

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

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6	ALVOTECH USA INC. and	)	
7	ALVOTECH HF,	)	
8	Petitioners,	)	Case No. PGR2025-00085
9	vs.	)	
10	REGENERON PHARMACEUTICALS,	)	
11	INC.,	)	
12	Patent Owner.	)	
13	_____		

DEPOSITION OF ROBERT FALCONER

SAN DIEGO, CALIFORNIA

MAY 27, 2026

REPORTED BY KAYLEE G. WOOD, RPR, CRR, CSR NO. 14348

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Petitioners, Case No. PGR2025-00085

vs.

REGENERON PHARMACEUTICALS, INC.,

Patent Owner.

15 VIDEO RECORDED DEPOSITION OF ROBERT FALCONER,
 16 commencing at the hour of 8:07 a.m. PST, Wednesday,
 17 May 27, 2026, 12860 El Camino Real, Suite 400, San
 18 Diego, California 92130, before Kaylee G. Wood,
 19 Certified Shorthand Reporter, Registered Professional
 20 Reporter, and Certified Realtime Reporter in and for
 21 the State of California.

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TIM HUNTER, VIDEOGRAPHER

1 I N D E X

2

3 WITNESS: Robert Falconer

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1 SAN DIEGO, CALIFORNIA; MAY 27, 2026; 8:07 A.M. PST

2 PROCEEDINGS

3 THE VIDEOGRAPHER: And here begins the
4 videotaped deposition of Robert Falconer in the matter
5 of Alvotech versus Regeneron. This deposition is being
6 held at 12860 El Camino Real, Suite 400, San Diego,
7 California 92130. Today's date is May 27, 2026. The
8 time on the record is 8:07 a.m. My name is Tim Hunter,
9 your legal videographer. Our court reporter today is
10 Kaylee Wood. Counsel, would you please introduce
11 yourselves and state whom you represent for the record
12 starting with noticing counsel? And the witness will
13 be sworn.

14 MR. TRASK: Andrew Trask of Williams &
15 Connolly on behalf of patent owner Regeneron
16 Pharmaceuticals. With me in person today are my
17 colleagues Kathryn Kayali and Rhochelle Krawetz, and
18 joining us remotely through Zoom is in-house counsel at
19 Regeneron, Petra Scamborova.

20 MR. CHEN: I'm Philip Chen from Fish &
21 Richardson on behalf of the petitioner Alvotech and the
22 witness, Dr. Robert Falconer. I'm joined remotely by
23 my colleague Mike Kane also from Fish & Richardson.

24 COURT REPORTER: My name is Kaylee Wood, CSR
25 Number 14348.

1 ROBERT FALCONER,
2 having first been duly sworn, was examined and
3 testified as follows:

4 EXAMINATION BY COUNSEL FOR THE PATENT OWNER,
5 REGENERON PHARMACEUTICALS, INC.

6 BY MR. TRASK:

7 Q. Good morning, Dr. Falconer.

8 A. Good morning.

9 Q. State your full name for the record, please.

10 A. My name is Robert John Falconer.

11 Q. Is there any reason you can't give truthful
12 and accurate testimony today?

13 A. No, I don't believe so.

14 Q. You've been deposed before?

15 A. No. This is my first -- is it deposition?

16 Q. Correct.

17 A. Yep.

18 Q. Okay. Well, throughout the day today I'll be
19 asking questions and you'll be providing answers. I'd
20 ask that if you don't understand any question that I
21 ask, that you please ask me to clarify, okay?

22 A. Okay.

23 Q. And if you don't ask me to clarify a question
24 then I'm going to assume that you understood my
25 question. Is that all right?

1 A. Okay.

2 Q. What did you do to prepare for this
3 deposition today?

4 A. This is going back to the initial stages of
5 the interaction with Fish & Richardson?

6 Q. Well, I was going to ask specifically
7 preparing for the deposition today?

8 A. Oh, today.

9 Q. We can later address the preparation of your
10 declaration.

11 A. Okay. Yeah. We had a meeting yesterday. It
12 was around about six hours. We went through the
13 deposition. I answered some model questions.

14 Q. And just to -- I'm not asking for any
15 privileged communications with your counsel, just to be
16 clear.

17 A. Sure. I was given advice on the appropriate
18 way of answering those questions.

19 Q. Who was in this six-hour meeting that took
20 place?

21 A. Philip Chen, who's on my left, and Michael
22 Kane via Zoom. I think Zoom or Teams.

23 Q. Did you have any other meetings other than
24 the six-hour meeting you had yesterday to prepare for
25 this deposition?

1 A. No. Actually, I'll clarify that. I had a
2 chat with Philip just before this meeting.

3 Q. Okay. Thank you for that. Now, did you
4 review any documents in preparation for this
5 deposition?

6 A. The declaration itself, the -- there's about
7 five patents that are mentioned in the declaration, and
8 I also reviewed the scientific documents I mentioned in
9 the background technology part.

10 Q. Okay. Did you review anything in preparation
11 for this deposition that's not mentioned in your
12 declaration?

13 A. Not that immediately comes to mind, no.

14 Q. So you have a copy in front of you of the
15 declaration you submitted in this case?

16 A. Yes.

17 Q. That was provided by counsel?

18 A. Yes.

19 Q. Okay. I'm -- this is going to be a duplicate
20 then but I'm going to mark for the record what has
21 already been marked as Alvotech Exhibit 1004. This is
22 also a copy of your deposition.

23 (Whereupon, Exhibit 1004, previously marked,
24 was proffered to the witness.)

25 MR. TRASK: Would you like a copy or --

1 COURT REPORTER: Eventually, yeah.

2 MR. TRASK: Yeah. Oh, I guess you can have
3 his ultimately.

4 COURT REPORTER: Yeah.

5 MR. TRASK: Yeah. Why don't I take it back
6 so we don't clutter it up?

7 MR. CHEN: Oh, thanks.

8 BY MR. TRASK:

9 Q. The copy of your declaration that was
10 provided by counsel, did that have any markings in it
11 that were not in the originally printed deposition?

12 A. I don't believe so.

13 Q. In reviewing your declaration in preparation
14 for this deposition did you spot any errors that you'd
15 like to correct?

16 A. No, no. I think it's all correct.

17 Q. Okay. And you reviewed it front to back,
18 your declaration?

19 A. I've read it several times, yes.

20 Q. And you stand by all the opinions in your
21 declaration sitting here today?

22 A. Yes.

23 Q. When were you first retained by Alvotech for
24 this matter?

25 A. To be honest I don't have the date. It's

1 many months ago.

2 Q. Who contacted you?

3 A. I've had a reasonably long-standing -- well,
4 five-year professional relationship with Michael Kane,
5 so I suggest it was almost certainly Michael who
6 contacted me.

7 Q. Okay. What is that professional
8 relationship?

9 A. I'm -- I've acted as his expert, acting as a
10 consultant on cases such as this.

11 Q. Any matters involving Alvotech?

12 A. Yes.

13 Q. Other than this one?

14 A. Yes.

15 Q. Which matters are those?

16 A. There was a case involving Humira. I think
17 it was AbbVie.

18 Q. Okay. Any others?

19 A. Not that have got to a stage where -- okay.
20 We've looked at some other monoclonals, but this is
21 very preliminary. There's one that I must admit I
22 struggle to pronounce. It begins with a V. I believe
23 it's -- is it inflammatory bowel disease?

24 THE VIDEOGRAPHER: Michael, Michael, we can
25 hear you.

1 MR. KANE: Sorry about that.

2 A. That was just a preliminary looking at some
3 patents.

4 Q. Do you know anyone at -- who works at
5 Alvotech?

6 A. I've met -- I had a meeting in Washington. I
7 believe it was August last year where I met a guy, his
8 first name was Phillip, and I hate to say it but I've
9 forgotten his family name.

10 Q. And that person --

11 A. And he was an employee of Alvotech.

12 Q. Okay. And what was that meeting about, if
13 you can say?

14 MR. CHEN: And Dr. Falconer, I'll caution you
15 not to reveal the substance of any privileged
16 communications you would have had with counsel, but if
17 you can answer the question without doing so then go
18 ahead?

19 A. I must admit I can't remember exactly which
20 one of the active ingredients we were discussing, but
21 we did discuss the use of excipients in creating stable
22 formulations for therapeutic proteins.

23 Q. Okay. Was that in connection with a legal
24 matter, that meeting?

25 A. Could you define a legal matter?

1 Q. Well, was it in connection with this legal
2 matter that we're here for today?

3 A. Yes. I don't recall, but it could have
4 included this.

5 Q. Was the person named Phil from Alvotech with
6 whom you met a lawyer?

7 A. No. He was a company employee. I don't
8 think he was a lawyer.

9 Q. Okay. Was -- did the meeting involve
10 providing technical advice?

11 A. Yes. That's what I'd call it.

12 Q. Okay. Did it relate to aflibercept?

13 A. That's what I don't recall. I can't remember
14 which active ingredients we were discussing.

15 Q. Okay. Is that the only person from Alvotech
16 that you know?

17 A. To the best of my knowledge, yes. They did
18 have a consultant, but he wasn't an -- he was
19 consulting for Alvotech on patent matters, and I don't
20 recall his name.

21 Q. Okay. Can you turn to paragraph 25 of your
22 declaration, Exhibit 1004? Are you there?

23 A. Yes.

24 Q. So this is the beginning of your materials
25 considered section, right?

1 A. Mm-hmm.

2 Q. You say in the second sentence, I've also
3 considered in whole or in party [sic] the materials
4 listed before. Party should say part, right?

5 A. I assume part is better grammar.

6 Q. Okay. You mean you haven't fully considered
7 all the materials listed below in full. Is that what
8 you're trying to convey there?

9 A. I've -- I've certainly read everything there
10 possibly with the exception of the prosecution history
11 and the Regeneron application for extension of patent
12 terms.

13 Q. So you considered in full all of the
14 documents listed in the table in paragraph 25 other
15 than the Exhibit 1002, the prosecution history, and
16 Exhibit 1013, the Regeneron application, is that right?

17 A. I don't recall reading Exhibit 12 either,
18 though I might have -- you know, I wouldn't discount
19 the fact that I -- I can't guarantee I haven't.

20 Q. Okay. So other than Exhibits 1002, 1012, and
21 1013, you considered in full all of the documents
22 listed in the table in paragraph 25, correct?

23 MR. CHEN: Objection to the extent it
24 mischaracterizes.

25 A. Yes. I think I'm familiar with the remaining

1 material. Yes.

2 Q. And that's not exactly what I asked.

3 A. Sorry.

4 Q. I'm not asking whether you're familiar with
5 them. I asked whether you reviewed them in full.

6 A. Yes. I did review them in full.

7 Q. All right. You did not review the
8 declaration submitted by Dr. D'Amico as part of the
9 materials you considered in providing your declaration,
10 right?

11 A. Yes. I don't recall seeing Dr. D'Amico's
12 declaration.

13 Q. Okay. Do you know that he submitted a
14 declaration in this case?

15 A. I expect he has.

16 Q. There are no materials listed in the table in
17 paragraph 25 that you considered in preparation for
18 your declaration that are not listed in that table,
19 correct? Strike that.

20 There are no materials that you reviewed in
21 forming your opinions in your declaration that are not
22 listed in the table in paragraph 25, correct?

23 A. As an academic I'm quite widely read in this
24 field, so broader opinions may have been generated from
25 an education over many years reading quite a diverse

1 range of literature, but these are the key pieces of
2 literature which we used in the production of this
3 declaration, yes.

4 Q. I understand that you're saying you also
5 considered your knowledge and professional experience,
6 but as to specific documents reviewed in forming your
7 opinions, the full set is listed in paragraph 25?

8 A. Yes.

9 Q. Do you know that Dr. D'Amico considered your
10 declaration in forming his opinions in this case?

11 A. I don't know what Dr. D'Amico -- whether he's
12 seen this or not.

13 Q. Okay. Did you ever ask to see his
14 declaration submitted in this case?

15 A. No. I don't recall. Don't think so.

16 Q. You weren't interested in seeing his opinions
17 in this matter in forming your own?

18 MR. CHEN: Objection. Form.

19 A. I had a Zoom meeting with Dr. D'Amico. I
20 don't recall the date.

21 Q. It says in paragraph 26 it was on
22 September 16, 2025. Does that sound right?

23 A. It could well be right, yes.

24 Q. Okay. How long did that Zoom meeting last?

25 A. This is very rough approximation, but it

1 would have been roughly 30 minutes.

2 Q. Is that the only time you've ever spoken to
3 Dr. D'Amico?

4 A. I believe so, yes.

5 Q. You relied on some of the information that
6 Dr. D'Amico provided during that conversation to form
7 your opinions in this case, correct?

8 A. Yes.

9 Q. Had you formed your opinions in this case
10 before speaking with Dr. D'Amico?

11 A. No.

12 Q. Okay. So the opinions that you've provided
13 in your declaration that rely on Dr. D'Amico's opinions
14 you formed after speaking with Dr. D'Amico, right?

15 A. Yes.

16 Q. Okay. What did you do after speaking with
17 Mr. D'Amico vis-a-vis preparing your declaration?

18 MR. CHEN: Dr. Falconer, I'll just caution
19 you here again to not reveal the substance of any
20 communications that you may have had with your
21 attorneys.

22 A. The information that Dr. D'Amico provided
23 that was sort of outside of the scope of what I would
24 normally know was with respect to the dose, the
25 injection volume. Those are the key parts. And also

1 would have, I recall, covered the use of narrow bore
2 needles because that's what they use when injecting
3 material into the eye.

4 Q. What time of day was that Zoom meeting you
5 had with Dr. D'Amico?

6 A. Depends which continent you're talking about.

7 Q. Local time for you, Australia, I assume.

8 A. Okay. Again this is not accurate, exact, but
9 I think it was -- I was at a conference and it was
10 about 10 o'clock in the evening.

11 Q. Where was that conference?

12 A. In Melbourne.

13 Q. That's quite late.

14 A. Yes. So I left the conference dinner to take
15 the call.

16 Q. Now, the declaration you have before you,
17 Exhibit 1004, was signed by you on September 17, 2025,
18 correct?

19 A. So we're talking about the declaration here?

20 Q. Correct.

21 A. What was the date again?

22 Q. It's on page -- it's the page marked 120,
23 one, two, zero. So I'll ask the question again.

24 A. Yes.

25 Q. You signed the declaration you submitted in

1 this case, Exhibit 1004, on September 17, 2025,
2 correct?

3 A. Yes.

4 Q. Do you remember what time of day you signed
5 this declaration?

6 A. No, I don't recall.

7 Q. Okay. But it was on -- that date is
8 accurate, correct?

9 A. I believe so.

10 Q. Yeah. So you testified that you formed your
11 opinions regarding dose and volume of administration
12 and needle bore size after speaking with Dr. D'Amico,
13 correct?

14 A. That's how I recall it.

15 Q. Okay. And that conversation was 24 hours or
16 less before you signed your declaration in final form?

17 A. I don't know the date of when I talked to
18 Dr. D'Amico.

19 Q. Well, it says in paragraph 26 that it was on
20 September 16, 2025, which is the day before you signed
21 your declaration. Is that accurate?

22 A. Sorry. Paragraph --

23 Q. 26.

24 A. 26. That sounds correct. Yes.

25 Q. Okay. So all of your opinions that are based

1 on the concept of a dose or an administration volume or
2 a needle size were formed within a 24-hour span of
3 time, is that right?

4 MR. CHEN: Objection. Form.

5 A. The dose, that's -- that was -- I wouldn't
6 have known that. The fact that intravitreal requires a
7 low volume, that would have been, you know, prior
8 knowledge. Exactly what that volume was, I wouldn't
9 have necessarily known that. The fact that it's a
10 narrow bore needle I think is common knowledge
11 certainly within, you know, my profession. Yes.

12 Q. So all of your opinions that are based on a
13 specific dose or a specific volume of administration
14 were formed within 24 hours of speaking with
15 Dr. D'Amico, correct?

16 MR. CHEN: Objection. Form.

17 A. The prior art sort of knowledge I'd have
18 known was that I think it's 100 microliters is the
19 maximum. I wouldn't have known the preferred dose.
20 Sorry, the -- sorry. The 100 microliters is the
21 maximum injection volume. I would have had the
22 assumption that the clinicians like it to be lower
23 because that is the maximum. As far as the dose went,
24 I don't recall knowing that value at that time.

25 Q. So the opinions you have that are based on a

1 dose were formed within a 24-hour time period after
2 speaking with Dr. D'Amico, correct?

3 MR. CHEN: Objection. Form.

4 Dr. Falconer, please give me a moment to
5 raise my objection.

6 Objection. Form.

7 You can answer.

8 A. From a formulation point of view if somebody
9 tells you the dose and the volume, you can quickly then
10 get to the concentration. That's, you know, a
11 calculation that takes less than a minute. And it's
12 the concentration that's the value for the formulation
13 scientist that's important.

14 Q. I don't think you're answering my specific
15 question --

16 A. Okay. Sorry.

17 Q. -- which is the following: Did you form all
18 of your opinions that are based on a dose within the 24
19 hours after speaking with Dr. D'Amico?

20 MR. CHEN: Objection. Form.

21 A. I believe so, yes.

22 Q. And did you form all of your opinions that
23 are based on the concept of administration volume
24 within the 24 hours after speaking with Dr. D'Amico?

25 MR. CHEN: Objection. Form.

1 A. I would have known roughly what the injection
2 volume was likely to be, but the decision on the end
3 injection volume I wouldn't have known.

4 Q. And so I still don't think you're answering
5 this question. Did you form your opinions based on the
6 concept of a specific administration volume within the
7 24 hours after speaking with Dr. D'Amico?

8 A. Yes.

9 Q. And did you draft your report containing
10 those opinions within the 24 hours after speaking with
11 Dr. D'Amico?

12 A. The parts associated with the dose and the
13 injection volume, yes, I believe so.

14 Q. Were you at a conference in Melbourne at the
15 time?

16 A. Yes.

17 Q. So you drafted the report during the
18 conference?

19 A. I'm quite used to doing that sort of thing.

20 Q. So you were sitting -- were you presenting or
21 sitting in the audience?

22 A. I presented on the last day.

23 Q. Okay.

24 A. Yeah.

25 Q. The day that you were drafting your report

1 were you in the audience or presenting?

2 A. I don't recall which day it was. It could
3 well have been after.

4 Q. Sorry. The day that you were drafting your
5 report based on the opinions of Dr. D'Amico, were you
6 sitting in the audience of the conference or were you
7 presenting at the conference that day?

8 A. I don't recall.

9 Q. Okay. So you were either -- you drafted the
10 portions of your report containing your opinions based
11 upon dose and administration volume either sitting in
12 the audience of the conference or while presenting at
13 the conference, correct?

14 A. Yes. I don't recall exactly the time scale
15 of that. Yes. I don't recall.

16 Q. It was one or the other, right?

17 A. No. I would have taken time out to, you
18 know, do the job. I wouldn't have been sitting in the
19 audience doing it.

20 Q. So you left the conference audience to draft
21 those sections of your report that day?

22 A. Well, afterwards --

23 MR. CHEN: Objection.

24 Dr. Falconer, please give me a moment to
25 object.

1 Objection. Misstates prior testimony.

2 You can answer.

3 A. So could you repeat the question?

4 Q. To draft those sections of your report
5 regarding the dose and administration volume opinions
6 of Dr. D'Amico you left the conference, correct?

7 MR. CHEN: Same objection.

8 A. I had a hotel room very close to the
9 conference where I could work and do the work I was
10 required. So that's what I understand I would have
11 done.

12 Q. Okay. But you don't recall one way or the
13 other?

14 A. No. I don't recall that day.

15 Q. What was the name of this conference?

16 A. It's the BioProcess Network Conference which
17 was held in Melbourne that year.

18 Q. Okay. I don't think this conference is
19 listed on your CV. Is your CV out of date?

20 A. Yes.

21 Q. What was the subject of your presentation at
22 that conference?

23 A. It was the manufacturing of mRNA precision
24 vaccines.

25 Q. Are there any other omissions from the CV

1 that you provided in this case?

2 A. Okay. This is the CV at the end of the
3 declaration?

4 Q. Correct.

5 A. This is at least six months out of date.
6 Yes. When I was checking this last night the
7 university name that I worked for has changed, so the
8 University of Adelaide merged with the University of
9 South Australia and is now called Adelaide University.

10 Q. Okay.

11 A. And --

12 Q. Are there publications that are missing from
13 your CV?

14 A. Yes. I think we've published two papers
15 since then.

16 Q. What is the subject matter of those papers?

17 A. One was on the self-assembly of lipid
18 nanoparticles used for mRNA vaccines. That's the one
19 I -- jumps to mind that's missing there.

20 Q. You said there was two. Is there another one
21 that you've published since submitting this CV?

22 A. We've got two that are in the process of
23 going through review and proofreading before release,
24 so I assume the other one I was thinking of was that
25 one.

1 Q. How long did it take you to draft the
2 portions of your opinion that are based on the opinions
3 of Dr. D'Amico?

4 A. I don't recall.

5 Q. Was it most of the day?

6 A. It would have been part of the day.

7 Q. Okay. An hour?

8 A. I don't recall.

9 Q. You understand that the patent being
10 challenged in this proceeding by Alvotech is patent
11 number 12,168,036, right?

12 A. I recall the 036.

13 Q. Can we call that the '036 patent?

14 A. Or Graham.

15 Q. Or Graham. You'll understand it if I refer
16 to either of those terms?

17 A. Okay.

18 Q. You provided your opinions from the
19 perspective of a person of ordinary skill in the art,
20 correct?

21 A. Correct.

22 Q. Can I use the term POSA, P-O-S-A, to refer to
23 that person?

24 A. Sure.

25 Q. You'll understand what I mean?

1 A. Yes.

2 Q. You define the POSA as being
3 multidisciplinary team, right? Paragraph 40 of your
4 declaration if you need to refer to that.

5 A. Correct.

6 Q. And the multidisciplinary team included a
7 medical doctor and someone with a Ph.D. in
8 pharmaceutical sciences or a similar field, right?

9 A. Yes.

10 Q. And that collective team is the POSA for
11 purposes of the '036 patent?

12 A. Correct.

13 Q. And on paragraph 42 -- actually, the top of
14 the page 22 --

15 A. This is 22 bottom or --

16 Q. It's the bottom number I'm referring to. You
17 say at the end of that sentence, I consider myself to
18 have at least the qualifications of a person of
19 ordinary skill in the art at the time of the alleged
20 invention. Do you see that?

21 A. Yes.

22 Q. Is that accurate?

23 A. Yes.

24 Q. Okay. So you have -- are you a medical
25 doctor?

1 A. No.

2 Q. Okay. The POSA is a multidisciplinary team
3 that includes both a medical doctor and a Ph.D. in
4 pharmaceutical sciences, right?

5 A. Yes.

6 Q. You don't have the qualifications of a POSA
7 for the '036 patent, right?

8 A. I have qualifications of the second part of
9 the POSA. Correct.

10 Q. You refer to that person as the skilled
11 formulator?

12 A. That sounds correct.

13 Q. But the POSA also includes a medical doctor,
14 right?

15 A. Yes.

16 Q. And so you do not have at least the
17 qualifications of a POSA for purposes of the '036
18 patent, right?

19 MR. CHEN: Objection. Mischaracterizes.

20 A. Okay. Well, I'm definitely not a medical
21 doctor in ophthalmology, but I am definitely an expert
22 on the formulation of therapeutic proteins.

23 Q. So you are -- in your opinion you have part
24 of the skills of a POSA but not all of the skills of a
25 POSA, right?

1 A. That's correct. Yes.

2 Q. Okay. So in saying that I consider myself to
3 have at least the qualifications of a person of
4 ordinary skill in the art at the time of the alleged
5 invention, that's not entirely accurate, right?

6 MR. CHEN: Objection. Mischaracterizes.

7 A. It should have been more precise.

8 Q. How would you word it today?

9 A. I'd consider myself to have at least the
10 qualifications of a personally -- person of ordinary
11 skill in the art pertaining to part two, the Ph.D. in
12 pharmaceutical sciences or a similar field.

13 Q. Okay. Turn to paragraph 24, please, of your
14 declaration. This paragraph contains a summary of your
15 opinions in this case?

16 A. Yes. That's what the title says. Well, the
17 first sentence. Yep.

18 Q. Okay. Is this an accurate summary of your
19 opinions in this case?

20 A. Yes.

21 Q. In grounds one and four your opinions are
22 based on the references Vitti and Larson, correct?

23 A. Correct.

24 Q. Your opinions are not based on any other
25 specific references for grounds one and four, right?

1 A. Yes. My opinions are based on Vitti and
2 Larson. I don't recall seeing the Australian Eylea
3 label.

4 Q. All right. You don't have any opinions
5 regarding the Australian label, correct, Exhibit 1009?

6 A. I don't believe I've seen it.

7 Q. Your opinions in grounds two and five rely on
8 the references Furfine, Dix, Fiedler, and Larson,
9 correct?

10 A. Sorry. Which paragraph is this?

11 Q. Still in paragraph 24.

12 A. Sorry. I turned the page.

13 Q. I mean, I'm asking about your opinions
14 generally, but we were talking about the summary
15 specifically.

16 A. Sure.

17 Q. Your opinions in this case regarding grounds
18 two and five rely on the references Furfine, Dix,
19 Fiedler and Larson, correct?

20 A. Correct.

21 Q. You don't have any opinions concerning the
22 2011 Eylea clinical review document, correct?

23 A. No.

24 Q. And you have no opinions on the POSA's
25 motivation to combine any of their references in any of

1 the obviousness grounds in this case, correct?

2 A. Could you repeat the question?

3 Q. You don't have an opinion about the POSA's
4 motivation to combine any of the references in any of
5 the obviousness grounds in this case, correct?

6 MR. CHEN: Objection. Form.

7 A. Could you repeat the question?

8 Q. You don't have an opinion about the POSA's
9 motivation to combine any of the references in any of
10 the obviousness grounds in this case, correct?

11 MR. CHEN: Same objection.

12 A. Yes. This is language that as a scientist
13 I'm not particularly familiar with.

14 Q. Well, why don't you turn to paragraph 23 of
15 your declaration? This paragraph sets forth the --
16 your understanding about the opinions that Dr. D'Amico
17 provides, correct?

18 A. Correct.

19 Q. And he provides the opinion for -- about what
20 a POSA would have been motivated to combine, correct,
21 for example in ground one, ground two, grounds four,
22 and grounds five?

23 A. Correct.

24 Q. You don't offer an opinion on that topic,
25 correct?

1 MR. CHEN: Objection. Form.

2 A. I don't believe so.

3 Q. I'm handing you what's been previously marked
4 as Exhibit 1007.

5 (Whereupon, Exhibit 1007, previously marked,
6 was proffered to the witness.)

7 Q. Do you recognize this document, Doctor?

8 A. Yes.

9 Q. What is it?

10 A. It's the patent we refer to as Vitti.

11 Q. Okay. You can keep that handy, but I'd ask
12 you to turn to paragraph 172 of your declaration. Are
13 you there?

14 A. Yes.

15 Q. In the second line of --

16 A. Could you wait a minute? Sorry. The
17 paragraph number?

18 Q. 172.

19 A. Yes.

20 Q. Are you there?

21 A. Yep.

22 Q. The first two lines of that paragraph you
23 state that Vitti teaches high concentration aqueous
24 pharmaceutical formulations that contain up to 115 mgs
25 per ml of aflibercept. You see that?

1 A. Yes.

2 Q. You agree with that?

3 A. Yes.

4 Q. Now, you're citing paragraph 94 of Vitti
5 there, right?

6 A. Yes.

7 Q. Okay. So you're relying on the passage in
8 paragraph 94 of Vitti that says 100 plus or minus 15
9 milligrams per milliliter of VEGF antagonist, is that
10 right?

11 A. Correct.

12 Q. You're also citing paragraph 127 in that
13 statement, paragraph 127 of Vitti.

14 A. Okay. Sorry.

15 Q. Are you at paragraph 127 of Vitti?

16 A. Yes. I'm reading it at the minute.

17 Q. Well, why don't I ask the question first?

18 A. Okay.

19 Q. Paragraph 127 of Vitti doesn't refer to 115
20 milligrams per milliliter at all, right?

21 A. Correct.

22 Q. If I say mgs per ml, do you understand that
23 to mean milligrams per milliliter?

24 A. Yes.

25 Q. So that statement then in paragraph 172 of

1 your declaration cites both paragraph 94 and paragraph
2 127 of Vitti, but the only disclosure that you're
3 really relying on there is the one in paragraph 94 that
4 says 100 plus or minus 15 mgs per ml of VEGF
5 antagonist, right?

6 MR. CHEN: Objection. Form.

7 A. That is the more precise wording, yes.

8 Q. Okay.

9 A. Yeah.

10 Q. Now, Vitti uses that term 100 mgs per ml plus
11 or minus 15 mgs per ml elsewhere in connection with a
12 VEGF antagonist, right? Do you recall that?

13 A. I recall it says somewhere else in the
14 patent, yes.

15 Q. None of those references refer to 100 plus or
16 minus 15 mgs per mill of aflibercept, specifically,
17 right?

18 MR. CHEN: Objection to the extent it
19 mischaracterizes the document.

20 Q. Well, for example, paragraph 94 doesn't say
21 100 plus or minus 15 mgs per ml of aflibercept, right?

22 MR. CHEN: Same objection.

23 A. Yes. It talks about the VEGF antagonist.

24 Q. But your opinion assumes that VEGF antagonist
25 is synonymous with aflibercept here?

1 MR. CHEN: Objection. Form.

2 A. Yes. If you look later on in the same
3 paragraph it does talk about a VEGF antagonist such as
4 aflibercept.

5 Q. But that's not a disclosure of plus or minus
6 100 mgs per ml, right?

7 MR. CHEN: Objection. Form.

8 A. Certainly my reading of this is it links the
9 VEGF antagonist to being at least the possibility of
10 being aflibercept.

11 Q. You read VEGF antagonist as synonymous with
12 aflibercept, right?

13 MR. CHEN: Objection. Misstates testimony.

14 A. My reading of this is that it certainly can
15 include aflibercept, yes.

16 Q. It can include other molecules too?

17 A. I don't recall it mentioning another VEGF
18 antagonist.

19 Q. What do you mean by --

20 A. But I do -- okay.

21 Q. Let me ask to understand that answer. When
22 you say I don't recall it mentioning another VEGF
23 antagonist, is it Vitti there?

24 A. Yes. It is Vitti.

25 Q. Okay.

1 A. Can I explain the answer?

2 Q. Please.

3 A. Yes. Obviously VEGF antagonist is a -- you
4 know, potentially is a broader family than just the one
5 specific molecule which in this case is aflibercept,
6 but my reading of this is that it is talking about
7 aflibercept.

8 Q. So when Vitti uses the term VEGF antagonist
9 it's using it to refer to aflibercept, correct?

10 MR. CHEN: Objection. Form.

11 A. So it would be my reading of it is that it
12 could definitely include aflibercept, yes.

13 Q. Well --

14 A. It's --

15 Q. Is it --

16 A. Okay.

17 Q. Does VEGF antagonist mean aflibercept or does
18 it mean something else?

19 MR. CHEN: Objection. Form.

20 A. My reading of this is it is alluding to
21 aflibercept but by using the wording VEGF antagonist it
22 could include variants on the theme, you know, other
23 therapeutic proteins that are VEGF antagonists. It's a
24 less precise use of the English language.

25 Q. So when you say Vitti teaches 115 mgs per ml

1 of aflibercept, you're actually referring to 115 mgs
2 per ml of a group of proteins called VEGF antagonists?

3 MR. CHEN: Objection. Misstates the
4 testimony.

5 A. And one of those is definitely aflibercept,
6 yes.

7 Q. But Vitti doesn't include 115 mgs per ml of
8 aflibercept specifically, right?

9 MR. CHEN: Asked and answered.

10 A. Vitti doesn't say aflibercept, but as I
11 pointed out, there is a very strong link in the same
12 paragraph that points out that that VEGF antagonist can
13 be aflibercept.

14 Q. What else can it be?

15 MR. CHEN: Objection. Asked and answered.

16 A. Proteins are made up of sequences of amino
17 acids, and a protein engineer could come up with
18 something which is very similar to aflibercept that has
19 a slightly different sequence, and that would be a VEGF
20 antagonist who wouldn't necessarily fit under the
21 definition of aflibercept which has a specific
22 sequence.

23 Q. So is that the meaning you understand Vitti
24 to be referring to when it refers to VEGF antagonist?

25 MR. CHEN: Objection. Form.

1 A. My reading is when it talks about VEGF
2 antagonist it is alluding to aflibercept or a similarly
3 related protein, yes. It's just less precise English.

4 Q. So VEGF antagonist refers to aflibercept and
5 other molecules, is that fair?

6 A. Yeah, and related.

7 Q. What do you mean by related?

8 A. The same binding. There's a sort of
9 functionality.

10 Q. So what is -- can you please tell me what you
11 understand Vittti to be -- what meaning of VEGF
12 antagonist Vittti is using?

13 MR. CHEN: Objection. Asked and answered.

14 A. Yes. I think the opinion in paragraph 115 on
15 page 51 of the declaration.

16 Q. What about that paragraph?

17 A. I think it spells out my opinion quite
18 nicely.

19 Q. The meaning of VEGF antagonist in Vittti is
20 not specific to aflibercept, correct?

21 MR. CHEN: Objection. Asked and answered.

22 A. Yes. A VEGF antagonist is not as well
23 defined a title as being precise in saying aflibercept.
24 The exemplary, you know, example here is aflibercept.

25 Q. You agree that Vittti does not specifically

1 disclose 115 mgs per ml of aflibercept, correct?

2 MR. CHEN: Objection. Asked and answered.

3 A. Yeah. My reading of this is that Vitti was
4 alluding to aflibercept and was using less precise
5 English, so it could include some -- the related
6 proteins to aflibercept.

7 Q. I don't know if that answers my question.
8 I'll ask it again.

9 A. Okay.

10 Q. You agree that Vitti does not specifically
11 disclose 115 mgs per ml of aflibercept, correct?

12 MR. CHEN: Same objection.

13 A. Yes. It doesn't specifically disclose it.
14 Correct.

15 Q. Now, if you turn to paragraph 85 of the Vitti
16 reference, are you there?

17 A. Yes.

18 Q. Vitti is defining the term VEGF antagonist in
19 this paragraph, correct?

20 A. Yes.

21 Q. You agree with this definition?

22 A. Yes.

23 Q. Now, you don't have an opinion in this case
24 about how many different molecules fall within Vitti's
25 definition of VEGF antagonist, correct?

1 A. Could you repeat the question?

2 Q. You don't have an opinion in this case about
3 how many different molecules fall within Vitti's
4 definition of VEGF antagonist, correct?

5 A. Correct.

6 Q. You'd agree with me it encompasses a very
7 large number of possible distinct molecules?

8 MR. CHEN: Objection. Form.

9 A. This definition does include a range of
10 different molecules, yes.

11 Q. It's a very large number of possible distinct
12 molecules, right?

13 MR. CHEN: Objection. Form.

14 A. It's a significant number, yes.

15 Q. The definition includes anti-VEGF antibodies?

16 A. Yes.

17 Q. Aflibercept's not an antibody, right?

18 A. No.

19 Q. How many anti-VEGF antibodies would a POSA
20 understand to fall within the scope of Vitti's VEGF
21 antagonist definition?

22 MR. CHEN: Objection. Form.

23 A. There are potentially numerous antibodies
24 that could fall under this definition, yes.

25 Q. Does Vitti disclose to the POSA aqueous

1 formulations suitable for intravitreal administration
2 containing every VEGF antibody falling within the scope
3 of the VEGF antagonist definition?

4 MR. CHEN: Objection. Form.

5 A. No.

6 Q. Why not?

7 A. Well, for an -- sorry. For instance, the
8 examples are only -- actually, I should check that
9 first. Yes. The VEGF antagonist in the examples, such
10 as example seven, is named as aflibercept.

11 Q. I'll ask the question again because I don't
12 think I got an answer to it.

13 A. Okay.

14 Q. Does Vitti disclose to the POSA aqueous
15 formulations suitable for intravitreal administration
16 including every VEGF antibody falling within the scope
17 of its VEGF antagonist definition?

18 A. No.

19 MR. CHEN: Objection. Form.

20 THE WITNESS: Sorry.

21 MR. CHEN: Give me a moment to raise my
22 objections, Dr. Falconer.

23 Q. And am I understanding correctly that you
24 said no to that question because there's no data in the
25 patent for any anti-VEGF antibodies, correct?

1 MR. CHEN: Objection to the extent it
2 mischaracterizes testimony.

3 A. Could you repeat the question?

4 Q. I think you just offered the opinion that
5 Vitti does not disclose or describe to the -- strike
6 that.

7 I think you just offered the opinion that
8 Vitti does not describe to the POSA any aqueous
9 formulations suitable for intravitreal administration
10 including every anti-VEGF antibody falling within the
11 scope of its VEGF antagonist, definition, correct?

12 MR. CHEN: Objection. Mischaracterizes
13 testimony.

14 A. Yes.

15 Q. Is the reason you provided that opinion
16 because there's no data in the patent for any anti-VEGF
17 antibody?

18 A. Yes. I don't recall there being any
19 anti-VEGF antibody in data in the patent.

20 Q. Okay. So in order for Vitti to disclose to
21 the POSA an aqueous formulation of a particular
22 molecule at a particular concentration, Vitti needs to
23 provide data for that particular molecule at that
24 particular concentration, correct?

25 MR. CHEN: Objection. Misstates testimony.

1 A. The POSA's reading or POSA associated with
2 the formulation science reading of this isn't solely
3 based on the examples, but it's based on the whole
4 patent. Sorry. Could you repeat the question?

5 Q. Let me ask the question again.

6 A. Yes.

7 Q. In your opinion in order for Vitti to
8 disclose to the POSA an aqueous formulation of a
9 particular molecule at a particular concentration,
10 Vitti needs to provide data for that particular
11 molecule at that particular concentration, correct?

12 MR. CHEN: Objection. Misstates testimony.

13 A. Sorry. No.

14 Q. No? So I don't then understand why you have
15 the opinion that Vitti doesn't describe formulations
16 with anti-VEGF antibodies. I thought you looked at the
17 examples and you didn't see any data for those
18 antibodies in the examples and so you concluded that
19 they weren't described. Did I misunderstand that?

20 MR. CHEN: Objection. Misstates testimony.

21 A. Could you repeat the question?

22 Q. I'm just trying to understand --

23 A. Yes.

24 Q. -- the boundaries of your opinion here.

25 A. Yes.

1 Q. I asked if Vitti describes the formulations
2 with anti-VEGF antibodies, and I think you answered no,
3 correct?

4 MR. CHEN: Objection. Misstates testimony.

5 A. The parts where it refers to the VEGF
6 antagonist -- yeah. The definition in the patent is
7 broad. So the -- sorry. Could you repeat the
8 question?

9 Q. I thought I heard you testify --

10 A. Yes.

11 Q. -- and correct me if I'm wrong -- that Vitti
12 does not describe formulations containing anti-VEGF
13 antibodies. Is that right or wrong?

14 MR. CHEN: Objection to the extent it
15 misstates testimony.

16 A. The parts of the patent -- sorry. Yes.
17 Sorry. I'm elaborating when I should just answer yes
18 or no. Could you repeat the question?

19 Q. I'll ask it in hopefully a clean -- in a more
20 precise way.

21 A. Yes, no. I understand the importance of
22 this.

23 Q. Does Vitti describe formulations of anti-VEGF
24 antibodies? Yes or no?

25 MR. CHEN: Objection. Form.

1 A. Yes.

2 Q. It does? Which formulations of anti-VEGF
3 antibodies does Vitti disclose?

4 A. The definition of VEGF antagonists is broad
5 enough that the parts that are talking about -- there's
6 a lot of the examples that are in the part before, that
7 section of the patent where it does mention things like
8 100 milligrams per ml. That definition is broad enough
9 that that could include the monoclonals. Yes.

10 Q. So in your opinion Vitti discloses aqueous
11 formulations suitable for intravitreal administration
12 containing at least 100 mgs per ml of every anti-VEGF
13 antibody falling within the scope of Vitti's anti-VEGF
14 antagonist definition?

15 MR. CHEN: Objection to the extent it
16 mischaracterizes testimony.

17 Q. I'm going to ask the question again because I
18 think I misspoke.

19 A. Yes.

20 Q. In your opinion Vitti discloses aqueous
21 formulations suitable for intravitreal administration
22 containing at least 100 mgs per ml of every anti-VEGF
23 antibody falling within the scope of Vitti's VEGF
24 antagonist definition, right?

25 MR. CHEN: Same objection.

1 A. Okay. Could you repeat the question, please?

2 Q. In your opinion Vitti discloses aqueous
3 formulations suitable for intravitreal administration
4 containing at least 100 mgs per ml of every anti-VEGF
5 antibody falling within the scope of Vitti's VEGF
6 antagonist definition, correct?

7 MR. CHEN: Same objection.

8 A. Sorry. Could you repeat the question?

9 Q. In your opinion Vitti discloses aqueous
10 formulations suitable for intravitreal administration
11 containing at least 100 mgs per ml of every anti-VEGF
12 antibody falling within the scope of Vitti's VEGF
13 antagonist definition, correct?

14 MR. CHEN: Same objection.

15 A. Incorrect. Yes.

16 Q. Why is that statement incorrect?

17 A. It's the imprecision of the English used in
18 the patent. The definition of a VEGF antagonist is
19 broad. It specifically then goes on to aflibercept in
20 that same paragraph, mentioning it as the example. And
21 then in the examples in the patent itself, they all
22 focus in on aflibercept, so it's -- from my reading
23 it's -- they've used a reasonably imprecise term that
24 has a broad family associated with it, and then they're
25 discussing aflibercept as the exemplar example. So

1 that's my reading of this -- of Vitti.

2 Q. Well, I was asking about anti-VEGF
3 antibodies.

4 A. Yes, yes.

5 Q. Is it your position that Vitti discloses no
6 aqueous formulations suitable for intravitreal
7 administration containing at least 100 mgs per ml of an
8 anti-VEGF antibody falling within the scope of Vitti's
9 VEGF antagonist definition?

10 MR. CHEN: Same objection.

11 A. Yeah. Not directly. These -- is it 49 in
12 the Vitti? Yeah. That section in 49 is imprecise
13 enough to cover the other VEGF antagonists as defined
14 in the patent.

15 Q. When you say 49 I don't know what you're
16 referring to.

17 A. Okay. This is Vitti page 15.

18 Q. You mean 94?

19 A. Oh, apologies. Yes.

20 Q. Okay. Well, I'm not asking about paragraph
21 94 specifically. I'm asking generally, is it your
22 position that Vitti doesn't disclose aqueous
23 formulations suitable for intravitreal administration
24 containing at least 100 mgs per ml of any anti-VEGF
25 antibody falling within the scope of Vitti's VEGF

1 antagonist definition?

2 MR. CHEN: Same objection.

3 A. Sorry. Could you repeat the question?

4 Q. Is it your opinion that Vittti does not
5 disclose aqueous formulations suitable for intravitreal
6 administration containing at least 100 mgs per ml of
7 any anti-VEGF antibody falling within the scope of
8 Vittti's VEGF antagonist definition?

9 MR. CHEN: Same objection.

10 A. Yes. My reading of this is that it doesn't
11 cover the anti-VEGF antibodies.

12 Q. This being the Vittti reference, right?

13 A. The Vittti reference, yes.

14 Q. Okay. So the POSA would not have a
15 reasonable expectation of success based on Vittti in
16 achieving aqueous formulations suitable for
17 intravitreal administration containing an anti-VEGF
18 antibody falling within the scope of Vittti's VEGF
19 antagonist, right?

20 MR. CHEN: Objection. Form. Misstates the
21 testimony.

22 A. Correct.

23 Q. And I assume the same opinion holds for small
24 molecule inhibitors of VEGF, but I'll ask that one too.
25 So I understand that the definition of VEGF antagonist

1 in paragraph 85 of Vitti encompasses small molecule
2 inhibitors of VEGF?

3 A. Correct, yes.

4 Q. Vitti does not disclose to the POSA any
5 aqueous formulations suitable for intravitreal
6 administration containing at least 100 mgs per ml of a
7 small molecule inhibitor of VEGF falling within the
8 scope of Vitti's VEGF antagonist definition, correct?

9 MR. CHEN: Same objections.

10 A. Correct.

11 Q. And Vitti would not have provided the POSA
12 with a reasonable expectation of success in achieving
13 aqueous formulations suitable for intravitreal
14 administration containing at least 100 mgs per ml of a
15 small molecule inhibitor of VEGF falling within Vitti's
16 definition of VEGF antagonist, right?

17 MR. CHEN: Same objections.

18 A. Yeah. Correct.

19 Q. Vitti's definition of VEGF antagonist
20 includes VEGF receptor-based chimeric molecules or
21 VEGF-inhibiting fusion proteins, also referred to as
22 VEGF traps, correct?

23 A. This is quote from the patent?

24 Q. Paragraph 85.

25 A. Yes. It's the part at the bottom of the

1 patent -- of the paragraph, I believe.

2 Q. So I'll just ask the question again.

3 A. Yes.

4 Q. Vitti's definition of VEGF antagonist
5 includes VEGF receptor-based chimeric molecules and
6 VEGF-inhibiting fusion proteins, also referred to as
7 VEGF traps, right?

8 A. Yes. That's the wording in the patent.

9 Q. Okay. That's a genus of molecules, correct?

10 MR. CHEN: Objection. Form.

11 A. I'm not familiar with your use of the word
12 genus with therapeutic proteins.

13 Q. I'll rephrase. That portion of the
14 definition of VEGF antagonist in Vitti is referring to
15 a collection of molecules, correct?

16 A. Correct.

17 Q. It's not referring specifically to
18 aflibercept, correct?

19 A. Correct.

20 Q. How many different VEGF traps would the POSA
21 be aware of?

22 MR. CHEN: Objection. Form.

23 A. I couldn't give you an exact number, but
24 there were several from the sort of earlier development
25 phase to the best of my knowledge. I'm -- yeah.

1 That's sort of outside the scope of the material that
2 I've been, you know, covering for this.

3 Q. So you have an understanding that these
4 VEGF-inhibiting fusion proteins is a class of
5 molecules, but you don't have an opinion about how
6 large that class is, correct?

7 MR. CHEN: Objection to the extent it
8 mischaracterizes testimony.

9 A. Yes. I don't know how many VEGF traps were
10 in the original development work. Yes. I don't know a
11 number.

12 Q. Does Vitti disclose to the POSA aqueous
13 formulations suitable for intravitreal administration
14 containing at least 100 mgs per ml of every
15 VEGF-inhibiting fusion protein falling within the scope
16 of Vitti's VEGF antagonist definition?

17 MR. CHEN: Objection to form.

18 A. No.

19 Q. How many VEGF-inhibiting fusion proteins --
20 strike that.

21 When Vitti discloses aqueous pharmaceutical
22 formulations suitable for intravitreal administration
23 containing a VEGF-inhibiting fusion protein within the
24 meaning of Vitti definition of VEGF antagonist, how
25 many VEGF-inhibiting fusion proteins is Vitti

1 disclosing in your opinion?

2 MR. CHEN: Objection. Form.

3 A. Yeah. Within the definition of the VEGF
4 antagonists that could be quite a broad number, broad
5 number of different proteins. Yes.

6 Q. So Vitti is disclosing aqueous formulations
7 suitable for intravitreal administration containing a
8 broad number of VEGF-inhibiting fusion proteins falling
9 within the scope of Vitti's definition of VEGF
10 antagonist?

11 MR. CHEN: Objection. Form. And to the
12 extent it mischaracterizes testimony.

13 A. Could you repeat the question?

14 Q. I'm going to ask a slightly different
15 question. Does Vitti disclose aqueous formulations
16 suitable for intravitreal administration containing at
17 least 100 mgs per ml of a broad number of
18 VEGF-inhibiting fusion proteins following within the
19 scope of Vitti's VEGF antagonist definition?

20 MR. CHEN: Objection. Form.

21 Counsel, we've been going on for about an
22 hour and a half.

23 MR. TRASK: We're in the middle of a question
24 right now.

25 MR. CHEN: Yeah.

1 A. Yes. I'll get you to just repeat the
2 question.

3 MR. TRASK: We can take a break shortly.

4 MR. CHEN: Yeah.

5 MR. TRASK: But I'd ask that you not
6 interrupt in the middle of a question when I'm waiting
7 for an answer, okay?

8 MR. CHEN: Yeah.

9 Q. Does Vitti disclose aqueous formulations
10 suitable for intravitreal administration containing at
11 least 100 mgs per ml of a broad number of
12 VEGF-inhibiting fusion proteins falling within the
13 scope of Vitti's VEGF antagonist definition?

14 A. No.

15 Q. How many formulations suitable for
16 intravitreal administration containing at least 100
17 milligrams per milliliter of a VEGF-inhibiting fusion
18 protein falling within the scope of Vitti's VEGF
19 antagonist definition does Vitti disclose to the POSA?

20 MR. CHEN: Objection. Form.

21 A. Sorry. Could you repeat the question?

22 Q. How many formulations suitable for
23 intravitreal administration containing at least 100 mgs
24 per ml of a VEGF-inhibiting fusion protein falling
25 within the scope of Vitti's VEGF antagonist definition

1 does Vitti disclose to the POSA?

2 MR. CHEN: Objection. Form.

3 A. None.

4 Q. And the POSA would not have a reasonable
5 expectation of success based upon Vitti in achieving
6 aqueous formulations suitable for intravitreal
7 administration containing a VEGF-inhibiting fusion
8 proteins falling within the scope of Vitti's VEGF
9 antagonist definition wherein the concentration is at
10 least 100 mgs per ml, correct?

11 MR. CHEN: Objection. Form.

12 A. Okay. I'll get you to repeat the question.

13 Q. Sure. I'll ask it slightly differently and
14 hopefully clear it [sic].

15 A. Yes.

16 Q. The POSA would not have a reasonable
17 expectation of success based upon Vitti in achieving
18 aqueous formulations suitable for intravitreal
19 administration containing at least 100 mgs per ml of a
20 VEGF-inhibiting fusion protein falling within the scope
21 of Vitti's VEGF antagonist definition, correct?

22 MR. CHEN: Objection. Form.

23 A. Sorry. I'm going to get you to repeat the
24 question again.

25 Q. The POSA would not have a reasonable

1 expectation of success based upon Vittti in achieving
2 aqueous formulations suitable for intravitreal
3 administration containing at least 100 mgs per ml of
4 VEGF-inhibiting fusion protein falling within the scope
5 of Vittti's VEGF antagonist definition, correct?

6 MR. CHEN: Objection. Form.

7 A. My answer to that question is that it doesn't
8 cover -- wouldn't cover all the VEGF fusion proteins.

9 Q. Let me just ask the question again because I
10 don't think that answers it.

11 A. Yes.

12 Q. And I understand we've been going for a while
13 so we can take a break shortly thereafter.

14 A. Yes, yes. I think the answer is incorrect
15 because -- yes.

16 Q. Do you mind if I ask the question?

17 A. Okay. I think we probably do need to take a
18 break.

19 Q. A lot of colloquy here. Here's the question.

20 A. Yeah.

21 Q. The POSA would not have a reasonable
22 expectation of success based upon Vittti in achieving
23 aqueous formulations suitable for intravitreal
24 administration containing at least 100 mgs per ml of a
25 VEGF-inhibiting fusion protein falling within the scope

1 of Vitti's VEGF antagonist definition, correct?

2 MR. CHEN: Objection. Form.

3 A. That's correct because the definition is so
4 broad. Yes.

5 MR. TRASK: Okay. Why don't we take a short
6 break?

7 THE WITNESS: Thank you.

8 THE VIDEOGRAPHER: Going off the record at
9 9:40 a.m.

10 (Whereupon, a recess was taken.)

11 THE VIDEOGRAPHER: And we're back on the
12 record at 9:56 a.m.

13 BY MR. TRASK:

14 Q. Doctor, during the break did you discuss your
15 testimony with counsel?

16 A. No.

17 Q. In your opinion, Doctor, does the Vitti
18 patent publication provide written description support
19 for aqueous pharmaceutical formulations suitable for
20 intravitreal administration containing at least 100 mgs
21 per ml of aflibercept falling within the scope of -- or
22 strike that.

23 In your opinion does Vitti disclose -- strike
24 that.

25 In your opinion does Vitti provide written

1 description support for aqueous formulations suitable
2 for intravitreal administration containing at least 100
3 mgs per ml of aflibercept?

4 MR. CHEN: Objection. Form.

5 A. Okay. I'm going to get you to repeat the
6 question, but --

7 Q. In your opinion does Vitti provide written
8 description support for aqueous formulations suitable
9 for intravitreal administration containing at least 100
10 mgs per ml of aflibercept?

11 MR. CHEN: Objection. Form.

12 A. Yes.

13 Q. In your opinion does Vitti provide written
14 description support for aqueous formulations suitable
15 for intravitreal administration containing at least 100
16 mgs per ml of aflibercept with a viscosity of 5 to 15
17 centipoise?

18 MR. CHEN: Objection. Form.

19 A. Could you repeat the question?

20 Q. In your opinion does Vitti provide written
21 description support for aqueous formulations suitable
22 for intravitreal administration containing at least 100
23 mgs per ml of aflibercept with a viscosity of 5 to 15
24 centipoise?

25 MR. CHEN: Objection. Form.

1 A. Yes.

2 Q. In your opinion does Vitti provide written
3 description support for aqueous formulations suitable
4 for intravitreal administration containing 114.3 mgs
5 per ml of aflibercept with a viscosity of between 5 and
6 15 centipoise?

7 MR. CHEN: Objection. Form.

8 A. I'll get you to repeat the question as well.

9 Q. In your opinion does Vitti provide written
10 description support for aqueous formulations suitable
11 for intravitreal administration containing 114.3 mgs
12 per ml of aflibercept with a viscosity of between 5 and
13 15 centipoise?

14 A. Yes.

15 Q. In your opinion does Vitti provide written
16 description support for aqueous formulations suitable
17 for intravitreal administration containing about 103 to
18 126 mgs per ml of aflibercept with a viscosity of
19 between 5 and 15 centipoise?

20 MR. CHEN: Objection. Form.

21 A. Could you repeat the question?

22 Q. In your opinion does Vitti provide written
23 description support for aqueous formulations suitable
24 for intravitreal administration containing about 103 to
25 126 mgs per ml of aflibercept with a viscosity of

1 between 5 and 15 centipoise?

2 MR. CHEN: Objection. Form.

3 A. I don't recall it having that support for
4 those numbers, no.

5 Q. Vitti doesn't disclose 103 to 126 mgs per ml
6 of aflibercept?

7 MR. CHEN: Objection. Form.

8 A. I don't recall it mentioning those numbers.

9 Q. So you don't have an opinion that Vitti
10 discloses 103 to 126 mgs per ml of aflibercept,
11 correct?

12 MR. CHEN: Objection. Misstates testimony.

13 A. My reading is it doesn't cover 126.

14 Q. Why not?

15 A. The highest value from my reading of this
16 patent is they're talking about 100 plus or minus 15
17 which takes it up to 115 milligrams per ml.

18 Q. You agree that if Vitti disclosed a higher
19 concentration of aflibercept than 100 plus or minus 15
20 then Vitti may disclose the range of 103 to 126 mgs per
21 ml, correct?

22 MR. CHEN: Objection. Misstates testimony.

23 A. Again I'll get you to repeat the question.

24 Q. Your opinion that Vitti doesn't disclose --
25 this is a different question. Your opinion that Vitti

1 doesn't disclose the range of 103 to 126 mgs per ml of
2 aflibercept is based on your opinion that Vitti doesn't
3 disclose above 115 mgs per ml of aflibercept, correct?

4 A. Correct.

5 MR. CHEN: Objection. Misstates testimony.

6 THE WITNESS: Sorry.

7 Q. Turn to paragraph 87 of Vitti, please.

8 A. Go ahead.

9 Q. Are you there?

10 A. Yes.

11 Q. Do you see about five lines up from the
12 bottom on page 14 in Vitti it says, insert embodiments
13 that pharmaceutical formulations are liquid
14 formulations that may contain 5 plus or minus 0.75 mgs
15 per ml to 150 plus or minus 22.5 mgs per ml of VEGF
16 antagonist?

17 A. Yes. I can see that.

18 Q. Vitti does disclose above 115 mgs per ml of
19 aflibercept, correct?

20 A. Again it's using the wording of VEGF
21 antagonist, but yes, that would be my reading of it.
22 Yes.

23 Q. Your reading of VEGF antagonist is synonymous
24 with aflibercept there, right?

25 MR. CHEN: Objection. Misstates testimony.

1 A. Yes.

2 Q. So Vitti does in fact provide written
3 description support for an aqueous pharmaceutical
4 formulation containing about 103 to is 26 mgs per ml of
5 aflibercept with a viscosity of between 5 and 15
6 centipoise, correct?

7 MR. CHEN: Objection. Form.

8 A. It doesn't actually mention the route of
9 administration, so I would say incorrect.

10 Q. What do you mean by it doesn't actually
11 mention the route of administration?

12 A. There's no allusion to viscosity or the --
13 where it's being administered.

14 Q. Vitti doesn't disclose the route of
15 administration of aflibercept?

16 MR. CHEN: Objection. Misstates testimony.

17 A. It does, but it doesn't in this part of
18 the -- in this paragraph.

19 Q. So the disclosures of aflibercept in Vitti
20 are not disclosures of administration by intravitreal
21 injection, correct?

22 MR. CHEN: Objection. Misstates testimony.

23 A. Could you repeat the question?

24 Q. I think you provided testimony that Vitti
25 does not provide written description support for an

1 aqueous pharmaceutical formulation containing about 103
2 to 126 mgs of aflibercept with a viscosity between 5
3 and 15 centipoise, correct?

4 A. Yes. That's what I said earlier. Yes.

5 Q. And that's because the range of aflibercept
6 that is disclosed in your opinion in paragraph 87 does
7 not mention the route of administration?

8 A. It doesn't mention a viscosity directly
9 there.

10 Q. Is viscosity mentioned -- oh, I'm sorry.
11 Finish your answer.

12 A. Yes.

13 Q. Are you done?

14 A. Yes, yes, yes. This paragraph doesn't
15 directly discuss viscosity or its intended application.
16 Sorry. That doesn't answer your question. Could you
17 repeat the question?

18 Q. Let me ask a different question. If Vitti
19 disclosed the route of administration and mentioned
20 viscosity, then it would provide written description
21 support for an aqueous pharmaceutical formulation
22 containing about 103 to 126 mgs per ml of aflibercept
23 with a viscosity of between 5 and 15 centipoise,
24 correct?

25 MR. CHEN: Objection. Form. Incomplete

1 hypothetical.

2 A. I apologize, but I'm going to get you to
3 repeat the question again.

4 Q. If Vitti disclosed the route of
5 administration and mentioned viscosity --

6 A. Yes.

7 Q. -- then it would provide written description
8 support for an aqueous pharmaceutical formulation
9 containing about 103 to 126 mgs per ml of aflibercept
10 with a viscosity between 5 and 15 centipoise, correct?

11 MR. CHEN: Same objections.

12 A. Yes.

13 Q. The POSA would understand from reading a
14 patent document that a reference to viscosity is a
15 disclosure -- or strike that.

16 A POSA would understand reading a patent
17 document that a reference to viscosity and a disclosure
18 of intravitreal administration would be written
19 description support for the viscosity range of 5 to 15
20 centipoise, correct?

21 MR. CHEN: Objection. Form.

22 A. Apologies.

23 Q. A POSA would understand reading a patent
24 document that a reference to viscosity and a disclosure
25 of intravitreal administration would constitute written

1 description support for the viscosity range of 5 to 15
2 centipoise, correct?

3 MR. CHEN: Objection. Form.

4 A. Yes.

5 Q. And if the patent disclosure contained
6 viscosity data, that would further provide written
7 description support for the POSA of that viscosity
8 range, correct?

9 MR. CHEN: Objection. Form. Incomplete
10 hypothetical.

11 A. Correct.

12 Q. The POSA would understand based on the
13 disclosure of viscosity data that the inventors
14 possessed the viscosity range of 5 to 15 centipoise,
15 correct?

16 MR. CHEN: Objection. Form. Incomplete
17 hypothetical.

18 A. Correct.

19 Q. Do you agree that protein stability is a key
20 issue for formulators?

21 A. Yes.

22 Q. What does stability mean?

23 A. Oh, it's a broad term. You could write a
24 book on it.

25 Q. Does it include physical stability?

1 A. Yes.

2 Q. Chemical stability?

3 A. Yes.

4 Q. Minimizing aggregation?

5 A. Yes.

6 Q. And you agree that formulations suitable for
7 intravitreal administration need to be stable?

8 A. Yes.

9 Q. Is stability more of a concern with
10 intravitreal formulations than other types of
11 formulations?

12 MR. CHEN: Objection. Form.

13 A. Sorry. I'll repeat the --

14 Q. Is stability more of a concern for
15 intravitreal formulations than other types of protein
16 formulations?

17 A. No.

18 Q. Why not?

19 A. The actual application isn't a concern
20 because if it's, say, a low dose, low volume,
21 intravitreal, it's not a particularly high concern.
22 Conversely, you could have a subcutaneous high
23 concentration, you know, high dose, reasonably low
24 volume. It's the concentration that is the important
25 factor as opposed to what the route of administration

1 is.

2 Q. Have you ever formulated a protein for
3 intravitreal administration?

4 A. No.

5 Q. Are you an expert in formulating proteins for
6 intravitreal administration or would you defer to
7 Dr. D'Amico on that subject?

8 A. From the formulation perspective the route of
9 administration, whether it's sub -- if it's
10 subcutaneous, intramuscular or intravitreal, has
11 similar concerns. And that's usually the -- they need
12 to be isotonic. The pH doesn't want to be too extreme.
13 And of course concentration, concentration is the
14 important factor. But that's, you know, independent of
15 which application you're using it for. So I'd say
16 somebody who could do a subcutaneous product could also
17 do an intravitreal product. It's -- the formulation
18 science itself is the same science.

19 Q. Why is it important not to have aggregation
20 of particulates in an intravitreal formulation?

21 A. There's a danger of information. There's --
22 I'm not an expert in this field. From the formulation
23 point of view you want to just keep aggregation as low
24 as possible because there are known side effects
25 associated with it. Exactly what reactions an

1 aggregate triggers in the eye, I don't know. But the
2 rule of thumb is you keep aggregation as low as
3 possible for all the different applications.

4 Q. Do you know if the tolerance for aggregation
5 for an intravitreal formulation is the same as for a
6 subcutaneous formulation?

7 A. No. I don't know the answer to that.

8 Q. Are you holding yourself out as an expert in
9 this proceeding on formulating proteins for
10 intravitreal administration?

11 A. I would argue that the formulation scientist
12 could work on intravitreal, subcutaneous, intravenous,
13 intramuscular, that a skilled person in the art would
14 be able to cover the different applications.

15 Q. Let me ask the question again. Are you
16 holding yourself out as an expert in this proceeding on
17 formulating proteins for intravitreal administration?

18 A. Yes.

19 Q. Even though you've never formulated a protein
20 for intravitreal administration?

21 A. Yes.

22 Q. What is the target viscosity for an
23 intravitreal formulation?

24 A. From the formulation science point of view
25 it's as low as possible.

1 Q. What is the value or range of values?

2 A. I agree with the approach that is in Larson,
3 in the Larson patent. The target is, you know, 10
4 centipoise or less. That's where you'd like to be.

5 Q. Does Larson state that the threshold for
6 intravitreal formulations is 10 centipoise or less in
7 your opinion?

8 A. No.

9 Q. Do you know what the threshold is for
10 intravitreal formulations with respect to viscosity?

11 A. There isn't an exact threshold.

12 Q. On what are you basing that opinion?

13 A. There's a series of factors. Viscosity's
14 one. The syringe is another. The type of needle is
15 another. So somebody skilled in the art would be
16 aiming for as low a viscosity as possible, knowing that
17 there will be a limit, which is dependent on things
18 like what type of bore needle the clinician wants to
19 use. And the formulation scientist, you know, doesn't
20 necessarily know what sort of bore needle the clinician
21 will require.

22 Q. So the person of ordinary skill in the art
23 would not understand there to be a viscosity threshold
24 for intravitreal formulations, correct?

25 MR. CHEN: Objection to the extent it

1 mischaracterizes prior testimony.

2 A. Sorry. I'll get you to repeat the question.

3 Q. The person of ordinary skill in the art would
4 not understand there to be a viscosity threshold for
5 intravitreal formulations, correct?

6 MR. CHEN: Same objection.

7 A. The person skilled in the art would know
8 there's not a clear-cut threshold because the person
9 skilled in the art doesn't know what bore needle the
10 clinician will require. And so it's -- that threshold
11 will move depending on the bore of the needle. The
12 rule of thumb from the formulation's perspective is
13 keep it low and then, you know, everything is fine. If
14 the viscosity gets too high you might be forced to use
15 a wider bore needle in which the clinician may disagree
16 with.

17 Q. What bore needle is used for intravitreal
18 administration in your opinion?

19 A. Yes. I'm not an expert on needle gauges.

20 Q. Okay. So without an understanding of the
21 gauge of needle that's used in intravitreal
22 administration how can you provide an opinion about
23 what viscosity the POSA would target in formulating a
24 protein for intravitreal administration?

25 MR. CHEN: Objection. Form.

1 A. The information about the needle gauge I'd be
2 sourcing from a clinician such as Dr. D'Amico.

3 Q. Did you --

4 A. Sorry. Can you repeat the question?

5 Q. Without an understanding of the gauge of the
6 needle that's used for intravitreal administration how
7 can you provide an opinion about what viscosity the
8 POSA would target in formulating a protein for
9 intravitreal administration?

10 MR. CHEN: Objection. Form.

11 A. Again I'd argue you want to drive it as low
12 as you go, and I'd be following the guidance from the
13 Larson patent in this which was, you know, ideally
14 below 10 centipoise, but it also mentions, you know,
15 the next level up is 20 centipoise.

16 Q. Well, it mentions a lot of other viscosities
17 as well, right?

18 A. Yes. It does. Yes.

19 Q. Are all those suitable for intravitreal
20 administration in the POSA's view?

21 A. I don't have a view on that.

22 Q. You don't have a view as to which viscosities
23 disclosed in Larson are suitable for intravitreal
24 administration?

25 MR. CHEN: Objection. Form.

1 A. Again I'll restate. The aim is to take it as
2 low as you can, and like Larson points, preferably, you
3 know, 10 centipoise or less.

4 Q. Is under 50 centipoise, five, zero, an
5 acceptable threshold for intravitreal administration in
6 the view -- in the POSA's view?

7 A. You would need to check the force that needs
8 to be applied using a specific syringe and a specific
9 needle and whether that's practical. If the answer is
10 it's not practical, it's too high.

11 Q. Have you checked that in forming your
12 opinions in this case?

13 A. Not in this case, no.

14 Q. So you don't have an opinion as to whether 50
15 centipoise is a suitable threshold for intravitreal
16 administration in the POSA's view?

17 MR. CHEN: Objection. Form.

18 A. The teaching from Larson would suggest that
19 -- what I was saying earlier, that you try to push it
20 lower and that 10 centipoise is the goal is my opinion.
21 Sorry. Could you repeat the question?

22 Q. Yeah. You don't have an opinion as to
23 whether 50 centipoise is a suitable threshold for
24 intravitreal administration in the POSA's view,
25 correct?

1 MR. CHEN: Objection. Form.

2 A. Correct.

3 Q. Would -- does the size of a protein affect
4 its propensity to aggregate?

5 A. It is one of the factors.

6 Q. And is a higher molecular weight protein more
7 prone to aggregation than a lower weight molecular
8 protein?

9 A. It's not directly linked.

10 Q. So you can't say as a general matter that
11 higher molecular weight proteins are generally more
12 prone to aggregation than lower molecular weight
13 proteins?

14 A. There's plenty of examples of lower molecular
15 weight proteins that aggregate.

16 Q. So you can't predict the aggregation of a
17 protein without experimental data, is that right?

18 MR. CHEN: Objection. Form.

19 A. Correct.

20 Q. Okay. But it's critical to know that a
21 protein is stable at a given concentration in order to
22 be able to formulate it for intravitreal
23 administration, right?

24 A. Correct.

25 Q. Okay. Does Vitti teach that aqueous

1 formulations of aflibercept at greater than 100 mgs per
2 ml are stable?

3 MR. CHEN: Objection. Form.

4 A. Yes. Paragraph -- sorry. Wait a second.

5 Q. I can repeat the question if it's helpful.

6 A. In a minute. Yes. I was looking at Vitti in
7 108 where it does discuss stability, but looking at
8 that particular paragraph it's talking about antibody
9 stability.

10 Q. Right. And so Vitti doesn't teach that
11 aqueous formulations of aflibercept at greater than 100
12 mgs per ml are stable, right?

13 A. No. I don't believe it does.

14 Q. And Vitti doesn't teach that aqueous
15 formulations of aflibercept at 114.3 mgs per ml are
16 stable, correct?

17 A. Correct.

18 Q. And Vitti doesn't teach that aqueous
19 pharmaceutical formulations of about 103 to 126 mgs per
20 ml of aflibercept would be stable, correct?

21 A. Correct.

22 Q. Okay. Vitti also doesn't teach the viscosity
23 of aqueous pharmaceutical formulations of aflibercept
24 at greater than 100 mgs per ml, correct?

25 A. Correct.

1 Q. And Vitti doesn't teach the viscosity of
2 aqueous pharmaceutical formulations of 114.3 mgs per ml
3 of aflibercept, correct?

4 A. Correct.

5 Q. And Vitti doesn't teach the viscosity of
6 aqueous pharmaceutical formulations of about 103 to 126
7 mgs per ml of aflibercept, correct?

8 A. Correct.

9 Q. And you agree that if the POSA didn't have an
10 understanding from Vitti that aflibercept formulations
11 would be stable then the POSA wouldn't have a
12 reasonable expectation of its success in achieving
13 formulations of aflibercept that would be suitable for
14 intravitreal administration, right?

15 MR. CHEN: Objection. Form.

16 A. Could you repeat the question?

17 Q. Because the POSA doesn't have an
18 understanding from Vitti that aflibercept would be
19 stable, the POSA wouldn't have a reasonable expectation
20 of success in achieving formulations of aflibercept
21 that would be suitable for intravitreal administration,
22 correct?

23 MR. CHEN: Objection. Form.

24 A. Correct.

25 Q. Vitti contains no stability data for

1 aflibercept at all, correct?

2 A. Yes.

3 Q. Withdraw that question.

4 A. Okay.

5 Q. Vitti contains no stability data for
6 aflibercept at 100 mgs per ml or above, correct?

7 A. Correct.

8 Q. Now, the '036 patent contains data showing
9 that aflibercept formulations at 100 mgs per ml or
10 above are stable, correct?

11 A. Can I have a copy of the patent?

12 Q. We'll get there. We don't need to address
13 that now if you don't recall. You don't recall off the
14 top of your head?

15 A. Not off the top of my head.

16 Q. Okay. Can you turn to paragraph 245 of your
17 declaration? Are you there?

18 A. Yes. Sorry. Thought it was 145.

19 Q. Let me know when you're at paragraph two,
20 four, five of your declaration.

21 A. I'm there. Yes.

22 Q. This -- your opinions here are part of your
23 opinions of -- for ground two, correct, which start on
24 page 78?

25 A. Mm-hmm.

1 Q. Sorry. I'll just need a yes or no rather
2 than a mm-hmm.

3 A. Correct.

4 Q. And you're providing here in paragraph 245 an
5 opinion as part of ground two that Vitti teaches stable
6 liquid pharmaceutical formulations containing up to 100
7 plus or minus 15 mgs per ml of VEGF antagonist, right?

8 A. Correct.

9 Q. And that opinion is part of your opinion in
10 support of ground two?

11 A. Correct.

12 Q. So you're relying on Vitti's disclosure as
13 part of your ground two opinion, correct?

14 MR. CHEN: Objection. Form.

15 A. Ground two also contains Dix, Furfine, and
16 Fiedler.

17 Q. Understood. I'm just asking if you're also
18 relying on Vitti for purposes of your ground two
19 opinion.

20 A. Oh, partly. Yes, yes.

21 Q. Okay. Now, your ground two is also based
22 on -- in part on the Furfine document, correct?

23 A. Correct.

24 Q. Okay. You stated in paragraph 191 of your
25 declaration that Furfine teaches stable aflibercept

1 formulations containing at least 100 mgs per ml of
2 aflibercept, correct?

3 A. That's what it says here, yes.

4 Q. Furfine doesn't teach over 100 mgs per ml of
5 aflibercept, right?

6 A. It says 1 to 100.

7 Q. So this statement's not accurate insofar as
8 it's suggesting that Furfine teaches greater than 100
9 mgs per ml of aflibercept, right?

10 MR. CHEN: Objection. Form.

11 A. Yes. Furfine in isolation does not teach
12 over 100.

13 Q. Okay. So do you retract this statement in
14 your declaration regarding Furfine?

15 MR. CHEN: Objection. Form.

16 A. Yes. I think preferred wording would be up
17 to.

18 Q. Okay. Okay. And does Furfine contain any
19 data for any aflibercept formulations at or above 100
20 mgs per ml?

21 A. Can I have a copy of Furfine?

22 Q. Yeah. All right. I'm handing you what's
23 been previously marked as Exhibit 1005. That's the
24 Furfine patent, right?

25 A. Yes.

1 (Whereupon, Exhibit 1005, previously marked,
2 was proffered to the witness.)

3 Q. Okay. I'll repeat the question. Does
4 Furfine contain any data for any aflibercept
5 formulations at or above 100 mgs per ml?

6 A. I'll get you to repeat the question.

7 Q. Furfine does not contain any data for any
8 aflibercept formulation at or above 100 mgs per ml of
9 aflibercept, correct?

10 A. Correct.

11 Q. And Furfine does not contain any stability
12 data for any aflibercept formulation at or above 100
13 mgs per ml of aflibercept, correct?

14 A. Correct.

15 Q. And Furfine does not contain any viscosity
16 data for any aflibercept formulation at or above 100
17 mgs per ml of aflibercept, correct?

18 A. Correct.

19 Q. Furfine contains no disclosure to the POSA
20 about any formulation with an aflibercept concentration
21 of 100 mgs per ml or above, correct?

22 MR. CHEN: Objection. Form.

23 A. Could you repeat the question?

24 Q. Furfine contains no disclosure to the POSA of
25 any formulation with an aflibercept concentration of

1 100 mgs per ml or above, correct?

2 MR. CHEN: Objection. Form.

3 A. If you look at section -- column two, is it
4 four to nine.

5 Q. Yes.

6 A. It discusses formulation there in broad
7 terms.

8 Q. And that disclosure does not contain any data
9 regarding an aflibercept formulation at 100 mgs per ml
10 or above, correct?

11 A. Correct.

12 Q. And the POSA wouldn't view it as a disclosure
13 regarding any properties regarding an aflibercept
14 formulation at 100 mgs per ml or above, correct?

15 MR. CHEN: Objection. Form.

16 A. Could you define your use of the word
17 properties or rephrase it?

18 Q. I'll ask a different question. The POSA
19 wouldn't view the passage in Furfine at column two,
20 line 4 through 9, as a disclosure regarding the
21 viscosity of a 100-mg-per-ml formulation of
22 aflibercept, correct?

23 A. Correct.

24 MR. CHEN: Objection. Form.

25 Q. You also provided opinions as part of ground

1 two based on the Dix patent, is that right?

2 A. That's correct.

3 Q. Dix is not a patent about intravitreal
4 administration, right?

5 A. Do you have a copy of Dix?

6 Q. Yeah.

7 A. Yeah.

8 Q. So I'm handing you what's been marked
9 previously as Exhibit 1006.

10 A. Thank you.

11 (Whereupon, Exhibit 1006, previously marked,
12 was proffered to the witness.)

13 Q. This is the Dix patent, right?

14 A. Yes.

15 Q. Dix is not a patent about intravitreal
16 administration, correct?

17 A. If you give me a minute. Yes. Dix is --
18 sorry. Repeat the question.

19 Q. Dix is not a patent about intravitreal
20 administration, correct?

21 A. Correct.

22 Q. Dix is -- refers to subcutaneous and
23 intravenous administration, correct?

24 A. Correct.

25 Q. Dix doesn't provide any viscosity data,

1 right?

2 A. Correct.

3 Q. Dix doesn't contain any disclosure to the
4 POSA of an injection volume, correct?

5 A. Correct.

6 Q. And Dix doesn't contain any disclosure to the
7 POSA about the dose of aflibercept, correct?

8 A. Correct.

9 Q. And Dix doesn't contain any disclosure to the
10 POSA of a formulation of greater than 100 mgs per ml of
11 aflibercept, correct?

12 A. Correct.

13 Q. You agree that whether a formulation is
14 stable doesn't inform the POSA anything about whether
15 the formulation is viscous or not, correct?

16 A. Correct.

17 Q. A formulation -- a protein formulation can be
18 stable and viscous or stable and not viscous, correct?

19 A. Correct.

20 Q. The two aren't related to one another?

21 A. Not directly.

22 Q. In other words, a disclosure to the POSA that
23 formulation is stable doesn't tell the POSA anything
24 about whether the formulation will have any given
25 viscosity, correct?

1 MR. CHEN: Objection. Form.

2 A. Could you repeat the question?

3 Q. Sure. I'll ask it a little more
4 specifically. A disclosure to the POSA that an
5 aflibercept formulation is stable doesn't inform the
6 POSA that that formulation will or will not be viscous,
7 correct?

8 A. Correct.

9 Q. You can put that aside. I'm handing you now
10 what's previously been marked as Exhibit 1011. This is
11 the Fiedler patent application.

12 (Whereupon, Exhibit 1011, previously marked,
13 was proffered to the witness.)

14 Q. Do you see that?

15 A. Yes.

16 Q. You rely on Fiedler for your ground two
17 opinions as well?

18 A. Yes.

19 Q. Does Fiedler disclose the viscosity of any
20 aflibercept formulations?

21 A. I'll get you to repeat the question.

22 Q. Does Fiedler disclose the viscosity of any
23 aflibercept formulations?

24 A. No.

25 Q. Fiedler doesn't teach the POSA anything about

1 the viscosity of an aflibercept formulation at any
2 particular concentration, right?

3 MR. CHEN: Objection. Form.

4 A. Correct.

5 Q. I'm handing you what's been previously marked
6 as Exhibit 1010.

7 (Whereupon, Exhibit 1010, previously marked,
8 was proffered to the witness.)

9 Q. This is the Larson patent application that
10 you referred to earlier, correct, Doctor?

11 A. Correct.

12 Q. Now, every claim in the '036 patent contains
13 a viscosity limitation, right?

14 A. I can't remember that level of detail.

15 Q. Okay. Some of the claims at least in the
16 '036 patent contain viscosity limitations?

17 A. Can I have a copy of the patent?

18 Q. Sure.

19 A. Sorry. I'll just be thorough.

20 Q. No problem. I'm handing you what's been
21 marked as -- previously as Exhibit 1001.

22 (Whereupon, Exhibit 1001, previously marked,
23 was proffered to the witness.)

24 Q. This is the '036 patent, correct?

25 A. Correct.

1 Q. Okay. Do you agree that the challenged
2 claims of the '036 patent include viscosity
3 requirements?

4 A. There are claims which specify viscosity.
5 Correct.

6 Q. Do you know if all the claims require
7 viscosity?

8 A. My reading of this patent is that they all go
9 back to claim one, which does specify viscosity.
10 Sorry. Would you like to repeat the question?

11 Q. Do you agree that the challenged claims of
12 the '036 patent all include viscosity requirements?

13 A. That's correct.

14 Q. And you agree that viscosity was a notorious
15 technical challenge associated with high concentration
16 formulations to the POSA?

17 MR. CHEN: Objection. Form.

18 A. I'd probably challenge the word challenge.
19 It's -- could you rephrase that?

20 Q. Well, let me just ask and you tell me if you
21 agree or disagree. Do you agree that viscosity was a
22 notorious technical challenge associated with high
23 concentration formulations to the POSA?

24 MR. CHEN: Objection. Form.

25 A. Well, I disagree.

1 Q. I'm handing you what's been marked Exhibit
2 1045.

3 (Whereupon, Exhibit 1045, previously marked,
4 was proffered to the witness.)

5 Q. Are you familiar with this paper, Doctor?

6 A. I've seen this before, yes.

7 Q. You cited this paper in your declaration,
8 right?

9 A. Yes.

10 Q. This is the Wang 2021 paper?

11 A. Yes.

12 Q. If you turn to page 269. One second. Okay.
13 Are you on page 269 of Wang?

14 A. I am.

15 Q. Do you see in the right-hand column about
16 halfway down it says, two notorious technical
17 challenges associated with high concentration
18 formulation are high viscosity and aggregation?

19 A. I do.

20 Q. Is that a correct statement?

21 A. I'd agree with as far as it's -- they are
22 challenge -- well, they are technical attributes that
23 you need to meet. I think calling it a notorious
24 technical challenge is probably exaggeration.

25 Q. This paper that you cited in support of your

1 declaration contains an exaggeration in your opinion?

2 MR. CHEN: Objection. Form.

3 A. I wouldn't necessarily agree with the wording
4 in this case.

5 Q. And that's because you believe, Doctor, that
6 the viscosity limitations in the '036 patent would have
7 been obvious to the POSA, right?

8 MR. CHEN: Objection. Form.

9 A. Yes.

10 Q. And that's -- strike that.

11 Your obviousness opinion regarding the
12 viscosity limitations is based on the notion that the
13 POSA was aware of several strategies for achieving
14 suitable viscosities, right?

15 A. Sorry. Could you -- I'll get you to re-ask
16 it.

17 Q. Your obviousness opinions regarding the
18 viscosity limitations in the '036 patent are based on
19 the notion that the POSA was aware of several
20 strategies for achieving suitable viscosities, correct?

21 A. Correct.

22 Q. And in your opinion the formulation
23 strategies known and available to the POSA for reducing
24 viscosity included adding amino acids?

25 A. Correct.

1 Q. They included adding salts?

2 A. Correct.

3 Q. They included minimizing the use of sugars or
4 sugar alcohols?

5 A. Correct.

6 Q. They included adjusting the pH?

7 A. Correct.

8 Q. They included adding viscosity, lowering
9 water-soluble dyes?

10 A. Correct.

11 Q. And they included emulsification?

12 A. Correct.

13 Q. And those were strategies and techniques for
14 optimizing the viscosity of high-concentration protein
15 formulations that in your view were well known to the
16 POSA, correct?

17 A. I'll probably -- well, there's not a correct
18 or incorrect answer to that. It's a nuanced answer.
19 The amino acids were well known. The salts were well
20 known. The reduction in sugar was published and should
21 have been well known. The water-soluble dyes is what
22 you'd call an interesting excipient. It's in Larson.
23 I hadn't seen that before, so that isn't so well known.
24 And the emulsification, I think I've only seen that in
25 one document, so I wouldn't say that's a normal

1 approach to reducing viscosity.

2 Q. Okay. And when you say the strategies of
3 using amino acids, using salts, minimizing sugars, and
4 adjusting pH were well known, you mean they were well
5 known to the POSA, right?

6 A. Yes.

7 Q. Okay. Were those extensively described in
8 the prior art?

9 MR. CHEN: Objection. Form.

10 A. Those strategies are in multiple references
11 of which there's a sample in the -- that had been
12 provided in the document, in the declaration.

13 Q. Okay. And as of 2018 -- strike that.

14 It's your opinion that as of 2018 optimizing
15 the viscosity of a protein formulation was a
16 well-established technique, correct?

17 A. Correct.

18 Q. And it's also your opinion that as of 2018
19 high viscosity -- strike that.

20 It's your opinion that as of 2018 high
21 concentration protein formulations with suitable
22 viscosities were well known to the POSA?

23 A. Correct.

24 Q. And the POSA reading the '036 patent would
25 have understood that the viscosity of high

1 concentration aflibercept formulations could be
2 optimized using these known viscosity-reducing
3 strategies, correct?

4 A. Correct.

5 Q. And the POSA reading the '036 patent also
6 would have understood that known viscosity-reducing
7 strategies could be employed with high concentration
8 aflibercept formulations to achieve viscosities of
9 between 5 and 15 centipoise?

10 A. Incorrect.

11 Q. The POSA reading the '036 patent would have
12 understood that known viscosity-reducing strategies
13 could be employed with high concentration aflibercept
14 formulations, right?

15 A. Correct.

16 Q. And that those strategies could be used to
17 obtain viscosities suitable for intravitreal
18 administration?

19 MR. CHEN: Objection. Form.

20 A. This is one where there's certainty and a
21 high degree of confidence, and so a straight yes-no
22 answer -- from the prior art we've discussed you'd be
23 confident you can get there but not absolutely
24 guaranteed. There's always a little bit of doubt.

25 Q. So the POSA reading the '036 patent would

1 have been confident that known viscosity-reducing
2 strategies could be employed with high concentration
3 aflibercept formulations to achieve viscosities of 5 to
4 15 centipoise?

5 A. I'll get you to repeat the question.

6 Q. Sure. The POSA reading the '036 patent would
7 have been confident that known viscosity-reducing
8 strategies could be employed with high concentration
9 aflibercept formulations to achieve viscosities of 5 to
10 15 centipoise?

11 A. Yes.

12 Q. Now, of the strategies that you provided in
13 your declaration for reducing viscosity, the ones that
14 we just enumerated, would the POSA view that list as
15 being incomplete in any way?

16 MR. CHEN: Objection. Form.

17 A. Yes.

18 Q. What strategies are missing from that list
19 from the POSA's perspective?

20 A. The sorts of variables that are not covered
21 by that list that the POSA would be interested in is
22 all of those, for instance the surfactant. The
23 evidence of -- with the sugars, the evidence I've seen
24 was just restricted to sucrose. You can of course swap
25 out sucrose with a sugar alcohol and that might be

1 beneficial. So there are other strategies that are not
2 necessarily listed here.

3 Q. Okay.

4 A. There are different types of salts that may
5 or may not be used, so there are other strategies you
6 could employ.

7 Q. What do you mean by the term high
8 concentration aflibercept formulation?

9 A. Could you be more precise?

10 Q. Yeah. Is there an understanding in the field
11 of the term high concentration in connection with a
12 protein formulation?

13 A. The general understanding to my best
14 knowledge is that sort of 100 mgs per ml would be where
15 people started to find it a high concentration, but 100
16 milligrams, you know, it's 100. You know, it's a nice,
17 round number.

18 MR. CHEN: Counsel, before you ask your next
19 question, we've been going on for a little bit over an
20 hour now. Can we go on a break once you finish this
21 line?

22 MR. TRASK: That's fine. Doctor, would you
23 like to take a break now or in a few minutes?

24 THE WITNESS: How many questions do you want
25 for this session?

1 MR. TRASK: We can stop now. That's fine.

2 THE WITNESS: Okay.

3 MR. TRASK: Yeah.

4 THE VIDEOGRAPHER: We're going off the record
5 at 11:07 a.m.

6 (Whereupon, a recess was taken.)

7 THE VIDEOGRAPHER: And we're back on the
8 record at 11:22 a.m.

9 BY MR. TRASK:

10 Q. Doctor, did you discuss your testimony at all
11 with counsel during the break?

12 A. No.

13 Q. We were talking about the strategies known to
14 the POSA for reducing viscosity. Do you recall that?

15 A. Yeah.

16 Q. And this is in connection with your opinion
17 that the viscosity limitation of the '036 patent would
18 have been obvious to the POSA, correct?

19 A. Yes.

20 Q. Now, one of the viscosity-reducing strategies
21 that you said would be well known to the POSA would be
22 using salts, correct?

23 A. Correct.

24 Q. What are salts?

25 A. Combinations of usually a metal and a halide

1 or a metal and something like a phosphate or an
2 sulfate. The most common salt of course is sodium
3 chloride, sodium being the metal, chloride being the
4 halide.

5 Q. What are kind of the structural features that
6 are common to the category of salts that you just
7 described?

8 A. One of them --

9 MR. CHEN: Objection. Form.

10 THE WITNESS: Sorry.

11 A. Yes. One has a positive charge and one has a
12 negative charge.

13 Q. You said sodium chloride is a salt known to
14 the POSA to reduce viscosity?

15 A. Yes.

16 Q. Sodium phosphate is a salt known to the POSA
17 to reduce viscosity?

18 A. I don't know whether sodium phosphate
19 would -- it's one of the options that you could play
20 around with.

21 Q. Okay. Salts can also be buffers, right?

22 A. Yes.

23 Q. Like sodium phosphate?

24 A. Like sodium phosphate.

25 Q. Another strategy that you said was well known

1 to the POSA for reducing viscosity in high
2 concentration protein formulations was using amino
3 acids, right?

4 A. Correct.

5 Q. What's an amino acid?

6 A. It's an organic molecule. It's the subunit
7 that's used for making up proteins. There's -- 20 of
8 them go into proteins. They have an amine and a
9 carboxyl group and then a side chain which varies, and
10 each of those 20 has a different side chain, the
11 exception being proline which is a different structure.

12 Q. Okay.

13 A. Stands alone.

14 Q. So I think you may have answered this
15 question at least in part already, but what are the
16 common structural features of the category of amino
17 acids that you just described?

18 MR. CHEN: Objection. Form.

19 A. Could you rephrase that?

20 Q. Yeah. I'll just repeat.

21 A. Yeah.

22 Q. What are the common structural features of
23 the category of amino acids that you just described?

24 MR. CHEN: Objection. Form.

25 A. They have an amine, carbon, carboxyl group,

1 and that's what polymerizes to make the protein.

2 Q. Okay. And what are examples of amino acids
3 that can be used to reduce viscosity as known by the
4 POSA?

5 A. The most obvious example is arginine. The --
6 lysine has been used. Histidine has been used. There
7 are other amino acids, but I'm not aware of them being
8 used in the literature, but they might be.

9 Q. Okay. But at least arginine, lysine, and
10 histidine fell within the category of amino acids that
11 the POSA would have understood could be used to reduce
12 viscosity in high concentration protein formulations?

13 A. They're the three choice options, yes.

14 Q. Now, amino acids can be buffers, correct?

15 A. Yes.

16 Q. And histidine is a buffer, right?

17 A. Yes.

18 Q. Now, do you agree that without experimental
19 data the POSA can't be certain whether any given known
20 viscosity-reducing strategy will work to reduce
21 viscosity with a specific protein at a specific
22 concentration?

23 MR. CHEN: Objection. Form.

24 A. Repeat the question, please.

25 Q. Sure. You agree that without experimental

1 data the POSA can't be certain whether any given known
2 viscosity-reducing strategy will work to reduce
3 viscosity with a specific protein at a specific
4 concentration?

5 A. Correct.

6 MR. CHEN: Same objection.

7 Q. But experimental data helps guide the POSA in
8 understanding which viscosity-reducing strategies can
9 be used to achieve optimum viscosities in high
10 concentration protein formulations, right?

11 A. Yes.

12 Q. Are you familiar with partial factorial
13 experimental design?

14 A. Yes.

15 Q. What is that?

16 A. It's a statistical approach where you can
17 determine whether specific factors that you're -- such
18 as amino acid presence, concentration, different
19 combinations of different excipients, whether they're
20 having a significant effect on whatever you're
21 measuring or not. So it's a way of screening different
22 excipients to see if they're having a significant
23 effect on a particular outcome.

24 Q. Is it also a strategy for helping understand
25 which excipients may help to reduce viscosity without

1 having to test every possible permutation of those
2 excipients?

3 A. Yes.

4 Q. And how does it work to allow the POSA to
5 kind of extrapolate from one excipient that's been
6 tested to other excipients that haven't been tested?

7 MR. CHEN: Objection. Form.

8 A. It doesn't extrapolate out to different
9 excipients. It tells you whether the excipient that
10 you've screened using the experimental approach has a
11 significant effect or not, so it's --

12 Q. And from that type of data the POSA can take
13 experimental results from one excipient falling within
14 a particular viscosity-reducing strategy and get some
15 degree of assurance that other excipients within that
16 viscosity-reducing strategy may likewise work to reduce
17 viscosity, is that right?

18 MR. CHEN: Objection. Form.

19 A. The way you've worded it is not correct.

20 Q. Okay. How would you word it?

21 A. The outcome -- the learning you get from sort
22 of the actual factorial experimental approach, its
23 beauty is you can screen a lot of different excipients
24 and work out which ones have an effect and which ones
25 don't. It can also detect interactions. So let's say

1 high pH, histidine might react. But what it doesn't
2 tell you, it doesn't tell you anything about the
3 excipients you didn't screen. It just tells you about
4 the ones you tested. So if I was screening and I used
5 sucrose, I would be guessing if I said that would also
6 be the same for maltose or trehalose which are closely
7 related. I might make the assumption, but the data I'm
8 getting doesn't tell me that.

9 Q. Okay. But -- I think that makes sense, but
10 I'm trying to understand -- I understood this technique
11 as you described it before as one that would allow you
12 to avoid having to screen every possible permutation,
13 is that right?

14 A. It stops you from having to test every
15 permutation.

16 Q. Okay. And is that because -- oh, go ahead.

17 A. But it's a screen. You can get evidence
18 which will suggest that a particular combination might
19 be better, but then you do the full factorial to show,
20 you know, where you want to be.

21 Q. Okay.

22 A. So it's the first step of, you know,
23 effectively two steps to get to your final formulation.

24 Q. Okay. So once a POSA has an understanding
25 that certain examples within a given viscosity-reducing

1 strategy will actually work to reduce the viscosity of
2 a high concentration protein, can the POSA leverage
3 that knowledge to draw any inferences about any other
4 members of that viscosity-reducing strategy?

5 A. You're talking about assumptions. If your
6 viscosity-reducing strategy was sodium chloride is a
7 salt, extrapolating that to calcium chloride would be
8 reckless. The -- but then again if you looked at
9 arginine and you said, okay, histidine has a high
10 probability of having a similar effect, that would have
11 a logic behind it.

12 Q. Okay. Histidine and arginine do have similar
13 effects in -- frequently when you try these types of
14 viscosity-reducing experiments?

15 MR. CHEN: Objection. Form.

16 A. The references that I provide would give
17 you -- I was trying to think if there's a comparable
18 histidine parallel with arginine, but I don't recall
19 whether there's one where it was side by side. But
20 they have similar -- well, they're similar types of
21 amino acids, but they also have differences.

22 Q. Right.

23 A. So you can say they're both positively
24 charged, but if you change the pH, histidine can change
25 its charge but arginine stays charged. So it's one of

1 these answers where there's a yes and a no and you
2 could argue both ways.

3 Q. Okay. But if you have data showing for
4 example that histidine serves to reduce viscosity with
5 a given protein at a given concentration, you may be
6 able to predict that arginine could do the same?

7 MR. CHEN: Objection. Form.

8 A. You would be optimistic without being
9 certain.

10 Q. By you, you mean the POSA, right?

11 A. Yeah.

12 Q. Okay. So the -- if you had data showing that
13 histidine reduced viscosity for a particular protein at
14 a particular concentration the POSA would be optimistic
15 that arginine could also serve to reduce the viscosity
16 of that protein at that concentration?

17 MR. CHEN: Objection. Form.

18 A. Yes. I think the correct word is optimistic.

19 Q. And those are both positively charged amino
20 acids, arginine and histidine at a given pH?

21 A. At a given pH, yes.

22 Q. Both have side chains with a low charge
23 density group at the end?

24 A. When they're charged, yes.

25 Q. And that's guanidinium for arginine and

1 imidazole for histidine?

2 A. That's correct.

3 Q. Okay. And those amino acids are predictable
4 in terms of reducing viscosity, generally speaking?

5 A. They're certainly in the palette of
6 excipients that you would test if you want to reduce
7 viscosity, yes.

8 Q. Okay. And more than just testing them, if
9 you knew that one would reduce viscosity, you'd be
10 optimistic that the other could as well, right?

11 A. It certainly increases the likelihood of you
12 including it in your palette. If one didn't work, the
13 other might work. So it's nuanced. It's not a
14 clear-cut answer.

15 Q. Okay. Okay. Would it be fair to say that
16 the guanidyl group of arginine functions analogously to
17 the imidazole group of histidine, allowing both to
18 screen electrostatic and hydrophobic interactions?

19 MR. CHEN: Objection. Form.

20 A. They're structurally different. They both
21 can carry a positive charge, and they're both
22 reasonably low charge density. So they have their
23 similarities while being structurally different.

24 Q. They have different structures but they
25 function analogously?

1 MR. CHEN: Objection. Form.

2 Q. With respect to --

3 A. Yes.

4 Q. With respect to viscosity reduction?

5 A. Yeah. On the whole, yes.

6 Q. Now, when developing formulations some
7 proteins can be more predictable than others. Do you
8 agree with that?

9 MR. CHEN: Objection. Form.

10 A. Yes.

11 Q. And designer proteins like fusion proteins
12 can represent a challenge as there are a broad
13 population of protein structures and functionalities?

14 MR. CHEN: Objection. Form.

15 A. At the early stage of development, you're
16 correct.

17 Q. Whereas monoclonal antibodies by comparison
18 as a class can be more predictable?

19 A. Yes. As a class they're more predictable.
20 There's always exceptions that prove the rule. Yeah.

21 Q. Aflibercept is an example of one of those
22 designer proteins?

23 A. It's a designer protein. Yes.

24 Q. And when you develop formulations with fusion
25 proteins it's important to have data showing which

1 types of viscosity-reducing strategies work with that
2 protein?

3 MR. CHEN: Objection. Form.

4 A. Yes.

5 Q. But your opinion is that the viscosity
6 limitations for aflibercept in the '036 patent are
7 obvious even though there's no data in the prior art
8 about the viscosity of aflibercept formulations, right?

9 A. Sorry. Could you repeat the question?

10 Q. Your opinion is that the viscosity
11 limitations for aflibercept formulations in the '036
12 patent are obvious even though there's no data in the
13 prior art about the viscosity of aflibercept
14 formulations, correct?

15 A. Okay. I'll get you to repeat the question
16 again.

17 Q. Your opinion is that the viscosity claim
18 limitations for aflibercept in the '036 patent are
19 obvious even though there's no data in the prior art
20 about the viscosity of aflibercept formulations,
21 correct?

22 A. Apologies. It's the structure of the
23 question that's throwing me. I'll get you to repeat it
24 again, I'm afraid.

25 Q. Your opinion is that the viscosity claim

1 limitations for aflibercept in the '036 patent are
2 obvious even though there's no data in the prior art
3 about the viscosity of aflibercept formulations?

4 A. Yes.

5 Q. And why is that?

6 A. It's because we -- sort of the understanding
7 is that that is the viscosity range that you want for a
8 product that is likely to be going through a narrow
9 bore needle and the restriction on the force that, you
10 know, a human hand can apply to that. So we know that
11 there's a desire to get down to a low viscosity, and as
12 Larson points out, you know, what you're aiming at is
13 that 10 centipoise law. That's where you -- as a
14 formulator you'd like to be.

15 Q. And the POSA would understand that they could
16 achieve that particular viscosity with aflibercept
17 formulations?

18 A. Yes.

19 Q. Without any data at all? Any viscosity data,
20 I apologize.

21 A. The Dix patent, the Furfine, the Fiedler, and
22 the Vittti all sort of combine to give you confidence
23 that the 100 milligram per milliliter product was what
24 you'd call fit for purpose. In other words, you know,
25 it could be used for the applications that those

1 patents mention.

2 Q. Does that hold true for aflibercept
3 formulations of 114.3 mgs per ml?

4 A. If you take the understanding that the 100
5 milligrams per ml from Dix and Furfine is correct, then
6 you think, okay, 15 percent on top of that is not a big
7 shift. Then if you go back to the Vitti where it talks
8 about 100 milligrams plus or minus 15, you think the
9 authors of the Vitti patent didn't see that 15 percent
10 difference as being, you know, outrageous, that it
11 fitted within their comfort zone, that they're willing
12 to say, okay, it's 100 mgs per ml plus or minus 15,
13 which means they were on the face of it confident that
14 115 milligrams per ml was a viable concentration to aim
15 at.

16 Q. Okay. And Vitti also discloses 150 plus or
17 minus 22.5 mgs per ml, right? We looked at that
18 earlier.

19 A. Yes. Yes, it does. Yes.

20 Q. And in your view that's a disclosure of
21 suitable viscosity set formulations up to 172.5 mgs per
22 ml of aflibercept?

23 MR. CHEN: Objection. Misstates testimony.

24 A. From the formulations scientist perspective,
25 a jump from 100 to 115 is relatively small and you

1 would have a reasonably high confidence that you can go
2 from that -- you could increase the concentration that
3 far. Going up to say 150 to 160, they would be well
4 aware that the probability of meeting an acceptable
5 viscosity goes down because it's an exponential
6 relationship between concentration of a protein and the
7 viscosity.

8 Q. Viscosity increases exponentially with the
9 concentration of the proteins, correct?

10 A. That's correct.

11 Q. And so what is your basis for saying that a
12 jump from 100 to 115 mgs per ml of aflibercept is a
13 relatively small increase from the standpoint of
14 viscosity?

15 A. If you look at the data for the different
16 monoclonal antibodies which is in the literature, it's
17 apparent that there's this, you know, definite curve
18 which is an exponential curve. So if you make a small
19 change, the jump in viscosity is not going to be
20 particularly large, but if you make a large jump in
21 concentration you know that you're going to -- you're
22 likely to run into -- the probability of running into
23 difficulties with the viscosity goes up.

24 Q. Well, doesn't that depend where you are in
25 the curve?

1 A. Oh, sure. If you're going say from 135 to
2 160, that might be a small move in the curve, and you'd
3 get a similar sort of proportional increase in
4 viscosity.

5 Q. It's not proportional. It's exponential,
6 right?

7 A. Yes, but I mean, if you're confident that
8 you've -- a point in the curve and you're only making a
9 small change, it's a relatively small change in the
10 viscosity.

11 Q. I guess what I don't understand is -- did you
12 finish?

13 A. Yes.

14 Q. Sorry. What I don't understand is how you
15 have any confidence at all about where you are in the
16 curve for aflibercept viscosity relative to
17 concentration. There is no such curve in the prior
18 art, right?

19 A. There isn't a curve for aflibercept.

20 Q. POSA wouldn't be aware of a concentration
21 viscosity curve for aflibercept in the prior art,
22 right?

23 A. Not that I know of.

24 Q. So the POSA had -- would have no idea where
25 they are on that curve for aflibercept based on

1 information in the prior art, right?

2 A. Yes.

3 Q. So in that case, how can you say that a jump
4 of 15 mgs per ml is relatively small when you don't
5 know where on that curve you're making that jump?

6 A. It's because it's a jump of 15 percent.
7 Exponential works -- what's the best way of putting
8 this in English? Yes. It's -- yeah. The way
9 exponential curves work -- and this is just
10 mathematics -- is if you sort of extend the axis one
11 way and then the other way, basically the shape is
12 similar. And, you know, the proportion change, if you,
13 say, do a 15 percent increase in concentration you
14 would expect that same proportion change in the
15 viscosity. Now, that's where the math works.

16 Q. Well, let me ask this.

17 A. Yeah.

18 Q. Portions of an exponential curve are -- some
19 portions of an exponential curve are steeper than
20 others, correct?

21 A. Correct.

22 Q. And without knowing where you are in the
23 exponential curve the POSA has no way of knowing
24 whether a 15 percent increase will result in a
25 relatively small increase in viscosity or a relatively

1 large increase in viscosity, right?

2 A. My understanding is the proportional change
3 is the same. So let's say you're at 100 milligrams per
4 ml and it's sitting at 10, and you get a 15. You
5 increase the concentration by 15 percent, and you get a
6 20 percent increase in viscosity. Doing a similar
7 change down the curve, you get the same proportional
8 change, but I'm not a mathematician so don't cite me on
9 that one.

10 Q. Right.

11 A. That's my understanding.

12 Q. Well, a 20 percent increase of a high
13 viscosity is a very high viscosity, right?

14 A. Yes.

15 Q. So without knowing where you are in the curve
16 you don't know whether the 15 percent increase is going
17 to put you in an area of the curve that has acceptable
18 viscosity or not for aflibercept, correct?

19 A. I guess the understanding that the viscosity
20 is acceptable at 100 milligrams per ml comes from the
21 combination of the different patents.

22 Q. But you're talking about the prior art
23 patents?

24 A. Yes.

25 Q. There's no viscosity data in any of those

1 prior art patents that you've cited, correct?

2 A. Well, they did talk about the route of
3 administration. It was Furfine --

4 Q. You already testified that there's no
5 viscosity data in Furfine.

6 A. Oh, there's no -- it doesn't give you
7 viscosity in centipoise. That's correct.

8 Q. I think your opinion that these viscosity
9 values are obvious is based on the fact that you have
10 these different strategies that you could employ with a
11 reasonable expectation of success to reduce viscosity,
12 correct?

13 A. Incorrect. That's only partially correct.
14 Because you know you've got a palette of different
15 excipients you can bring to play to reduce viscosity,
16 if you find yourself getting -- creeping higher than
17 your preferred value, then that's partially set due to
18 the choice of the gauge needle, that you can then
19 employ that palette of excipients to help you bring
20 back the viscosity down to an acceptable level.

21 Q. So once the POSA has data showing that an
22 example within a given viscosity-reducing strategy can
23 work to achieve a suitable viscosity, then the POSA has
24 some confidence that they could employ other members of
25 that category to similarly achieve suitable viscosities

1 for intravitreal formulations?

2 MR. CHEN: Objection. Form. Incomplete
3 hypothetical.

4 A. I'll get you to repeat that one.

5 Q. Once the POSA has data showing that an
6 example within a given viscosity-reducing strategy can
7 work to achieve a suitable viscosity for a particular
8 protein at a particular concentration, then the POSA
9 will have some confidence that they could employ other
10 members of that category to similarly achieve suitable
11 viscosities for intravitreal formulations?

12 MR. CHEN: Same objections.

13 A. It's a yes-or-no answer. The answer yes is
14 that it could well work, but because they're working on
15 similar principles on histidine and arginine, you know
16 that there's the possibility that they're both doing
17 the same thing and you're better off employing a
18 strategy like adjusting the pH. That is, you know, a
19 different strategy. So it's not a straight yes-no
20 answer, I'm afraid.

21 Q. Do you agree that a formulation viscosity
22 that's suitable for intravenous injection may not be
23 suitable for subcutaneous injection?

24 MR. CHEN: Objection. Form.

25 A. Could you repeat that.

1 Q. Do you agree that a formulation viscosity
2 that's suitable for intravenous injection may not be
3 suitable for subcutaneous injection?

4 A. Agreed.

5 MR. CHEN: Objection. Form.

6 Q. Do you agree that a formulation viscosity
7 that's suitable for subcutaneous injection may not be
8 suitable for intravitreal injection?

9 MR. CHEN: Objection. Form.

10 A. Okay. Could you repeat that one? Sorry.

11 Q. Do you agree that a formulation viscosity
12 that's suitable for subcutaneous injection may not be
13 suitable for intravitreal injection?

14 MR. CHEN: Objection. Form.

15 A. Again that's a yes-no answer. They're --
16 both subcutaneous and intravitreal are both constrained
17 by the desire to use narrow bore needles in both cases,
18 so there's commonalities between those two methods of
19 administration which is quite different to intravenous
20 where you don't have those constraints.

21 Q. Do you know if subcutaneous formulations are
22 administered with the same gauge needle as
23 intravenous -- excuse me. Do you know if subcutaneous
24 formulations are administered with the same gauge
25 needle as intravitreal formulations?

1 A. I'm not a clinician, so I would answer that
2 I'm the wrong person to answer that question to be
3 honest.

4 Q. Okay. So if you don't know the gauge of the
5 needle that's used as between subcutaneous and
6 intravitreal, and the gauge of the needle is critical
7 for understanding what's a suitable viscosity --

8 A. Yes.

9 Q. -- you don't know whether a formulation
10 that's suitable for subcutaneous administration will be
11 suitable for intravitreal administration, is that fair?

12 MR. CHEN: Objection. Form. Misstates
13 testimony.

14 A. Okay. I'll get you to repeat that.

15 Q. If you don't know the gauge of the needle
16 that's used --

17 A. Yes.

18 Q. -- for subcutaneous and intravitreal
19 administrations, and the gauge of the needle is
20 critical for understanding the suitable viscosity for
21 the particular application, then you can't know whether
22 a formulation that's suitable for subcutaneous
23 administration will necessarily be suitable for
24 intravitreal administration, correct?

25 MR. CHEN: Objection. Form. Misstates

1 testimony.

2 A. That is correct, but this is why you have a
3 clinician as part of the team so you can answer those
4 questions directly.

5 Q. So you rely on Dr. D'Amico to understand what
6 the viscosity for -- you rely on Dr. D'Amico's opinion
7 for the specific question of what viscosity would be
8 suitable for administration through a needle used for
9 intravitreal administration?

10 MR. CHEN: Objection. Form.

11 A. Yes. Once you know that -- what the needle
12 is you can work out what is an acceptable viscosity.

13 Q. And Dr. D'Amico presumably knows what gauge
14 needle is used for intravitreal administration?

15 MR. CHEN: Objection. Form.

16 A. I should hope so.

17 Q. And so you'd rely on his opinion with respect
18 to the suitable viscosity for an intravitreal
19 administration through the particular needle used for
20 intravitreal administration, right?

21 MR. CHEN: Objection. Form.

22 A. Well, once you know the -- once you know the
23 bore of the needle there are mathematical ways of
24 working out what the viscosity should be, and then it's
25 pointed out in I think it's Fiedler, the patent, there

1 are experimental ways of testing it too.

2 Q. Okay. But --

3 A. So the missing part of the equation as far as
4 the formulation person is concerned is once you know
5 the gauge of the needle, you know the internal
6 diameter, that's the critical piece of information you
7 need to -- now, that -- the strategy that's used might
8 be different. You know, it could be maths, it could be
9 experimental, or it could be relying on previous
10 experience.

11 Q. But you're relying on Dr. D'Amico for doing
12 that math based on the gauge of the needle that's used
13 for intravitreal administration, right?

14 MR. CHEN: Objection. Form.

15 A. I personally don't know if Dr. D'Amico would
16 go from a gauge to a natural viscosity. I would assume
17 that the formulation scientist would answer that
18 question whether it's experimentally, whether it's
19 mathematically, or whether it's from prior experience.

20 Q. Okay. But you haven't done that calculation
21 yourself, right?

22 A. I have in the past.

23 Q. But for this case you haven't done the
24 calculation of what a suitable viscosity for
25 intravitreal administration would be based on the gauge

1 of the needle that's used for intravitreal
2 administration?

3 A. I did look at it in the Excel spreadsheet.
4 The maths is relatively simple. It's well within, you
5 know, capabilities of somebody such as myself.

6 Q. I didn't see that opinion in your
7 declaration. You didn't provide that opinion in this
8 case, correct?

9 A. Correct.

10 Q. Okay. What Excel spreadsheet are you
11 referring to?

12 A. Oh, the -- there is a formula which doesn't
13 spring off -- I don't recall what it's called. But
14 like all mathematical formulas, it's a useful guide to
15 what we're -- you know, what may or may not work. But
16 the approach taken I think it's in Fiedler is a lot
17 safer because it's an experimental approach.

18 Q. You don't have an opinion apart from the
19 numbers that you identified in Larson as to what a
20 suitable viscosity is for an intravitreally
21 administered formulation, correct?

22 A. Correct.

23 Q. And those values that you identified in
24 Larson are not disclosed together with a discussion of
25 intravitreal administration, correct?

1 MR. CHEN: Objection. Form.

2 A. Or let me see. Could you remind me of the
3 question?

4 Q. Sure. Let me do it this way. Do you have
5 Larson in front of you? This is Exhibit --

6 A. I do. Yes.

7 Q. -- 1010. Now, one of the passages you relied
8 on in Larson for the suitable viscosity -- and in fact,
9 you know, keep Larson open but look at paragraph 94 of
10 your declaration which talks about Larson. Of your
11 declaration, 94. Are you there?

12 A. Yep.

13 Q. Okay. You see at the very end of that
14 paragraph which is at the -- on the next page, it's
15 citing these viscosities you've been talking about in
16 Larson, 20 centipoise, 10 centipoise, right? You see
17 that?

18 A. Yes.

19 Q. And as support for those values you're citing
20 Larson at paragraph 75 and 77, right?

21 A. Correct.

22 Q. Okay. Now if you could turn to Larson at
23 paragraph 75 to 77, are you there?

24 A. Yes.

25 Q. Okay. This discussion falls under the

1 headline formulations on page -- well, it's page 9 at
2 the bottom of Larson, right?

3 A. Yep.

4 Q. And the discussion of formulations starts off
5 in the very first sentence talking about formulations,
6 quote, useful for subcutaneous, SC, and intramuscular,
7 IM, injections, end quote. Do you see that? I'm on
8 paragraph 74, of 74.

9 A. 74?

10 Q. Yeah. Paragraph 74 in Larson, the first
11 sentence refers to subcutaneous, SC, and intramuscular,
12 IM, injections. Do you see that?

13 A. Yes.

14 Q. Okay. And this discussion continues and
15 talks about preferable viscosities for such
16 formulations, and you cite some values in paragraph 75
17 and 77, correct?

18 A. Correct.

19 Q. And paragraph 75 repeats its reference to
20 subcutaneous and intramuscular injections about -- one,
21 two, three, four, five, six -- eight lines up from the
22 bottom of paragraph 75. It refers to SC or IM
23 injection. Do you see that?

24 A. Yes.

25 Q. There's no reference here in connection with

1 these viscosities of intravitreal injections, correct?

2 A. Correct.

3 Q. So these are not disclosures of viscosities
4 that are suitable for intravitreal injection in Larson,
5 correct?

6 MR. CHEN: Objection. Form.

7 A. Again, that depends on the choice of needle.

8 Q. But you don't know the gauge needle that's
9 used for intravitreal administration, do you, Doctor?

10 A. Yes, but I know they're both narrow bore.

11 Q. Are they the same or are they different,
12 subcutaneous and intravitreal, in your expert opinion
13 sitting here today?

14 A. My expert opinion is that I'd confirm this
15 with Dr. D'Amico.

16 Q. You did confirm it with Dr. D'Amico?

17 A. No. That's where I would ask the question.

18 Q. You'd ask him?

19 A. Yes.

20 Q. When you had the conversation with him did
21 you ask him that question?

22 A. I don't specifically recall asking that
23 question.

24 Q. Okay. So sitting here today you don't know
25 whether the gauge needle used for subcutaneous

1 injection and the gauge needle used for intravitreal
2 injection are the same or different, right?

3 A. My understanding is that subcutaneous is a
4 family of different injections, and the move has been
5 towards using as narrow bore needles as possible to
6 reduce pain on injection, so different motives to
7 intravitreal. And the move towards narrow bore needle
8 with intravitreal is to minimize damage to the cornea.
9 So different motives, but both of them are pushing
10 towards the range of narrow bore needles. Now, exactly
11 where they locate and how much they overlap you'd have
12 to ask Dr. D'Amico. But from a formulation point of
13 view we know that, you know, the pressure is to make
14 sure that the viscosity is compatible with those -- the
15 needle that the clinician requires.

16 Q. How do you know --

17 A. So --

18 Q. Finish your answer.

19 A. I'll let you ask the question again.

20 Q. Sitting here today you don't know whether the
21 gauge needle used for subcutaneous injection and the
22 gauge needle used for intravitreal injection are the
23 same or different, correct?

24 MR. CHEN: Objection. Form.

25 A. Again, my understanding is that the

1 population of needles they use overlap. So there's a
2 high probability that they're using the same or similar
3 bore needles.

4 Q. And on what is that opinion based, Doctor?

5 A. Background knowledge.

6 Q. What is the gauge needle that you're
7 referring to that overlaps between subcutaneous and
8 intravitreal?

9 A. Okay. From my understanding it is a narrow
10 bore needle. I don't person -- I don't know the number
11 of that gauge, but I know it's a narrow bore needle.

12 Q. You don't know what viscosity range is
13 suitable for intravitreal administration sitting here
14 today, correct?

15 MR. CHEN: Objection. Form.

16 A. I know from the learning of Larson that I'd
17 be aiming for as low a viscosity as I can because that
18 gives you the option of using narrow bore needles.

19 Q. Doctor, what about the passage in Larson that
20 we just looked at or anything else in Larson teaches
21 you the suitable viscosity range for intravitreal
22 administration?

23 MR. CHEN: Objection. Form. Asked and
24 answered.

25 A. From the formulation perspective there's

1 nothing particularly magical about intravitreal. It's
2 the bore of the needle that's the key, parameter that
3 you're interested in.

4 Q. And what is the bore of the needle that's
5 used for intravitreal injection, Doctor?

6 A. I can't give you a number for that straight
7 off. No.

8 Q. So without that information you can't tell me
9 what is the viscosity that's suitable for intravitreal
10 administration, correct?

11 MR. CHEN: Objection. Form.

12 A. Correct.

13 Q. Okay. And you agree that the disclosures
14 that -- strike that.

15 Now, your declaration refers to a trend
16 toward high concentration protein formulations,
17 correct?

18 A. Correct.

19 Q. Okay. What was the big driver of that trend
20 in the industry up to 2018?

21 A. Two major motives. One was to bring
22 injection volume down, and the other one was to
23 obviously increase the dose.

24 Q. Now, some of the references you cited discuss
25 the desire to move away from intravenous administration

1 and towards subcutaneous administration for patient
2 convenience, correct?

3 A. Could you cite -- show me where that's --

4 Q. Yeah. Do you have that Wang 2021 paper in
5 front of you? I think I marked that as an exhibit. I
6 did. It's Exhibit 1045. Yeah. So if you look at -- I
7 think this is -- well, let's start with your
8 declaration on paragraph 43 which I think makes that
9 point pretty clearly. Are you there?

10 A. Yes.

11 Q. So this paragraph in your declaration says,
12 as the need for protein-based therapeutics has grown
13 high concentration protein formulations have become
14 increasingly important in the pharmaceutical industry,
15 correct?

16 A. Correct.

17 Q. And you cite an exhibit here, Exhibit 1032,
18 and you quote in part saying, efforts are currently
19 being made to convert the existing low concentration IV
20 mAb products for high concentration SC products. Do
21 you see that?

22 A. Yes.

23 Q. So you agree that the driver behind moving
24 from lower to higher protein concentration was driven
25 by the desire to transition from intravenous to

1 subcutaneous formulations, right?

2 MR. CHEN: Objection. Form.

3 A. It's one of the drivers, yes.

4 Q. Okay. And then further in that paragraph you
5 say, over the last three decades -- I'm not quoting
6 exactly here -- the FDA has approved more and more high
7 concentration protein formulations with at least 100
8 mgs per ml protein concentration. Do you see that?

9 A. Yes.

10 Q. With a significant increase starting in 2015.
11 Do you see that?

12 A. Yes.

13 Q. And you cite a graph here from that Wang 2021
14 paper, correct?

15 A. Correct.

16 Q. Do you know how many of these high
17 concentration formulations shown in the graph,
18 reproduced in paragraph 43 of your report, from the
19 start of the graph all the way up through 2018 were
20 intravitreal formulations?

21 A. No. I don't know the answer to that.

22 Q. Okay. But you rely on this trend towards
23 higher protein concentration as one of the factors that
24 would motivate the POSA to develop a higher
25 concentration formulation of aflibercept for

1 intravitreal administration, correct?

2 MR. CHEN: Objection. Form.

3 A. Incorrect.

4 Q. Let's turn to paragraph 246 of your
5 declaration. See, you say, a skilled formulator would
6 have been aware of the trend in the industry towards
7 higher concentration therapeutic protein formulations
8 and --

9 A. Sorry. Could you repeat which paragraph?

10 Q. Oh, sorry. 246 in your declaration.

11 A. 246.

12 Q. Yeah. Are you there?

13 A. Yes.

14 Q. This paragraph states, furthermore, a skilled
15 formulator would have been aware of the trend in the
16 industry towards higher concentration therapeutic
17 protein formulations and the numerous successfully
18 developed high concentration therapeutic protein
19 formulations already FDA approved and commercially
20 available at the time, citing Wang 2021, right?

21 A. Correct.

22 Q. And then you say, accordingly, in paragraph
23 247, given the small increase -- the relatively small
24 increase in concentration, blah, blah, blah, a skilled
25 formulator would have reasonably expected to succeed in

1 obtaining an aqueous pharmaceutical formulation with
2 114 mgs per ml as claimed, right?

3 A. Correct.

4 Q. So you're relying on this trend in Wang
5 towards higher concentration protein formulations as
6 part of your justification for why the POSA would have
7 expected to succeed in obtaining high concentration
8 aflibercept formulations, right?

9 MR. CHEN: Objection. Form.

10 A. Could you repeat the question?

11 Q. Your opinions in this case as shown by
12 paragraph 246 and 247 of your declaration show that you
13 are relying on this supposed trend in the industry
14 towards higher concentration therapeutic protein
15 formulations such -- as exhibited by Wang in support of
16 the notion that the POSA would have a reasonable
17 expectation of success in obtaining an aqueous
18 pharmaceutical formulation with a high concentration of
19 aflibercept, right?

20 A. Correct.

21 MR. CHEN: Objection. Form.

22 THE WITNESS: Sorry.

23 A. Correct.

24 Q. But you don't know how many of these high
25 concentration therapeutic protein formulations shown in

1 Wang were intravitreal formulations, correct?

2 A. My understanding is most of them would have
3 been subcutaneous.

4 Q. Are all of them subcutaneous? Let me ask the
5 question more precisely.

6 A. Okay. Yes.

7 Q. Of the formulations discussed in Wang from
8 2018 and earlier, how many of those formulations with
9 high concentration proteins are intravitreal
10 formulations? Do you know?

11 A. I don't know the answer to that, no.

12 Q. Do you think that is a relevant piece of
13 information to know before concluding based upon this
14 exhibit that the POSA would have a reasonable
15 expectation of success?

16 MR. CHEN: Objection. Form. Argumentative.

17 A. Can I have a minute?

18 Q. Can you answer the question? Or do you need
19 time to answer the question?

20 A. I need -- just -- well, I started this, so
21 I'm just going to have a quick look through it.

22 Q. Okay. I understand you're going to look
23 through Wang, and that's fine. But let me just ask
24 you, before opening Wang you don't know how many
25 formulations in Wang up to 2018 were known to the POSA

1 with an intravitreal administration route, correct?

2 A. What I'm trying to do is I can't recall when
3 the other intravitreals were introduced on to the
4 market. Yeah. It's just knowledge I haven't -- it
5 would be easy enough to find out.

6 Q. Right. But you didn't do that analysis in
7 preparing your opinions in this case, correct?

8 MR. CHEN: Objection. Form.

9 A. Yes. I don't recall that being part of the
10 analysis.

11 Q. Okay. Do you know whether a high
12 concentration protein formulation for intravitreal
13 administration have ever been prepared from -- in 2018
14 or earlier?

15 MR. CHEN: Objection. Form.

16 A. I don't recall the dates when those
17 intravitreal products were brought on the market.

18 Q. Okay. That's not --

19 A. That's -- sorry. Repeat the question.

20 Q. Well, based on the answer you just gave I
21 think I understand that in forming your opinions you
22 did not seek to determine whether the POSA was aware of
23 any previous high concentration protein formulations
24 for intravitreal administration, correct?

25 MR. CHEN: Objection. Form. Misstates

1 testimony.

2 A. Yeah. Correct.

3 Q. Do you want to take a look at Wang?

4 A. I'd first like -- just -- yes. Could we just
5 have a minute?

6 Q. Of course.

7 A. Thank you.

8 Q. Do you want to take a break?

9 A. Can I read this while I'm taking a break?

10 Q. Of course.

11 A. Okay. Yeah.

12 THE VIDEOGRAPHER: Going off the record --

13 THE WITNESS: Yeah. You can start lunch now
14 and I'll join you in a minute.

15 MR. TRASK: That's fine. Whatever you want
16 to do. Does that work for you?

17 MR. CHEN: Yeah.

18 MR. TRASK: Okay. Why don't we take a lunch
19 break then? Does that work?

20 THE WITNESS: Yeah. Yes.

21 THE VIDEOGRAPHER: Going off the record at
22 12:23 p.m.

23 (Whereupon, a recess was taken.)

24 THE VIDEOGRAPHER: We're back on the record
25 at 1:18 p.m.

1 BY MR. TRASK:

2 Q. Doctor, during the lunch break did you
3 discuss your testimony at all with counsel?

4 A. No.

5 Q. Did you discuss your declaration?

6 A. No.

7 Q. Did you discuss any of the references cited
8 in your declaration with counsel during the break?

9 A. No.

10 Q. Okay. When we left off I think we were
11 talking about the Wang reference. Do you still have
12 that in front of you, Exhibit 1045?

13 A. Yes.

14 Q. I just want to see if you agree with me.
15 Turn to the bottom of the second page under the heading
16 administration route analysis. Do you see where I am?

17 A. Yes.

18 Q. Do you see that it refers to different types
19 of administration routes in that paragraph?

20 A. Yes.

21 Q. And intravitreal injection is abbreviated
22 IVI?

23 A. Correct.

24 Q. Intravenous is IV, intramuscular IM, and
25 subcutaneous SC. Do you see that?

1 A. Yes.

2 Q. Okay. So then let's look at the table one in
3 Wang which is on the next page, the third page. Do you
4 see there's a couple in this table for administration
5 route? It's the next to last column on the right?

6 A. Yes.

7 Q. I'd like you to look through this table which
8 spans several pages and let me know how many
9 intravitreal high concentration formulations are
10 included in this table.

11 A. There's the two.

12 Q. The first one is SUSVIMO, ranibizumab,
13 correct? It's the first entry in the table.

14 A. Correct.

15 Q. And that was approved in 2021, correct?

16 A. Correct.

17 Q. And the other one is Beovu which was approved
18 in 2019, correct?

19 A. Correct.

20 Q. So you agree with me that the POSA wasn't
21 aware of any high concentration formulations suitable
22 for intravitreal administration as of 2018, correct?

23 MR. CHEN: Objection. Form.

24 A. I'd agree there was no high concentration
25 intravitreal products that had been approved at that

1 date, yes.

2 Q. And therefore you agree that the POSA was
3 aware of no such formulations, correct?

4 MR. CHEN: Objection. Form.

5 A. Correct.

6 Q. And so the trend that the POSA was aware of
7 that you referenced in your declaration of making --
8 moving towards high concentration protein formulations
9 was not a trend that the POSA associated with
10 intravitreal formulations as of 2018, correct?

11 MR. CHEN: Objection. Form.

12 A. Correct.

13 MR. TRASK: Kat, I'm going to need some
14 copies that don't have highlighting on them.

15 Q. Okay. Do you have Larson in front of you?
16 This is Exhibit 1010.

17 A. Yes.

18 Q. Yes. Now, Larson is a patent publication
19 about the viscosity-reducing strategy of using
20 water-soluble organic dyes, correct?

21 A. Correct.

22 Q. And you see in the abstract on the first page
23 there are administration routes mentioned in Larson?

24 A. Correct.

25 Q. What are the administration routes that

1 Larson teaches that their strategy is applicable to?

2 MR. CHEN: Objection. Form.

3 A. It mentions administered by subcutaneous or
4 intramuscular injection rather than by lengthy
5 intravenous infusion.

6 Q. So Larson is directed to the administration
7 routes of subcutaneous and intramuscular injection, is
8 that right?

9 MR. CHEN: Objection. Form.

10 A. According to the abstract that's the
11 impression you get, yes.

12 Q. Okay. And you've read the paper as a whole,
13 correct?

14 A. Yes.

15 Q. And that's also the impression -- you get the
16 impression from the paper as a whole that Larson is
17 directed to subcutaneous and intramuscular injection?

18 MR. CHEN: Objection. Form.

19 A. Could you repeat my question -- your question
20 again?

21 Q. Sure. Larson is generally directed to
22 achieving viscosity suitable for subcutaneous and
23 intramuscular injection, correct?

24 MR. CHEN: Objection. Form.

25 A. Could you repeat the question?

1 Q. Sure. Larson is generally directed to
2 achieving viscosity suitable for subcutaneous and
3 intramuscular injection, correct?

4 MR. CHEN: Objection. Form.

5 A. Correct.

6 Q. How many working examples are there in the
7 Larson patent? Do you know?

8 MR. CHEN: Objection. Form.

9 Q. Okay. Have you looked for working examples
10 in the Larson patent prior to the question I just asked
11 you?

12 A. Yes. I know what I'm looking for, but I just
13 haven't got to it yet.

14 Q. I'll tell you what. Why don't you turn to
15 page 25 at the bottom of Larson?

16 A. Page 25?

17 Q. Yeah. At the bottom.

18 A. Okay.

19 Q. You there?

20 A. Yes.

21 Q. You see this is a section called examples?

22 A. Yes.

23 Q. And you see there's one working example in
24 Larson, right, example one?

25 A. Yes.

1 Q. There are a number of aqueous solutions of
2 therapeutic monoclonal antibodies described in this
3 example and presented in the table in paragraph 258,
4 correct?

5 A. Correct.

6 Q. In your opinion are any of the working
7 examples in Larson suitable for intravitreal
8 administration?

9 MR. CHEN: Objection. Form.

10 A. To the best of my knowledge these are all --
11 none of these are intravitreal.

12 Q. Why do you say that?

13 A. With the exception of two of them. Yes. I'm
14 relying on memory.

15 Q. Sorry. Your testimony is that two of the
16 aqueous solutions --

17 A. Sorry. Carry on.

18 Q. Okay. Sorry. I interrupted you. I was
19 trying to understand your last answer. Is your
20 testimony that two of the aqueous solutions of
21 therapeutic antibodies described in Larson's working
22 example are suitable for intravitreal administration?

23 A. No. That was not my answer.

24 Q. Okay. What is your answer?

25 A. That to the best of my knowledge none of

1 these are intravitreal.

2 Q. So none of the working examples in the Larson
3 publication disclose formulations suitable for
4 intravitreal administration, correct?

5 A. Incorrect.

6 Q. How is that statement incorrect?

7 A. The formulations that he used were
8 subcutaneous, designed to meet a lot of the factors --
9 well, the factors that are also used to design an
10 intravitreal formulation.

11 Q. Which of the formulations in the working
12 example is suitable for intravitreal administration in
13 your expert opinion?

14 A. In the table in 258 the viscosity value is
15 given there, a rule on the high side for use in an
16 intravitreal formulation.

17 Q. I don't know if I'm understanding. I asked
18 you --

19 A. Sorry. Could you repeat the question?

20 Q. I said, none of the working examples in the
21 Larson publication disclose formulations suitable for
22 intravitreal administration, correct? And you answered
23 incorrect. So I'm assuming from that answer that there
24 is at least one formulation disclosed in a working
25 example of Larson is suitable for intravitreal

1 administration. Is that right or wrong?

2 A. Could you repeat the question?

3 Q. I'll just ask it again.

4 A. Yes.

5 Q. Is there a formulation disclosed in Larson
6 that is suitable for intravitreal administration?

7 MR. CHEN: Objection. Form.

8 A. The examples in the table in 258, the answer
9 is no.

10 Q. So Larson -- strike that.

11 A. Yes.

12 Q. Am I correct in saying that Larson does not
13 disclose any formulations suitable for intravitreal
14 administration?

15 MR. CHEN: Objection. Form. And to the
16 extent it mischaracterizes prior testimony.

17 A. Correct.

18 Q. I'm handing you what's previously been marked
19 as Exhibit 1028.

20 (Whereupon, Exhibit 1028, previously marked,
21 was proffered to the witness.)

22 Q. This is the Inoue publication if I'm
23 pronouncing that correctly from 2013, is that right?

24 A. 2014. It was received in 2013.

25 Q. It says available online 20 November, 2013.

1 Do you see that right above the abstract?

2 A. Yes.

3 Q. Okay. You're familiar with this paper,
4 correct?

5 A. I've read it, yes.

6 Q. The first paragraph of the paper under the
7 abstract says that therapeutic proteins account for an
8 increasingly large portion of pharmaceutical drugs in
9 recent years, correct?

10 A. Correct.

11 Q. The POSA would agree with that?

12 A. (No audible response given.)

13 Q. It says, these proteins are normally
14 administered via subcutaneous injection. The POSA
15 would agree with that?

16 A. Sorry. Which line are we looking at?

17 Q. The second line of the paper.

18 A. Correct.

19 Q. POSA would agree with that?

20 A. Yes.

21 Q. Do you see further down in that same
22 paragraph it says -- actually the last sentence of that
23 paragraph says, maintaining a solution viscosity below
24 50 centipoise is a primary goal when developing high
25 concentration formulations of therapeutic proteins?

1 A. Correct.

2 Q. Would the POSA agree with that?

3 A. Yes. That's what's written there. Yes.

4 Q. The POSA would understand that the threshold
5 for viscosity for a subcutaneous formulation is 50
6 centipoise, correct?

7 A. Correct.

8 Q. Okay. Okay. You can put that aside. Okay.
9 I'm handing you what I'm marking now as Exhibit 2038.

10 (Whereupon, Exhibit 2038, Alvotech's Petition
11 For Post-Grant Review, was marked for identification.)

12 Q. Do you know what this document is, Doctor?

13 A. I haven't read it before, no.

14 Q. You understand it to be Alvotech's petition
15 for post-grant review in this proceeding?

16 A. Correct.

17 Q. You haven't seen this before?

18 A. No.

19 Q. Okay. Turn to page 71 of the petition. Are
20 you there?

21 A. Yes.

22 Q. I'm going to read from the very last line on
23 to the next page. It says, on the other end, a POSA
24 would not have been motivated to go above 115 mgs per
25 ml, the upper limit disclosed in Vitti. Do you see

1 that?

2 A. Yes.

3 Q. Do you agree or disagree with that statement?

4 A. I agree with the whole paragraph. Yes.

5 Q. Do you agree that 115 mgs per ml is the upper
6 limit disclosed in Vitti?

7 MR. CHEN: Objection. Form.

8 A. No, because we found a higher one. Well, you
9 found a higher one. Yes.

10 Q. Right. You agree that 115 mgs per ml is not
11 the upper limit disclosed in Vitti, right?

12 MR. CHEN: Objection. Form.

13 A. Could you repeat the question?

14 Q. You agree that 115 mgs per ml is not the
15 upper limit disclosed in Vitti, correct?

16 A. Correct.

17 Q. And so the basis for that conclusion about
18 the POSA's motivation is incorrect in -- on pages 71 to
19 72 of this exhibit, correct?

20 MR. CHEN: Objection. Form.

21 A. Could you repeat the question? Sorry. It's
22 just the wording.

23 Q. The basis for the conclusion about the POSA's
24 motivation on pages 71 to 72 of this exhibit is
25 incorrect, true?

1 MR. CHEN: Objection. Form.

2 A. Could you repeat the question?

3 Q. I will. You agree that the basis for the
4 conclusion on pages 71 to 72 of Exhibit 2038 regarding
5 the POSA's motivation is incorrect?

6 MR. CHEN: Same objection.

7 A. Okay. Could you repeat the question?

8 Q. You agree that the basis for the conclusion
9 on pages 71 to 72 of Exhibit 2038 regarding the POSA's
10 motivation is incorrect?

11 MR. CHEN: Same objection.

12 A. I would say the motivation was correct.

13 Q. The basis for the POSA's motivation as
14 described on pages 71 to 72 in Exhibit 2038 is that the
15 POSA would not have been motivated to go above 115 mgs
16 per ml, the upper limit disclosed in Vitti, correct?

17 MR. CHEN: Objection. Form.

18 A. Could you repeat it? Sorry.

19 Q. The basis for the POSA's motivation as
20 described on pages 71 to 72 of Exhibit 2038 is that the
21 POSA would not have been motivated to go above 115 mgs
22 per ml, the upper limit disclosed in Vitti, correct?

23 MR. CHEN: Same objection.

24 A. Okay. One more time.

25 Q. The basis for the POSA's motivation as

1 described on pages 71 to 72 of Exhibit 2038 is that the
2 POSA would not have been motivated to go above 115 mgs
3 per ml, the upper limit disclosed in Vitti, correct?

4 MR. CHEN: Same objection.

5 A. Incorrect.

6 Q. Does this sentence on -- from paragraph 71 to
7 72 state that the POSA would not have been motivated to
8 go above 115 mgs per ml, the upper limit disclosed in
9 Vitti?

10 A. The skilled formulation scientist wouldn't be
11 taking a single sentence to form the basis of an
12 opinion.

13 Q. Isn't this passage conveying that the POSA
14 would not have been motivated to go above 115 mgs per
15 ml because that is the upper limit disclosed in Vitti?

16 A. Yes. It does say the upper limit disclosed
17 in Vitti is 115.

18 Q. And because it's not true that 115 mgs per ml
19 is the upper limit disclosed in Vitti, the basis for
20 this statement about the POSA's motivation is
21 incorrect, right?

22 MR. CHEN: Objection. Form.

23 A. Correct.

24 Q. Now, if you turn to paragraph 251 of your
25 declaration, are you there?

1 A. Yes.

2 Q. Paragraph 251 says, while it may have been
3 possible to obtain an aflibercept formulation with a
4 protein concentration above 115 mgs per ml, a skilled
5 formulator would have understood that high
6 concentration protein formulations carry a greater risk
7 of failure due to increased risk of aggregation and
8 increased viscosity, correct?

9 A. Apologies. I moved to 151, not 251.

10 Q. Sorry. I meant 251.

11 A. Yes. Carry on.

12 Q. All right. Rather than reading it I'll just
13 explain how I understand this. Does paragraph 251 of
14 your declaration convey that the skilled formulator
15 would not seek to achieve formulations above 115 mgs
16 per ml because they carry a greater risk of failure?

17 A. As you increase the product concentration
18 they carry a greater risk of failure, yes.

19 Q. Okay. And this is a statement about an
20 aflibercept formulation specifically, right?

21 A. Yes.

22 Q. None of the three references you cite in
23 support of this statement have anything to do with
24 aflibercept, right?

25 A. Do you have a copy of Dear? And Neergaard.

1 Q. Without looking at these references, you
2 don't recall whether they address --

3 A. Yes. I think --

4 (Reporter clarification.)

5 Q. Without looking -- thank you. Without
6 looking at these references, you don't recall whether
7 they address aflibercept or not, correct?

8 A. My belief is they follow the monoclonal
9 antibodies and serum albumin, which is not aflibercept.

10 Q. So without looking at these references, you
11 believe these references do not address aflibercept,
12 correct?

13 A. Correct.

14 Q. Here's -- I'm handing you what's marked as
15 Exhibit 1021. This is the Dear reference. And the
16 other reference you asked for is Neergaard which I'm
17 handing you now which has been previously marked as
18 Exhibit 1033.

19 (Whereupon, Exhibit 1021, previously marked,
20 was proffered to the witness.)

21 (Whereupon, Exhibit 1033, previously marked,
22 was proffered to the witness.)

23 Q. With all of these references in front of you
24 now, Doctor, you agree that the references you cite in
25 support of this statement that a skilled formulator

1 would believe that concentrations of greater than 115
2 mgs per ml of aflibercept -- strike that.

3 I'll rephrase the question. You offered an
4 opinion in paragraph 251 that concentrations of
5 aflibercept above 115 mgs per ml carry a greater risk
6 of failure, correct?

7 A. Correct.

8 Q. And you cited three references in support of
9 that statement, correct?

10 A. Correct.

11 Q. None of those three references have anything
12 to do with aflibercept, correct?

13 A. Correct.

14 Q. Do you have any other support beyond the
15 three references cited here for that statement in
16 paragraph 251?

17 A. The relationship between protein
18 concentration and viscosity is something which is a
19 property of proteins as a whole, and these examples of
20 proteins which show the relationship between viscosity
21 and protein concentration, and the understanding is the
22 protein concentration goes up, the viscosity goes up.
23 And aflibercept is a protein. Sorry.

24 Q. You're not saying -- sorry, Doctor. You're
25 not saying that all proteins have a limit of 115 mgs

1 per ml above which they carry a risk of a failed
2 formulation, right?

3 A. No.

4 Q. Okay. What are you citing in support other
5 than these three references which have nothing to do
6 with aflibercept in support of this statement about
7 aflibercept?

8 A. I have no additional support.

9 Q. Now, we covered this previously, but just to
10 restate, you agree that Vitti discloses 150 plus or
11 minus 22.5 mgs per ml of a VEGF antagonist, correct?

12 MR. CHEN: Objection to the extent it
13 mischaracterizes prior testimony.

14 A. Could you cite the -- I know we've said it
15 before, but --

16 Q. For example, in paragraph 87. And I'm in
17 Vitti Exhibit 1007.

18 A. Yes. I can see it.

19 Q. And so the upper range of that concentration
20 in your view is 172.5 mgs per ml, correct?

21 MR. CHEN: Same objection.

22 A. Correct.

23 Q. And your understanding from your conversation
24 with Dr. D'Amico is that it would have been preferable
25 to deliver an 8-milligram dose of aflibercept, right?

1 A. Correct. Was it milligram? Wait a second.

2 Apologies. Yes.

3 Q. And you also understand from Dr. D'Amico that
4 the POSA would have sought to formulate an intravitreal
5 formulation of aflibercept at 50 microliters if
6 possible, correct?

7 A. Correct.

8 Q. So if you take the 8-milligram dose of
9 aflibercept that the -- you understand the POSA would
10 seek to use and you put it into a 50-microliter volume
11 which you understand is the volume that the POSA would
12 seek to use, that results in a concentration of 160 mgs
13 per ml, correct?

14 A. Correct.

15 Q. And that's well below the upper limit
16 disclosed in Vitti of 172.5 mgs per ml, correct?

17 A. Correct.

18 Q. And so the POSA wouldn't have any motivation
19 then to alter the volume of that formulation, correct?

20 MR. CHEN: Objection. Form.

21 A. In light of -- incorrect. Sorry. Repeat the
22 question.

23 Q. The POSA wouldn't have any motivation to --
24 strike that.

25 In light of the upper limit disclosed in

1 Vitti of 172.5 mgs per ml --

2 A. Yes.

3 Q. -- the POSA could have formulated an
4 8-milligram dose of aflibercept in a volume of 50
5 microliters, correct, to achieve a concentration of 160
6 mgs per ml?

7 A. That --

8 MR. CHEN: Objection. Form.

9 A. Correct.

10 Q. And the POSA wouldn't have had any motivation
11 to further alter that -- those formulation parameters,
12 correct?

13 MR. CHEN: Objection. Form.

14 A. I would disagree with that.

15 Q. Why?

16 A. Because the teachings from Furfine and Dix
17 and Fiedler have a comfort zone of 100 milligrams per
18 ml, and a 60 percent increase is a sizable increase in
19 concentration, whereas 15 percent increase is a -- you
20 know, it's not negligible, but it's a much smaller
21 increase in concentration.

22 Q. So you're discounting the disclosure in Vitti
23 of 150 plus or minus 22.5 mgs per ml, is that right?

24 MR. CHEN: Objection. Form.

25 A. Well, the practicing formulation scientist

1 with a knowledge of the relationship between protein
2 concentration and viscosity, a 60 percent increase in
3 concentration will have a serious effect on the
4 viscosity whereas a 15 percent is a much more
5 manageable increase of viscosity. And there's a much
6 higher probability of success.

7 Q. None of the references you just discussed --
8 Vitti, Dix, Furfine, Fiedler -- disclose any data about
9 viscosity, correct?

10 A. Correct.

11 Q. On what are you basing your opinion that an
12 increase of 15 mg per ml would be -- achieve a suitable
13 viscosity but 116 mgs per ml and above would not?

14 A. Yes. If you go to the declaration, paragraph
15 190, 191, the role of the Furfine patent is spelled
16 out.

17 Q. Now, ground one doesn't include Furfine,
18 right?

19 A. This is 191 -- yes. It's ground two.

20 Q. Ground one does not rely upon Furfine,
21 correct?

22 A. Correct.

23 Q. So putting aside ground two for a moment,
24 ground one has no support for the notion that an
25 increase of 115 -- strike that.

1 Ground one in your declaration has no support
2 for the notion that increasing from 100 mgs per ml of
3 aflibercept to 115 mgs per ml of aflibercept would
4 achieve a suitable viscosity for intravitreal
5 administration but increasing to 116 mg per ml of
6 aflibercept and beyond would not achieve a suitable
7 viscosity for intravitreal administration, correct?

8 MR. CHEN: Objection. Form.

9 A. Yes. It does not say that.

10 Q. You don't have support for that point,
11 correct?

12 A. In the declaration, correct.

13 Q. Just to make sure we're on the same page,
14 ground one in your declaration has no support for the
15 notion that the POSA would view 115 mgs per ml of
16 aflibercept as an acceptable viscosity but 116 mgs per
17 ml and above as an unacceptable viscosity, correct?

18 MR. CHEN: Same objection.

19 Q. I'll just ask the question again because I
20 don't know if it was entirely clear.

21 A. Yes.

22 Q. Ground one in your declaration contains no
23 support for the proposition that the POSA would view
24 115 mgs per ml of aflibercept as having an acceptable
25 viscosity for intravitreal administration but 116

1 milligrams per ml of aflibercept and above as having an
2 unacceptable viscosity, correct?

3 MR. CHEN: Same objection.

4 A. Where was the 160 again? Sorry. Which
5 paragraph?

6 Q. I'm not referring to a particular paragraph.

7 A. Yes.

8 Q. I'm just asking a question. I'll restate it.
9 Ground one in your declaration contains no support for
10 the proposition that the POSA would view up to 115 mgs
11 per ml of aflibercept as having an acceptable viscosity
12 for intravitreal administration but 116 mgs per ml of
13 aflibercept and above as having an unacceptable
14 viscosity for intravitreal administration, correct?

15 MR. CHEN: Same objection.

16 A. Correct.

17 THE WITNESS: Sorry.

18 Q. You agree that a volume of 70 microliter for
19 intravitreal injection is disclosed nowhere in the
20 prior art, correct?

21 MR. CHEN: Objection. Form.

22 A. Could you define the prior art?

23 Q. Sure. The -- I'll phrase it a different way.

24 A. Yes.

25 Q. The POSA would have been unaware of any

1 disclosure of a 70-microliter injection volume for
2 intravitreal administration, correct?

3 MR. CHEN: Objection. Form.

4 A. That's correct to the best of my knowledge.
5 Yes.

6 Q. Did Dr. D'Amico tell you that the POSA would
7 select an injection volume of 70 microliters?

8 A. No.

9 Q. Dr. D'Amico's opinion is that 50 microliters
10 is the preferable volume for intravitreal
11 administration, correct?

12 MR. CHEN: Objection. Form.

13 A. Correct.

14 Q. Dr. D'Amico told you that the POSA would seek
15 to administer 8 milligrams of aflibercept as a dose for
16 intravitreal injection, correct?

17 A. Correct.

18 Q. Do you know how Dr. D'Amico arrived at the
19 value of 8 milligrams?

20 A. No.

21 Q. Dr. D'Amico didn't identify any other dose of
22 aflibercept as being one that the POSA would seek to
23 administer intravitreally other than 8 milligrams,
24 correct?

25 MR. CHEN: Objection. Form.

1 A. Correct.

2 MR. TRASK: Is now a good time for a break?

3 MR. CHEN: Yeah.

4 MR. TRASK: Okay. Let me take a short break.

5 THE VIDEOGRAPHER: We are going off the

6 record at 2:21 p.m.

7 (Whereupon, a recess was taken.)

8 THE VIDEOGRAPHER: Back on the record at 2:37

9 p.m.

10 BY MR. TRASK:

11 Q. Okay. Could you turn to your -- back to your
12 declaration, paragraph 35? Are you there?

13 A. Yes.

14 Q. So paragraphs 35 through 37 of your
15 declaration set forth the standard for written
16 description that you followed in forming your written
17 description opinions in this case, correct?

18 A. Correct.

19 Q. Okay. Now, you said in paragraph 35 in part,
20 I understand that the written description analysis
21 focuses on what the four corners of the priority
22 document specification conveys to one of ordinary skill
23 in the art. Do you see that?

24 A. Yes.

25 Q. So your written description analysis in this

1 case was based on the four corners of the '036 patent
2 specification, correct?

3 A. Correct.

4 Q. Okay. Your written description analysis was
5 not based on other documents beyond the '036 patent
6 specification, correct?

7 A. This is some legelese that I don't fully
8 understand. Could you --

9 Q. Well, you rendered opinions in this case on
10 the subject of written description, correct?

11 A. Yes.

12 Q. And specifically ground three in your
13 declaration alleges that the claims of the '036 patent
14 lack written description, right?

15 A. Yes.

16 Q. And you applied a legal standard in
17 determining whether the claims complied with the
18 written description requirement or not, correct?

19 A. Correct.

20 Q. And I'm trying to understand the standard you
21 applied in reaching your conclusions in this case on
22 written description, okay?

23 A. Okay.

24 Q. Your written description analysis in this
25 case was based on the four -- I already asked that one.

1 Sorry.

2 A. Yes.

3 Q. Strike that.

4 Your written description analysis in this
5 case was not based on documents other than the '036
6 patent specification, correct?

7 A. Correct.

8 Q. Your written description analysis didn't
9 consider any information that was well known to the
10 POSA but was not disclosed in the four corners of the
11 '036 patent, correct?

12 MR. CHEN: Objection. Form.

13 A. What was the paragraph with the four corners?

14 Q. Paragraph 35.

15 A. 35.

16 Q. I'll ask the question again.

17 A. Does -- the four corners, are they the four
18 points in 36?

19 Q. I'm --

20 A. Sorry.

21 Q. I'm not here to answer questions. I'm here
22 to ask them, Doctor.

23 A. Okay.

24 Q. Let me ask the question again. Your written
25 description analysis didn't consider any information

1 that was well known to the POSA but was not disclosed
2 within the four corners of the '036 patent, correct?

3 A. Could you define the four corners again?

4 Q. I didn't define four corners.

5 A. Okay.

6 Q. I'm just reading from this phrase in your own
7 declaration.

8 A. Yes.

9 Q. So let me ask the question again and you can
10 tell me -- tell me your answer. Your written
11 description analysis didn't consider any information
12 that was well known to the POSA but was not disclosed
13 within the four corners of the '036 patent, correct?

14 MR. CHEN: Objection. Form.

15 A. I can't answer the question on the basis that
16 my understanding of the four corners is beyond what I
17 know, my understanding.

18 Q. So you don't understand the written
19 description legal standard that you applied in
20 rendering your written description opinions in this
21 case, correct?

22 MR. CHEN: Objection. Form.

23 A. Correct.

24 Q. Now, when you formed your written description
25 opinions in this case you read the full text of the

1 '036 patent and then you determined whether or not the
2 written description standard was met, correct?

3 A. To the best of my ability, yes.

4 Q. Okay. And in doing so you didn't also
5 consider information that was not set forth in the text
6 of the '036 patent including information that was well
7 known to the POSA, correct?

8 MR. CHEN: Objection. Form.

9 Q. I can ask the question again, Doctor, if that
10 would be helpful.

11 A. Just give me one minute. Yes. Could you
12 repeat your question?

13 Q. Yes. When you formed your written
14 description opinions in this case you read the full
15 text of the '036 patent but you didn't also consider
16 information that was not set forth in the '036 patent
17 including information that was well known to the POSA,
18 correct?

19 A. Correct.

20 Q. Now, if a class of structures is known to the
21 POSA does a patent need to provide an exhaustive
22 description of that class in order to satisfy written
23 description?

24 MR. CHEN: Objection. Form.

25 A. Can you repeat the question?

1 Q. If a class of structures is known to the
2 POSA --

3 A. Yes.

4 Q. -- does the patent need to provide an
5 exhaustive description of that class in order to
6 satisfy written description?

7 MR. CHEN: Same objection.

8 A. I don't know the answer to that question.

9 Q. Did you consider -- strike that.

10 In reaching your conclusions on written
11 description about the '036 patent did you consider
12 whether a known class of structures needs to be
13 exhaustively described in the specification of the '036
14 patent?

15 MR. CHEN: Objection. Form. Calls for a
16 legal conclusion.

17 A. Okay. I'll get you to repeat the question,
18 I'm afraid.

19 Q. In reaching your conclusions on written
20 description about the '036 patent did you consider
21 whether a known class of structures needs to be
22 exhaustively described in the specification of the '036
23 patent?

24 A. I believe the answer is no.

25 Q. If something is well known in the art to the

1 POSA does the patent need to describe it in order to
2 satisfy written description?

3 MR. CHEN: Objection. Form. Calls for legal
4 conclusion.

5 A. I don't know the answer to that.

6 Q. In reaching your conclusions on written
7 description about the '036 patent did you consider
8 whether something well known in the art needed to be
9 described expressly in the '036 patent in order to
10 satisfy written description?

11 MR. CHEN: Same objection.

12 A. Could you repeat the question?

13 Q. In reaching your conclusions on written
14 description about the '036 patent did you consider
15 whether something well known in the art needed to be
16 described expressly in the '036 patent in order to
17 satisfy written description?

18 MR. CHEN: Same objections.

19 A. I don't know the answer to that question.

20 Q. Well, I'm asking whether you considered that
21 or not.

22 A. Okay.

23 Q. So I think you probably do know the answer to
24 this question.

25 A. Okay. Yes.

1 Q. In reaching your conclusions on written
2 description about the '036 patent did you consider
3 whether something well known in the art needed to be
4 described expressly in the '036 patent in order to
5 satisfy written description?

6 MR. CHEN: Same objections.

7 A. My assumption is that it would need to be
8 described, yes.

9 Q. Is that the standard you applied in reaching
10 your written description opinions --

11 A. Yes.

12 Q. -- in this case?

13 A. Yes.

14 Q. Do you agree that a claim with an open-ended
15 upper range may be adequately described for purposes of
16 written description where the upper bound would be
17 limited by what a POSA would understand to be workable?

18 MR. CHEN: Objection. Form. Calls for legal
19 conclusion.

20 A. Could you repeat the question?

21 Q. Yeah. And I'll ask it a little differently.
22 Do you agree that a claim with an open-ended upper end
23 of its range may be adequately described for purposes
24 of written description where the upper bound would be
25 limited by what the POSA would understand to be

1 workable and where the patent specification adequately
2 supports that range?

3 MR. CHEN: Same objections.

4 A. I'm sorry. You're going to have to repeat
5 that question again. It's a long one.

6 Q. I'll ask it a little differently. Hopefully
7 it's a little easier for you to answer.

8 A. Yes.

9 Q. In rendering your opinions on the subject of
10 written description in this case --

11 A. Yes.

12 Q. -- did you consider whether a claim with an
13 open-ended upper range may be adequately described for
14 written description purposes where the upper bound
15 would be limited by what a POSA would understand to be
16 workable and where the patent specification adequately
17 supports that range?

18 MR. CHEN: Same objections.

19 A. Yes. That seems reasonable.

20 Q. Is that something you considered in rendering
21 your opinions in this case?

22 MR. CHEN: Same objections.

23 A. To my understanding the question and answer
24 would be no.

25 Q. So in reaching your written description

1 opinions in this case you did not evaluate whether the
2 open-ended range of at least 100 mgs per ml of
3 aflibercept concentration may be adequately described
4 for purposes of written description if the upper bound
5 would be limited by what a POSA would understand to be
6 workable and where that patent specification adequately
7 supports the range?

8 MR. CHEN: Same objections.

9 A. I'm afraid I'm going to have to get you to
10 repeat it again.

11 Q. In reaching your written description opinions
12 in this case you did not evaluate whether the
13 open-ended range of at least 100 mgs per ml of
14 aflibercept may be adequately described in the '036
15 patent for purposes of written description if the upper
16 bound would be limited by what a POSA would understand
17 to be workable and where that patent specification
18 adequately supports the range?

19 MR. CHEN: Same objections.

20 A. I'm afraid I'm going to have to ask you to
21 repeat it.

22 Q. Okay. And just for context this question is
23 about whether you did or didn't do a particular
24 evaluation as part of your written description
25 analysis, okay?

1 A. Yes.

2 Q. So the question is in reaching your written
3 description opinions in this case is it true that you
4 did not evaluate whether the open-ended range of at
5 least 100 mgs per ml of aflibercept may be adequately
6 described in the '036 patent for purposes of written
7 description if the upper bound would be limited by what
8 a POSA would understand to be workable and where that
9 patent specification adequately supports the range?

10 MR. CHEN: Same objections.

11 A. The best answer I can give at this stage is I
12 don't know.

13 Q. You don't recall sitting here today
14 performing that evaluation, correct?

15 MR. CHEN: Same objections.

16 A. Could you ask the question in more sort of
17 standard English? Because --

18 Q. I think this is standard English. You
19 reached written description opinions in this case,
20 correct?

21 A. Correct.

22 Q. And as part of those opinions you performed
23 certain evaluations of the '036 patent, correct?

24 A. Yes.

25 Q. Was one of those evaluations the question of

1 whether the open-ended range of 100 mgs per ml of
2 aflibercept or higher adequately described in the '036
3 patent for purposes of written description if -- let me
4 restate it because I think I misspoke. Was one of the
5 evaluations that you performed in reaching your written
6 description opinions in this case the evaluation of
7 whether the open-ended range of at least 100 mgs per ml
8 of aflibercept may be adequately described in the '036
9 patent if the upper bound would be limited by what the
10 POSA would understand to be workable and where the
11 specification adequately supports the range?

12 MR. CHEN: Same objections.

13 A. I apologize. Could you repeat the question?

14 Q. Okay. Doctor, you have an understanding of
15 the evaluations you performed in reaching your written
16 description opinions in this case, correct?

17 A. I believe so, yes.

18 Q. Okay. So my question is directed at whether
19 you performed this particular evaluation, okay?

20 A. Okay.

21 Q. In arriving at your written description
22 opinions in this case did you evaluate whether the
23 open-ended range of at least 100 mgs per ml of
24 aflibercept may be adequately described in the '036
25 patent if the upper bound would be limited by what the

1 POSA would understand to be workable and where the
2 specification adequately supports the range?

3 MR. CHEN: Same objections.

4 A. Okay. One more time.

5 Q. In arriving at your written description
6 opinions in this case did you or did you not evaluate
7 whether the open-ended range of at least 100 mgs per ml
8 of aflibercept may be adequately described in the '036
9 patent if the upper bound of that range would be
10 limited by what the POSA would understand to be
11 workable and where the specification adequately
12 supports the range?

13 MR. CHEN: Same objections.

14 A. I'll give the answer as no on the basis that
15 I'm -- the language isn't what I'm used to, so --

16 Q. You don't recall doing the evaluation that I
17 just read to you, correct?

18 MR. CHEN: Same objections.

19 A. Not specifically, no.

20 Q. Okay. Is one of the strategies for reducing
21 viscosity known to the POSA the strategy of adding
22 buffers?

23 MR. CHEN: Objection. Form.

24 A. Yes.

25 Q. You didn't list that in your declaration

1 though, right, Doctor?

2 A. Buffers are mentioned numerous times in the
3 declaration.

4 Q. Right, but your declaration set out a series
5 of strategies well known to the POSA for reducing
6 viscosity. It started with adding amino acids, adding
7 salts, and so on, correct?

8 A. Correct.

9 Q. Your list of strategies known to the POSA for
10 reducing viscosity did not include adding buffers,
11 correct?

12 A. The amino acid histidine is also a buffer,
13 and the salt phosphate is also a buffer.

14 Q. So the strategy of adding buffers is
15 encompassed by the strategies of adding amino acids and
16 adding salts?

17 MR. CHEN: Objection. Form.

18 A. Buffers you could anticipate will have an
19 effect on viscosity, yes. Sorry. The question?

20 Q. The question is the strategy of adding
21 buffers to reduce viscosity is encompassed by the
22 strategies of adding amino acids and adding salts,
23 correct?

24 MR. CHEN: Objection. Form.

25 A. Well, incorrect.

1 Q. Buffers can be amino acids, correct?

2 A. Correct.

3 Q. And buffers can be salts, correct?

4 A. Correct.

5 Q. So the strategy -- the strategies of adding
6 amino acids and adding salts encompass adding buffers,
7 correct?

8 MR. CHEN: Objection. Form.

9 A. Correct.

10 Q. And these are strategies that the inventors
11 of the '036 patent were employing in seeking to reduce
12 the viscosity of high concentration aflibercept
13 formulations, correct?

14 MR. CHEN: Objection. Form.

15 A. Correct.

16 Q. These strategies are well known to the POSA,
17 correct?

18 A. Correct.

19 Q. And the '036 patent inventors provided
20 extensive data on viscosities of particular high
21 concentration aflibercept formulations in the patent,
22 correct?

23 A. Correct.

24 MR. CHEN: Objection. Form.

25 THE WITNESS: Apologies.

1 Q. Now, you agree that the claims of the '036
2 patent cover formulations both with and without an
3 excipient buffer, correct?

4 A. The claims, correct.

5 Q. The claims are silent about the presence or
6 absence of an excipient buffer in the formulation,
7 correct?

8 A. It isn't mentioned in the claims. Correct.

9 Q. They're silent on that point, correct?

10 A. Yes.

11 Q. Now, if the claims were intended to exclude
12 buffers they could say something like, wherein the
13 formulation contains no excipient buffer, right?

14 MR. CHEN: Objection. Form. Incomplete
15 hypothetical. Calls for legal conclusion.

16 A. Could you repeat the question?

17 Q. Sure. If the claims of the '036 patent were
18 intended to exclude excipient buffers they would have
19 said something like, wherein the formulation contains
20 no excipient buffer, correct?

21 MR. CHEN: Same objections.

22 A. Okay. One more time.

23 Q. If the claims of the '036 patent were
24 intended to exclude excipient buffer containing
25 formulations they would have said something like,

1 wherein the formulation contains no excipient buffer,
2 correct?

3 MR. CHEN: Same objections.

4 A. I don't really know the answer to that
5 question.

6 Q. Do you agree that the '036 patent does not
7 claim as its invention formulations without an
8 excipient buffer?

9 MR. CHEN: Objection. Form.

10 A. My reading of the patent is the claims just
11 make no mention of buffer.

12 Q. Right. And so the -- oh, I'm sorry.

13 A. And it's just imprecise on that subject.

14 Q. And you agree that the '036 patent does not
15 claim as its invention formulations without an
16 excipient buffer?

17 A. My reading of it is that's correct.

18 Q. And I think in your written description
19 opinion you concluded that even though the '036 patent
20 does not claim as its invention formulations without an
21 excipient buffer, the '036 patent nevertheless must
22 describe formulations without an excipient buffer to
23 satisfy the written description requirement, right?

24 MR. CHEN: Objection. Mischaracterizes.

25 A. Could you repeat the question?

1 Q. In your written description opinion you
2 concluded that even though the '036 patent does not
3 claim at its invention formulations without an
4 excipient buffer the '036 patent nevertheless must
5 describe formulations without an excipient buffer to
6 satisfy the written description requirement, correct?

7 MR. CHEN: Objection. Mischaracterizes.

8 A. Correct.

9 Q. Now, in your view -- strike that.

10 In your opinion in this case an excipient
11 buffer is essential to the claimed formulations in the
12 '036 patent, correct?

13 A. Correct.

14 Q. And your written description analysis
15 considered whether the '036 patent inventors viewed an
16 excipient buffer as essential to their invention,
17 correct?

18 MR. CHEN: Objection. Form.

19 A. Correct.

20 Q. In deciding that a buffer is an essential
21 element to the claimed invention in the '036 patent,
22 did you analyze the claims that were submitted by the
23 inventors in their originally filed application?

24 MR. CHEN: Objection. Form. Calls for legal
25 conclusion.

1 A. The only version of Graham is the one in
2 front of us that I've seen.

3 Q. Let me ask the question again.

4 A. Yes.

5 Q. In deciding that a buffer is an essential
6 element to the claimed invention in the '036 patent did
7 you analyze the claims that were submitted by the
8 inventors in their originally filed application?

9 A. No.

10 Q. Have you seen those claims before?

11 A. I don't believe so.

12 Q. Do you know whether for purposes of written
13 description the originally filed claims are considered
14 part of the specification of the patent?

15 MR. CHEN: Objection. Calls for legal
16 conclusion.

17 A. I don't know.

18 Q. If the originally filed claims for the
19 application that issued as the '036 patent included
20 claims to a method for treating an angiogenic eye
21 disorder comprising administering an intravitreal
22 injection of a VEGF receptor fusion protein without
23 requiring a buffer would that provide written
24 description support in your opinion?

25 MR. CHEN: Objection. Form. Calls for legal

1 conclusion. Incomplete hypothetical.

2 A. Yes.

3 Q. I'm handing you what's been marked as Exhibit
4 1002. This is a portion of the file history of the
5 '036 patent. You said you had reviewed portions of the
6 file history of the '036 patent, correct?

7 A. I don't recall.

8 (Whereupon, Exhibit 1002, previously marked,
9 was proffered to the witness.)

10 Q. Exhibit 1002 is on your list of materials
11 considered on page 15 of the declaration.

12 A. Sorry. Wrong page number.

13 Q. That's the lower page number.

14 A. Yeah.

15 Q. Confusing, I know.

16 A. You'd think I'd have caught on by now,
17 wouldn't you?

18 Q. Do you see Exhibit 1002 in paragraph 125?

19 A. Yes.

20 Q. You considered Exhibit 1002 in forming your
21 opinions, right?

22 A. No.

23 Q. You didn't?

24 A. No.

25 Q. Okay. It's listed among the materials

1 considered formed as part of rendering your opinions in
2 this declaration?

3 A. To the best of my knowledge I haven't seen
4 that document before.

5 Q. Okay. So Exhibit 1002 is erroneously listed
6 among your list of materials considered in your
7 declaration, correct?

8 A. Correct.

9 Q. Well, I represent to you then that what I've
10 handed you marked Exhibit 1002 is a portion of the full
11 prosecution history of the '036 patent.

12 A. Okay.

13 Q. The full prosecution history is hundreds of
14 pages long and for the sake of the environment I
15 printed just a portion of it, okay?

16 A. Yes.

17 Q. And this is the portion for the record that
18 is at pages 4920 through 4932, okay?

19 A. Okay.

20 MR. TRASK: Counsel, do you have any
21 objection to my use of a portion of this file history
22 as an exhibit in this deposition?

23 MR. CHEN: No objection.

24 Q. I want you to turn to claim 30. It's on the
25 bottom of the page ending in 4931.

1 A. Yes.

2 Q. Do you see that claim 30 is directed to a
3 method for treating an angiogenic eye disorder and a
4 subject in need thereof comprising administering an
5 intraocular injection of more than about 2 milligrams
6 of a VEGF receptor fusion protein to the eye of the
7 subject?

8 A. Yes.

9 Q. Then I want you to turn to claim 31. Are you
10 there?

11 A. Yes.

12 Q. Claim 31 depends from claim 30?

13 A. Yes.

14 Q. And it recites the method of claim 30
15 comprising administering about 4 milligrams, about 6
16 milligrams, about 8 milligrams, or about 10 milligrams
17 of the VEGF receptor fusion protein to the eye of the
18 subject, correct?

19 A. Correct.

20 Q. Claim 43 depends from among others claim 31,
21 right?

22 A. Yes.

23 Q. And claim 34 narrows claim 31 to wherein the
24 intraocular injection is an intravitreal injection,
25 correct?

1 A. Correct.

2 Q. Claim 35 narrows claim 34 among others to
3 particular angiogenic eye disorders, correct?

4 A. Correct.

5 Q. And claim 36 narrows claim 35 among others to
6 wherein the VEGF receptor fusion protein is
7 administered in about 100 microliters or less, about 90
8 microliters, about 80 microliters, about 75
9 microliters, about 70 microliters, about 60
10 microliters, or about 50 microliters, correct?

11 A. Correct.

12 Q. You agree that claims 30 through 36 disclose
13 methods of treating an angiogenic eye disorder by
14 administering a VEGF fusion protein for intravitreal
15 injection with particular doses and particular volumes,
16 correct?

17 A. Correct.

18 Q. None of these claims require a buffer,
19 correct?

20 A. That's correct. The claims don't require a
21 buffer.

22 Q. Turn to paragraph 277 of your declaration,
23 please. Are you there?

24 A. I am, yes.

25 Q. Now, you provide an opinion here that the

1 claims lack written description support because they do
2 not require a buffer which the specification makes
3 clear is required, correct?

4 A. Okay. I'm going to read part of this
5 document to try and figure out exactly what it's
6 referring to in specification.

7 Q. Well, you're welcome to look at what you want
8 to, Doctor, but my question is just about paragraph 277
9 and whether -- effectively whether I read it correctly,
10 so maybe I'll ask the question again and you can decide
11 what else you need to look at if anything.

12 A. Sure.

13 Q. You provide an opinion in paragraph 277 of
14 your declaration that the claims lack written
15 description support because they do not require a
16 buffer which the specification makes clear is required,
17 correct?

18 A. That is a correct reading, yes.

19 Q. So in your opinion the '036 patent does not
20 contain language indicating that the use of a buffering
21 agent is optional, right?

22 A. Okay. Could you repeat the question?

23 Q. In your opinion the '036 patent lacks
24 language indicating that the use of a buffering agent
25 is optional, right?

1 A. Yes.

2 Q. Now, if the specification of the '036 patent
3 incorporated language indicating that the use of a
4 buffering agent was optional, then you agree that this
5 written description opinion wouldn't apply, correct?

6 MR. CHEN: Objection. Form. Calls for legal
7 conclusion. Incomplete hypothetical.

8 A. Repeat the question. Thank you.

9 Q. If the specification of the '036 patent
10 incorporated language indicating that the use of a
11 buffering agent was optional, then you would agree that
12 your written description opinion would not apply,
13 correct?

14 A. Correct.

15 MR. CHEN: Same objections.

16 Q. Now I'm going to read you a sentence, okay?
17 And the sentence is this: The composition, if desired,
18 can also contain minor amounts of wetting or
19 emulsifying agents or pH buffering agents. Did you
20 hear that?

21 A. Yes.

22 Q. Okay. That language indicates that a buffer
23 is not required, correct?

24 MR. CHEN: Objection. Form.

25 A. Okay. I'll get you to reread that. Thank

1 you.

2 Q. Sure. The sentence is, the composition, if
3 desired, can also contain minor amounts of wetting or
4 emulsifying agents or pH buffering agents. Did you get
5 that? That sentence indicates that a buffer is not a
6 requirement, correct?

7 MR. CHEN: Same objection.

8 A. Correct.

9 Q. That sentence indicates that a buffer is used
10 only if desired, correct?

11 MR. CHEN: Same objection.

12 A. That would be my interpretation of that
13 sentence.

14 Q. Okay. And if that language that I just read
15 were incorporated into the '036 patent then you agree
16 that the '036 patent would include language indicating
17 that the use of a buffer is optional, correct?

18 A. Correct.

19 MR. CHEN: Objection. Form. Calls for legal
20 conclusion. Incomplete hypothetical.

21 Dr. Falconer, please give me a moment to
22 raise my objections.

23 THE WITNESS: Yes.

24 MR. CHEN: Thank you.

25 Q. Do you know how many formulations are

1 disclosed in the '036 patent with viscosity data
2 demonstrating about 5 to 15 centipoise?

3 A. Without counting them, there are numerous
4 examples in the figures in the patent.

5 Q. Well, not just in the figures but also in the
6 specification, right, the written description portion
7 of the patent? Why don't I ask the question again?
8 There are numerous examples in the patent, both in the
9 figures and in the written description portion
10 describing formulations of aflibercept with at least
11 100 mgs per ml and viscosities of about 5 to 15
12 centipoise, correct?

13 A. Correct.

14 Q. And the description of those formulations
15 provides adequate written description support for
16 claims claiming at least 100 mgs per ml of aflibercept
17 with 5 to 15 centipoise viscosity, correct?

18 A. Correct.

19 MR. CHEN: Objection. Form. Calls for legal
20 conclusion.

21 Q. And the description in the specification also
22 provides adequate written description support for
23 claims containing 114.3 mgs per ml of aflibercept with
24 5 to 15 centipoise viscosity, correct?

25 MR. CHEN: Same objections.

1 A. Okay. Could you repeat the question?

2 Q. Sure. The description in the specification
3 in the '036 patent, including the many working
4 examples, provide adequate written description support
5 for claims containing 114.3 mgs per ml of aflibercept
6 with 5 to 15 centipoise viscosity, correct?

7 MR. CHEN: Objection. Form.

8 Q. Let me know if you need that question again,
9 Doctor.

10 A. Yes. I will ask for it again shortly. Okay.
11 Can you repeat the question?

12 Q. So first of all I'll ask a different
13 question. You reviewed the specification of the '036
14 patent carefully in rendering your opinions in this
15 case, right?

16 A. Yes.

17 Q. Front to back?

18 A. Yes.

19 Q. Okay. The description in the specification
20 of the '036 patent, including its many working
21 examples, provide adequate written description support
22 for claims containing 114.3 mgs per ml of aflibercept
23 with 5 to 15 centipoise viscosity, correct?

24 MR. CHEN: Objection. Form.

25 A. There's certainly more than one example with

1 114.3 milligrams, yes.

2 Q. So let me just ask the question again.

3 A. Yes.

4 Q. The description in the specification of the
5 '036 patent, including its many working examples,
6 provide adequate written description support for claims
7 containing 114.3 mgs per ml of aflibercept with 5 to 15
8 centipoise viscosity, correct?

9 MR. CHEN: Objection. Form.

10 Q. When did you last review the '036 patent,
11 Doctor?

12 A. A couple of weeks ago.

13 Q. Okay. You still recall it fairly well?

14 A. Reasonably well, yes.

15 Q. Okay.

16 A. Yes.

17 Q. Well, let me just ask this one more time.
18 The description in the specification of the '036
19 patent, including its many working examples, provide
20 adequate written description support for claims
21 containing 114.3 mgs per ml of aflibercept with 5 to 15
22 centipoise viscosity, correct?

23 MR. CHEN: Objection. Form.

24 A. What I was looking for was confirmation of
25 the last part of that statement.

1 Q. Do you not know the answer to that question,
2 Doctor? I've got multiple questions pending so why
3 don't I just kind of ask the question cleanly and then
4 you can give me an answer and we can move on, okay,
5 Doctor?

6 A. Could you give me a minute? Could you repeat
7 the question?

8 Q. Yes. The description in the specification of
9 the '036 patent, including its many working examples,
10 provides adequate written description support for
11 claims containing 114.3 mgs per ml of aflibercept with
12 between 5 to 15 centipoise viscosity, correct?

13 MR. CHEN: Same objection.

14 A. Yes. I can neither confirm nor disagree with
15 the very last part of that statement.

16 Q. Okay. So you don't know the answer to that
17 question, is that fair?

18 A. That's fair, yes.

19 MR. TRASK: I think we've probably been going
20 close to an hour. Should we take another break.

21 MR. CHEN: Yeah.

22 Q. Does that work for you, Doctor?

23 A. Sure.

24 THE VIDEOGRAPHER: Going off the record at

25 3:35 p.m.

1 (Whereupon, a recess was taken.)

2 THE VIDEOGRAPHER: We're back on the record
3 at 3:56 p.m.

4 BY MR. TRASK:

5 Q. Doctor, did you converse with your -- with
6 Alvotech's counsel during the break?

7 A. We did talk.

8 Q. Okay. Did you discuss anything relating to
9 this case?

10 A. No.

11 Q. Okay. Not your testimony?

12 A. No.

13 Q. Not any of the documents that have been
14 introduced as exhibits?

15 A. No.

16 Q. Okay. Do you have the '036 patent handy,
17 Doctor?

18 A. Mm-hmm.

19 Q. Can you turn to column 16 of the patent? It
20 has a page number of 55 at the bottom. Are you there?

21 A. Yes.

22 Q. Do you see in column 16 at about lines 14 to
23 15 there are two U.S. patents referenced there? It's
24 U.S. patent number 7,396,664 and U.S. patent 7,354,579?

25 A. Yes.

1 Q. Okay. Have you reviewed those patents,
2 Doctor?

3 A. I don't recognize the numbers.

4 Q. Okay. Do you see them listed in your list of
5 materials considered in paragraph 25 of your
6 declaration?

7 A. Which line was it again that the numbers are
8 on?

9 Q. Column 16, lines 13 to 14.

10 A. Yes. I don't see them on the exhibit list.

11 Q. Okay. So would you agree that you did not
12 review or consider either of these patents at column
13 16, lines 13 to 14 of the '036 patent in forming your
14 opinions in this case?

15 A. I don't recall the numbers.

16 Q. Okay. Well, the list of materials considered
17 is a list of the materials you considered in forming
18 your opinions, right?

19 A. Yes, yes.

20 Q. And those two patents are not included in
21 your list of materials considered?

22 A. Correct.

23 Q. So would it be fair for me to understand that
24 you did not consider either of those patents in forming
25 your opinion in this case?

1 A. Correct.

2 Q. Do you see that following those two patent
3 numbers in column 16, line 14 of the '036 patent it
4 states that those patents are, quote, incorporated
5 herein for all purposes, unquote?

6 A. Yes. That's what it says.

7 Q. What do you take that to mean?

8 MR. CHEN: Objection. Form. Calls for legal
9 conclusion.

10 A. My reading of that as a scientist as opposed
11 to a lawyer is that those two patents are pertinent to
12 this patent. Could you repeat the question?

13 Q. When you reviewed the '036 patent --

14 A. Yes.

15 Q. -- did you ask counsel for Alvotech for
16 copies of those two patents?

17 A. Not to the best of my knowledge.

18 Q. But you understood them to be pertinent to
19 the '036 patent, right?

20 A. Yes. I believe they are pertinent to this
21 patent.

22 Q. And you understand that the '036 patent
23 incorporates those patents herein for all purposes,
24 right?

25 A. That's what the sentence says, yes.

1 Q. Why didn't you choose to ask counsel for
2 copies of those patents to review in arriving at your
3 opinions in this case?

4 A. I didn't understand their importance.

5 Q. Do you understand now that it might have been
6 a good idea to ask to review those patents in rendering
7 your opinions regarding the '036 patent?

8 A. With --

9 MR. CHEN: Objection. Form.

10 THE WITNESS: Sorry. Go for it.

11 MR. CHEN: I've raised my objection.

12 THE WITNESS: Yes.

13 MR. CHEN: You can answer.

14 A. With hindsight I believe it would have been a
15 good idea to read those patents, yes.

16 Q. Counsel for Alvotech never provided you with
17 copies of those patents, right?

18 A. I don't recognize the patent numbers.

19 Q. If you'd reviewed them you would have listed
20 them among your materials considered in paragraph 25 of
21 your declaration, correct?

22 A. Correct.

23 Q. Okay. Do you recall asking counsel for
24 copies of any references, patents, publications that
25 are cited in the '036 patent?

1 A. I don't recall requesting directly material
2 from this patent, no.

3 Q. Do you recall requesting indirectly material
4 from the '036 patent as part of your review?

5 A. I don't recall it, no.

6 Q. To the best of your understanding did you
7 review any documents that are incorporated by reference
8 into the '036 patent as part of your analysis regarding
9 the '036 patent?

10 MR. CHEN: Objection. Form. Calls for legal
11 conclusion.

12 A. Could you point out where those documents are
13 listed?

14 Q. Well, why don't I ask at a general level and
15 then we can get specific?

16 A. Okay.

17 Q. To the best of your knowledge did you review
18 any documents incorporated by reference into the '036
19 patent as part of your analysis regarding the '036
20 patent?

21 MR. CHEN: Same objections.

22 A. I don't recall requesting documents because
23 they were cited here in the '036 patent.

24 Q. Turn to paragraph 22 of the -- sorry. Strike
25 that.

1 Turn to column one of the '036 patent. It's
2 at the page ending in 48.

3 A. Yep.

4 Q. There is a paragraph under cross-reference to
5 related applications in the top left.

6 A. I can see it, yes.

7 Q. There's a number of patent applications
8 number -- excuse me. Strike that.

9 There are a number of patent application
10 numbers recited in that paragraph at column one, lines
11 8 through 16, correct?

12 A. Correct.

13 Q. And the paragraph ends by stating that each
14 of those patent applications is herein incorporated by
15 reference in its entirety?

16 A. Correct.

17 Q. Did you review any of those patent
18 applications to your knowledge in rendering your
19 opinions about the '036 patent?

20 A. To the best of my knowledge, no.

21 Q. There's also a U.S. patent number referenced
22 in the second line of that -- or the third line of that
23 paragraph, patent number 11,103,552. Do you see that?

24 A. Yes.

25 Q. Did you review that patent incorporated by

1 reference into the '036 patent?

2 A. Not that I know of, no.

3 Q. Turn to paragraph 266 of your declaration,
4 please, Doctor. Are you there?

5 A. Yes.

6 Q. And you see the heading of this section,
7 number one towards the top of this page, refers to your
8 opinion on written description support, correct?

9 A. Correct.

10 Q. And in the first paragraph under that
11 heading, paragraph 266 you say, the '036 patent claims
12 cover a method for treating an angiogenic eye disorder
13 comprising intravitreal administration of a broad genus
14 of potential formulations having a concentration of at
15 least 100 mgs per ml of a specified VEGF receptor
16 fusion protein and it goes on, correct?

17 A. Correct.

18 Q. So this opinion here is limited to claims
19 that recite at least 100 mgs per ml of a VEGF receptor
20 fusion protein, correct?

21 MR. CHEN: Objection. Form.

22 A. Sorry. Could you repeat the question?

23 Q. Sure. Your opinion in this section starting
24 on the page marked 106 in your declaration is limited
25 to claims in the '036 patent that have a concentration

1 of at least 100 mgs per ml of a specified VEGF receptor
2 fusion protein, correct?

3 MR. CHEN: Same objection.

4 A. Correct.

5 Q. And if you turn to paragraph 274 in that same
6 section, it's the page ending -- page number 110 at the
7 bottom. This is part of the same section of your
8 written description opinion, right?

9 A. Right.

10 Q. And your opinion here says that moreover, the
11 claims recite concentrations of at least 100 mgs per ml
12 of the VEGF fusion protein with no stated upper limit,
13 correct?

14 A. Correct.

15 Q. And so you're rendering an opinion in section
16 XII.1 that claims reciting concentrations of at least
17 100 mgs per ml with no stated upper limit lack written
18 description support, right?

19 A. Can I have the question again?

20 Q. Sure. You're rendering an opinion in section
21 XII.1 of your declaration that claims reciting
22 concentrations of at least 100 mgs per ml with no
23 stated upper limit lack written description support,
24 correct?

25 A. Correct.

1 Q. And that opinion doesn't apply to claims that
2 include a stated upper limit, correct?

3 MR. CHEN: Objection. Form.

4 A. Correct.

5 Q. Do you have the '036 patent in front of you
6 still, Doctor?

7 A. Yes.

8 Q. Turn to claim 31 at the back of the patent.
9 Are you there?

10 A. Yes.

11 Q. Do you see claim 31?

12 A. Yes.

13 Q. Claim 31 recites among other things about
14 114.3 mgs per ml of aflibercept, correct?

15 A. Correct.

16 Q. That claim doesn't have no stated upper
17 limit, correct? Let me rephrase that in a positive.
18 That claim has a stated upper limit, correct?

19 MR. CHEN: Objection. Form.

20 Q. Of -- let me recite the question again.
21 Claim 31 has a stated upper limit for its aflibercept
22 concentration, correct?

23 MR. CHEN: Objection. Form.

24 A. Yes. It has a target concentration that I
25 assume is the upper limit for what it's stating, yes.

1 Q. Right. And you don't have an opinion that
2 claim 31 lacks written description support, right?

3 MR. CHEN: Objection. Form.

4 A. Could you repeat the question?

5 Q. Right. I'll just first direct your attention
6 to paragraph 274 of your declaration.

7 A. Yes.

8 Q. Your written description here is directed to
9 claims with no stated upper limit, correct?

10 A. That is the wording. Correct.

11 Q. Okay. And claim 31 has a target
12 concentration for aflibercept which inherently contains
13 a stated upper limit, correct?

14 A. Correct.

15 Q. So you don't have a written description
16 opinion -- strike that.

17 You don't have an opinion that claim 31 lacks
18 written description support, right?

19 MR. CHEN: Object to the extent it
20 mischaracterizes.

21 A. Repeat the question, please.

22 Q. Sure. Your written description opinion is
23 limited to claims with no stated upper limit, correct?

24 A. Correct.

25 MR. CHEN: Same objection.

1 THE WITNESS: Sorry.

2 Q. Claim 31 of the '036 patent has a target
3 concentration for aflibercept --

4 THE VIDEOGRAPHER: Hey, Michael. We can hear
5 you.

6 Q. Why don't I start over? Your written
7 description opinion is directed to claims with no
8 stated upper limit, correct?

9 MR. CHEN: Same objections.

10 A. Correct.

11 Q. Okay. Claim 31 has a target concentration
12 for aflibercept of 114.3 mgs per ml which inherently
13 contains a stated upper limit for the concentration of
14 aflibercept, correct?

15 A. Correct.

16 MR. CHEN: Same objection.

17 THE WITNESS: Sorry.

18 Q. And you don't have an opinion that claim 31
19 lacks written description support, correct?

20 MR. CHEN: Same objection.

21 A. Correct.

22 Q. Claim 35 of the '036 patent recites an
23 aflibercept concentration range of 103 to 126 mgs per
24 ml of aflibercept, correct?

25 A. Correct.

1 Q. Claim 35 also has a stated upper limit to
2 aflibercept concentration, correct?

3 A. Correct.

4 Q. And you don't have an opinion that claim 35
5 lacks written description support, correct?

6 MR. CHEN: Same objections.

7 A. Correct.

8 Q. Okay. You can put that aside for the moment.
9 Turn to paragraph 177 of your declaration, please,
10 Doctor.

11 A. Yes.

12 Q. This paragraph describes your analysis of why
13 POSA would have selected an aqueous pharmaceutical
14 formulation containing about 114.3 mgs per ml of
15 aflibercept, correct?

16 A. Correct.

17 Q. Now, you don't consider any dose here other
18 than 8 milligrams of aflibercept, correct?

19 A. Correct.

20 Q. And that's because Dr. D'Amico told you that
21 the POSA would consider only an 8-milligram dose,
22 correct?

23 A. Correct.

24 Q. If he had told you that other doses would be
25 considered by the POSA, you would have included those

1 in your analysis, correct?

2 A. Correct.

3 Q. But the POSA wouldn't have been interested in
4 a dose of 7 milligrams of aflibercept?

5 MR. CHEN: Objection. Form.

6 A. To the best of my knowledge that's correct.

7 Q. And the POSA wouldn't have considered a dose
8 of 9 milligrams of aflibercept, correct?

9 MR. CHEN: Objection. Form.

10 A. The dosage is the domain of the clinician.
11 If they want 8 milligrams, that's what you formulate.

12 Q. And you discussed this topic during your
13 conversation with Dr. D'Amico on September 16, 2025,
14 correct?

15 A. Correct.

16 Q. And he told you in no uncertain terms that
17 the POSA would consider only an 8-milligram dose of
18 aflibercept, right?

19 MR. CHEN: Objection. Form.

20 A. That was the dose that he mentioned.
21 Correct.

22 Q. And you didn't have any doubt about that
23 following the conversation with him, correct?

24 A. He's the formulation scientist. I leave that
25 decision-making to the clinician.

1 Q. Understood. Now, I think you also testified
2 that Dr. D'Amico told you that the POSA would prefer an
3 injection volume of 50 microliters, correct?

4 MR. CHEN: Objection. Form.

5 A. My recollection is that's correct, yes.

6 Q. Okay. And he didn't suggest that any
7 injection volume other than 50 microliters would be
8 selected by the POSA, correct?

9 MR. CHEN: Objection. Form.

10 A. There's a difference between an absolute
11 injection volume and a preferred injection volume. My
12 understanding of this field is that 100 microliters is
13 considered the maximum, and 50 is the preferred.

14 Q. What is your understanding that 100
15 microliters is the maximum injection volume based upon?

16 A. I'm not a clinician, so I've never injected
17 anybody in the eye and never intend doing so. My
18 understanding is that if you inject too large a volume
19 into the eye it increases the pressure inside the eye
20 which can cause discomfort, and it potentially could
21 cause bleed back by the puncture hole. But I'm not a
22 clinician.

23 Q. Those are topics outside of your area of
24 expertise?

25 A. Yeah, yeah.

1 Q. And so ultimately you would defer to
2 Dr. D'Amico as to the suitable injection volume for
3 intravitreal aflibercept injection, correct?

4 A. Correct.

5 Q. And he told you that 50 microliters would be
6 the volume to be selected by a POSA, correct?

7 MR. CHEN: Objection. Form.

8 A. He would have said the preferred volume.
9 It's -- when you know the dose, he would know the
10 administration and the type of needle or whatever, so
11 there's a component to this decision-making that's
12 definitely on his shoulders. From the formulation
13 scientist perspective you always can -- you're
14 concerned if you drift out of what is the sort of
15 accepted or understood to be sort of a safe
16 concentration you want to minimize moving away from
17 that as much as possible because you don't want
18 aggregation or unanticipated increase in viscosity.
19 And so that decision-making process is often a
20 compromise. So obviously from a -- with the
21 perspective of a formulation scientist if you can keep
22 the concentration low the probability of success is
23 higher, and if you go to a high concentration such as
24 160, you don't know that you're going to run into
25 difficulties but the probability is that it's going to

1 be harder work keeping the stability and the viscosity
2 within a target range.

3 Q. Now, of all the concentrations listed in the
4 table in paragraph 177 of your declaration, you don't
5 have -- strike that.

6 Of all the concentrations listed in paragraph
7 177 of your declaration the POSA didn't have any data
8 demonstrating the stability or viscosity of aflibercept
9 at any of those concentrations, correct?

10 MR. CHEN: Objection. Form.

11 A. The -- both Dr. D'Amico and myself, I can't
12 speak for Dr. D'Amico, but the understanding that 100
13 milligrams isn't based on a measured viscosity.

14 Q. Okay. I think you misspoke. Did you say --
15 you said 100 milligrams. We're talking about an
16 8-milligram dose, correct?

17 A. Sorry. The 100 milligrams per ml.

18 Q. Ah, so let me re-ask the question.

19 A. Yes. Okay.

20 Q. I was getting confused.

21 A. Yes.

22 Q. Of all the concentrations listed in paragraph
23 177 of your declaration, the POSA didn't have any data
24 demonstrating the stability or viscosity of aflibercept
25 at any of those listed concentrations, correct?

1 MR. CHEN: Same objection.

2 A. The -- incorrect.

3 Q. Okay. What data -- putting aside the '036
4 patent, which of course has data --

5 A. Yes, yes.

6 Q. -- but what data in the prior art did the
7 POSA have demonstrating the stability or viscosity of
8 an aflibercept formulation at any of these
9 concentrations listed in paragraph 177 of your
10 declaration?

11 A. Yes. If you go to paragraph 192, there's a
12 discussion on -- from the work published in Dix which
13 presents stability data for -- I believe they call it
14 here VEGF trap which I understand to be aflibermab --
15 aflibercept.

16 Q. There's no viscosity data index, is there,
17 Doctor?

18 A. In Dix's it's stability data. It was half of
19 your question.

20 Q. Right. So --

21 A. Would you like the other half?

22 Q. Yes.

23 A. Furfine -- actually, I'll find it in the --
24 yes. In paragraph 195 it discusses the use --
25 formulation containing what I believe to be aflibercept

1 that has -- that is stated to be suitable for
2 intravitreal injection.

3 Q. There's no viscosity data for a formulation
4 in Furfine of at least 100 mgs per ml of aflibercept,
5 correct?

6 A. Correct.

7 Q. And so the POSA evaluating the concentrations
8 set forth in paragraph 177 of your declaration in your
9 view would have an understanding of the viscosity below
10 100 mgs per ml but not above, correct?

11 MR. CHEN: Objection. Form. Misstates
12 testimony.

13 A. Could you re-ask the question?

14 Q. Sure. The POSA evaluating the concentrations
15 that are set forth in paragraph 177 of your declaration
16 for aflibercept formulations --

17 A. Yes.

18 Q. -- would have an understanding of the
19 viscosity of those formulations in your view below 100
20 mgs per ml but not above 100 mgs per ml of aflibercept,
21 correct?

22 MR. CHEN: Same objections.

23 A. Based on Dix and Furfine, one is 1 to 100 and
24 the other one has data for 100. If it's -- well, the
25 assumption of viscosity is appropriate if they're

1 claiming that it's used for intravitreal injection.

2 It's for one -- you know, up to 100.

3 Q. Right.

4 A. Yes.

5 Q. And so the POSA would not have any data to
6 draw upon indicating the viscosity of an aflibercept
7 formulation at over 100 mgs per ml? You agree with
8 that?

9 A. Yes.

10 Q. And so if the POSA were going to choose from
11 among the different concentrations shown in your table
12 on paragraph 177 of your declaration, the most
13 conservative option for the skilled formulator would be
14 to choose a concentration of aflibercept for which in
15 your view the POSA has data demonstrating the viscosity
16 of that aflibercept formulation, correct?

17 MR. CHEN: Objection. Form.

18 A. I'll get you to re-ask the question because
19 the wording is important in this case. Yes.

20 Q. If a POSA were choosing from among the
21 different aflibercept concentrations --

22 A. Yes.

23 Q. -- shown in the table in paragraph 177 of
24 your declaration, the most conservative options for the
25 skilled formulator would be to choose a concentration

1 of aflibercept for which in your view the POSA has data
2 demonstrating the viscosity of that aflibercept
3 formulation, correct?

4 A. Correct.

5 MR. CHEN: Objection. Form.

6 Q. And those formulations are the aflibercept
7 concentration of 80 mgs per ml, correct?

8 MR. CHEN: Same objection.

9 A. Could you repeat the question?

10 Q. Sure. The conservative concentrations for a
11 skilled formulator to select from among those shown in
12 the table in paragraph 177 of your declaration include
13 the concentration of 80 mgs per ml, correct?

14 MR. CHEN: Same objection.

15 A. Okay. I'll get you to -- and I'll focus on
16 the wording.

17 Q. The most conservative concentrations of
18 aflibercept for a skilled formulator to select from
19 among those shown in the table on paragraph 177 of your
20 declaration include the concentration of 80 mgs per ml
21 of aflibercept, correct?

22 MR. CHEN: Same objection.

23 A. From the perspective of the formulation
24 scientist, that's correct.

25 Q. Right. And it would also include the

1 concentration of 88.9 mgs per ml of aflibercept,
2 correct?

3 MR. CHEN: Same objection.

4 A. That's correct.

5 Q. Okay. If it were up to the skilled
6 formulator to select which concentration of aflibercept
7 to use in an aflibercept formulation for intravitreal
8 injection the skilled formulator would select either 80
9 or 88.9 mgs per ml of aflibercept in your opinion,
10 correct?

11 MR. CHEN: Objection. Form. Incomplete
12 hypothetical.

13 A. I think the skilled formulator would be
14 comfortable with 100, 88.9, and 80.

15 Q. Okay. And as long as the clinician POSA
16 informed the skilled formulator that injection volumes
17 up to 100 microliter were clinically acceptable, then
18 the POSA would select one of the three concentrations
19 you just identified, 80, 88.9, or 100 mgs per ml of
20 aflibercept, correct?

21 MR. CHEN: Same objections.

22 A. I would target that question to Dr. D'Amico
23 because what I think is clinically acceptable is likely
24 to be of lesser value than the clinician's view on
25 that.

1 Q. Okay. But I think I was just posing this as
2 a -- well, let me ask the question again because I
3 don't think I'm asking you to decide what's clinically
4 acceptable. I think the question is asking you to draw
5 a conclusion based upon what the clinician would inform
6 the skilled formulator, if that makes sense to you.

7 A. Okay.

8 Q. So I'll ask the question again. If the
9 clinician POSA informed the skilled formulator that
10 injection volumes up to 100 microliters were clinically
11 acceptable, then the POSA would select one of the three
12 concentrations you just identified, 80, 88.9, or 100
13 mgs per ml of aflibercept for an intravitreal
14 formulation, correct?

15 MR. CHEN: Objection. Form. Incomplete
16 hypothetical.

17 A. Correct.

18 Q. And selecting instead a concentration of
19 114.3 mgs per ml of aflibercept for an intravitreal
20 formulation would be a riskier decision for the skilled
21 formulator to make, correct?

22 MR. CHEN: Objection. Form.

23 A. Incorrect.

24 Q. Skilled formulator has no data on the
25 viscosity of a formulation of 114.3 mgs per ml,

1 correct?

2 A. Correct.

3 Q. So wouldn't the most -- the more conservative
4 option to be -- to choose a concentration of
5 aflibercept for which the skilled formulator has in
6 your view certainty about the viscosity of that
7 formulation?

8 MR. CHEN: Objection. Form.

9 A. That is the most conservative option.

10 Q. Selecting 114.3 mgs per ml of aflibercept for
11 an intravitreal formulation would be a riskier decision
12 for the skilled formulator, correct?

13 MR. CHEN: Same objection.

14 A. My opinion on this subject is that the level
15 of risk associated with approximately 15 percent, there
16 is a risk. You would test it experimentally, but you
17 also know that you've got that palette of excipients
18 that you can work with if you find that either the
19 stability is quite up to scratch or the viscosity is
20 drifting towards an unacceptable value.

21 Q. As protein concentration increases, viscosity
22 tends to increase as well, right?

23 A. Yes.

24 Q. As protein concentration increases, the risk
25 of aggregation tends to increase as well, right?

1 A. Yes.

2 Q. Selecting a concentration of 114.3 mgs per ml
3 is a riskier decision for the skilled formulator to
4 make than to select a lower concentration such as 100
5 mgs per ml or below, correct?

6 MR. CHEN: Objection. Form.

7 A. I would word it as a manageable risk rather
8 than an unmanageable risk.

9 Q. I didn't ask whether it was manageable or
10 not.

11 A. Yes. Okay. Please rephrase the question.
12 Sorry. Re-ask the question.

13 Q. Selecting a concentration of 114.3 mgs per ml
14 of aflibercept for an intravitreal formulation is a
15 riskier decision for the skilled formulator to make
16 than selecting a lower concentration of aflibercept for
17 an intravitreal formulation such as 100 mgs per ml or
18 below in your opinion, correct?

19 A. Correct.

20 MR. CHEN: Objection. Form.

21 Q. The selection of the concentration of
22 aflibercept to use in an intravitreal formulation is
23 one on which you'd ultimately defer to the clinician,
24 Dr. D'Amico, right?

25 MR. CHEN: Objection. Form.

1 A. This decision would be a joint decision.
2 They would take in the opinion of Dr. D'Amico and the
3 natural tendency for the formulation scientist to be
4 conservative. The judgment call would be where you
5 assign an acceptable risk, knowing that if you run into
6 any difficulties you still do have a palette of
7 excipients to work it.

8 Q. Who would make the ultimate decision as to
9 what concentration of aflibercept is safe to administer
10 into the eye of a patient?

11 MR. CHEN: Objection. Form.

12 A. It's a joint decision.

13 Q. Okay. Did you get the opinion of Dr. D'Amico
14 on what concentration of aflibercept is safe to
15 administer into the eye of a patient?

16 A. No.

17 Q. So because this is a joint decision you're
18 not able to render an opinion definitively on which
19 concentration of aflibercept the POSA would have found
20 to be acceptable for administration intravitreally into
21 the eye of a patient, correct?

22 MR. CHEN: Objection. Form.

23 A. The decision-making in this case has two
24 aspects to it, the desire of the clinician to have the
25 smaller injection volume and the natural conservatism

1 of the formulation scientist to not stray too far away
2 from their comfort zone when it comes to the
3 concentration. So it has two aspects to the
4 decision-making.

5 Q. Because it's a joint decision about what
6 concentration of aflibercept to administer
7 intravitreally into the eye of a patient, you as a
8 non-clinician are not able to offer a definitive
9 opinion alone about what concentration of aflibercept
10 the POSA would have found to be acceptable for
11 administration intravitreally into the eye of a
12 patient, correct?

13 A. Okay. I lost it again.

14 Q. Because the decision about what concentration
15 of aflibercept to administer intravitreally into the
16 eye of a patient is a joint decision between the
17 clinician and the formulator, you as a non-clinician
18 are not offering a definitive opinion about what
19 concentration of aflibercept the POSA would have found
20 to be acceptable for administration intravitreally into
21 the eye of a patient, correct?

22 A. Correct.

23 Q. Okay. You can put that aside. I'm handing
24 you, Doctor, what's been marked Exhibit 2039.

25 (Whereupon, Exhibit 2039, Advances in Liquid

1 Formations of Parental Therapeutic Proteins, was marked
2 for identification.)

3 Q. Do you recognize this paper?

4 A. Yes. I believe I wrote it about 17 years
5 ago. No, it isn't. Sorry.

6 Q. Time flies, but not that fast.

7 A. Time flies. It just feels like it. Yes.
8 Biotech advances. I was thinking of another one.

9 Q. This was published in 2019, right?

10 A. Correct.

11 Q. It's a research review paper, is that right?

12 A. Correct.

13 Q. What is a research review paper?

14 A. It is where it looks at -- there's -- well,
15 there's more than one answer to that question, I'm
16 afraid. Some research reviews are effectively
17 literature reviews of all the published work. This one
18 looks at formulations of products that were on the
19 market, so it used package inserts as one of the
20 sources of information which isn't traditional for
21 research review.

22 Q. Okay. And review papers like this aren't
23 breaking new ground from an experimental standpoint;
24 they're reviewing the available information in the
25 field, correct?

1 A. Yes. This is backward looking.

2 Q. Okay. And so even though this paper was
3 published in 2019 do you think it's fair to say that
4 this reflects what the POSA would have known as of the
5 2018 priority date?

6 A. There might be some exceptions in there, but
7 yes, most of it.

8 Q. Okay. Turn to the second page of the
9 article. There's a heading, 2.1 buffers in the
10 left-hand column. Do you see that?

11 A. Yes.

12 Q. The second paragraph under that heading says,
13 the therapeutic protein has some buffering capacity in
14 its own right. At higher protein concentrations over
15 50 mgs per ml the protein's buffering capacity may be
16 sufficient to hold the pH at the desired value.

17 Do you see that?

18 A. Yes.

19 Q. The POSA would have understood that?

20 A. Yes.

21 Q. Was the POSA aware of liquid formulations of
22 therapeutic proteins that did not include excipient
23 buffers?

24 A. Around about this period there was some work
25 published that talked about not having buffers, but I

1 must admit I don't recall the date.

2 Q. Do you see figure one on page 3 of your
3 paper?

4 A. Yes.

5 Q. And this describes buffers used in
6 therapeutic monoclonal antibody liquid formulations
7 separated by decade, right?

8 A. Yes.

9 Q. And the green bars are from the 2000s and the
10 blue bars are from the 2010s, right?

11 A. Correct.

12 Q. Okay. And all the way at the right side of
13 that graph there's a segment titled none. Do you see
14 that?

15 A. Correct.

16 Q. And that's indicating that as of the relevant
17 time period -- well, strike that.

18 The graph is indicating that in the 2000s
19 there was one formulation of a therapeutic monoclonal
20 antibody in liquid form that contained no excipient
21 buffer, correct?

22 A. Correct.

23 Q. And in the 2010s there was also one other
24 formulation of a therapeutic monoclonal antibody in
25 liquid form that contained no excipient buffer,

1 correct?

2 A. Correct.

3 Q. Did you put this table together?

4 A. Yes.

5 Q. Okay. Do you know what either of those
6 formulations was?

7 A. I don't recall.

8 Q. But suffice to say starting in the 2000s the
9 POSA was familiar with the concept of a therapeutic
10 monoclonal antibody formulation in liquid form that did
11 not require an excipient buffer, correct?

12 A. Correct.

13 Q. Okay. And then if you could turn to figure
14 four, this figure shows buffers used in therapeutic
15 protein other than monoclonal antibody and insulin
16 liquid formulations, correct?

17 A. Correct.

18 Q. And this graph shows that in the 2010s there
19 were four therapeutic protein formulations other than
20 monoclonal antibodies and insulin that contained no
21 excipient buffer in the formulation, correct?

22 A. Correct.

23 Q. And in the 1990s there was one formulation of
24 a therapeutic protein other than a monoclonal antibody
25 or insulin that did not contain an excipient buffer,

1 correct?

2 A. Correct.

3 Q. You put this chart together?

4 A. Yes.

5 Q. Do you recall what any of those formulations
6 was?

7 A. I'm afraid not.

8 Q. But the POSA would have been aware from the
9 1990s that therapeutic proteins other than monoclonal
10 antibodies and insulin could be formulated in liquid
11 formulations without requiring an excipient buffer,
12 correct?

13 A. That assumes they read that package insert
14 and had seen that there was no buffer in that
15 formulation.

16 Q. The POSA is assumed to know all relevant
17 information in the field, correct?

18 A. Nobody knows all relevant information in the
19 field, but you would hope they know the majority of it,
20 yes.

21 Q. Well, the POSA that you envisioned or --
22 strike that.

23 The POSA that you applied for purposes of
24 your analysis in this case, did that POSA have an
25 understanding of all the relevant literature in the

1 field as of the priority date of the '036 patent?

2 A. Yes.

3 Q. Okay. And so the POSA would have understood
4 as of the 1990s that you could formulate a therapeutic
5 protein other than a monoclonal antibody or insulin in
6 a liquid formulation without an excipient buffer,
7 correct?

8 A. Yes.

9 Q. Now, the POSA would understand that
10 aflibercept protein has buffering capacity, correct?

11 A. Correct.

12 Q. And the POSA would understand that
13 aflibercept could be formulated without an excipient
14 buffer, correct?

15 A. Correct.

16 Q. And in view of the disclosure of the '036
17 patent the POSA would understand that a formulation
18 with at least 100 mgs per ml of aflibercept could be
19 formulated without an excipient buffer?

20 MR. CHEN: Objection. Form.

21 A. Correct.

22 Q. And given the information conveyed in your
23 2019 review paper reflecting the POSA's knowledge, you
24 agree that as of the early 2000s the POSA would have
25 understood that aflibercept could be formulated in a

1 liquid formulation without an excipient buffer,
2 correct?

3 A. Could you rephrase the question -- sorry,
4 re-tell the question?

5 Q. You agree that as of the early 2000s the POSA
6 would have understood that aflibercept could be
7 formulated in a liquid formulation without an excipient
8 buffer, correct? In fact, let me rephrase the
9 question. You agree that as of the early 2000s
10 researchers in the field understood that a protein like
11 aflibercept could be formulated in a liquid formulation
12 without an excipient buffer, correct?

13 A. Sorry. Yes. Sorry I was --

14 Q. You agree that as of the early 2000s
15 researchers in the field understood that a protein like
16 aflibercept could be formulated into liquid
17 pharmaceutical formulation without an excipient buffer,
18 correct?

19 A. Yes.

20 MR. TRASK: Why don't we take a quick break?

21 THE VIDEOGRAPHER: Going off the record at
22 5:02 p.m.

23 (Whereupon, a recess was taken.)

24 THE VIDEOGRAPHER: And we're back on the
25 record at 5:25 p.m.

1 BY MR. TRASK:

2 Q. All right. Doctor, did you discuss your
3 testimony with counsel for Alvotech during the break?

4 A. I did not.

5 Q. Okay. You testified earlier today that you
6 are a skilled formulator POSA for purposes of the '036
7 patent, right?

8 A. Correct.

9 Q. At what point in time did you gain the
10 qualifications of being a skilled formulator POSA?

11 A. The skill set that I developed started in the
12 1980s. I worked with -- well, we called them proteins
13 in the 1990s. In the 1980s it was a mixture of
14 expression of proteins. In those days it was bacteria
15 as the expression host, and then I used to do
16 purification. And then back in those days you'd follow
17 that up by lyophilizing the recombinant protein.
18 Liquid formulations in those days weren't common.
19 That's probably -- to be -- yeah. The default was
20 lyophilizing.

21 Q. Okay. So let me ask you this. Would you
22 consider yourself a person of ordinary skill in the art
23 in the field of liquid protein pharmaceutical
24 formulations as of the early 2000s?

25 A. I would have put it at the late 2000s.

1 Q. Okay. Okay. I'm handing you what I just
2 marked as Exhibit 2040.

3 (Whereupon, Exhibit 2040, Conference Program,
4 was marked for identification.)

5 Q. Doctor, this is the program of the conference
6 that you testified about earlier at which you presented
7 in September of 2025, correct?

8 A. Correct.

9 Q. And it looks like you presented on the next
10 to last page of this exhibit at 11:30 a.m. on day three
11 of the conference, September 17th, correct?

12 A. Correct.

13 Q. Okay. This is the same day that you were
14 drafting your expert report based on all of the
15 information that you had obtained from your
16 conversation with Dr. D'Amico on September 16th,
17 correct?

18 A. It's the same day. Correct.

19 Q. Okay. Did you attend the session before you
20 spoke at the conference at 11:30 a.m.? Sorry. I'll
21 make it more clear. Strike that.

22 Did you attend the presentation starting at 9
23 a.m. up until your own presentation at 11:30 a.m.?

24 MR. CHEN: Objection. Form.

25 A. I went to the first talk which was Jessica

1 Boutros. It was incorrectly recorded here as being
2 University of Melbourne. She was University of
3 Adelaide. I don't recall going to the other talks that
4 morning.

5 Q. Did you attend any of the talks after you
6 presented at 11:30 a.m. that day?

7 A. Yes. I recall attending the talk, Vincent
8 Liden [sic] at 2:20.

9 Q. Would you have attended a number of the talks
10 at the conference on September 17th?

11 A. Normally I would, yes.

12 Q. So much of your day on September 17th was
13 taken up by attending talks at the conference and
14 giving your own talk at the conference, right?

15 A. Yes.

16 MR. CHEN: Objection. Form. And to the
17 extent it mischaracterizes prior testimony.

18 A. Certainly part of the day was -- involving
19 presenting a talk and hearing two of the talks which
20 are from students from the same university as myself.
21 Yes.

22 Q. Okay. It looks like the last talk ended
23 around 3:30 p.m. on the 17th, is that right?

24 A. Correct.

25 Q. Did you go home after that?

1 A. I'd have flown home that evening.

2 Q. Okay. How long is the flight home?

3 A. From Melbourne it's about an hour.

4 Q. Okay. And there's obviously time with
5 security and everything, so what was your -- roughly
6 the time spent in transit that day from the conference
7 back home?

8 A. With taxis, probably two and a half hours.

9 Q. Okay. How much time did that leave you to
10 actually focus on writing the portions of your report
11 that rely on Dr. D'Amico's opinions?

12 A. I don't recall exactly how much time I spent
13 working on it.

14 Q. Okay. But you signed -- you finalized and
15 signed your declaration on September 17th, correct?

16 A. Correct.

17 Q. Do you remember if you did that at the
18 conference or at home?

19 A. I don't recall.

20 Q. Okay. You'd say at most you'd spent about
21 how many hours preparing those opinions in your
22 declaration?

23 A. Yes. I don't recall.

24 Q. Well, no more than 24 certainly, correct?

25 A. Sure.

1 Q. Maybe no more than 12?

2 A. I'd say it was -- yeah. Correct.

3 Q. Okay. Would you say it was more than 6 hours
4 that day with everything else you had going on?

5 A. It could have been 6 or 8. Yes.

6 Q. So after speaking with Dr. D'Amico you spent
7 roughly 6 or 8 hours drafting the obviousness opinions
8 in your expert report, signed it that day, and e-mailed
9 it to counsel?

10 MR. CHEN: Objection. Form.
11 Mischaracterizes prior testimony.

12 A. I don't recall how many hours I spent working
13 on this.

14 Q. Your best guess is 6 to 8 hours?

15 MR. CHEN: Same objections.

16 A. That is a guess.

17 Q. Okay. Do you have another guess or is that
18 the best one we have at present?

19 A. That's as good a working guess as any.

20 Q. Okay. So your best estimate sitting here
21 today is that you spent roughly 6 or 8 hours drafting
22 the obviousness opinions in your expert report, signed
23 it, and e-mailed it to counsel that day, correct?

24 MR. CHEN: Same objections.

25 A. The parts where it required Dr. D'Amico's

1 input, yes.

2 Q. Okay. Which are all of the obviousness
3 grounds in your declaration, right?

4 MR. CHEN: Objection. Mischaracterizes
5 testimony and the document.

6 A. Yes. The key part that was discussed between
7 myself and Dr. D'Amico was the part that led up to
8 section 177, and it was the negotiation about injection
9 volume and dose.

10 Q. Your opinions relating to injection volume
11 and dose were drafted in a roughly 6-to-8-hour period
12 on September 17th, correct? I'll rephrase the
13 question.

14 A. Yeah. So --

15 Q. Your opinions based upon -- I'll rephrase it
16 again. Your opinions involving the concepts of
17 injection volume and dose were drafted in a roughly
18 6-to-8-hour period on September 17th of 2025, correct?

19 MR. CHEN: Objection. Form.

20 A. The component that required Dr. D'Amico's
21 input was in that reasonably short period of time, yes.

22 MR. TRASK: Okay. No further questions.
23 Thank you for your time, Doctor. Much appreciated.
24 Should we go off the record?

25 MR. CHEN: Yeah. Let's go off the record.

1 COURT REPORTER: Before we go off the record,
2 just confirming your rough draft and copy.

3 MR. CHEN: Let's -- I'm not -- we're not
4 closing the deposition yet. I want to just take a look
5 at my notes, see if I have any follow-up questions.

6 COURT REPORTER: Okay.

7 THE VIDEOGRAPHER: Off the record at 5:38
8 p.m.

9 (Whereupon, a recess was taken.)

10 THE VIDEOGRAPHER: And we're back on the
11 record at 5:57 p.m.

12 EXAMINATION BY COUNSEL FOR THE PETITIONERS,
13 ALVOTECH USA INC. AND ALVOTECH HF
14 BY MR. CHEN:

15 Q. All right. Dr. Falconer, do you recall a
16 discussion with counsel earlier on today about Vitti
17 and a formulation of 150 plus or minus 22.5 mgs per ml
18 of VEGF antagonist in paragraph 87 of Vitti? Do you
19 recall the discussion?

20 A. I don't recall the discussion.

21 Q. Okay. Well, we'll talk more -- we'll start
22 by talking more generally about Vitti. You considered
23 and read all of Vitti in rendering your opinions
24 regarding obviousness and expectation of success in
25 your declaration, correct?

1 A. Correct.

2 MR. TRASK: Objection. Leading.

3 Q. Okay. So let's take -- let's turn to
4 paragraph 94. Please take a moment and read that full
5 paragraph to yourself and let me know when you're done
6 reading.

7 A. I've [sic] done reading.

8 Q. Okay. Does paragraph 94 of Vitti
9 specifically discuss aflibercept formulations?

10 A. Yes.

11 Q. Does paragraph 94 of Vitti teach aflibercept
12 formulation having a concentration of aflibercept of up
13 to 115 milligrams per milliliter?

14 A. Yes.

15 Q. Does paragraph 94 of Vitti specifically say
16 anything about an aflibercept formulation with a
17 concentration of more than 115 milligrams per
18 milliliter?

19 A. No.

20 Q. Did you take paragraph 94 into account in
21 rendering your opinions based on Vitti?

22 A. No. I was asked directly about the paragraph
23 87.

24 Q. I'll re-ask the question.

25 A. Okay.

1 Q. I'm not sure if you heard me correctly.

2 A. Okay. Sorry.

3 Q. In rendering the opinions set out in your
4 declaration --

5 A. Yes.

6 Q. -- did you take paragraph 94 of Vitti into
7 your -- into account?

8 A. Yes.

9 Q. Okay. Let's take a look at a different
10 portion of Vitti. I'd like to -- I'd like you to turn
11 to paragraph 127, and take a moment again to read the
12 full paragraph to yourself and let me know when you're
13 done.

14 A. Yes. Read it.

15 Q. Okay. Does paragraph 127 of Vitti discuss
16 formulations containing aflibercept?

17 A. Yes.

18 Q. Is it your opinion that paragraph 127 of
19 Vitti teaches formulations containing aflibercept that
20 have a concentration of aflibercept of up to 100 mg per
21 ml?

22 A. Yes.

23 Q. Does paragraph 127 of Vitti say anything
24 about specifically an aflibercept formulation with a
25 concentration of more than 115 mgs per ml of

1 aflibercept?

2 A. No.

3 Q. Did you take paragraph 127 into account in
4 rendering your opinions based on Vitti?

5 A. Yes.

6 Q. Now, when we started I had alluded to some
7 discussion that you had with counsel earlier on in the
8 deposition regarding paragraph 87 of Vitti, so I'd like
9 you to turn there now. And again take a moment and
10 please read the entire paragraph to yourself and let me
11 know when you're done.

12 A. I've read it. Yes.

13 Q. Okay. Now, the portion that was discussed in
14 Vitti -- you were focused on this language about 150
15 plus or minus 22.5 milligrams per milliliter of VEGF
16 antagonist. Does that ring a bell?

17 A. Yes.

18 Q. Okay. Does paragraph 87 of Vitti say
19 anything about a formulation containing specifically
20 aflibercept at a concentration of 115 mgs per ml?

21 A. No.

22 Q. Does the word aflibercept show up in
23 paragraph 87 at all?

24 A. No.

25 Q. Now taking a look -- so let's step away from

1 paragraph 87. I want to ask you about Vitti as a
2 whole, okay? Taking -- now considering the entire
3 disclosure of Vitti, does Vitti contain any disclosure
4 of a formulation containing specifically aflibercept at
5 a concentration of more than 115 milligrams per
6 milliliter?

7 A. No.

8 Q. Based on your review of Vitti is it your
9 understanding -- is it your opinion that a person of
10 skill -- a skilled formulator -- strike that. I'll
11 start over.

12 Based on your analysis of Vitti, is it your
13 opinion that a skilled formulator would have reasonably
14 expected to succeed in obtaining an aflibercept
15 formulation with a concentration of greater than 100
16 mgs per ml?

17 A. Yes.

18 Q. Based on your analysis of Vitti is it your
19 opinion that a skilled formulator would have reasonably
20 expected to succeed in obtaining an aflibercept
21 formulation with a concentration of up to 115 mgs per
22 ml?

23 A. Yes.

24 Q. Does that include 114.3 mgs per ml?

25 A. Yes.

1 Q. Okay. You can set aside Vitti. Now I want
2 to move on to Larson but before you go to Larson I want
3 to talk about -- I want to talk about a couple
4 paragraphs in your declaration, specifically paragraphs
5 123 and 125. We'll start with 125, okay? Let me
6 know -- when you're there, go ahead and read the full
7 paragraph to yourself and let me know when you're done.

8 MR. TRASK: I'm going to object to this
9 question as outside the scope of the examination. I
10 don't think I asked any questions about paragraph 125
11 of his declaration.

12 Q. All right, Doctor. Have you had a chance to
13 fully review paragraph 125?

14 A. Yes.

15 Q. Okay. So you recall discussion earlier today
16 counsel asked you regarding needle gauges for
17 intravitreal injections and also Larson?

18 A. Yes.

19 Q. Okay. Does paragraph 125 of your declaration
20 contain some of your opinions related to those issues?

21 MR. TRASK: Objection. Scope.

22 A. It mentions the gauge of needles in two
23 places, yes.

24 Q. Okay. And after having read paragraph 125 of
25 your declaration does it refresh your memory regarding

1 your opinion on the gauge of needles that can be used
2 for intravitreal injection?

3 MR. TRASK: Objection. Scope.

4 A. Yes. It does mention 30-gauge needle. It
5 also discusses the range of needle sizes that could be
6 used, between 18 and 32. And that's broader because it
7 talks about subcutaneous, intramuscular, and other
8 injections.

9 Q. Okay. Let's turn to -- again remaining on
10 topic of needle gauges for intravitreal injection, I
11 want to turn to paragraph 123 of your declaration, and
12 then take a moment to read that to yourself, and again
13 let me know when you're done and I'll ask my questions.

14 MR. TRASK: I'll be objecting to all
15 questions about paragraph 123 as outside the scope of
16 the examination as I didn't ask any questions about
17 this paragraph either.

18 A. Yes. I've finished reading it.

19 Q. Okay. Having reviewed paragraph 123, does
20 this refresh your memory regarding whether Larson
21 teaches any intravitreal formulations?

22 MR. TRASK: Objection. Scope.

23 A. Yes. It mentions Eylea, which is
24 aflibercept.

25 Q. Okay. And just to -- just for the record are

1 you referring to -- are you referring to the language
2 in -- the language that you quote regarding paragraph
3 167 of Larson?

4 MR. TRASK: Objection. Scope. Leading.

5 A. Yes. That directly talks about aflibercept.

6 Q. Is it your opinion that Larson teaches
7 formulations containing aflibercept?

8 MR. TRASK: Objection. Scope. Leading.

9 A. Yes.

10 Q. Okay. You can set aside Larson. Let's turn
11 to paragraph 113 of your declaration. And so I want to
12 talk about your -- some of your opinions regarding
13 expectation of success, okay?

14 A. Okay.

15 Q. And in paragraph 113 you provided your
16 opinion that a skilled formulator would have had a
17 reasonable expectation of success in obtaining an
18 aqueous pharmaceutical formulation for intravitreal
19 administration comprising at least 100 mgs per ml of
20 aflibercept, a VEGF receptor fusion protein that has a
21 viscosity of about 5 to 15 centipoise as required by
22 claim one. Did any of your testimony and discussion
23 with counsel today change that opinion?

24 MR. TRASK: Objection. Scope.

25 A. No.

1 Q. Okay. Let's go -- let's move on to paragraph
2 178. Okay. So in paragraph 178 you provided your
3 opinion that in light of Vitti a skilled formulator
4 would have reasonably expected to succeed in optimizing
5 for and obtaining a aqueous pharmaceutical formulation
6 for intravitreal administration with about 114 mgs per
7 ml of aflibercept. Did any of your testimony and
8 discussion with counsel today change that opinion?

9 MR. TRASK: Objection. Scope. Leading.

10 A. No.

11 Q. Okay. Let's turn to paragraph 189. Okay.
12 And so the first -- the first -- those two paragraphs
13 that we just went over, 113 and 178, were related to
14 ground one, and just table that. We are now in ground
15 two, paragraph 189 of your declaration. And in
16 paragraph 189 you provide your opinion that a skilled
17 formulator would have had a reasonable expectation of
18 success in obtaining an aqueous pharmaceutical
19 formulation for intravitreal administration comprising
20 at least 100 mgs per ml of aflibercept, a VEGF receptor
21 fusion protein that has a viscosity of about 5 to 15
22 centipoise as required by claim one. Did any of your
23 testimony and discussion with counsel today change that
24 opinion?

25 MR. TRASK: Objection. Scope. Leading. And

1 probably talking too fast for the court reporter.

2 A. No.

3 Q. Okay. Turn to paragraph 253. And in
4 paragraph 253 you provided your opinion that a skilled
5 formulator would have reasonably expected to succeed in
6 obtaining an aqueous pharmaceutical formulation
7 suitable for intravitreal injection with a protein
8 concentration of 114.3 mgs per ml based on Furfine,
9 Dix, and Fiedler as a matter of routine optimization.
10 Did any of your testimony and discussion with counsel
11 today change that opinion?

12 MR. TRASK: Objection. Scope. Leading.

13 A. No.

14 Q. Okay. All right. I want to change gears and
15 talk about your -- some of your testimony today
16 regarding your written description opinions, okay?

17 MR. TRASK: Objection. Foundation.

18 Q. I'll direct you to paragraph 36 of your
19 declaration. And again take some time to read the full
20 paragraph and let me know when you're done reading.

21 A. I've read it.

22 Q. Okay. Do you recall counsel asking you
23 earlier on in the day about this paragraph and in
24 particular the factors used to evaluate the sufficiency
25 of disclosure?

1 MR. TRASK: Objection. Foundation. Scope.

2 A. Yes.

3 Q. And so here you list certain factors, the
4 existing knowledge in the particular field, the extent
5 and content of the prior art, the maturity of the
6 science or technology, and the predictability of the
7 claimed method or invention. Is it your understanding
8 that these are the factors used to evaluate the
9 sufficiency of a disclosure for purposes of the written
10 description requirement?

11 MR. TRASK: Objection. Scope. Leading.

12 A. Yes.

13 Q. We can go through each one one at a time.
14 Did you consider and apply factor one in your written
15 description analysis which is the existing knowledge in
16 the particular field?

17 MR. TRASK: Objection. Leading.

18 A. Yes.

19 Q. Did that include what was known to skilled
20 formulators at the time of the alleged invention of the
21 '036 patent?

22 MR. TRASK: Same objection.

23 A. Yes.

24 Q. Did you consider and apply factor two, the
25 extent and content of the prior art?

1 MR. TRASK: Objection. Leading.

2 A. Yes.

3 Q. Did you consider and apply factor three, the
4 maturity of the science or technology?

5 MR. TRASK: Objection. Leading.

6 A. Yes.

7 Q. Did you consider and apply factor four, the
8 predictability of the claim method or analysis?

9 MR. TRASK: Same objection.

10 A. Yes.

11 Q. Do you recall testifying earlier that you
12 reviewed the full text of the '036 patent in your
13 analysis on written description?

14 A. Yes.

15 Q. In that analysis did you perform your
16 analysis from the perspective and background knowledge
17 of a skilled formulator at the time of the alleged
18 invention of the '036 patent?

19 MR. TRASK: Objection. Leading.

20 A. Yes.

21 Q. Okay. Staying on the topic of written
22 description, you recall counsel asking you some
23 questions about your opinions on the example
24 formulations notice '036 patent and their viscosity
25 data? Do you recall the discussion?

1 A. Yes.

2 Q. Does the specification of the '036 patent
3 including the examples include any viscosity data for a
4 bufferless, 100 mg per ml aflibercept formulation?

5 MR. TRASK: Objection. Scope.

6 A. No.

7 Q. Does the specification of the '036 patent
8 including the examples include any viscosity data for a
9 bufferless 114.3 mgs per ml aflibercept formulation?

10 MR. TRASK: Objection. Scope.

11 A. No.

12 Q. Does the specification of the '036 patent
13 include any examples include any viscosity data for a
14 bufferless 103 to 126 mgs per ml aflibercept
15 formulation?

16 MR. TRASK: Objection. Scope.

17 A. No.

18 Q. Does the specification of the '036 patent
19 including examples include any viscosity data for any
20 bufferless aflibercept formulation having a
21 concentration of more than 100 mgs per ml of
22 aflibercept?

23 MR. TRASK: Objection.

24 (Reporter clarification.)

25 MR. TRASK: Scope.

1 A. Could you repeat the question? Sorry. I was
2 distracted.

3 Q. Yes. Does the specification of the '036
4 patent including its examples include any viscosity
5 data for any bufferless aflibercept formulation having
6 a concentration of more than 100 mgs per ml of
7 aflibercept?

8 MR. TRASK: Same objection.

9 A. No.

10 MR. CHEN: Okay. No further questions. I'll
11 pass the witness.

12 EXAMINATION BY COUNSEL FOR THE PATENT OWNER,

13 REGENERON PHARMACEUTICALS, INC.

14 BY MR. TRASK:

15 Q. Doctor, you provided testimony in response to
16 about seven hours of questions that I asked today on
17 the record, correct?

18 A. Correct.

19 Q. Did you have your declaration in front of you
20 the entire time that you provided that testimony?

21 A. Yes.

22 Q. You were never denied access to your
23 declaration in providing that testimony, correct?

24 A. No.

25 Q. You provided all of your testimony today

1 under oath, correct?

2 A. Yes.

3 Q. And all of your testimony today is truthful
4 and accurate, correct?

5 A. Yes.

6 Q. And you stand by all of the questions --
7 strike that.

8 You stand by all of the answers you provided
9 in response to the questions I asked today, correct?

10 A. Correct.

11 MR. TRASK: No further questions.

12 COURT REPORTER: Confirming your copy order
13 and/or rough draft.

14 MR. CHEN: Yeah. Let's do the rough
15 expedited. How long does that take?

16 COURT REPORTER: The rough I can have to you
17 today.

18 MR. CHEN: Okay. Yeah. Let's do that. And
19 then what's standard delivery for the certified?

20 COURT REPORTER: 10 business days is
21 standard.

22 MR. CHEN: Okay. I think that's probably
23 fine.

24 COURT REPORTER: Okay.

25 MR. TRASK: And we already discussed

1 arrangements.

2 THE VIDEOGRAPHER: And we're going off the
3 record at 6:33 p.m.

4 (Off the record at 6:33 p.m.)

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1 Declaration Under Penalty of Perjury

2

3 I, Robert Falconer, declare under penalty of
4 perjury under the laws of the State of California that
5 the foregoing is true and correct; that I have read my
6 deposition and have made the necessary corrections,
7 additions, or changes to my answers that I deem
8 necessary.

9 Executed on this _____ day of
10 _____, 2026.

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Robert Falconer

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1 : : : CERTIFICATE OF REPORTER : : :

2

3 I, Kaylee G. Wood, a Certified Shorthand
4 Reporter, holding a valid and current license issued by
5 the State of California, No. 14348, duly authorized to
6 administer oaths, do hereby certify:

7 That the witness in the foregoing deposition
8 was administered an oath to testify to the whole truth
9 in the within-entitled cause;

10 That said deposition was taking down by me in
11 shorthand at the time and place therein stated and
12 thereafter transcribed into typewriting, by computer,
13 under my direction and supervision.

14 (X) Reading and signing was requested.

15 () Reading and signing was waived.

16 () Reading and signing was not requested.

17 Should the signature of the witness not be
18 affixed to the deposition, the witness shall not have
19 availed himself/herself of the opportunity to sign or
20 the signature has been waived.

21 I further certify that I am neither counsel
22 for nor related to any party in the foregoing
23 depositions and caption named nor in any way interested
24 in the outcome thereof.

25

26

27 Dated: This 29th day of May, 2026.

28 at Julian, California.

29

30

31

32

KAYLEE G. WOOD

33

CSR NO. 14348

34

1 CORRECTION CERTIFICATE

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2 To add testimony, indicate "Add" and print the exact
  words you wish to add. To delete testimony, indicate
3 "Delete" and print the exact words you wish to delete.
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5 Deposition of: Robert Falconer
Proceedings Date: May 27, 2026

7 I, Robert Falconer,
have the following changes to my proceedings
8 transcript:

9	PAGE	LINE	CHANGE TESTIMONY TO READ AS FOLLOWS:
10	_____	_____	_____
11	_____	_____	_____
12	_____	_____	_____
13	_____	_____	_____
14	_____	_____	_____
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22			

23 _____
 24 _____ Date _____

25 Robert Falconer