PH20 is to human PH20?
11 A. I think it's about -- roughly 60 percent,
12 similar.
13 Q. Do you know how similar the guinea pig
14 PH20 sequence is to modified PH20 polypeptides?
15 A. I don't know that. I can't -- I can't
16 offer an opinion. I don't know.
17 Q. You did not make that --
18 A. No, I didn't.
19 Q. -- determination?
20 The guinea pigs that were injected with
21 PH20, both male and female, generated polyclonal
22 antibodies, correct?
23 MR. POWERS: Objection. Form.
24 THE DEPONENT: Generated antibodies,
25 circulating antibodies, in the serum.

1 Q. (By Ms. Wang) The male guinea pigs
2 generated polyclonal antibodies against PH20?
3 A. Yes, they did.
4 Q. And the female guinea pigs also generated
5 polyclonal antibodies against PH20?
6 A. Yes, they did.
7 Q. Would you agree that PH20 is a
8 self-antigen?
9 MR. POWERS: Objection. Form.
10 THE DEPONENT: Excuse me, sorry.
11 It's a self-anti- -- self-antigen in
12 males.
13 Q. (By Ms. Wang) And that's because male
14 guinea pigs naturally express PH20?
15 A. Yes.
16 Q. And that means a self-antigen in male
17 guinea pigs would have to overcome immune tolerance
18 in order to be successful?
19 A. Well, they -- they generate an
20 inflammatory response when PH20's administered. So
21 that -- but that also involves an antibody
22 response.
23 Q. Would you agree that a vaccine using a
24 self-antigen must overcome immune tolerance to be
25 successful?

1 MR. POWERS: Objection. Form.
2 THE DEPONENT: It -- it doesn't have to.
3 It -- depending on how it's presented to the
4 animal.
5 Q. (By Ms. Wang) What do you mean by
6 "depending on how it is presented"?
7 A. Well, if it's presented as, for example,
8 a denatured protein or as a linear polypeptide, an
9 animal may see that as a foreign antigen even
10 though it's a self-antigen.
11 Q. A denatured protein or a linear
12 polypeptide would not have the three-dimensional
13 structure of the self-antigen, would it?
14 A. That is correct.
15 Q. You testified that in the guinea pig
16 studies in males, injection with PH20 generated an
17 inflammatory response; is that correct?
18 A. Yes, it is.
19 Q. And is that the orchitis and epididymitis
20 we discussed earlier?
21 A. Yes.
22 Q. And that inflammatory response was an
23 immune response against tissues in the guinea pig
24 that naturally expressed PH20?
25 MR. POWERS: Objection. Form.

1 THE DEPONENT: I believe they also had
2 circulating polyclonal antibodies, as well, in the
3 serum. But, yes, there -- there was what's called
4 breakthrough in the male reproductive tract.
5 Q. (By Ms. Wang) The inflammatory response
6 seen orchitis and epididymitis -- epididymi- -- let
7 me rephrase.
8 The inflammatory response seen in the
9 orchitis in male guinea pigs, that was because the
10 guinea pig raised an immune response -- I'm sorry.
11 Let me rephrase again.
12 The inflammatory response seen in
13 orchitis in male guinea pigs was due to a response
14 against tissue in the guinea pig expressing PH20,
15 right?
16 A. Yes.
17 Q. Do you know whether guinea pigs have a
18 unique immune system compared to other mammals?
19 MR. POWERS: Objection. Form.
20 THE DEPONENT: They don't have a unique
21 immune system, but the lumen of the male tract is
22 not a barrier to circulating immunoglobulin as it
23 is in any other animals.
24 Q. (By Ms. Wang) But you don't think guinea
25 pigs have a different immune system compared to

1 other mammals?
2 MR. POWERS: Object to form.
3 THE DEPONENT: No, I don't believe they
4 have a different immune system. It may just be the
5 testes-blood barrier that's common in most mammals.
6 Q. (By Ms. Wang) You cited the guinea pigs
7 studies in your declaration as evidence of
8 successful use of PH20 polypeptides as
9 contraceptive vaccines before 2012, correct?
10 A. Yes.
11 Could you point to where you're looking?
12 I just want to make sure --
13 Q. Paragraph 35.
14 A. Okay. Yes.
15 Q. You did not cite any other study before
16 2012 demonstrating PH20 polypeptide as an effective
17 contraceptive vaccine in other species?
18 A. The guinea pig was the -- kind of the
19 proof-of-concept animal model where it worked
20 exceedingly well.
21 Q. But you did not cite any study in any
22 other animal model where the PH20 polypeptide
23 worked as a contraceptive vaccine?
24 MR. POWERS: Object to form.
25 THE DEPONENT: That's correct, but that

1 has to do with administration or the route of
2 administration.
3 Q. (By Ms. Wang) You did not identify any
4 other successful animal study in which PH20
5 polypeptide worked as a contraceptive vaccine?
6 A. That is correct.
7 Q. At paragraph 49 of your declaration --
8 A. Yes.
9 Q. -- you talk about the Pomering 2002
10 paper, which is Exhibit 1020.
11 A. Yes.
12 Q. And you agree that Pomering 20- -- of
13 2002 reports that "rabbits receiving PH20
14 polypeptides via the subcutaneous route induced
15 high levels of" polyclonal antibodies?
16 A. Yes, in the plasma.
17 Q. And Pomering used recombinant rabbit
18 PH20?
19 A. Yes, correct.
20 Q. And you agree this was unmodified rabbit
21 PH20?
22 A. Yes.
23 Q. And the rabbits were injected
24 subcutaneously?
25 A. Yes.

1 Q. And you agree they were injected with an
2 adjuvant?
3 A. They were.
4 Q. You agree they were also injected with
5 booster immunizations?
6 A. Yes, they were.
7 Q. And both male and female rabbits were
8 immunized?
9 A. Yes, correct.
10 Q. And Pomering 2002 reported that the
11 rabbits generated polyclonal antibodies that bound
12 native PH20, correct?
13 A. Circulating in the plasma, yes, but not
14 in the reproductive tract.
15 Q. Regardless of where it was, the rabbits
16 generated polyclonal antibodies that bound native
17 PH20, correct?
18 MR. POWERS: Objection. Form.
19 THE DEPONENT: Yes, they did.
20 Q. (By Ms. Wang) And you agree that even
21 though the rabbits generated polyclonal antibodies
22 to PH20, this did not result in infertility in any
23 of the rabbits?
24 MR. POWERS: Objection. Form.
25 THE DEPONENT: They -- they only -- the

1 only stimulation of polyclonal antibodies was in
2 the plasma, not in the reproductive tract, which is
3 where it needs to be for contraception.
4 Q. (By Ms. Wang) So is it your opinion that
5 for there to be successful contraception, there
6 must be polyclonal antibodies in the reproductive
7 tract?
8 A. Yes, and Pomering addresses that
9 extensively in their paper.
10 Q. And it is your opinion that subcutaneous
11 injection can never be an effective way to deliver
12 a contraceptive vaccine?
13 MR. POWERS: Objection. Form.
14 THE DEPONENT: Can you define "never."
15 Q. (By Ms. Wang) Well, I'm trying to
16 understand.
17 So the rabbits were injected
18 subcutaneously, and you acknowledge they raised
19 polyclonal antibodies.
20 A. In the plasma, yes.
21 Q. And it's your opinion that they were not
22 raised in the right location?
23 A. That's correct.
24 Q. So in your opinion, the location of the
25 immune response matters to whether modified PH20

1 polypeptide can be a successful contraceptive?
2 A. Yes.
3 Q. Just raising polyclonal -- rephrase.
4 Just inducing a polyclonal antibody
5 response is insufficient for there to be successful
6 contraception?
7 MR. POWERS: Objection. Form.
8 THE DEPONENT: That's a very broad
9 question. I think it needs to be defined a little
10 bit more.
11 In other words, raising polyclonal
12 antibodies where and how?
13 Q. (By Ms. Wang) Well, that's what I'm
14 trying to understand.
15 Just raising polyclonal antibodies
16 against PH20 is, by itself, in your opinion,
17 insufficient for there to be contraception?
18 MR. POWERS: Objection.
19 THE DEPONENT: I can't agree or --
20 MR. POWERS: Form.
21 THE DEPONENT: -- disagree with that
22 statement. It's too -- it's too broad.
23 So, I mean, the location has to be part
24 of that question.
25 Q. (By Ms. Wang) Raising a polyclonal

1 antibody response to PH20 in the wrong location
2 would be insufficient to cause contraception?
3 MR. POWERS: Object to form.
4 THE DEPONENT: I mean, I -- I would
5 answer "yes," but there's further details that --
6 with that question.
7 Q. (By Ms. Wang) Is it fair that generating
8 polyclonal antibodies against PH20 is necessary but
9 not sufficient to cause contraception?
10 MR. POWERS: Objection to form.
11 THE DEPONENT: If -- if the polyclonal
12 antibodies are generated in the female tract,
13 particularly the upper female tract, it would be
14 sufficient.
15 Q. (By Ms. Wang) It's your opinion that
16 polyclonal antibodies need to be generated in the
17 upper female tract, and that would be sufficient
18 for contraception?
19 A. Yes, that is correct.
20 Q. I will direct your attention to
21 paragraph 50 of your declaration.
22 A. Okay.
23 Q. And paragraph 50 refers to the Hardy 2004
24 paper, which is Exhibit 1019.
25 A. Yes.

1 Q. You agree that Hardy 2004 reports testing
2 mice with PH20?
3 MR. POWERS: Objection. Form.
4 THE DEPONENT: Well, that was the heading
5 of the overall study, but in this case, Hardy
6 clearly states the mouse PH20 antibodies generated
7 in the reproductive tract were insufficient to
8 cause infertility.
9 Q. (By Ms. Wang) My question was, Hardy
10 2004 reports the testing of mice with PH20 as a
11 contraceptive --
12 A. Yes.
13 Q. -- correct?
14 And they used unmodified mouse PH20?
15 A. Recombinant, yes.
16 Q. And you agree Hardy 2004 tested both male
17 and female mice?
18 A. Yes.
19 Q. They delivered the mouse PH20 by
20 intraperitoneal injection?
21 A. Yes, correct.
22 Q. And you agree they used an adjuvant?
23 A. They did.
24 Q. And you agree they used three booster
25 doses?

1 A. Yes.
2 Q. And you agree they tested a formulation
3 involving direct injection of the protein --
4 MR. POWERS: Objection. Form.
5 Q. (By Ms. Wang) -- right?
6 A. I'm sorry, could you repeat that.
7 Q. The Hardy authors tested a formulation of
8 PH20 involving direct injection of the protein into
9 mice?
10 MR. POWERS: Objection. Form.
11 THE DEPONENT: Intraperitoneal, yes.
12 Q. (By Ms. Wang) They also tested a
13 formulation of PH20 using recombinant virus
14 administration?
15 A. Yes.
16 Q. And Hardy 2004 reported neither
17 recombinant mouse PH20 vaccine formulation
18 significantly reduced the fertility of either male
19 or female mice?
20 MR. POWERS: Objection. Form.
21 THE DEPONENT: Yes, that is correct.
22 Q. (By Ms. Wang) It's your opinion, though,
23 that Hardy 2004 did not use an optimized
24 immunization strategy, right?
25 A. That's my opinion, and that's also what

1 Hardy indicates in their discussion, as well.
2 Q. It's your testimony that the Hardy
3 authors claim that immunization strategy is the
4 reason they were unable to achieve infertility?
5 MR. POWERS: Objection. Form.
6 THE DEPONENT: When you say "immunization
7 strategy," could you define that, what you mean by
8 that.
9 Q. (By Ms. Wang) Well, I asked you, it's
10 your opinion that Hardy did not use an optimized
11 immunization strategy, right?
12 And you said that's also what Hardy
13 indicates in their discussion, as well.
14 Do you recall that testimony?
15 A. Yes.
16 Q. And so it is your testimony that Hardy
17 says that they did not use an optimized
18 immunization strategy, and that was the reason they
19 couldn't --
20 MR. POWERS: Objection.
21 Q. (By Ms. Wang) -- achieve effective
22 contraception?
23 MR. POWERS: Objection. Form.
24 THE DEPONENT: It's my view that they
25 were not -- unable -- and Hardy says the same

1 thing. They were unable to elicit a response in
2 the female tract because of the intraperitoneal
3 approach.
4 Q. (By Ms. Wang) Hardy says that their
5 inability to cause contraception was due to the
6 intraperitoneal approach?
7 MR. POWERS: Objection. Form.
8 THE DEPONENT: Well, again, I probably --
9 I would like to look at that reference just --
10 before I offer an answer.
11 Q. (By Ms. Wang) We can move on.
12 You don't disagree that the Hardy authors
13 still generated a polyclonal antibody response in
14 mice with PH20, do you?
15 A. In plasma they did, yes.
16 Q. So the mice still raised polyclonal
17 antibodies against PH20?
18 A. Yes, that is correct.
19 Q. It's your opinion that the antibodies
20 were not in the right location?
21 A. Yes.
22 Q. In your declaration, you also discuss the
23 Rosengren 2015 paper.
24 Do you recall that?
25 A. Yes, I do.

1 Q. And that's Exhibit 1061?
2 A. Yes.
3 Q. Rosengren 2015 tested serum antibody of
4 human patients who were injected with PH20,
5 correct?
6 A. Yes.
7 Could you provide me with that paragraph
8 you're looking at.
9 Q. Paragraph 45.
10 A. Thank you.
11 Yes, thank you.
12 Q. So Rosengren 2015 tested serum antibody
13 of human patients who were injected with PH20?
14 A. Yes, correct.
15 Q. And the human patients were injected with
16 unmodified recombinant human PH20?
17 A. Yes, without an adjuvant.
18 Q. And serum antibody means the patient had
19 an immune response to the injected PH20, correct?
20 MR. POWERS: Objection. Form.
21 THE DEPONENT: Yes, it -- it could mean
22 that.
23 Q. (By Ms. Wang) The serum antibody -- let
24 me rephrase.
25 The serum antibodies that were tested

1 were anti-PH20?
2 MR. POWERS: Objection. Form.
3 THE DEPONENT: Yes, in some of the
4 patients.
5 Q. (By Ms. Wang) Meaning the Rosengren 2015
6 authors found that the serum antibodies in some of
7 the patients bound native PH20?
8 MR. POWERS: Object to form.
9 THE DEPONENT: I -- I think bound
10 recombinant PH20.
11 Q. (By Ms. Wang) You don't think any of the
12 serum antibodies found in patients bound native
13 PH20?
14 A. I don't think -- I don't think they
15 looked at that in terms of sperm -- native being
16 sperm PH20.
17 Q. Do you think antibodies that bind
18 recombinant PH20 would not bind native sperm PH20?
19 A. Native serum.
20 MR. POWERS: Objection. Form.
21 THE DEPONENT: Sorry, say that again.
22 I just want to...
23 Q. (By Ms. Wang) So you testified that you
24 think Rosengren 2015 tested serum antibodies and
25 found that they bound recombinant PH20, correct?

1 A. I believe that's right, yes.
2 Q. And you don't think that they tested
3 whether the serum antibody bound native sperm --
4 A. That is --
5 Q. -- PH --
6 A. Right, that is correct.
7 Q. And do you think that the testing that
8 found that serum antibody bound recombinant PH20
9 does not prove that the antibodies would have bound
10 native sperm PH20?
11 MR. POWERS: Objection. Form.
12 THE DEPONENT: Well, that wasn't tested,
13 so I -- I can't really offer an opinion on that.
14 Q. (By Ms. Wang) I understand that binding
15 to native sperm PH20 was not tested.
16 But what I'm trying to understand is,
17 testing of the serum -- or binding of the serum
18 antibodies to recombinant human PH20, does that
19 tell you something about whether those serum
20 antibodies would bind sperm PH20?
21 A. Yes, in a theoretical way, that's true.
22 I believe, though, the titers they
23 identified in these patients were extremely low
24 titers.
25 Q. Well, I'm not asking about titers.

1 A. Yeah.
2 Q. I'm just asking about binding, so --
3 A. Just theoretically, yeah.
4 Q. So serum antibodies that bound
5 recombinant human PH20 antibody would theoretically
6 also bind human sperm PH20, correct?
7 MR. POWERS: Object to form.
8 THE DEPONENT: Could, yes.
9 Q. (By Ms. Wang) You said it "could."
10 Are there instances where it wouldn't?
11 A. Well, I would -- I would say that a POSA
12 would have predicted that it would.
13 But also, the Rosengren -- both Rosengren
14 studies were well after 2012. So in principle, a
15 POSA wouldn't have even looked at those, you know,
16 to think about PH20 binding in humans.
17 Q. So setting aside the timing -- and I
18 appreciate you have your opinions on that -- what
19 I'm trying to understand is, someone looking at
20 serum antibodies that bound recombinant human PH20
21 antibody, is there any reason they would think it
22 would not also bind human sperm PH20?
23 MR. POWERS: Object to form.
24 THE DEPONENT: No.
25 Q. (By Ms. Wang) Would one need to test

1 polyclonal antibodies raised against recombinant
2 PH20 to know if they would bind to the PH20 on
3 sperm?
4 MR. POWERS: Objection. Form.
5 THE DEPONENT: No, it would be -- a POSA
6 would predict that it would or expect that it
7 would.
8 Q. (By Ms. Wang) The Rosengren authors
9 found that serum antibodies bound recombinant human
10 PH20, but they found no instance in any serum
11 sample of antibodies that neutralized PH20 enzyme
12 activity, did they?
13 MR. POWERS: Object to form.
14 THE DEPONENT: I believe that's true.
15 Q. (By Ms. Wang) Are you aware that
16 Rosengren 2015 was authored by employees of
17 Halozyme?
18 A. Yes, I was.
19 Q. And Halozyme is the patent owner in this
20 proceeding, correct?
21 A. Yes.
22 Q. So inducing a polyclonal antibody
23 response against PH20 does not always result in
24 infertility in the subject, correct?
25 MR. POWERS: Objection. Form.

1 THE DEPONENT: Well, the qualifier is, if
2 it's a serum response, there -- there has to be a
3 response and a significant response in the
4 reproductive tract to affect sperm. And the
5 responses they report in the papers were very
6 minimal, barely detectable. They were present, but
7 ti- -- yeah, the antibodies were present but very
8 low levels, even in the serum.
9 Q. (By Ms. Wang) So your opinion is, you
10 need the polyclonal antibody response against PH20
11 to be in a particular location in the body for
12 there to be effective contraception?
13 A. Yes, similar to what I stated earlier,
14 right.
15 Q. And also said a "significant response."
16 So does that mean you need a particular
17 amount of polyclonal antibody response against PH20
18 in a particular location for there to be effective
19 contraception?
20 MR. POWERS: Objection. Form.
21 THE DEPONENT: Well, an adequate --
22 adequate response for -- to have enough to bind to
23 sperm.
24 Q. (By Ms. Wang) So just a little bit of
25 polyclonal antibody in the reproductive tract would

1 not be enough to be effective as a contraception?
2 A. Well, I can't opine on that specifically,
3 but it's similar in -- I've talked about the
4 mucosal response eliciting -- or an intranasal
5 administration and a mucosal response eliciting a
6 high -- relatively high level of antibody that
7 is -- that's been shown for other antigens. Not
8 related to sperm, but to HIV and herpes.
9 And that's plenty of antibody response to
10 completely neutralize HIV and herpes virus.
11 Q. Do you know how much antibody response
12 would be needed against PH20 for there to be an
13 effective contraception?
14 MR. POWERS: Object to form.
15 THE DEPONENT: Again, I can't opine on
16 that because I don't have specific amounts.
17 Q. (By Ms. Wang) You don't know what the
18 specific amounts are?
19 A. No, I don't.
20 Q. Across the studies that we have talked
21 about, subcutaneous administration of native PH20
22 did not cause contraception in several species,
23 right?
24 A. Yes, that's true.
25 Q. So is it your opinion that the route of

1 administration matters to getting effective
2 contraception with a modified PH20 polypeptide?
3 A. Yes, I believe that's one of the most
4 important factors.
5 Q. So the usefulness of the modified PH20
6 polypeptides as contraceptive vaccines depends on
7 how they are delivered?
8 MR. POWERS: Object to form.
9 THE DEPONENT: Yes, I believe it is.
10 Q. (By Ms. Wang) Is it your opinion that in
11 2012, the POSA would have understood that
12 subcutaneous immunization would never work to cause
13 contraception?
14 MR. POWERS: Objection. Form.
15 THE DEPONENT: Are you referring --
16 excuse me, are you referring to human or to animals
17 or general or...
18 Q. (By Ms. Wang) Well, is it your opinion
19 that a POSA would have understood in 2012 that
20 subcutaneous immunization would not work in humans
21 to cause contraception?
22 A. So based on the papers that were
23 published that had used subcu and intraperitoneal
24 and even intramuscular, there was not an adequate
25 response in the reproductive tract to result in

1 contraception.
2 And, again, that's discussed in -- in the
3 discussions of the papers from 2002, 2004 and --
4 and other papers, even from the late '90s. So a
5 POSA would have been aware that that is a major
6 issue.
7 Q. And a POSA in 2012 would not expect
8 subcutaneous immunization to be -- to work in
9 humans to cause contraception?
10 MR. POWERS: Objection. Form.
11 THE DEPONENT: Yes, in humans. It might
12 work in guinea pigs but not humans.
13 Q. (By Ms. Wang) A POSA in 2012 would not
14 expect subcutaneous immunization to work in mice to
15 cause contraception?
16 MR. POWERS: Objection. Form.
17 THE DEPONENT: Probably, yes. Again,
18 based on the discussions of -- of those studies
19 that did not elicit an adequate immune response in
20 the reproductive tract.
21 Q. (By Ms. Wang) We've talked about your
22 opinion that where the location in the body, where
23 the polyclonal response is generated, matters to
24 contraception, right?
25 A. Yes.

1 Q. And it's your testimony that the route of
2 administration also matters to contraception?
3 A. So those are interrelated, yes.
4 Q. Is it also your opinion that the use of
5 adjuvants matters to effective use of modified PH20
6 polypeptide as a contraceptive vaccine?
7 A. Yes. That would increase the efficiency
8 of the response tremendously.
9 Q. Does a depend on a particular adjuvant?
10 A. Depends -- again, it depends. In your
11 question, are you talking about in mucosal response
12 or the reproductive tract, or are you talking the
13 circulating plasma?
14 Q. Well, your opinion is that there needs to
15 be a mucosal response for there to be effective
16 contraception, right?
17 A. Yes, correct.
18 Q. And you need adjuvants with the mucosal
19 route as well, right?
20 A. That's what's been used, yes.
21 Q. Would you use the same adjuvants in the
22 mucosal route as were used in the subcutaneous
23 route?
24 A. Probably not.
25 Q. But it's your opinion that even

1 subcutaneous administration with adjuvants would be
2 insufficient to cause contraception in animals
3 other than guinea pigs?
4 MR. POWERS: Object to form.
5 THE DEPONENT: Yes, essentially that's
6 what was done with the Hardy and Pomering studies.
7 Q. (By Ms. Wang) In your opinion, does the
8 particular dosage matter to effective contraception
9 with a modified PH20 polypeptide?
10 A. Well, I can't give an opinion on specific
11 amounts that would be necessary for an adequate
12 response, but yes. I mean, if it's an extremely
13 low level, there may not be a response. It may
14 have to be of an adequate level, but I can say what
15 that is. Or I can't offer an opinion on w
16 is.
17 Q. So you do need enough modified PH20
18 polypeptide for an adequate immune response?
19 A. Yes, and I think would be probably on par
20 to what have been used to achieve plasma levels
21 circulating.
22 Q. But you don't know what amount that would
23 be --
24 A. Well --
25 Q. -- sitting here today?

1 A. They're in the microgram -- microgram per
2 million quantities.
3 Q. But you don't specific quantities?
4 MR. POWERS: Objection. Form.
5 THE DEPONENT: Again, I -- I need to look
6 through references to -- to tell you specifically
7 what was used in those studies.
8 Q. (By Ms. Wang) So we discussed this
9 earlier, but it's your opinion that the polyclonal
10 antibodies generated against any of the modified
11 PH20 polypeptides would bind to the PH20 poly- --
12 PH20 polypeptide of sperm in the reproductive tract
13 of the female mammal and cause contraception?
14 A. Yes. If it's an adequate response, yes,
15 that's correct.
16 Q. And that would include humans?
17 A. Yeah.
18 Q. Are you aware of any evidence published
19 before 2012 of modified PH20 polypeptides causing
20 polyclonal antibodies that bind native human PH20?
21 MR. POWERS: Objection. Form.
22 THE DEPONENT: I am not other than
23 recombinant -- just recombinant proteins, native
24 protein structure.
25 Q. (By Ms. Wang) You are aware of

1 recombinant native proteins but not of modified
2 PH20 polypeptides generating --
3 A. Yeah.
4 Q. -- polyclonal responses against native
5 human PH20?
6 MR. POWERS: Objection. Form.
7 THE DEPONENT: Correct, or at least I'm
8 unaware.
9 Q. (By Ms. Wang) Are you aware of any
10 evidence published after 2012 of modified PH20
11 polypeptides causing antibodies that bind native
12 human PH20?
13 A. No, I am not aware of that.
14 Q. Are you aware of any evidence published
15 before 2012, of successful contraception in humans
16 using native PH20 as a vaccine?
17 A. I am not aware of any studies on that.
18 Q. And you are not aware of studies before
19 2012 of successful contraception in humans using
20 modified PH20 polypeptides as a vaccine?
21 A. I'm not aware, no.
22 Q. Are you aware of any evidence published
23 after 2012 of successful use of a modified PH20
24 polypeptide as a vaccine?
25 MR. POWERS: Objection. Form.

1 THE DEPONENT: No, I am not.
2 Q. (By Ms. Wang) In humans or in any other
3 mammals?
4 A. No, I am not.
5 Q. So is fair to say there's no evidence of
6 modified PH20 polypeptide being used successfully
7 for contraception in humans?
8 MR. POWERS: Objection. Form.
9 THE DEPONENT: Not that I'm aware of.
10 Q. (By Ms. Wang) Your opinion that
11 polyclonal antibodies generated against any of the
12 modified PH20 polypeptides would cause
13 contraception also applied to nonhuman mammals,
14 correct?
15 A. You mean using -- so using the modified
16 human PH20 polypeptides in other mammals?
17 Q. Yes.
18 A. Yes. It -- that's right.
19 Q. So your opinion is you can take the
20 modified human polypeptide -- PH20 polypeptide, use
21 it as contraception in nonhuman mammals, and it
22 would be effective?
23 A. Yes, as long it was done, again, in the
24 appropriate -- getting the antibodies in the
25 appropriate place in the reproductive tract.

1 Q. And those mammals would include rabbits,
2 right?
3 A. Uh-huh.
4 Q. Mice?
5 A. Yes.
6 Q. Rats?
7 A. Yes.
8 Q. And cynomolgus monkeys?
9 A. Yes.
10 Q. And that opinion is based on the opinion
11 that immunization with recombinant human modified
12 PH20 would cause the nonhuman mammal to generate
13 polyclonal antibodies in response and those
14 polyclonal antibodies would bind the nonhuman
15 mammals native PH20 on sperm?
16 MR. POWERS: Objection. Form.
17 THE DEPONENT: Yes. Again, if it's
18 administered in the appropriate way to elicit a
19 response in the reproductive tract of those
20 animals.
21 Q. (By Ms. Wang) Do you agree that in 2012
22 the POSA's expectation would have been that in
23 order to test contraception efficiency in a certain
24 species, PH20 from that species must be used as an
25 immunogen?

1 MR. POWERS: Objection. Form.
2 THE DEPONENT: No, because of the percent
3 homology of the human PH20 to those other animals
4 theoretically is high enough, kind of in the
5 50 percent and higher range, and that should elicit
6 an immune response, and those polyclonal antibodies
7 should bind to that animal's PH20 that's in their
8 sperm.
9 Q. (By Ms. Wang) Are you aware of any
10 evidence published before 2012 investigating the
11 effect of human PH20 on fertility in nonhuman
12 mammals?
13 MR. POWERS: Objection. Form.
14 THE DEPONENT: No, I am not aware.
15 Q. (By Ms. Wang) Are you aware of any
16 evidence published before 2012 of using modified
17 human PH20 polypeptide to see its effect on
18 fertility in nonhuman mammal?
19 MR. POWERS: Same objection.
20 THE DEPONENT: No, I am not.
21 Q. (By Ms. Wang) Are you aware of any
22 instances in which immunogens with less than
23 60 percent sequence identity to the native PH20 in
24 an animal were used in vivo and caused infertility
25 in that animal?

1 MR. POWERS: Same objection.
2 THE DEPONENT: No. I am not aware of
3 that.
4 Q. (By Ms. Wang) Would you agree that an
5 immunogen with a higher sequence identity to the
6 native PH20 would be more likely to present
7 epitopes that would cause the production of
8 antibodies that would bind to the native PH20?
9 MR. POWERS: Objection. Form.
10 THE DEPONENT: I think for -- excuse
11 me -- for polyclonal antibodies, that kind of
12 sequence identity should be sufficient in -- in a
13 theory -- in theory to result in antibody
14 production, and those antibodies would bind to the
15 animal's PH20.
16 Q. (By Ms. Wang) You said "that kind of
17 sequence identity," what sequence identity --
18 A. Kind of -- in the -- 50 percent or
19 higher. Most of those animals are above
20 60 percent.
21 Q. And the opinion that most animal are
22 above 60 percent identity, is that something you
23 independently developed?
24 A. No, I did not do that.
25 Q. Where did you -- repeat.

How did you come to the belief that most animals have above 60 percent identity?

A. You mean with those animals that were listed originally, or which animals?

Q. I think you -- I think your testimony was that most animals are in the 50 percent or higher identity; is what you said?

A. I think I was referring to the animals that were listed in my declaration, not -- I can't really speak to all the other ones.

Q. Fair enough.

So it's your belief that the animals listed in paragraph 30 of your declaration all have above 50 percent sequence identity to human PH20?

A. Yes, approximately.

Q. And you did not form that belief independently?

A. No, Dr. Moon refers to that in his declaration.

MR. POWERS: Sue, is now a good time for lunch?

MS. WANG: Just a couple more questions from me.

MR. POWERS: Okay.

Q. (By Ms. Wang) It's okay, Dr. Cherr?

A. That's fine.
Q. Your opinion that modified PH20 polypeptides would cause contraception in nonhuman mammals is based on the belief that those nonhuman mammals have above 50 percent sequence identity, right?
A. Or -- or near 50 percent, yes.
Q. And that belief that those human -- nonhuman mammals in paragraph 30 -- are near or above 50 percent sequence identity; that is from Dr. Moon?
A. Yes, that's right.
Q. Are you aware of any evidence published after 2012 investigating the effect of native human PH20 on fertility in nonhuman mammals?
A. No, I am not aware.
Q. What about any evidence after 2012 of using modified PH20 polypeptides to investigate fertility in nonhuman mammals?
A. No, I am not aware of that.
Q. Are you aware of any evidence published after 2012 that immunizing nonhuman mammals with recombinant human PH20 caused infertility in those nonhuman mammals?
MR. POWERS: Objection. Form.

1 THE DEPONENT: I'm sorry. Can you say
2 that again?
3 Q. (By Ms. Wang) Are you aware of any
4 evidence published after 2012 --
5 A. After.
6 Q. -- that immunizing nonhuman mammals with
7 recombinant human PH20 caused infertility in the
8 nonhuman mammals?
9 MR. POWERS: Same objection.
10 THE DEPONENT: I'm not aware.
11 MR. POWERS: That's a lot more than a
12 couple questions, Sue, for me. Can we have lunch
13 now?
14 Would you like a break, Doctor?
15 THE DEPONENT: Sure.
16 MS. WANG: Okay.
17 THE VIDEOGRAPHER: Okay. The time is
18 12:13 p.m. Pacific time. We are off the record.
19 (Recess taken.)
20 THE VIDEOGRAPHER: The time is 1:06 p.m.
21 Pacific time. We are on record.
22 Q. (By Ms. Wang) Welcome back, Dr. Cherr.
23 During the lunch break, did you speak
24 with counsel?
25 A. No, I did not.

1 Q. So before the break, we were talking -- I
2 was asking about evidence published regarding the
3 effect of human PH20 on fertility in nonhuman
4 mammals.
5 Do you recall that?
6 A. I do.
7 Q. And you are not aware of any evidence
8 published regarding using human PH20 and its effect
9 on fertility in nonhuman mammals?
10 MR. POWERS: Objection. Form.
11 THE DEPONENT: Could you -- I'm sorry.
12 Q. (By Ms. Wang) Let me rephrase that.
13 You are not aware of any published
14 evidence before 2012 regarding the effect of native
15 human PH20 on fertility in nonhuman mammals --
16 MR. POWERS: Objection. Form.
17 Q. (By Ms. Wang) -- right?
18 A. Cor- -- I'm not aware, yes.
19 Q. Are you aware of any evidence published
20 after 2012 describing non- -- describing immunizing
21 nonhuman mammals with recombinant human PH20 to
22 investigate the effect on infertility in those
23 nonhuman mammals?
24 MR. POWERS: Objection. Form.
25 THE DEPONENT: I'm not aware.

1 Q. (By Ms. Wang) Would you agree that
2 experimental evidence testing human PH20 and its
3 effect on fertility would be useful to determining
4 whether the PH20 would work as a contraception?
5 MR. POWERS: Objection. Form.
6 THE DEPONENT: I -- I really can't offer
7 an opinion on that because there's so many details
8 regarding how those kinds of approaches would be
9 taken. So just to make a blanket statement, I -- I
10 can't necessarily offer an opinion.
11 Q. (By Ms. Wang) You don't think evidence
12 showing PH20's effect on fertility experimentally
13 would be useful to know whether it would be useful
14 as a contraceptive?
15 A. Again, it would have -- it would depend
16 on how -- how those experts were done. And, again,
17 I come back to this routinely, that -- if they were
18 able to -- so making a general statement about
19 that, I don't agree with. But it was done where
20 there was mucosal -- appropriate mucosal response,
21 that it could be. But, again, those details -- not
22 very simple. Those are complicated details.
23 Q. So experimentation -- experimental
24 evidence showing PH20's effect on fertility that is
25 not delivered mucosally in your opinion would just

not be relevant?

MR. POWERS: Objection. Form.

THE DEPONENT: Would not be -- I think based on what a POSA would know in -- by 2012 that an administration, that did not elicit a mucosal response, there would be failure or no contraception.

Q. (By Ms. Wang) Is it your opinion that the POSA would ignore experimental evidence using PH20 in various animals but injected subcutaneously?

MR. POWERS: Object to form.

THE DEPONENT: I don't know if a POSA would ignore, but I think that a POSA -- their expectation would be that you would need to elicit a mucosal response in order to see it or observe an effect.

Q. (By Ms. Wang) So in your mind, experimental evidence showing the effect of PH20 injected subcutaneously on fertility in an animal would not be relevant to the POSA's determination of whether PH20 would be useful as a contraceptive vaccine?

MR. POWERS: Objection. Form.

THE DEPONENT: I'm sorry. Could you

1 can you further define "relevant," what you mean by
2 that?
3 Q. (By Ms. Wang) Well, would experimental
4 evidence showing the effect of the PH20 injected
5 subcutaneously be probative for the POSA in
6 determining whether PH20 would be useful as a
7 contraceptive vaccine?
8 A. I'm sorry. "Prohibitive"?
9 Q. "Probative."
10 A. "Probative." You're talking about prior
11 to 2012?
12 Q. Well, I'm asking generally about
13 experimental evidence.
14 MR. POWERS: Objection. Form.
15 THE DEPONENT: I think it -- I think that
16 assessing the immune response and the location of
17 the immune response would be absolutely critical;
18 otherwise, it may not be very useful.
19 Q. (By Ms. Wang) Are you saying the POSA
20 would look at experimental evidence generated from
21 injecting PH20 subcutaneously to assess the
22 location of the immune response to determine if it
23 was probative?
24 MR. POWERS: Objection. Form.
25 THE DEPONENT: No, because -- well,

1 again, prior to 2012, it -- it was, in my mind,
2 clear that a POSA would understand that experiments
3 with -- with experimental animals, subcutaneous
4 injections are not successful in eliciting an
5 appropriate response in the reproductive tract.
6 And I don't think that would change after 2012
7 either.
8 Q. (By Ms. Wang) Are you aware of any
9 evidence, period, whether published or not,
10 investigating the effect of native human PH20 on
11 fertility in nonhuman mammals?
12 MR. POWERS: Object to form.
13 THE DEPONENT: No, I am not.
14 Q. (By Ms. Wang) Are you aware of any such
15 evidence for modified PH20 polypeptide on fertility
16 in nonhuman mammals?
17 A. No, I am not.
18 Q. Are you aware that scientists at Halozyme
19 investigated whether immunization of nonhuman
20 mammals with recombinant human PH20 would cause
21 infertility in those mammals?
22 A. I'm not aware of that. Is that published
23 or --
24 Q. So you haven't review any expert --
25 A. I haven't reviewed it, no.

1 Q. Were informed these experiments had been
2 performed?
3 MR. POWERS: Objection. Form.
4 (Court Reporter asks for clarification.)
5 THE DEPONENT: No.
6 Q. (By Ms. Wang) And confirm you have not
7 spoken to any Halozyme scientists in connection
8 with this case?
9 A. No, no.
10 Q. So in connection with your opinion that
11 by December 2012 POSAs would have expected the
12 polyclonal antibodies generated female mammals in
13 response to any of the modified PH20 polypeptides
14 would cause contraception, did you thoroughly
15 investigate the literature before 2012 in forming
16 your opinions?
17 MR. POWERS: Objection. Form.
18 THE DEPONENT: I did.
19 Q. (By Ms. Wang) And you thoroughly
20 investigated the literature before 2012 on efforts
21 to use PH20 as an immunocontraception before you
22 prepared your declaration?
23 A. Yes, that's correct.
24 Q. And do you believe that the evidence you
25 presented in your declaration is the most probative

1 on the question?
2 A. I believe so.
3 Q. And that question would be whether a POSA
4 would have considered PH20 to be a useful antigen
5 for inclusion in immunocontraceptive vaccines?
6 MR. POWERS: Objection. Form.
7 THE DEPONENT: Yes, with -- well, with
8 the caveat of, again, coming back to the immune
9 response in the female tract. So that -- that
10 would be critical.
11 Q. (By Ms. Wang) Right.
12 But you believe the evidence cited in
13 your declaration is the most probative of the
14 question, whether a POSA would have considered
15 modified PH20 polypeptides to be useful for
16 inclusion in immunocontraceptive vaccines?
17 A. Yes, I believe so.
18 Q. And you identified no studies outside of
19 the guinea pigs where a polyclonal antibody
20 response to PH20 caused contraception, correct?
21 MR. POWERS: Objection. Form.
22 THE DEPONENT: That is correct based on
23 the literature I reviewed, yes.
24 Q. (By Ms. Wang) And you don't think it's
25 possible that someone before you reviewing the

1 data from nonprimate models would conclude that
2 PH20 is not a useful antigen for inclusion in
3 immunocontraceptive vaccines?
4 MR. POWERS: Objection. Relevance.
5 THE DEPONENT: I think if you look at the
6 discussion in those key papers that I've presented
7 in my declaration, they're very clear in their
8 discussion of potentially why they did not have
9 contraceptive effects. And, again, it comes back
10 to the antibodies being at the right place at the
11 right time in sufficient quantities.
12 Q. (By Ms. Wang) So you don't think someone
13 reviewing those key papers would conclude that PH20
14 is not a useful antigen for inclusion in
15 immunocontraceptive vaccines?
16 MR. POWERS: Objection. Relevance.
17 THE DEPONENT: I just want to make sure I
18 have it right. Say it, please.
19 Q. (By Ms. Wang) Yeah.
20 You don't think it's possible someone
21 reviewing the key papers you cited in your
22 declaration would conclude that PH20 is not a
23 useful antigen for inclusion in immunocontraceptive
24 vaccines?
25 MR. POWERS: Same objection.

1 THE DEPONENT: Correct, if they did a
2 careful analysis of what was in those papers.
3 Q. (By Ms. Wang) Earlier we talked about
4 the Hardy 2004 paper.
5 Do you recall that?
6 A. Yes.
7 Q. And you confirmed for me that the Hardy
8 authors delivered mirroring PH20 by virus
9 administration?
10 A. But I think the -- the actual route of
11 exposure in the Hardy paper was intraperitoneal, I
12 believe. But, again, I -- I'd like to look at the
13 reference.
14 Q. I'll direct your attention to page 328 of
15 Exhibit 1019.
16 A. Yes.
17 Q. Let me ask the question again so I can
18 get the right answer.
19 So Hardy -- the Hardy authors delivered
20 PH20 using recombinant virus administration,
21 correct?
22 A. That was one of the ways they did, yes.
23 Q. And recombinant virus administration also
24 generates polyclonal antibodies in serum?
25 A. It looks like it triggered an antibody

1 response in a proportion of the animals, not in all
2 of them.
3 Q. My question is, the recombinant viral
4 administration generates polyclonal antibodies in
5 serum, right?
6 MR. POWERS: Objection. Form.
7 THE DEPONENT: Right.
8 So I believe they found that serum from
9 several mice did not contain immunoglobulin
10 antibodies using that approach.
11 Q. (By Ms. Wang) And serum from other mice
12 did --
13 A. Did, yes.
14 Q. But this recombinant viral approach
15 results in antibodies in serum and not the
16 reproductive tract, right?
17 A. Well, it only -- it only elicited
18 antibodies in serum in a proportion. I think it
19 was two out of the six of the animals, I believe.
20 Q. And it did not elicit antibody response
21 in the reproductive tract?
22 A. They didn't -- they did not study that.
23 Q. Okay. Is it your opinion that the POSA
24 would not view recombinant viral delivery of PH20
25 as a viable mechanism for causing contraception?

1 MR. POWERS: Objection. Form.
2 THE DEPONENT: No, I don't believe so,
3 because whether that was the recombinant viral or
4 just the recombinant expressed PH20, either way,
5 even if there was a serum titer, they did not
6 achieve contraception.
7 And, again, it had to do with the route
8 of exposure not -- not triggering mucosal response
9 in the reproductive tract.
10 Q. (By Ms. Wang) So the POSA would use not
11 recombinant viral delivery of PH20 because it would
12 not raise sufficient titer in the reproductive
13 tract?
14 MR. POWERS: Objection. Form.
15 THE DEPONENT: No, they might -- they
16 might use it because it may elicit a response
17 through a very different route of exposure than
18 what was used in the study. Again, coming back to
19 the -- an intranasal type of exposure.
20 Q. (By Ms. Wang) So your opinion is the
21 POSA could use recombinant viral delivery of PH20
22 as long as they delivered the recombinant virus
23 intranasally?
24 MR. POWERS: Object to form.
25 THE DEPONENT: To trigger, yes, a mucosal

1 response. So it might be effective -- very
2 effective for that.
3 Q. (By Ms. Wang) I'd like to direct your
4 attention to paragraph 33 -- you can set that
5 aside.
6 A. Okay.
7 Q. Paragraph 33 of your declaration.
8 A. Yes.
9 Q. And, actually, just before paragraph 33,
10 the last sentence of paragraph 32, you state,
11 "POSAs would have known that the binding of
12 antibodies to sperm PH20 polypeptide in the female
13 reproductive tract would cause contraception
14 irrespective of where the antibodies bind on the
15 PH20 polypeptides."
16 Do you see that?
17 A. Yes.
18 Q. And that is your opinion?
19 A. That is my opinion.
20 Q. In order for anti-PH20 antibodies to
21 cause contraception, those antibodies have to bind
22 sperm surface PH20, correct?
23 A. Sperm surface or inside the acrosome.
24 But probably all -- all places, wherever PH20 is.
25 Q. And on the sperm surface, there is a

1 portion of PH20 that is not exposed, correct?
2 MR. POWERS: Objection. Form.
3 THE DEPONENT: A portion?
4 I would -- what do you mean by "a
5 portion"?
6 Q. (By Ms. Wang) There's a part of the PH20
7 protein structure on sperm that is not exposed to
8 the surface?
9 MR. POWERS: Objection. Form.
10 THE DEPONENT: Okay. Are you referring
11 to sperm in -- that are coated with, like, a
12 glycocalyx coat?
13 Q. (By Ms. Wang) No.
14 Maybe let me ask a different question.
15 In your opinion, are there epitopes of
16 PH20 on sperm that are not available for antibody
17 binding, assuming the glycocalyx has been removed?
18 A. Assuming the glycocalyx has been removed.
19 Potentially, a small portion of the lipid
20 anchor, where it anchors to the membrane, the outer
21 leaflet of the membrane, that small region may not
22 be recognized by antibodies. But also maybe is
23 a -- it's a small portion of the molecule.
24 Q. In your opinion, does soluble PH20 have
25 the exact same epitopes as sperm PH20?

1 MR. POWERS: Objection. Form.
2 THE DEPONENT: That is not known. It is
3 endoproteolytically cleaved, but still connected
4 with a disulfide bond. But I'm not aware of
5 studies that have done a complete analysis
6 Q. (By Ms. Wang) So you don't know whether
7 soluble PH20 has different epitopes from sperm
8 PH20?
9 MR. POWERS: Object to form.
10 THE DEPONENT: I don't -- well, I don't
11 think it does.
12 Any sort of changes that occur during the
13 acrosome reaction, it really is not very relevant,
14 assuming there's a polyclonal antibody response,
15 because it would be expected that polyclonal
16 antibodies would bind to that soluble form as well
17 as the membrane-bound form. There's multiple --
18 multiple regions along the protein that would
19 available.
20 Q. (By Ms. Wang) Right.
21 I'm not asking about polyclonal
22 antibodies.
23 A. Right.
24 Q. I'm just asking about protein structure.
25 A. Okay.

1 Q. So do you know whether soluble PH20 has
2 the same epitopes as sperm PH20?
3 MR. POWERS: Objection. Asked and
4 answered.
5 THE DEPONENT: I don't know.
6 I can't say for sure.
7 Q. (By Ms. Wang) In paragraph 33 of your
8 opinion, you say the POSA would have known that
9 antibodies "would prevent sperm from fertilizing
10 the oocyte by, e.g., inhibiting sperm motility,
11 inducing sperm agglutination, reducing penetration
12 of cervical mucus by sperm, interfering with sperm
13 capacitation or the acrosome reaction, or
14 stimulating sperm lysis via the complement
15 pathway," correct?
16 A. Yes, yeah.
17 Q. Do you know which of these mechanisms
18 actually prevents fertilization?
19 A. Well, certainly, they all could, because
20 they could prevent sperm from getting up into the
21 oviduct or, once it's in the oviduct, prevent it
22 from -- prevent sperm from getting to the oocyte
23 itself.
24 So any sort of effect on mobility, on --
25 if it induced sperm agglutination, for example, any

1 sort of effect on cervical mucus penetration by
2 sperm, and then, of course, inhibition of either
3 capacitation or the acrosome reaction, all those
4 could contribute to lack of fertilization.
5 Q. Does contraception require all of these
6 mechanisms to occur?
7 MR. POWERS: Object to form.
8 THE DEPONENT: No, I don't believe
9 there's a requirement for all of them, but any --
10 any one or any one combination of them could
11 contribute to contraception.
12 Q. (By Ms. Wang) If only one of the
13 mechanisms occurred, is that, in your opinion,
14 enough to prevent fertilization?
15 A. If it was a mechanism that either
16 prevented sperm from reaching the oviduct or within
17 the oviduct caused agglutination or lysed killing
18 of sperm, of course that would have an effect.
19 But also, even if it was a mechanism -- I
20 mean, again, you're talking about choosing one of
21 the mechanisms. But if it was a mechanism on -- in
22 terms of the acrosome reaction or binding to the
23 zona pellucida, anything like that, that would
24 be -- that would definitely affect fertilization.
25 Q. Right.

1 But I'm trying to understand if there's
2 one mechanism that alone would prevent
3 fertilization.
4 A. Yeah, I -- I don't want to speculate, but
5 I -- I believe that if you have antibodies binding
6 to PH20 on sperm that potentially numerous
7 mechanisms are impacted, not just one, necessarily.
8 Q. Do you know which mechanisms are
9 impacted?
10 MR. POWERS: Object to form.
11 THE DEPONENT: Well, I don't -- I don't
12 know myself.
13 But a POSA would have derived that once
14 PH20 is exposed in the oviduct when sperm undergo
15 capacitation, and they bind those antibodies,
16 they're probably not going to be able to move
17 forward in the oviduct, and they certainly couldn't
18 enter the cumulus matrix. And then they wouldn't
19 acrosome-react and bind to the zona pellucida.
20 So I think from the basic mechanisms of
21 sperm and how they fertilize an oocyte that that
22 kind of information with -- with -- and antibodies
23 bound to them, that would be what -- what would be
24 expected, that you would have an effect at multiple
25 levels.

1 Q. (By Ms. Wang) Am I understanding you
2 correctly that the POSA would expect multiple
3 mechanisms but not know which one was actually
4 working?
5 A. Yes, I think that's right, yeah.
6 Q. They don't know the mechanism -- the
7 actual mechanism of action without testing for it?
8 MR. POWERS: Object to form.
9 THE DEPONENT: I don't -- I think they
10 don't need to know that to at least be able to move
11 forward with -- with the approach of developing a
12 contraceptive vaccine.
13 Q. (By Ms. Wang) Just to confirm, this is
14 your opinion for any and all of the modified PH20
15 polypeptides?
16 A. Yes, I think it would be the same sort of
17 thing we've been talking about, where those would
18 elicit a very similar level of antibody of response
19 in the upper tract, again, appropriately
20 administered to elicit a mucosal response.
21 Q. Is it your opinion that the
22 contraceptive -- rephrase.
23 Is it your opinion that modified PH20
24 polypeptides have to raise an antibody response in
25 the upper reproductive tract to be effective as

1 contraception?
2 MR. POWERS: Objection. Form.
3 THE DEPONENT: I believe it has to be
4 throughout the reproductive tract, ideally.
5 Q. (By Ms. Wang) Would modified PH20
6 polypeptides be effective as contraception if they
7 only raised antibody response in the upper
8 reproductive tract?
9 A. Yes, they would be effective, but that --
10 that would also be unlikely because of the mucosal
11 response and where that -- and that's throughout
12 the reproductive tract.
13 Q. Would modified PH20 polypeptides be
14 effective as contraception if they only raised
15 antibody response in the lower reproductive tract?
16 MR. POWERS: Object to form.
17 THE DEPONENT: I think that's kind of an
18 unlikely scenario if its administered in the --
19 again, in the appropriate way, whether -- to elicit
20 a mucosal response, because the upper reproductive
21 tract and the oviduct and the uterus are known to
22 be places where there's high secretion of mucosal
23 immunoglobulin A, IgA.
24 Q. (By Ms. Wang) Is it your belief that
25 mucosal administration of an antigen -- rephrase,

1 sorry.
2 Is it your belief that any mucosal
3 administration of an antigen would result in
4 antibody production in both the upper and lower
5 reproductive tracts?
6 A. I just want to be clear.
7 Could you please define your definition
8 of "lower."
9 I guess there's different regions to the
10 reproductive tract, so I just want to be sure I'm
11 understanding what you're referring to.
12 Q. Right.
13 Well, let me rephrase my question, then.
14 Your belief is that any mucosal
15 administration of modified PH20 polypeptides would
16 generate antibodies throughout the reproductive
17 tract?
18 A. If -- if administered to elicit a mucosal
19 response, yes, there would be -- and there may be
20 varying levels in different regions. But, yes, it
21 would be throughout the reproductive tract.
22 Q. But there would be varying levels in
23 different regions of the reproductive tract,
24 correct?
25 MR. POWERS: Objection. Form.

1 THE DEPONENT: Yes, because of where
2 mucosal secretion of antibodies occurs, which is in
3 the upper, in the oviduct and in the uterus and, to
4 some degree, in the cervix, there would be
5 throughout much of it, as well as, you know, some
6 movement of those antibodies down to the vagina, as
7 well.
8 Q. (By Ms. Wang) And the form of mucosal
9 administration doesn't matter to the level of
10 antibody production in different regions of the
11 reproductive tract?
12 A. So I think you need to define "form" --
13 Q. Okay.
14 A. -- when you say that.
15 Q. The type of administration that causes a
16 mucosal response, does it matter?
17 A. Well, as I opined in my declaration,
18 intranasal has been the most common, and it's known
19 to elicit the strongest response. But there's also
20 vaginal administration, rectal, you know. But all
21 of those will elicit at some different levels.
22 But intranasal has been the one that
23 seems to have really a high efficiency on antibody
24 production, IgA antibody production.
25 Q. Oral administration is also a form of

1 mucosal --
2 A. Oral can, probably less so than the
3 intranasal route.
4 Q. So oral administration would not
5 elicit --
6 A. Would not --
7 Q. -- would not elicit the necessary
8 antibody response in the reproductive tract?
9 MR. POWERS: Object to form.
10 THE DEPONENT: It could.
11 I mean, it hasn't -- oral has been used
12 with certain antigens, certain viral path- -- and
13 pathogens.
14 But, again, intranasal, in the -- for the
15 reproductive tract, intranasal seems to be the
16 strongest response that's been documented to date.
17 Q. (By Ms. Wang) Vaginal administration
18 would not elicit a strong enough antibody response
19 in the reproductive tract?
20 MR. POWERS: Objection. Form.
21 THE DEPONENT: It could, and they --
22 people have used intranasal and vaginal in
23 combination to elicit a very strong response.
24 Q. (By Ms. Wang) How about vaginal alone?
25 MR. POWERS: Same objection.

1 THE DEPONENT: I'm not sure, but I don't
2 think it's as effective as intranasal.
3 Q. (By Ms. Wang) Does vaginal
4 administration elicit an antibody response in a
5 different region of the reproductive tract than
6 intranasal?
7 A. So my understanding is that vaginal
8 administration elicits a mucosal response. So that
9 would be throughout -- not necessarily in the
10 vagina, but throughout the upper reproductive tract
11 where those -- as I mentioned, those secretory
12 centers are. But, again, it may just not be as
13 strong as the intranasal.
14 Q. And I guess I should confirm with you,
15 how are you defining "upper reproductive tract"?
16 A. Oh, I -- so I usually think of it as the
17 uterus and fallopian tube.
18 Q. And is the amount of mucosal secretion
19 different between the uterus and the fallopian
20 tube?
21 A. Those are pretty similar. It's that --
22 the iliac system in terms of secretion. And
23 there's also some in the cervix, but none in the
24 vagina.
25 Q. So if the DSA were able to elicit a

1 mucosal response, is it your opinion that there
2 would be similar amounts of antibody in the uterus
3 and the fallopian tube?
4 A. Yes, I mean, that would be the
5 expectation.
6 Q. You mentioned in your declaration at
7 paragraph 33 agglutination as a mechanism by which
8 antibody binding to sperm could cause
9 contraception.
10 A. Yes.
11 Q. What causes agglutination?
12 A. So this is -- a lot of this is known from
13 antisperm antibodies that women -- and this goes
14 back to the '60s and '70s. And their partners'
15 sperm tend to be agglutinated if they have auto
16 sperm -- or anti -- sorry, antisperm antibodies.
17 And it's usually because of the
18 immunoglobulin molecule having -- being polyvalent.
19 And so antibody bound to one sperm, especially when
20 they're so dense in the lower reproductive tract,
21 that the antibodies will essentially cross-link
22 sperm and cause them to agglutinate.
23 Q. So agglutination requires a large amount
24 of sperm?
25 A. That's right, and that's where it's

1 mainly been observed down in the lower tract.
2 Q. Would you expect agglutination in the
3 oviduct?
4 A. Probably less likely than the lower
5 tract. I mean, it certainly could happen, but...
6 Q. You said the earlier, the sperm density
7 in the oviduct is fairly low, right?
8 A. It's fairly low, but just -- as you
9 recall that figure, they're bound to those
10 oviductal cells, and so they're close to each other
11 when they're bound there. There's not that many of
12 them, but the ones that are bound there, they're
13 close.
14 So if antibodies are present as soon as
15 DEFB126 comes off, there's a possibility for
16 cross-linking of sperm and some degree of
17 agglutination there.
18 Q. You also talk in paragraph 34 of your
19 declaration about binding of antibodies to sperm
20 PH20 polypeptide causing allosteric effects
21 irrespective of where the antibodies bound on PH20
22 polypeptide.
23 A. Yeah.
24 Q. What do you mean "allosteric effect"?
25 A. Well, so there's kind of -- the idea of

1 steric effects of -- when an antibody's binding,
2 say, to an enzyme. In this case, it's a
3 hyaluronidase. But it's -- it's been more -- it's
4 been better studied in something like an enzyme
5 protease.
6 And it can bind to -- an antibody can
7 bind to the active site or to sites adjacent to the
8 active site and can induce some sort of steric --
9 sorry, confirmational change in the protein that
10 will affect the active site without actually
11 binding to the active site.
12 So that's just an example.
13 Q. Has the allosteric effect been studied in
14 PH20?
15 A. Not that I'm aware of.
16 Q. And in your opinion, the allosteric
17 effect interfering with PH20 enzyme activity could
18 occur regardless of where the antibody binds on
19 PH20?
20 MR. POWERS: Object to form.
21 THE DEPONENT: Yes, particularly in
22 relation to the size of the substrate, which is
23 many millions molecular weight the hyaluronic acid.
24 So, you know, it's not a small protein that's being
25 hydrolyzed. And so physically, antibodies bound

1 along much of PH20 could inhibit that interaction
2 with hyaluronic acid.
3 Q. (By Ms. Wang) Does your opinion assume
4 that there would be multiple antibodies bound to
5 PH20 in order for there to be an allosteric effect?
6 A. Yes, in terms of polyclonals, yes.
7 Q. So just one antibody may not generate an
8 allosteric effect?
9 MR. POWERS: Object to form.
10 THE DEPONENT: Again, that's -- the --
11 the assumption is that if you have a polyclonal
12 response and polyclonal antibodies are binding
13 along the PH20 protein, you know, it wouldn't just
14 be one, or one site.
15 Q. (By Ms. Wang) But if only one antibody
16 binds to PH20, that antibody may not cause an
17 allosteric effect?
18 A. Yeah, it's hard to opine on that kind of
19 speculation. I -- I, you know, I mean, that's --
20 that might be from -- from an in vivo perspective,
21 that probably wouldn't -- wouldn't happen, is not
22 relevant. One might study that in vitro, but,
23 again, it's -- you know, there's a disconnect there
24 because that just -- with a polyclonal response,
25 that just wouldn't happen.

1 Q. Well, you have an opinion also on
2 monoclonal antibodies, right?
3 A. Yes.
4 Q. A monoclonal antibody means an antibody
5 with one specificity --
6 A. Yes.
7 Q. -- right?
8 So a monoclonal antibody that only binds
9 one place on PH20 may not cause an allosteric
10 effect, right?
11 A. It might or might not.
12 The -- the full antibody is still --
13 is -- because of -- again, because of kind of a
14 steric sort of effect can certainly impact the
15 substrate hyaluronic acid of other functions of the
16 PH20 protein.
17 Q. But a monoclonal antibody may not because
18 it may not bind in the right place to cause a
19 steric effect, right?
20 MR. POWERS: Objection. Form.
21 THE DEPONENT: Again, I wouldn't want to
22 speculate. I mean, one can come up with some
23 hypothesis that it might not, but I really don't
24 know data that directly support that.
25 Q. (By Mr. Wang) Do you know data that

1 sorry, let me rephrase.
2 Do you know one way or the other, without
3 testing it, that a monoclonal antibody binding to
4 PH20 would cause an allosteric effect?
5 MR. POWERS: Object to form.
6 THE DEPONENT: Well, as it relates -- it
7 depends.
8 As a relation to the different functions
9 of PH20, it might have an effect on the HA binding
10 site, it might have an effect on the enzymatic
11 site, or both.
12 Q. (By Ms. Wang) But do you know the actual
13 effect it has without testing for it?
14 MR. POWERS: Objection. Form.
15 THE DEPONENT: No.
16 One would have to screen the monoclonals
17 for activity in binding.
18 Q. (By Ms. Wang) When we're talking about
19 allosteric effects from a polyclonal response, is
20 it your opinion that binding location on the PH20
21 doesn't matter?
22 A. So again -- sorry, could you just -- I
23 just want to make sure I'm clear on that.
24 Q. Sure.
25 You have an opinion that polyclonal

1 antibodies will cause an allosteric effect,
2 irrespective where the antibodies bind, on page 20,
3 right?
4 A. Because they are going to binding to many
5 regions on the PH20 polypeptide.
6 Q. And in your opinion, binding specificity
7 of those polyclonal antibodies doesn't matter?
8 A. No, because they're -- they are going to
9 be multiple epitopes. So functionally it should
10 inhibit PH20 function. Or when it's on sperm, bind
11 to it on sperm.
12 Q. Affinity of the polyclonal antibodies,
13 also doesn't matter?
14 MR. POWERS: Object to form. Foundation.
15 THE DEPONENT: I would think most of
16 those would be relatively high avidity.
17 Q. (By Ms. Wang) Avidity of the polyclonal
18 antibodies wouldn't matter?
19 A. What did you say?
20 Q. Avidity.
21 A. Avidity, yeah.
22 MR. POWERS: Same objection.
23 THE DEPONENT: Probably not.
24 MS. WANG: Okay to take a break?
25 MR. POWERS: Sure.

1 THE DEPONENT: Thanks.
2 THE VIDEOGRAPHER: Time is 1:56 p.m.
3 Pacific time. We are off the record.
4 (Recess taken.)
5 THE VIDEOGRAPHER: The time is 2:11 p.m.
6 Pacific time. We are on record.
7 Q. (By Ms. Wang) Dr. Cherr, in the last
8 break did you speak with counsel?
9 A. I did not.
10 Q. Okay. In order for modified PH20
11 polypeptides to be useful as contraceptive vaccines
12 in female mammals, they have to generate a
13 polyclonal immune response at the right place at
14 the right time in sufficient quantities, correct?
15 MR. POWERS: Objection. Form.
16 THE DEPONENT: I would agree with that.
17 Q. (By Ms. Wang) Your opinion on
18 paragraph 43 of your declaration is that a POSA
19 would have expected the modified PH20 polypeptides
20 with optimized administration to be useful as
21 contraceptive vaccines in female mammals.
22 That's your opinion, right?
23 A. Yes.
24 Q. What did you mean by "optimized
25 administration"?

A. Well, meaning mucosal and, again, talked about it in -- in here, but primarily an intranasal route since that's been shown to be most effective for other types of antigens.

Q. Would the POSA have expected the modified PH20 polypeptides to be useful as contraceptive vaccines in female mammals without optimized administration?

MR. POWERS: Objection. Form.

THE DEPONENT: I think in looking through the papers I cite, they would have an understanding that there's a need to elicit a response in the reproductive tract which, again, would be a mucosal response.

Q. (By Ms. Wang) So the modified PH20 polypeptides, without optimized administration, would not be use useful as contraception?

MR. POWERS: Objection. Form.

THE DEPONENT: With -- without -- without mucosal -- without triggering a mucosal response, yes, that would be true. Wouldn't -- probably wouldn't be useful.

Q. (By Ms. Wang) Does your concept of optimized administration require adjuvants?

A. Yes, that's how we are defining it here.

1 with -- adjuvants that have been used successfully
2 in mucosal and eliciting mucosal responses.
3 Q. So optimized administration requirements
4 intranasal?
5 A. That's what I'm referring to here, to
6 stimulate a mucosal response.
7 Q. And it requires adjuvants for mucosal
8 response?
9 MR. POWERS: Object to form.
10 THE DEPONENT: (Nods head.)
11 Q. (By Ms. Wang) Right?
12 A. Yes.
13 Q. And you also state that the POSA would
14 use an agent that removes beta-defensin, DEFB126.
15 Is that part of your optimized
16 administration?
17 A. And that -- and that is an optional step
18 to remove beta-defensin 126, but it's not
19 mandatory.
20 Q. But mandatory for optimized
21 administration, in your mind, is intranasal plus
22 adjuvant?
23 A. Yes, I think that's the step -- the main
24 step.
25 Q. Is the optimized administration of

1 modified PH20 polypeptides the same for all mammals
2 that are covered, in your opinion?
3 A. So again, "optimized" as defined, or what
4 was referred to here, is dealing with intranasal
5 administration. And yes, that -- that -- because
6 that's known that that would stipulate a mucosal
7 response in -- in most mammals that have been
8 studied.
9 Q. So in your opinion for modified PH20
10 polypeptides to be useful as contraceptive
11 vaccines, they would have to be delivered
12 intranasally to female mammals?
13 MR. POWERS: Object to form.
14 THE DEPONENT: Sorry, one more time. I
15 just want to make sure I heard the right word,
16 please.
17 Q. (By Ms. Wang) For modified PH20
18 polypeptides to be useful as contraception
19 vaccines, they would have to be delivered
20 intranasally to female mammals?
21 MR. POWERS: Same objection.
22 THE DEPONENT: They would have to be
23 administered such that an adequate immune response
24 occurred. An intranasal would be the primary way.
25 But as we talked about before, there could be a

1 vaginal delivery as well.
2 Q. (By Ms. Wang) But in your opinion for
3 modified PH20 polypeptides to be useful as
4 contraception, they would have to be delivered
5 mucosally?
6 A. Yes.
7 Q. Is your optimized administration the same
8 for all modified PH20 polypeptides?
9 A. Yes.
10 Q. And that would include modified PH20
11 polypeptides that are unfolded?
12 A. Yes.
13 Q. With regard to an adjuvant for intranasal
14 administration, would any adjuvant work?
15 A. Well --
16 MR. POWERS: Objection. Form.
17 Go ahead.
18 THE DEPONENT: When you say "any
19 adjuvant," you mean literally any -- anything or
20 known intranasal -- or known adjuvants that have
21 been used intranasally?
22 Q. (By Ms. Wang) I'm trying to understand
23 your opinion that adjuvants -- that the POSA would
24 know to include adjuvants.
25 THE DEPONENT: So typically cholera

1 toxin B the, nontoxic form -- portion of cholera
2 toxin is commonly used intranasally, and it has
3 been very successful.
4 Q. (By Ms. Wang) Is that the only one?
5 A. Well, there's -- there's others.
6 There's -- from E. coli. There's
7 flagellin/MAGELLAN, which is a toll receptor
8 protein. So there's several others that have been
9 used, but cholera toxin, at least for antiviral
10 usage or stimulation for antiviral antigens,
11 cholera toxin B has been very successful.
12 Q. Are you aware of any evidence of cholera
13 toxin B as a successful adjuvant with the delivery
14 of a -- of a self-antigen?
15 MR. POWERS: Object to form.
16 THE DEPONENT: I am not aware of --
17 you know, I haven't look into that, right.
18 Q. (By Ms. Wang) Are you aware of any
19 intranasal contraceptive vaccines that existed
20 before 2012?
21 A. Are you referring -- when you say
22 "contraceptive vaccines," you're referring to
23 eliciting an antibody response?
24 Q. Yes.
25 A. No, I am not.

1 Q. Are you aware of any intranasal
2 immunocontraceptive vaccines today?
3 A. Today? I'm sorry, today? Or --
4 Q. Yeah.
5 A. You meant recently or --
6 Q. After 2012 --
7 A. Oh, okay.
8 Q. -- are you aware of any intranasal
9 immunocontraceptive vaccines?
10 A. No, I am not.
11 Q. Are you aware of any mucosal
12 immunocontraceptive vaccines before 2012?
13 MR. POWERS: Object to form.
14 THE DEPONENT: No, I am not.
15 Q. (By Ms. Wang) How about after 2012?
16 MR. POWERS: Same objection.
17 THE DEPONENT: I am not aware of one.
18 Q. (By Ms. Wang) Are you aware of any
19 intranasal vaccines using an enzyme antigen before
20 2012?
21 A. I'm not.
22 Q. How about after 2012?
23 A. No, I am not aware of.
24 Q. Are you aware of any evidence published
25 before 2012 of the successful mucosal delivery of

1 PH20 to humans?
2 MR. POWERS: Objection. Form.
3 THE DEPONENT: I don't believe so. I
4 don't know of any.
5 Q. (By Ms. Wang) Any evidence of successful
6 mucosal delivery of modified PH20 polypeptides to
7 humans?
8 A. No, I am not.
9 Q. Are you aware of any evidence of mucosal
10 delivery of modified PH20 peptides to nonhumans?
11 A. No, I am not.
12 Q. Are you aware of any evidence published
13 before 2012 that PH20 is expressed in the female
14 reproductive tract of any mammal?
15 A. The only -- the only one I know of is the
16 BALB/c mice, genetically -- highly modified genetic
17 strain of mice that was used in the Hardy study.
18 Q. So besides the mice in the Hardy study,
19 you're not aware of any other evidence published
20 before 2012 of PH20 expression in female
21 reproductive tracts?
22 A. No, I'm not.
23 Q. You stated earlier that the POSA would
24 have optionally delivered an anti beta-defensin,
25 DFB126 agent, to the vaginal cavity of vaccinated

1 women just before intercourse to make modified PH20
2 polypeptides an effective contraceptive; is that
3 correct?
4 MR. POWERS: Object to form.
5 THE DEPONENT: Yeah.
6 Q. (By Ms. Wang) You identified in your
7 declaration, at paragraph 39, sialidase.
8 A. Yes, that's right.
9 Q. You didn't cite any study where sialidase
10 was administered vaginally to female primates
11 before 2012, did you?
12 A. That's correct. It has been found in the
13 vagina in humans, but not administered.
14 Q. And so there's also no study
15 administering sialidase to the human vagina before
16 2012?
17 A. Not that I'm wear of, no.
18 Q. And sialidase treatment of sperm prevents
19 sperm from penetrating cervical mucosal because of
20 removal of the negative charge on the sperm
21 surface, right?
22 A. Yes, that's correct.
23 Q. The sialidase prevention of sperm from
24 penetrating cervical mucus occurs whether or not
25 PH20 is bound by antibodies, right?

1 MR. POWERS: Object to form.
2 THE DEPONENT: No. It's -- so it's a way
3 of further enhancing any sort of antibody effect
4 down in the lower tract. I have a sialidase there.
5 Q. (By Ms. Wang) But just to confirm,
6 sialidase alone prevent sperm from penetrating
7 cervical mucus?
8 A. That is correct.
9 Q. In your opinion, would the POSA only
10 select sialidase to administered to humans?
11 MR. POWERS: Objection. Form.
12 THE DEPONENT: Probably not, because the
13 sialidase -- sialidase treatment is an optional or
14 enhancing approach. If there were sperm that got
15 through to the upper tract, you would still ideally
16 really want an antibody response in that upper
17 tract. And then whatever sperm did get up in the
18 upper tract, if they are lacking their sialic acid,
19 would be highly susceptible to any sort of
20 antibodies that would be present there. So I
21 viewed this as both working together.
22 Q. (By Ms. Wang) So if a POSA wanted to use
23 an anti-defensin agent, would they only select
24 sialidase?
25 MR. POWERS: Objection. Form.

1 THE DEPONENT: If you could define
2 "anti-defensin agent" or what you mean by that.
3 Q. (By Ms. Wang) Well, if a POSA wanted to
4 deliver an anti-beta-defensin, DEFB126 agent, would
5 they only select sialidase?
6 A. Sorry. I just push back a little bit on
7 the term "anti-beta-defensin" because it makes it
8 sound like you're talking about an antibody?
9 Q. No.
10 A. No?
11 Q. I'm talking about an agent that
12 removes --
13 A. That removes or affects its function,
14 yeah.
15 Q. Right.
16 So if a POSA wanted to use an agent that
17 removes the anti-defensin -- sorry, the
18 beta-defensin, would only select sialidase?
19 A. There's only approaches that could be
20 taken in terms of, you know, bicarbonate levels and
21 different incubation procedures that kind of mimic
22 what normally occurs in the upper tract. But the
23 sialidase is by far the more straightforward and
24 easiest has a single enzyme treatment versus more
25 complicated culture medium.

Q. You identified caffeine as an agent known to expose sperm surface protein?

A. Right. And that's not -- that's kind of an in vitro mimic of the physiology of what happens. It's not referring to drinking a lot of coffee. Sorry.

Q. The POSA would not be putting caffeine up the vagina?

A. Right.

Q. Okay. Same for Dibutyryl cAMP?

A. Cyclic. Yeah, same thing. So these are all kind of the normal metabolic physiological processes that are occurring up in the upper tract, and those are all in vitro chemicals that elicit a similar response.

Q. But the POSA would not be using them in vivo?

MR. POWERS: Object to form.

THE DEPONENT: I mean, it's a known possible treatment, but it would be very difficult. A sialidase would be much more straightforward.

Q. (By Ms. Wang) Do you think the delivery of an agent to remove the beta-defensin from sperm surface PH20 prior to intercourse would be practical in a wild animal population?

1 A. In -- in a what population?
2 Q. In a wild animal population.
3 A. Oh, wild.
4 Are you -- I guess, are you -- I'm trying
5 to understand the context. Are you talking about
6 wild animal, feral animal control?
7 Q. Well, your opinion is that the modified
8 PH20 polypeptides would be useful as contraception
9 in nonhuman mammals, right?
10 A. Right.
11 Q. And that would include primates?
12 A. Yes.
13 Q. Right?
14 A. Yes.
15 Q. And so do you think that delivery of an
16 agent to remove beta-defensin would be practical to
17 achieve contraception in wild primates?
18 MR. POWERS: Objection -- Objection.
19 Form.
20 THE DEPONENT: Yeah, I think the
21 operative term is "practical" and "wild." Because
22 if you're talking about laboratory animals that are
23 used for, you know, developing a certain drugs and
24 procedures, then yes. But when we're talking about
25 a disc or a ring, a vaginal ring, or even a gel,

1 you know, that probably wouldn't be practical in a
2 wild population for, I think, hopefully obvious
3 reasons, but...
4 Q. (By Ms. Wang) I'm trying to understand
5 though, is -- so is your opinion that modified PH20
6 polypeptides would be a useful contraception in
7 nonhuman mammals? Does that include wild mammals?
8 A. Well -- so, again, I think we are kind
9 of -- I just want to make sure we are kind of on
10 the same path here. You are talking about -- yes,
11 and I mentioned this appropriate, if there's an
12 appropriate mucosal response and it's administered
13 in an appropriate way. So I guess the optional
14 sialidase treatment certainly could be done in
15 population -- laboratory population of wild
16 animal -- or sorry, not wild animals -- laboratory
17 populations of nonhuman animals. But -- and that
18 would be irregardless of which polypeptides were
19 used.
20 Q. But the optional sialidase treatment
21 would not be used for wild mammals?
22 A. Well, I guess my opinion is theoretically
23 it could be, but it's not very practical.
24 Q. So your opinion is that modified PH20
25 polypeptides, in order for them to be effective as

1 contraceptive vaccines, the POSA would expect to
2 have to administer them mucosally with a potent
3 mucosal adjuvant?
4 MR. POWERS: Objection. Form.
5 THE DEPONENT: Well, it's not
6 administering them a mucosal -- administering them
7 so that there was a sufficient mucosal response,
8 yes.
9 Q. (By Ms. Wang) And that was not done in
10 the guinea pig studies reported by Primakov
11 (phonetic), correct?
12 MR. POWERS: Objection. Form.
13 THE DEPONENT: No that was not.
14 Q. (By Ms. Wang) The guinea pigs did not
15 receive mucosally administered or intranasally
16 administered PH20?
17 A. That's correct.
18 Q. Suppose the POSA wanted to use modified
19 PH20 polypeptides to make a rat contraceptive
20 vaccine.
21 Would they administer the PH20
22 polypeptide intranasally?
23 A. For controlling rats, you say, or for
24 rendering rats infertile?
25 Q. For controlling rats.

1 A. So yes, in rats they would want a --
2 intranasal or mucosal response to optimize that.
3 Q. So the POSA would administer modified
4 polypeptides intranasally to rats?
5 For a rat contraceptive vaccine, what
6 mucosal adjuvant would the POSA include?
7 A. I think in literature, again, for other
8 types of antigens, people have used the cholera
9 toxin B quite successfully for antiviral antigens.
10 Q. And how often would they -- sorry, let me
11 rephrase.
12 The POSA would also expect to need to
13 boost the rat population with vaccine, right?
14 MR. POWERS: Object to form.
15 THE DEPONENT: Potentially. There are
16 some studies that have found a single nasal
17 administration triggers a very long-lasting
18 antibody response. But certainly an option would
19 be to boost.
20 Q. (By Ms. Wang) So boosting is not a part
21 of your optimized administration?
22 A. No. I -- it would be part of it to -- to
23 maintain -- again, there's -- there's levels of the
24 immune response, and then there's time frame
25 maintaining it, and boosting comes in potentially

1 to both of those.
2 Q. And how would a POSA developing a rat
3 contraceptive vaccine boost the rat population with
4 vaccine?
5 MR. POWERS: Objection. Form.
6 THE DEPONENT: It's -- it's hard for me
7 to opine on that because I'm not familiar with
8 how -- you know, using it as a feral population
9 control, how these things would be done. So I
10 can -- I don't want to speculate on exactly how
11 that would be done.
12 Q. (By Ms. Wang) Earlier we talked about
13 you have an opinion regarding monoclonal
14 antibodies.
15 A. Uh-huh.
16 Q. And you state in your declaration --
17 let's go to paragraph 14 -- that you were asked to
18 consider -- I will wait.
19 A. Yes.
20 Q. You were asked to consider whether a POSA
21 would have expected anti-PH20 monoclonal antibodies
22 against any of the modified PH20 polypeptides when
23 administered into the vaginal cavity of human
24 females to cause contraception.
25 Do you see that?

1 A. Yes.
2 Q. Where did this question come from?
3 A. Well, I was asked to comment on that from
4 counsel.
5 Q. So counsel formulated the question for
6 you?
7 A. Not in those exact words, but the --
8 conceptually.
9 Q. Were you asked to consider administration
10 of monoclonal antibodies to any place other than
11 the vaginal cavity of human females?
12 A. No.
13 Q. Your opinion on monoclonal antibodies
14 we've -- let me start over.
15 As we talk about before, monoclonal
16 antibodies only have one specificity, right?
17 A. Yes, correct.
18 Q. And so they would have to be made and
19 screened in order to find the right antibody that
20 would cause contraception?
21 MR. POWERS: Object to form.
22 THE DEPONENT: I believe where this is
23 discussed further back -- this is just at the
24 beginning. Where this is discussed further back, I
25 think I talked about a mixture of different --

1 different monoclonal antibodies that would bind to
2 different epitopes would be used in the vaginal
3 cavity or delivered in the -- a gel or a vaginal
4 ring or vaginal disc.
5 Q. (By Ms. Wang) Is it your opinion that
6 you would need more than one monoclonal antibody
7 with more than one specificity in order to have
8 effective contraception?
9 A. I think would be advantageous to have a
10 number of -- that bind to different epitopes.
11 Q. Can you have effective contraception with
12 only one monoclonal antibody that only binds one
13 epitope?
14 A. Potentially, yes.
15 Q. That one monoclonal antibody would have
16 to be made and screened to determine if it could
17 potentially work, right?
18 MR. POWERS: Object to form.
19 THE DEPONENT: Well, I think the
20 monoclonal antibodies one would develop for this
21 kind of purpose, the POSA would be screening
22 numerous antibodies and then could decide how many
23 they wanted to employ for this purpose.
24 Q. (By Ms. Wang) The POSA would be making
25 numerous antibodies and screening them.

MR. POWERS: Same objection.
Q. (By Ms. Wang) Right?
A. Yes.
Q. These monoclonal antibodies are not being administered as immunocontraceptive vaccines, right?
A. Correct, they are being added to the vaginal cavity.
Q. And modified PH20 polypeptides are not monoclonal antibodies, right?
A. Yes, you're right on that.
Q. Did you, in forming your opinions, investigate any differences in the location of expression of PH20 on the sperm of different species?
MR. POWERS: Objection. Form.
THE DEPONENT: Sorry, could you ask that again.
Q. (By Ms. Wang) In forming your opinions, did you investigate any differences in the location of expression of PH20 on the sperm of different species?
MR. POWERS: Same objection.
THE DEPONENT: Yes.
I was aware of differences between

1 rodents and primates, in particular.
2 Q. (By Ms. Wang) Are you aware that the
3 location of expression of PH20 on guinea pig sperm
4 is different from the sperm of other mammals?
5 MR. POWERS: Objection. Form.
6 THE DEPONENT: Yes, I am aware.
7 Q. (By Ms. Wang) You did not investigate
8 any differences in the immune system of guinea pigs
9 versus other mammals, did you?
10 MR. POWERS: Objection. Form.
11 THE DEPONENT: I did not investigate it.
12 There's very little known, but like -- as
13 I mentioned earlier, it is known that guinea pigs
14 have leakage or breakthrough from the circulating
15 plasma if there's antibodies circulating into the
16 reproductive tract lumens of both males and
17 females.
18 Q. (By Ms. Wang) Right, and I'm just asking
19 about the immune system.
20 A. Yeah.
21 Q. You didn't investigate any differences in
22 the immune system between --
23 A. No.
24 I don't know, and I don't think that's
25 known.

Q. Okay.
MS. WANG: Okay to take a break?
MR. POWERS: Sure.
THE DEPONENT: Sure.
THE VIDEOGRAPHER: The time is 2:44 p.m. Pacific time. We are off the record.
(Recess taken.)
THE VIDEOGRAPHER: The time is 3:06 p.m. Pacific time. We are on the record.
Q. (By Ms. Wang) Dr. Cherr, did you speak with counsel during the last break?
A. I did not.
Q. The answers that you gave today, would any of them have been different for any of the four patents in the four proceedings?
A. For any of the -- yeah, I --
Q. Let me rephrase.
A. Yeah.
Q. The answers that you gave today would not have been different for any of the four patents in the four different proceedings, right?
A. Yes, that is correct.
Q. You provided your opinions from the perspective of a POSA in December 2012, right?
MR. POWERS: Objection. Form.

THE DEPONENT: Yes, that's true.

Q. (By Ms. Wang) Would your opinions have been different from the perspective of a POSA in December 2011?

MR. POWERS: Object to form.

THE DEPONENT: Probably need to think about that, but I -- my response would be, no, wouldn't be any different.

Q. (By Ms. Wang) Okay.

MS. WANG: All right. Thank you.

Those are all the questions I have for you today, Dr. Cherr.

Before we go off the record, I would like to ask for counsel for production of the near-final Moon declaration that Dr. Cherr testified he reviewed before signing his declaration.

MR. POWERS: We'll consider it, Counsel.

MS. WANG: Okay.

THE VIDEOGRAPHER: And before I read us off, I just need to grab --

MR. POWERS: We need time to consider whether or not there's going to be any redirect.

THE VIDEOGRAPHER: Okay.

MR. POWERS: So let's take a break.

MS. WANG: Okay.

1 THE VIDEOGRAPHER: Take a break?
2 Copy that.
3 The time is 3:08 p.m. Pacific time. We
4 are off the record.
5 (Recess taken.)
6 THE VIDEOGRAPHER: The time is 3:13 p.m.
7 Pacific time. We are on the record.
8 MR. POWERS: Thank you very for your time
9 to, Dr. Cherr. We have no questions for you.
10 The witness will read and sign.
11 MS. WANG: Okay.
12 MR. POWERS: Thank you, Counsel.
13 MS. WANG: And, sorry, one quick thing
14 before we go off the record.
15 Can we have Dr. Cherr's versions of his
16 declaration be part of the record.
17 MR. POWERS: Sure.
18 They're unmarked versions of his
19 declaration.
20 MS. WANG: That's fine, thank you.
21 THE VIDEOGRAPHER: Okay. If there is
22 nothing else, I will just grab orders real quickly.
23 Ms. Wang, you get the video, standard.
24 Did you need it synced to the transcript?
25 MS. WANG: Yes, I believe so.

THE VIDEOGRAPHER: All right. And then, Mr. Powers, did you need a copy of the video and/or transcript at this time?

MR. POWERS: Yes, we will.

THE VIDEOGRAPHER: Okay. Did you want them synced, as well?

MR. POWERS: Let me check about that.

THE VIDEOGRAPHER: Okay. I'll put you down for a follow-up.

And then will it just be the one order for both sides, or --

MR. POWERS: Yes.

THE VIDEOGRAPHER: Okay. Perfect.

In which case, this ends Volume 1 of the video deposition of Gary N. Cherr, Ph.D., in the matter of Merck Sharp & Dohme LLC v. Halozyme Incorporated.

The time is 3:14 p.m. Pacific time. We are off the record.

(TIME NOTED: 3:14 P.M.)

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1 I, GARY N. CHERR, Ph.D., do hereby declare
2 under penalty of perjury that I have read the
3 foregoing transcript; that I have made any
4 corrections as appear notes; that my testimony as
5 contained herein, as corrected, is true and
6 correct.
7 Executed this ____ day of _____,
8 2025, at _____, _____.
9
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12 _____
GARY N. CHERR, Ph.D.
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I, Rebecca L. Romano, a Registered Professional Reporter, Certified Shorthand Reporter, Certified Court Reporter, do hereby certify:

That the foregoing proceedings were taken before me at the time and place herein set forth; that any deponents in the foregoing proceedings, prior to testifying, were administered an oath; that a record of the proceedings was made stenographically by me and which was thereafter transcribed under my direction; that the foregoing transcript is a true record of the testimony given.

Further, that if the foregoing pertains to the original transcript of a deposition in a Federal Case, before completion of the proceedings, review of the transcript [ ] was [ ] was not requested.

I further certify I am neither financially interested in the action nor a relative or employee of any attorney or any party to this action.

IN WITNESS WHEREOF, I have this date subscribed my name.

Dated: November 17, 2025

Rebecca L. Romano, RPR, CCR
CSR No. 12340

DEPOSITION ERRATA SHEET

Case Name: Merck Sharp & Dohme LLC vs. Halozyme Inc.
Name of Deponent: Gary N. Cherr, Ph.D.
Date of Deposition: November 12, 2025
Job No.: 7005263-001
Reason Codes: 1. To clarify the record.
2. To conform to the facts.
3. To correct transcript errors.

Page _____ Line _____ Reason _____

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_____ Subject to the above changes, I certify that the transcript is true and correct

_____ No changes have been made. I certify that the transcript is true and correct.

_____
GARY N. CHERR, PH.D.

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