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UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF WEST VIRGINIA
Regeneron Pharmaceuticals, Inc.
Plaintiff,
VS. CIVIL ACTION NO.
1:22-cv-61
Mylan Pharmaceuticals, Inc., and
Biocon Biologics, Volume 7
Defendants.

- - -

Proceedings had in the bench trial of the above-styled
action on June 21, 2023, before Honorable Thomas S. Kleeh
District Judge, at Clarksburg, West Virginia.

- - -

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1 Wednesday Afternoon Session,
2 June 21, 2023, 9:00 a.m.

3 - - -

4 THE COURT: Day seven, I think, we convene for trial.
5 Counsel is present. Dr. MacMichael is on the stand. I believe
6 we're ready for redirect.

7 Is that correct, Counsel?

8 Madam Court Reporter is ready. You may proceed.

9 MR. SALMEN: Yes, Your Honor. For the first portion
10 of my redirect, I'm probably going to have to get into some
11 information that has been designated confidential. So pursuant
12 to your previous order, we ask for a sealed courtroom.

13 THE COURT: Understood.

14 In an effort to get everyone their steps in early
15 this morning, those of you not permitted to be here under the
16 Court's protective order, if I could ask you to step out. We
17 would certainly appreciate it.

18 We'll also ask the court security, once those folks
19 have vacated the premises, to seal our courtroom, please.
20 Thank you so much.

21 (The following proceedings (1527/23 to 1533/12) were
22 had under seal, and are filed under separate cover.)

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(Courtroom unsealed.)

THE COURT: Welcome back, everybody.
Counsel, you may proceed.

MR. SALMEN: Thank you, Your Honor.

BY MR. SALMEN:

Q. Dr. MacMichael, do you recall Mr. Berl asking you the question "Polysorbate in Claim 1 is being used as a surface-active agent to prevent aggregation and denaturation?"

A. I don't recall the specific question.

Q. That appears at trial transcript page 1455. Why don't we put that on the screen to refresh your recollection.

I'll give you a moment to read that.

A. Yes.

Q. Do you recall this question?

1 A. Yes.

2 Q. Let's take a look at the '865 patent Claim 1, please.

3 Claim 1 of the '865 patent does not require
4 polysorbate, does it?

5 A. It does not call out polysorbate.

6 Q. Dr. MacMichael, you were asked about Dr. Rabinow's
7 testimony. And to refresh your recollection, let's pull up
8 page 1482 to 1483.

9 Do you recall being shown this testimony from
10 Dr. Rabinow?

11 A. Yes, I do.

12 Q. And you see here Dr. Rabinow was being asked about
13 optimizing the stability of a protein formulation, a single
14 formulation, right?

15 A. Yes.

16 Q. Were you asked to provide an opinion regarding
17 whether the patent enables just a single formulation or whether
18 the patent enables the full scope of the universe of
19 formulations covered by the asserted claims?

20 A. Yes, I was asked.

21 Q. Were you asked whether the patent enables a single
22 formulation or whether the patent enables the full scope of
23 formulations covered by the asserted claims?

24 A. I apologize. I can't recall the specificity of that
25 question, but I can answer the question. But I believe it does

1 not give a description on how to make multiple formulations.

2 Q. Thank you.

3 Now, Dr. MacMichael, Mr. Berl asked you about undue
4 experimentation and your interpretation of that term. Do you
5 remember those questions?

6 A. Yes.

7 Q. Now, you've formed an opinion regarding the amounts
8 of experimentation required to practice the full scope of the
9 asserted claims; is that correct?

10 A. Correct.

11 Q. What level of experimentation, in your opinion, is
12 required for the person of ordinary skill in the art to
13 practice the full scope of the asserted claims?

14 A. It would take a significant amount of
15 experimentation.

16 Q. When you previously suggested that -- I'm sorry.
17 What was the term you used?

18 A. I used "significant" as opposed to "undue."

19 Q. Okay. When you previously suggested that significant
20 experimentation would be necessary, do you consider significant
21 experimentation to be undue in view of the full scope -- the
22 full scope of the '865 patent claims?

23 A. Yeah. I remember we had quite some discussion on
24 that.

25 Undue means so much experimentation that you wouldn't

1 be able to achieve it. What I was testifying yesterday is it
2 would be a significant amount of work, whether it was undue,
3 but it would take a lot of work on the part of the formulation
4 department. So --

5 Q. Now, Doctor -- I'm sorry.

6 A. I was just going to say whether you call that undue
7 or significant is a relative term.

8 Q. Dr. MacMichael, you were also asked by Mr. Berl
9 whether you identified any formulation that you would not be
10 able to make.

11 Do you recall those questions?

12 A. Yes.

13 Q. And is that the evaluation that you were asked to
14 make in determining enablement, whether you could not make a
15 certain formulation, or were you asked to form an opinion
16 regarding whether the skilled person could practice the full
17 scope of the claims?

18 A. I don't know if I can get to the specifics of the
19 question of how -- what was asked yesterday, but the second
20 part of the question was?

21 Q. Were you asked whether the skilled person could
22 practice the full scope of the asserted claims?

23 A. I believe I was.

24 Q. Dr. MacMichael, you were also asked about the
25 Kaisheva reference. Do you remember that one?

1 A. Yes.

2 Q. And in this line of questions Mr. Berl suggested that
3 the '865 patent informed the skilled person of an optimum pH
4 for the formulations in the asserted claims.

5 Do you recall that?

6 A. Yes, I do.

7 Q. And that appears for the record at trial transcript
8 pages 1488 to 1489.

9 Now, let's take a look at the '865 patent, Claim 1,
10 Dr. MacMichael.

11 Dr. MacMichael, is Claim 1 limited to a formulation
12 with a pH of 6.2 to 6.3?

13 A. No.

14 Q. The full scope of the formulation pH under Claim 1
15 would be much broader, right?

16 A. Well, it's not -- I don't see a definition for the
17 value of the pH in Claim 1, so one would assume it's broad.

18 Q. Now, let's take a look at Claim 4.

19 Is Claim 4 limited to a specific pH?

20 A. No.

21 Q. Let's take a look at Claim 5. Is Claim 5 limited to
22 a specific pH?

23 A. No.

24 Q. Let's take a look at the Kaisheva reference, Claim 1
25 of Kaisheva. This is DTX 3610, page 20 to 21. There is a copy

1 of it, Dr. MacMichael, in your cross-examination binder,
2 Volume 1, if that helps.

3 A. That's Volume 2. I'm sorry. Could you give me
4 the --

5 Q. Yes. DTX 3610. And I think Mr. Gibson has it up on
6 the screen now.

7 A. Okay. Okay.

8 Q. And you see there in the third line of Claim 1 it
9 reads "About 5 to 25 millimolar histidine buffer, having a pH
10 from about 5.5 to 6.5."

11 Do you see that?

12 A. Yes, I do.

13 Q. So, Dr. MacMichael, does the claim in the Kaisheva
14 reference identify the specific pH range?

15 A. Yes, it does -- it uses the term "about." Yes, it
16 does. It gives 5.5 to about 6.5.

17 Q. Right. And we don't see that specificity in the
18 '865 patent Claims 4 or 5, right?

19 A. No.

20 Q. Okay.

21 We can take that down.

22 Dr. MacMichael, you recall when Mr. Berl asked you
23 about certain internal documents from Regeneron where they used
24 the term "cosolvent," right?

25 A. Yes.

1 MR. SALMEN: And for the record, Your Honor, this is
2 at trial transcript pages 1476.

3 BY MR. SALMEN:

4 Q. Dr. MacMichael, you provided your opinion in this
5 case that polysorbate 20 is not -- sorry.

6 And you provided your opinion in this case that
7 polysorbate 20 is not an organic cosolvent in Mylan's product
8 under the Court's claim construction, right?

9 A. That's correct.

10 Q. Okay.

11 Mr. Gibson, you can take that down.

12 Were Mr. Berl's questions regarding the internal
13 Regeneron documents specific to the Court's claim construction?

14 A. I don't believe so.

15 Q. Do you have any idea whether Regeneron was applying
16 the Court's claim construction when it used the term
17 "cosolvent" in those internal documents?

18 A. No. I don't know the mind of the Regeneron
19 personnel.

20 Q. And would the person of ordinary skill in the art
21 have access to the Regeneron internal documents?

22 A. Well, they're internal documents. They're
23 confidential.

24 Q. Thank you.

25 Now, Dr. MacMichael, I'd like to ask you about when

1 Mr. Berl asked you several questions about preventing
2 aggregation using polysorbate. And I want to first ask you to
3 consider a hypothetical formulation of aflibercept without
4 polysorbate.

5 A. Okay.

6 Q. Are you with me?

7 A. Yes, I am.

8 Q. That solution would have to be in some kind of a
9 container, right?

10 A. Yes.

11 Q. And I believe you testified yesterday that protein
12 interactions with the surface of the container or interactions
13 with the air can result in protein adsorption which can lead to
14 aggregation. Was that right?

15 A. Yes. And denaturation.

16 Q. And denaturation. If I had the same solution in
17 three different containers -- one in a smooth glass, a second
18 in a jagged plastic container, and a third in a completely
19 rubber container -- are you still with me?

20 A. Yes, I am.

21 Q. The propensity for the protein to aggregate in those
22 various containers is going to be different, right?

23 A. Yes, it will be.

24 Q. Now, if I pick the best container, the one where the
25 protein showed the least amount of aggregation -- let's say the

1 glass. Okay? And I put my solutions in only glass, I would
2 have reduced the propensity for the protein to aggregate by
3 eliminating the rubber or the jagged plastic, right?

4 A. What you're saying -- you're saying -- through
5 experimentation, we demonstrated that we saw a greater
6 propensity in one container versus another? Is that your
7 question?

8 Q. Yes.

9 A. Yes.

10 Q. And so by putting it in the best container, I would
11 have reduced the propensity for the protein to aggregate now
12 that it's in the glass, right?

13 MR. BERL: Objection, Your Honor. This is leading.

14 THE COURT: Sustained.

15 BY MR. SALMEN:

16 Q. So, Dr. MacMichael, would you equate removing the
17 rubber interface which reduced the likelihood of protein to
18 aggregate the equivalent of using a cosolvent to increase the
19 protein solubility?

20 A. No, because if you start getting aggregation, that
21 container, once -- you might change the rate -- depending on
22 the container without polysorbate -- and, again, we're talking
23 hypothetical experimentation here -- once you initiated
24 aggregation, if you're going to see aggregation lesser in the
25 glass and faster in the rubber, ultimately, in the glass you're

1 still going to get -- hint at the final amount of aggregation.
2 So the rate might be different. So you'd need to add a
3 surfactant whether using glass or rubber to prevent that
4 aggregation.

5 Q. And would the fact that the surface is glass versus
6 rubber be the equivalent of adding a cosolvent to increase
7 solubility of the protein?

8 A. Well, first of all, adding a cosolvent -- we're using
9 a generic term -- "cosolvent" here -- to increase solubility?

10 Q. Yes.

11 A. The answer would be no.

12 Q. Thank you.

13 I think you also testified in response to Mr. Berl's
14 questions that adding hydrochloric acid to protein solutions
15 might cause aggregation by denaturing the protein; is that
16 right?

17 A. Yes. When you're adjusting the pH of a protein
18 solution, you have to be very careful that there's not -- as
19 you're adding it, that there's not high concentrations of acid
20 before it diffuses. In those areas, you can get denaturation.

21 Q. But would you then say that not adding hydrochloric
22 acid to my formulation would be the equivalent of using a
23 cosolvent to increase solubility?

24 A. No. It's two different things. The hydrochloric
25 acid would be a denaturing agent. And not using the

1 hydrochloric acid doesn't make it equivalent to using a
2 surfactant if that is the question.

3 Q. Thank you, Dr. MacMichael.

4 Last questions here, Dr. MacMichael.

5 You recall the analogy Mr. Berl presented to you
6 about driving your separate cars through a snowstorm, right?

7 A. Yes.

8 Q. Let me pose a similar hypothetical. But in mine
9 let's put the person skilled in the art of driving in snowy
10 conditions behind the wheel of the car. Okay?

11 Now, a person skilled in the art of driving through
12 snow would know that having a good set of snow tires on your
13 car is going to make that car sufficiently stable in the event
14 a snowstorm does occur, right?

15 A. Correct.

16 Q. And the skilled person might even have studded snow
17 tires which have been road tested and proven to be sufficiently
18 stable in pretty serious weather conditions, right?

19 A. Correct.

20 Q. And the skilled person of driving in the snow would
21 know the snow tires alone would be sufficient to prevent the
22 car from sliding off the road, right?

23 A. Correct.

24 Q. So adding chains on top of those snow tires would
25 merely provide the skilled person some added assurance; isn't

1 that right?

2 A. Correct.

3 MR. SALMEN: That's the end of my redirect, Your
4 Honor.

5 THE COURT: Thank you, Counsel.
6 Recross?

7 MR. BERL: Your Honor, I was going to start where
8 Mr. Salmen started; but, unfortunately, that's the confidential
9 document.

10 THE COURT: No. Understood.

11 Time for more steps, everyone. I'd like to ask you
12 to step out of the courtroom and ask court security to seal our
13 courtroom once everyone's had a chance to depart.

14 (The following proceedings (1544/16 to 1550/4) were
15 had under seal, and are filed under separate cover.)

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(Courtroom unsealed.)

THE COURT: Thank you, Officer.

Mr. Berl, you may proceed.

BY MR. BERL:

Q. Do you recall a few moments ago you were asked questions about the pH range and whether the claims in the '865 patent were limited to a particular pH range?

A. I recall the questioning around the pH, yes.

Q. You agree that the specification limits the formulation pH to within the range of 5.8 to 7, right?

A. If you could pull up the claims and the specifications, I'd like to see them so I can confirm.

Q. Let's just pull up your expert report, your reply report, PTX 62. This is your reply expert report, sir, correct?

A. I believe so, yes.

Q. And in the second to last bullet point on page 10 it says, "The pH. The specification only limits the formulation of pH to within the wide range of 5.8 and 7.0."

Do you see that?

A. Yes, I do.

Q. And that's a correct statement, right?

1 A. I made it.

2 Q. Now, finally, I want to ask you about the testimony
3 you gave about trying to distinguish between a formulation and
4 whether that's routine to make and multiple formulations.

5 Do you recall that in Mr. Salmen's questioning of
6 you?

7 A. Yes, I do.

8 Q. Doctor, just so everyone's clear, your opinion is
9 that protein formulations are routinely optimized to improve
10 the stability of their active ingredients, correct?

11 A. Yes.

12 Q. Not a protein formulation; protein formulations.
13 Right?

14 A. When I said protein formulations, I was talking about
15 the body of biotechnology and multiple companies and multiple
16 products. That's why I used the term in plural. Formulations
17 require significant amount of work. That was what I was
18 referring to.

19 Q. Okay. So final question. Protein formulations are
20 routinely optimized to improve the stability of their active
21 ingredients.

22 Do I have that right?

23 A. That's a fair statement.

24 MR. BERL: No more questions, Your Honor.

25 THE COURT: Rereredirect.

1 MR. SALMEN: No questions, Your Honor.

2 THE COURT: All right. Do we have any exhibits that
3 we need to -- one second, Doctor. Sorry.

4 MR. BERL: I just have two, Your Honor. I imagine
5 Mr. Salmen has a lot more than that. So maybe I'll just get my
6 two done, which are PTX 672 and PTX 1948.

7 THE COURT: Understood.

8 Any objection to those two documents?

9 MR. SALMEN: Let me just check, please.

10 THE COURT: Sure.

11 MR. SALMEN: Actually, Your Honor, we do object to
12 admitting those documents into evidence with this expert.
13 Those are the two Regeneron internal documents that
14 Dr. MacMichael stated he had not seen before. I don't think
15 this is the witness to properly authenticate those documents.

16 THE COURT: Mr. Berl.

17 MR. BERL: Yes, Your Honor. We can admit them
18 through someone else, but the point is we've been admitting
19 throughout the trial cross-examination testimony or -- and the
20 associated documents.

21 THE COURT: Is there any suggestion that these
22 documents are not actually authentic? That is a low
23 evidentiary hurdle the opponent has to climb over.

24 MR. SALMEN: We have no objection to their
25 authenticity, Your Honor. It's just -- and that was not the

1 basis of the objection, but these --

2 THE COURT: Then what is the basis?

3 MR. SALMEN: The lack of foundation with this expert.

4 THE COURT: With respect to authenticity. What other
5 foundation? They were used to cross the bases of the doctor's
6 many opinions, correct, Mr. Berl?

7 MR. SALMEN: I'll withdraw the objection, Your Honor.

8 THE COURT: With objection withdrawn, both of those
9 exhibits are hereby deemed admitted.

10 And, Counsel, if you want to review your list very
11 slowly, please.

12 (PTX 672 and PTX 1948 were admitted.)

13 MR. SALMEN: Yes. I'll go through them slowly, Your
14 Honor. DTX 0007, DTX 0030, DTX 2687, DTX 3463, DTX 3465,
15 DTX 3466, DTX 4116, DTX 4229, DTX 4430, DTX 5011, DTX 5012,
16 DTX 5053, DTX 5172, DTX 5196, DTX 5273, DTX 7087, DTX 8206,
17 DTX 8207, DTX 8208, and DTX 8209.

18 THE COURT: Any objection to any of those items on
19 the list?

20 MR. BERL: No, Your Honor.

21 THE COURT: Without objection, each of those shall be
22 deemed admitted.

23 (DTX 0007, DTX 0030, DTX 2687, DTX 3463, DTX 3465,
24 DTX 3466, DTX 4116, DTX 4229, DTX 4430, DTX 5011, DTX 5012,
25 DTX 5053, DTX 5172, DTX 5196, DTX 5273, DTX 7087, DTX 8206,

1 DTX 8207, DTX 8208, and DTX 8209 were admitted.)

2 THE COURT: Anything further we need from the good
3 doctor?

4 MR. SALMEN: No, Your Honor.

5 THE COURT: All right. Doctor, thank you so much,
6 sir. You can step down. I throw you back into the waters.
7 They're free to talk to you again.

8 THE WITNESS: Thank you.

9 THE COURT: Mylan may call its next witness.

10 MS. MAZZOCHI: Your Honor, Mylan does not have any
11 further live witnesses for its case in chief. I did, however,
12 before we closed yesterday we had talked about introducing
13 exhibits that were raised by Regeneron at Dr. Stewart's cross.

14 THE COURT: Correct.

15 MS. MAZZOCHI: We would like to move into evidence
16 PTX 3348, which is one of his publications that was used on
17 cross.

18 THE COURT: Any objection to 3348?

19 MR. GREGORY: No objection.

20 THE COURT: Without objection, 3348 deemed admitted.
21 (PTX 3348 was admitted.)

22 THE COURT: Were there any other loose ends from
23 Dr. Stewart's testimony in terms of exhibits?

24 MS. MAZZOCHI: I don't believe so. I think we got
25 all the rest of his exhibits into evidence.

1 THE COURT: Okay. Understood.

2 Regeneron, any remaining?

3 MR. GREGORY: Yes, Your Honor. Given that they're
4 moving 448, I'd like to take an opportunity to go back and take
5 a look at the other exhibits moved on cross and see if you
6 wanted to move a couple of those into evidence as well.

7 THE COURT: Continue to have Dr. Stewart's exhibits
8 at loose end then. That's fine.

9 So Mylan is resting its case in chief, correct?

10 MS. MAZZOCHI: Yes. With that, Your Honor, we would
11 rest our case in chief. And then as we had indicated
12 yesterday, however, Mylan does have some objections to the
13 witnesses and some of the deposition designations that
14 Regeneron is proposing to offer today.

15 I believe one of their next witnesses was going to be
16 Ms. Chu. There were objections that we had to Regeneron
17 calling her in her individual capacity to talk on particular
18 topics. I believe we filed a motion on that this morning.

19 THE COURT: I believe that you did, 6:49 a.m. It's
20 21 pages in length with attachments.

21 MS. MAZZOCHI: Yes. And I can certainly summarize
22 briefly what the issues are. And it's basically this.

23 THE COURT: Let's pause on that.

24 Given that Mylan has rested, are there any motions
25 from Regeneron at this juncture?

1 We'll come back to that.

2 MR. BERL: Yes, Your Honor. Regeneron moves for
3 judgment under Rule 52(c). I understand, Your Honor, that this
4 is a bench trial; so I'll be brief.

5 But I would note that beginning with the formulation
6 case, as it relates to invalidity, Mylan's combinations are
7 plainly deficient. Even taking their expert's testimony as
8 true, he failed to show multiple limitations of the claim were
9 met by the asserted combinations, including, but not limited
10 to, the requirement of an ophthalmologic formulation, which is
11 present in neither Fraser nor the Liu reference with which it
12 was combined; and the at least 98 percent native conformation
13 limitation, which is not present with respect to aflibercept in
14 any of their combinations and is not even tested for any
15 product or any molecule or any formulation with respect to the
16 combination of Fraser and Lucentis.

17 Absent a showing that all limitations of the claim,
18 the claim as a whole, is obvious, an obviousness case simply
19 cannot succeed.

20 With respect to the Dix reference, Mylan advanced no
21 evidence, zero, that the Dix application and the application at
22 issue here were not commonly owned or were not subject to a
23 common assignment by the same company, Regeneron. It's clear
24 from the face of that; they're all Regeneron's applications.
25 And, accordingly, under 35 U.S.C. 103(c), it cannot be used as

1 prior art for purposes of obviousness.

2 With respect to anticipation of Dix, even taking as
3 true everything their expert Dr. Rabinow said, regarding the
4 40 mg/mL limitation of the claim, it's just not there. He
5 relies only on the disclosure of 10 to 50 mg/mL, a range which
6 is not directed to aflibercept.

7 But in any event, the law is clear. Disclosure of a
8 range is not the disclosure of any number within that range,
9 and any anticipation argument that Mylan attempts to advance
10 simply is inconsistent with that controlling precedent, and so
11 it cannot succeed either.

12 Now, with respect to Section 112, Your Honor just
13 heard Dr. MacMichael, and the testimony was clear. He had
14 numerous opportunities, both on cross-examination and again
15 this morning on redirect, to tell Your Honor that the
16 experimentation to practice the claim was undue. He repeatedly
17 declined. And that's the standard from the *Wands* case all the
18 way down to *Alcon v. Barr*. It's routine experimentation or
19 undue experimentation.

20 They had two experts testify. We haven't gone yet,
21 of course. Their first expert, Dr. Rabinow, said it's routine.
22 Their second expert didn't disagree with that, and he doesn't
23 say it's undue experimentation either. You can't have an
24 enablement case without undue experimentation, and there's no
25 evidence that there is.

1 With respect to written description, he likewise
2 agreed that this claim recites structure and it's structurally
3 limited. The buffer is a known set of structures. The
4 stabilizing agent is a known set of structures. The organic
5 cosolvent in Claim 4 limited to polysorbate, that's a known
6 structure. The active ingredient, aflibercept, that's a known
7 structure.

8 These are known structures. A written description
9 case cannot lie where you are reciting structures in your claim
10 because the test for written description is whether a person of
11 skill can envisage or envision what you're claiming. Can they
12 recognize what it is?

13 And all of the foundational case from the Federal
14 Circuit, beginning with the *Wyeth* case and rapamycin all the
15 way to their en banc *Lilly v. Ariad* case stand for the
16 proposition that you can't just claim function, you can't say I
17 claim anything that will work without regard to what structures
18 it is, because the person of skill can't envision what
19 structures you are claiming.

20 That's not what we have here, according to
21 Dr. MacMichael himself. We have structures that are being
22 claimed. And Your Honor will search in vain for any claim that
23 is limited to structure which the Federal Circuit has said
24 doesn't meet the written description requirement in a situation
25 like this because, of course, you can envision is. He agreed

1 it's limited to structures.

2 The structures are known. And so it's, by
3 definition, something that the skilled artisan can envision.
4 They know this is in or this is out. If it doesn't have a
5 stabilizing agent, it's out. If it has one, it meets that
6 limitation. This is not some amorphous effort to claim only
7 function; and therefore, the written description requirement is
8 met as a matter of law.

9 Finally, with respect to indefiniteness,
10 Dr. MacMichael agreed that the person of ordinary skill can
11 understand the claims. He agreed that he lacks the expertise
12 to determine what is suitable and what is not suitable. And he
13 didn't consult with anyone, such as an ophthalmologist, who
14 would have that expertise.

15 So I submit, Your Honor, that we should have judgment
16 with regard to invalidity.

17 Regarding infringement, I actually think there are
18 not many factual disputes here between Dr. Trout and
19 Dr. MacMichael. Everyone agrees that, if you have polysorbate
20 in the formulation that Mylan has, more of the aflibercept
21 would be in solution under various conditions, conditions that
22 Your Honor has heard from every witness in the case are
23 important, such as going through the needle and creating the
24 shear stress that can make things fall out of solution.

25 THE COURT: Let me ask you this, Mr. Berl. Does the

1 label applied to polysorbate 20 matter? Is that a significant
2 issue or dispute?

3 MR. BERL: No.

4 THE COURT: Why not?

5 MR. BERL: The reason is that the question under the
6 Court's claim construction is does it increase the solubility
7 of the aflibercept?

8 It doesn't matter whether someone labels it a
9 stabilizing agent, a surfactant, or an organic cosolvent. The
10 reason is those are words. Words don't matter. Actions
11 matter. Is it actually increasing the solubility?

12 And Dr. MacMichael's own Graph 34 showed that it is.
13 Without polysorbate, it was going down like this. And I'm
14 showing for the record the curve where it's crashing out of
15 solution in the black on Slide 34. And he showed with
16 polysorbate, more is in solution. He agreed that that's what
17 happened, and Dr. Trout says that's what happened.

18 You could call it a stabilizing agent, a surfactant.
19 You can call it a duck. All that matters under Your Honor's
20 construction is is there more polysorbate -- is there more
21 aflibercept in solution with polysorbate than without? The
22 answer to that question I would say undisputedly, according to
23 this record, is yes.

24 I would also observe that "stabilizing agent" is a
25 general term. And one needs to ask what is it stabilizing

1 against? And I think both experts agreed what it's stabilizing
2 against is aggregation. And if it stabilizes against
3 aggregation, both experts testified clearly that aggregation
4 then leads to precipitation, which is the opposite of
5 solubility. You're either in solution or you precipitated out
6 of solution.

7 I don't think there's anything at all inconsistent
8 with calling this a stabilizing agent. That's not a problem
9 because it's stabilizing against it coming out of solution.
10 Put another way, it's stopping it from coming out of solution;
11 it's keeping it in solution. It is increasing the solubility
12 because there will be more with polysorbate in solution than
13 without polysorbate under various relevant conditions such as
14 shear stress.

15 So I don't think the label matters. As I've said
16 repeatedly, this is not some anthropomorphic exercise where the
17 polysorbate is running around saying, "I wonder what someone
18 calls me." That's not going on here.

19 We know what it's doing. It's stopping aggregation;
20 it's stopping precipitation; it's keeping the aflibercept in
21 solution. That's what the claim requires, more in solution
22 with than without and under relevant conditions.

23 I think both experts agreed. You can look at
24 Slide 34. That's exactly what's going on. Y axis there is
25 solubility of the aflibercept. If there's more with

1 polysorbate than without, I think that ends the infringement
2 inquiry, respectfully.

3 With respect to the method of treatment, happy to
4 answer any other questions Your Honor has.

5 THE COURT: Go ahead.

6 MR. BERL: With respect to the method of treatment,
7 Your Honor, we explained in our infringement case that their
8 label instructs practicing these claims. We heard no response
9 from them in their case, no expert testimony, no other
10 testimony indicating otherwise. The evidence is undisputed
11 that their label instructs use of the claim.

12 Now, if they have some argument that not everyone
13 practices the claim, that's not a defense to infringement under
14 35 U.S.C. 271(e), which is the section that we're addressing
15 here in this case. The *AstraZeneca* case clearly stands for
16 that proposition. We cited that in our pretrial papers.

17 It doesn't matter whether everyone practices the
18 claim. What matters is whether anyone practices the claim.
19 And the testimony was clear that some doctors practice the
20 claim. If that were not right, we would have heard an expert
21 for Mylan come in here and tell you that, but they withdrew
22 their noninfringement expert.

23 And so they have no contrary interpretation of the
24 evidence because the evidence is undisputed that some doctors
25 will practice this claim. They haven't disputed that their

1 label sets forth the claim. Under the *Warner-Lambert* case and
2 its progeny, that reflects Mylan's intent.

3 You can't say I didn't mean it, I don't really care
4 if people do it, I don't want to do it. That's not what
5 happens under Section 271(e). Your label reflects your intent.
6 The evidence is undisputed that their label hits every
7 limitation of the claim and instructs doctors to practice the
8 claim. That's sufficient for intent. That's the beginning and
9 the end of that inquiry.

10 With respect to invalidity on the method of treatment
11 claim, they have not advanced any argument that there are five
12 loading doses in the prior art for the DME and diabetic
13 retinopathy. It's just not there. They try to massage every
14 single reference they can to make three five or to may pro re
15 nata, prn, dosing somehow turn into five.

16 You heard yesterday from the witness stand from
17 Dr. Stewart that it's just not there. That's not what it says,
18 and they can't change what the prior art says. And based on
19 the record that they have created, there is no case of
20 obviousness because, again, every limitation in the claim as a
21 whole has to be obvious.

22 Finally, as to the Claim 6 of the '572 patent, you've
23 heard a lot of testimony about where the prior art was. It was
24 unclear what treatment regimens would go forward. The art was
25 trending away from the dosing regimen that is in the claim

1 here. Genentech had failed with their efforts to do extended
2 fixed dosing. People were moving toward pro re nata dosing.

3 Again, I don't think there are all that many factual
4 disputes on this point, and under the facts in the record,
5 there is no obviousness. It was not moving in the direction
6 where the claims went. And we did that, not anyone else.

7 With respect to their argument on the isotonic
8 limitation, Your Honor, they have not established how far
9 outside of the range of isotonic you would want to go or not
10 want to go. They had one witness testifying about this,
11 Dr. Albini, who said you wouldn't want to use something too
12 isotonic, over 800, because it could create some problems and
13 he provided a reference, but he declined to say how far outside
14 of that range of isotonic -- and we've seen what that is in the
15 record -- you would be willing to go or not willing to go.

16 And so while they have made some case crediting all
17 their evidence, as one does at the Rule 52 stage, that you
18 wouldn't want to venture too far, all the way over 800, they
19 have not made any case that you can't venture at all outside of
20 the isotonic range to practice the claims. So I think their
21 argument there is deficient as well.

22 So with that, obviously, open to any questions, but
23 we believe that we should have judgment at this stage on both
24 patents.

25 THE COURT: Understood. Thank you, Mr. Berl,

1 Counsel.

2 Ms. Mazzochi, my apologies. I had some reading
3 materials we discussed early this morning. This is my first
4 cup of coffee; so I somehow combined your name with
5 Mr. Rakoczy, name into one. I assume I'm not the first person
6 to do that, but with my apologies, ma'am, go right ahead.

7 MS. MAZZOCHI: No worries, Your Honor. I am used to
8 it. I got over that in about third grade, people
9 mispronouncing both my first and last names. So I'm good. As
10 long as you're not shooping me out in the courtroom, I'm happy.

11 All right. Your Honor, under 52(c), first of all,
12 I'll go in reverse order.

13 The plaintiffs have suggested -- as we stated in our
14 Rule 52(c) motion, we do not believe the plaintiffs have met
15 their burden, and similarly the evidence that we have set forth
16 in connection with our case in chief actually undermines
17 plaintiff's claims that it would be improper on the
18 infringement side to infer an intent to induce, not only
19 because of the miniscule number of individuals that they, in
20 theory, tried to come up with who might be practicing the
21 claims. They don't dispute that you have to first have a
22 direct infringer before you can have an active indirect
23 infringement. They simply don't have the proof on that.

24 Furthermore, the Federal Circuit case law is also
25 clear that, even if you want to assume a label indication is an

1 infringing one, if you have noninfringing label uses -- and
2 that discretion is left up to the clinical judgment of the
3 prescribing physician, which Dr. Csaky admitted it would be --
4 then there is no inference of an intent to deceive.

5 Furthermore, with regard to their issues with regard
6 to invalidity, they don't dispute that we really met our burden
7 because, again, they keep focusing on what was expressly stated
8 in a reference as opposed to what was inherently disclosed in a
9 reference. They have -- our experts were firm on that issue
10 that there was inherency through Dixon and other references.
11 Even their attempt to try to get Dr. Stewart to agree with them
12 backfired because he admitted that, as a person who is a
13 prescribing physician, if he was going to apply a prn dosing
14 regimen, he could easily envision how you could get to five
15 loading doses before you go to eight-week dosing. So that
16 pretty much backfired on them.

17 When it comes to obviousness, again, I'm not quite
18 sure exactly what Mr. Berl is really trying to argue here with
19 regard to the term "isotonic." If someone would have been
20 motivated to make the formulation isotonic, and the undisputed
21 evidence is that they would be, to say, "Well, I can come up
22 with some theory as to why something might not be isotonic"
23 does not negate the motivation of a person of ordinary skill in
24 the art to actually make the formulation obvious.

25 Likewise, when it comes to these particular dosing

1 regimens, the motivation in the art was very clear that there
2 was going to be -- that the doctors were already using
3 extension methods, including after a monthly loading dose
4 period. So the fact that Regeneron thinks that maybe they
5 optimized them at five, routine optimization is not something
6 that can be grounds for patentability.

7 With regard to indefiniteness and some of the other
8 Section 112 issues that Dr. Stewart identified, as Dr. Stewart
9 mentioned, Dr. Csaky has nothing in his expert report
10 suggesting that the particular disease indications he
11 identified will not work. So that nixes Claim 6.

12 And when it comes to the specification, again, the
13 fact that the number 4 or the number 5 might appear somewhere
14 in a specification does not satisfy the Federal Circuit's blaze
15 marks test.

16 So we have met our burden to show indefiniteness. We
17 have -- I'm sorry -- nonenablement, written description. We
18 put forth the evidence of indefiniteness. That wasn't even
19 addressed in terms of their inconsistent metrics that Regeneron
20 is trying to propose for the term "approximately." So we have
21 certainly met our burden on each of the elements with regard to
22 the dosing patents and all the defenses that we have raised.

23 With regard to the formulation, the '865 patent
24 claim, I'm sure Mr. Salmen will kick me off the podium if I say
25 anything wrong, and we'll probably want to add to it, but let

1 me just try to --

2 THE COURT: Probably in the form of a sticky note,
3 but go ahead.

4 MS. MAZZOCHI: We love those sticky notes, especially
5 if they are not going to keep a protein from falling out of
6 solution.

7 But, you know, on this question of aggregation,
8 again, what I think that Regeneron is really trying to do is
9 they are trying to renegotiate, reopen, and modify the Court's
10 claim construction. The claim construction was clear because
11 the scientific literature is clear that a cosolvent is
12 something that will in fact increase the amount of substance
13 that you have in solution.

14 And for all of the drama that's been going on back
15 here, nobody's disputing what the phenomenon is. It's just
16 that Dr. Trout is trying to say that, when you're preventing
17 aggregation, that's somehow the flip side of improving
18 solubility. It simply is not.

19 You know, Mr. Berl keeps saying you put more in
20 there. You are not putting more in there in the context of our
21 formulation. It starts in solution. It stays in solution.
22 And the fact that you've said, well, maybe you've put some
23 bumper guards up to make sure that you don't come out of
24 solution, that is not increasing the overall solubility of the
25 substance.

1 We're not starting at 30 mg/mL putting a material in
2 there and now it's getting us to 40 mg/mL. That's not --
3 what's what you actually use a cosolvent for. We're not
4 starting out with a lyophilized formulation that maybe was at
5 half the concentration stored that way for stability purposes.
6 Now we're going to add a cosolvent to it as we reconstitute it
7 so that we can expand the nature of the formulation. That's
8 not what's happening here.

9 All that's happening is we started at 40 mg/mL. We
10 stay at that concentration. And we don't need to have the
11 polysorbate in there to increase the concentration because
12 we're not increasing the concentration. We're not using it to
13 stuff more aflibercept into the existing formulation.

14 So, furthermore, when it comes to some of the
15 questions with regard to anticipation, again, I'm going to take
16 issue with Mr. Berl's suggestion that, when the prior art
17 disclosed 10 to 50, that that somehow is not good enough to
18 anticipate a milligram range of 40.

19 And the arguments that they're trying to make here
20 again, they either have an obvious and anticipation problem or
21 they have a Section 112 enablement problem and they also are
22 not going to be able to claim the benefit back to their earlier
23 applications. Because here again -- when the Federal Circuit
24 has identified situations where you have a range and you are
25 going to now say I've found something within the range I'm

1 going to call patentable, you also have the burden to come
2 forward and show that it's called a result-effective variable,
3 that there's something unique or special about this particular
4 point in the range that's not shared by other formulations that
5 are within the same scope of the range.

6 There is no evidence in the record that there's
7 something magical here about 40 mg/mL formulations that's
8 unique, distinct, and different from the 10- to 50-milligram
9 ones. And if it is, then their specification certainly hasn't
10 enabled the person of ordinary skill in the art how to identify
11 it, find it, or get there. And that's part of what our
12 Section 112 arguments are all about.

13 That's likewise the same argument that condemns their
14 ability to claim backwards in their priority applications. If
15 they're going to start to say that our particular
16 combination -- I call it their particular combination of the
17 jigsaw puzzle that's sitting in the claims.

18 If they want to say there's really something special
19 about each particular range that we've pinpointed as against
20 the prior art background of this being part of the normal
21 recipe that people were using -- a surfactant, a solubilizer, a
22 buffer -- then their specification doesn't enable it. And
23 that's why, again, they don't have any reason to say that these
24 are unique or distinct. And if they are, then it fails under
25 Section 112.

1 And that's why, Your Honor, we do keep getting back
2 to -- you know, again, Mr. Berl was saying, oh, well, look, we
3 can find some instances where somebody will routinely optimize
4 a formulation. Yeah, if you actually have an existing
5 formulation, there are routine steps that somebody can go
6 through to try to optimize it.

7 The problem is that these claims are not limited to
8 just a narrow scope or a narrow range. These claims in the
9 '865 patent are directed to an incredibly broad range. And
10 they have not actually taught the person of ordinary skill in
11 the art how to do that.

12 That's why -- when you start going through the undue
13 experimentation factors, that's why they exist to determine
14 is -- in the ultimate legal question for you, is it undue? Is
15 the amount of burden that the person of ordinary skill in the
16 art has to go through? Do we have broad claims? We sure do.

17 Are they saying the art is unpredictable when it
18 comes to the obviousness analysis? They sure are.

19 Are they saying things like, oh, a person of ordinary
20 skill in the art wouldn't be able to do these things because
21 they were teaching away with motivations against it? Yes.

22 So even when you have, then, the '865 patent in hand
23 and you ask the person of ordinary skill in the art would you
24 be able to make the full scope of what is claimed? the answer
25 then becomes no, not without a significant massive amount of

1 experimentation, where you are now back in trial-and-error
2 land.

3 So yes, could the person of ordinary skill in the art
4 take, for example, the existing census formulations that were
5 designed for intravitreal purposes and actually put them
6 forward -- you know, use them -- put aflibercept into them, for
7 example, or take the Fraser formulation that's existing and
8 optimize that? Of course they could.

9 But if you want to then say but what about -- but
10 Regeneron didn't limit themselves to just the narrow claim.
11 They went broad. And because they went broad, that's what the
12 *Amgen* case is all about. The minute you decide you're going to
13 go with a very broad claim, you better have the specification
14 disclosure to support it. And here, they simply don't.

15 So, Your Honor, I know that you're going -- I'm
16 assuming you're going to take all these under advisement and
17 these will be the subject of posttrial briefing; but, again,
18 that's essentially an outline of where things are here.

19 THE COURT: I'll ask you the same question counsel
20 asked Mr. Berl.

21 Why should polysorbate care what name we ascribe to
22 it?

23 MS. MAZZOCHI: I think that what we care about is the
24 Court's claim construction. The Court --

25 THE COURT: That's a living and breathing

1 construction, correct?

2 MS. MAZZOCHI: The Court's claim construction
3 contemplates a behavior profile.

4 THE COURT: Right. But that can change through
5 completion of trial, correct?

6 MS. MAZZOCHI: And that's exactly the point, is that
7 there are instances where polysorbate can behave as a
8 cosolvent, when it is driving more aflibercept versus your
9 starting point into solution.

10 That's not -- that is not what is happening here.
11 So -- and that's where we fundamentally just object to what
12 Dr. Trout is trying to do. He is trying to say that preventing
13 a protein from denaturing or preventing an existing amount of
14 protein from crashing out of solution, that that is somehow
15 equivalent to increasing the amount in solution. They're
16 fundamentally different things.

17 And I think that what you see, then, at least in
18 Mylan's BLA, is when we're using, for example, the terminology
19 that we do -- and I don't want to get -- I don't remember which
20 part is public or not.

21 But when we are talking about our -- things within
22 our BLA, we are making representations to the FDA this is the
23 behavioral consequence of what's happening. This is how it is
24 working. This is how it's functioning. This is how it's
25 behaving.

1 So our terminology that we have presented to the FDA
2 is describing how it's behaving in solution. And what we never
3 said is we are using this to make sure we can fit enough
4 aflibercept in the formulation in order to meet our
5 specification goals. If we did, it would be called a
6 cosolvent; since we're not, that's why it's not there.

7 So I agree that the Court should be looking at the
8 behavior of what's going on, but what they're trying to do is
9 refine the term "cosolvent" to give it a new scientifically
10 inaccurate reading. They're trying to basically graft the
11 function and behavior of a stabilizer, of a surfactant, into
12 the definition of cosolvent through semantic games. And we
13 just fundamentally disagree that that's appropriate to happen
14 here.

15 So I don't know if I've -- I don't know If I've
16 answered your question. Maybe I haven't answered your
17 question. But that to me is fundamentally where we're coming
18 from here.

19 THE COURT: It strikes me at this juncture -- I mean,
20 polysorbate 20, Tween 20, whatever we want to call it in terms
21 of what the substance is, is on the list of ingredients, right?

22 MS. MAZZOCHI: Sure.

23 THE COURT: There's no dispute about that. What
24 strikes me is the more operative dispute here is does it matter
25 whether or not the claims of the patent ascribe the right

1 moniker to it as to what its function is? Is that as
2 dispositive as I intuit at this point?

3 MS. MAZZOCHI: Yeah. And I think that it is
4 important because when the claim uses the term "cosolvent" --
5 and remember, Your Honor, they have claims that are specific to
6 polysorbate. That's Claim 51. So they had the ability to
7 say -- and they do have claims that say, "I hereby claim a
8 formulation with polysorbate in it, and we don't care about its
9 function. We don't care about its role."

10 They have those claims. Those aren't asserted here.

11 They've tried to use broader claims where they did
12 impart a functional concept, buffer, cosolvent, stabilizing
13 agent. They're trying to take those broad functionally defined
14 terms and say we're now going to cover this ingredient.

15 By the way, Your Honor, they also clearly thought
16 that the term "cosolvent" was different from a stabilizer.
17 They used both of those terms in Claim 1. So for Regeneron to
18 now turn around and say, oh, well, now I'm going to treat them
19 as if they are synonymous terms violates a whole host of claim
20 construction rules.

21 So here again, I understand -- and this is where I
22 think, Your Honor, there has been a lot that the parties have
23 agreed on. But what we fundamentally don't -- I mean, when it
24 comes to --

25 THE COURT: I may not need my second cup of coffee

1 after this, Counsel, all recently filed pleadings to the
2 contrary. But go ahead. We might just hear what all we've
3 agreed upon.

4 MS. MAZZOCHI: In the sense of the parties -- the
5 parties are not disputing what's in the formulation. They're
6 not disputing amounts in the formulation. And Regeneron, for
7 example, is not disputing that we have histidine. Histidine is
8 also helping to -- it performs a role within the formulation.

9 But if you start then getting away from, well, I'm
10 going to let them say that cosolvent can just mean anything
11 that helps or anything that prevents aggregation or anything
12 that helps prevent denaturation, that's fundamentally rewriting
13 the claims.

14 So they chose to put terms in their claims that had
15 functional aspects to them -- buffer, stabilizer, cosolvent.
16 Our evidence and everything that we've submitted to the FDA, we
17 submit, confirms we are not using that function with that
18 ingredient. We're not using polysorbate to achieve the
19 functional role of a cosolvent.

20 What is that functional role? It has to be
21 increasing, not keeping it in, not -- if you've got the same
22 number of players on the team or on the roster and you say I
23 want to increase the roster, that means you're putting more on.

24 But, by contrast, all we're saying is we've got
25 nonplayers on the field and we're just trying to make sure none

1 of them has to run off. That's not putting more people on the
2 roster; that's just trying to keep everything status quo.

3 What they're trying to say is that, well, if you're
4 trying to maintain the status quo, then somehow you're
5 increasing and you're changing something. It's just -- it's
6 not.

7 So that's why, you know, when it comes to what's
8 going on here, it is very important what they actually put in
9 their claim. And we can't start erasing those claim
10 limitations. We just can't.

11 And frankly, Your Honor, if they had wanted to make a
12 doctrine of equivalence argument, which it seems like they
13 might be trying to now make, they had every opportunity to do
14 that months ago. But then they also would have had to comply
15 with the Federal Circuit standards on equivalent function,
16 equivalent way, equivalent result, showing that they didn't
17 disclose but not claim things, which are legal restrictions.
18 They wouldn't have been able to meet those standards, which is
19 why we don't have a doctrine of equivalence analysis here.

20 So they offered literal infringement. They have a
21 claim construction. The claim construction requires that a
22 cosolvent has to actually help dissolve, get more things into
23 solution. And they haven't demonstrated that our ingredients
24 are going to do that.

25 Hopefully, that answers your question.

1 THE COURT: Understood.

2 MS. MAZZOCHI: Thank you.

3 THE COURT: Given the context of a bench trial
4 proceeding and the myriad of questions the Court has to sift
5 through, the Court's going to, under 52(c), decline to render
6 judgment at this point but proceed with hearing evidence on
7 that front.

8 Who will Regeneron's first rebuttal witness be?

9 MR. BERL: Your Honor, the first witness will be
10 Karen Chu.

11 THE COURT: All right. We're going to take ten
12 minutes at this point. I'll give Regeneron an opportunity to
13 respond to the motion concerning Ms. Chu, and we'll go from
14 there. We'll be at ease for ten minutes. Thank you.

15 (A recess was taken from 10:17 a.m. to
16 10:36 a.m.)

17 THE COURT: Regeneron's response to Motion 546.

18 MR. GREGORY: Good morning again, Your Honor.

19 THE COURT: Good morning.

20 MR. GREGORY: Your Honor, obviously, we have not had
21 a chance to fully brief this issue in response to the motion
22 that we received this morning at -- I believe it was around
23 7:00 a.m.

24 THE COURT: 6:49.

25 MR. GREGORY: I was close.

1 Respectfully, Your Honor, I think that we have a road
2 map for dealing with exactly this situation. We've -- we're
3 having this trial already. It's the same road map that we used
4 with Dr. Yancopoulos and Dr. Furfine. And that is,
5 respectfully, Your Honor, this is a bench trial. And I think
6 Ms. Chu should be able to take the stand, provide her
7 testimony.

8 If defense counsel feels that, in fact, we verge into
9 issues or material or documents that are inappropriate somehow
10 to use with Ms. Chu or to address through Ms. Chu, they could
11 raise that in the posttrial briefing or in the course of her
12 testimony.

13 I think that is, frankly, the beginning and end of
14 the issue. I'm happy to discuss with particularity some of the
15 arguments that I can discern from this brief that I've had a
16 little bit of time to digest now.

17 The overriding argument seems to be that Ms. Chu's
18 testimony -- the subject matter of her testimony is some sort
19 of surprise. I'm not sure how that can be the case. So the
20 facts are as follows:

21 Ms. Chu has been on our initial disclosures -- our
22 Rule 26 disclosures since --

23 THE COURT: Yes. I don't think there's any dispute
24 about that. She was deposed.

25 MR. GREGORY: And she was deposed for over seven

1 hours, a full day. You heard an hour of her testimony
2 yesterday.

3 THE COURT: I have not heard what the weather was in
4 the city of her deposition.

5 Sorry. I couldn't resist. Go ahead.

6 MR. GREGORY: So -- but to be clear, in those initial
7 disclosures starting back in September, in an interrogatory
8 response filed in January, in her deposition, in all these
9 places, Mylan-Biocon was informed what the subject matter of
10 her testimony would be. That's the conception, reduction to
11 practice of the inventions found in the '601 and the '572
12 patents as well as the clinical properties of aflibercept.
13 That's been consistent in every one of these written
14 communications.

15 Ms. Chu has been on both parties' witness lists since
16 the first witness lists were exchanged. I candidly don't know
17 how much more I can explain about what Ms. Chu's going to
18 testify to without actually putting on her testimony and
19 walking through it with Your Honor and with defense counsel
20 here.

21 THE COURT: Understood.

22 Counsel, she's been disclosed as a witness. You've
23 had the opportunity to depose her. I'll be candid with you.
24 I'm at a loss.

25 MS. MAZZOCHI: Sure. Your Honor, we were able to

1 depose her as a 30(b)(6) witness and a 30(b)(1). But at the
2 outset of her deposition, I put the initial disclosures in
3 front of her and said okay, what are you going to testify to at
4 trial?

5 THE COURT: Did you ask her what knowledge she had
6 about it?

7 MS. MAZZOCHI: Yeah. She didn't even --

8 THE COURT: The words matter. It's a completely
9 different question. I've read the exchange not only in the
10 last volley we had over Ms. Chu's testimony but also the motion
11 that was filed this morning.

12 The words matter. The objection to what are you
13 going to testify to at trial is, I think, a valid one. But
14 there's different questions that could have been asked, I
15 guess, is my point.

16 Let me get to this point as well. Ms. Chu testified
17 under oath. If she gets up here and all of a sudden has
18 learned a whole lot of new things that she didn't know at the
19 time, that sounds like a very compelling and rich
20 cross-examination that will weigh heavily in this Court's
21 assessment of her credibility.

22 But I'm not inclined -- I'll say I'm going to deny
23 the motion at this juncture. I don't think, as a matter of
24 law, it is proper to preclude her testimony consistent with the
25 Court's prior rulings. She was disclosed. She was deposed.

1 If she's changed her story or augmented her knowledge that she
2 did not have at the time, counsel is certainly welcome and no
3 doubt capable to expose that direct cross. So that motion will
4 be denied.

5 We'll take up the other motion with respect to
6 Drs. Ryder and Russell when we get to them if Regeneron intends
7 to call them.

8 Mylan may call its next witness -- I'm sorry.

9 Regeneron may call its next witness.

10 MR. GREGORY: Thank you, Your Honor.

11 Regeneron calls Ms. Karen Chu.

12 THE COURT: Counsel, before you begin, just a
13 warning, if I get a message that indicates I need to walk out
14 of here in 18 minutes because of traffic to retrieve a kid,
15 I'll let everybody know, but then we may take an early lunch
16 break today. Just FYI.

17 With apologies to you, Ms. Chu.

18 MR. GREGORY: Understand, Your Honor. I have a
19 4-year-old myself and I know how it goes.

20 THE COURT: Understood. I-79 has been a joy the last
21 few weeks.

22 With that, Counsel, you may proceed.

23 MR. GREGORY: Thank you.

24 **KAREN CHU, PLAINTIFF'S WITNESS, SWORN**

25 **DIRECT EXAMINATION**

KAREN CHU - DIRECT

1 BY MR. GREGORY:

2 Q. Ms. Chu, could you please introduce yourself to the
3 Court.

4 A. Yes. Good morning. My name is Karen Chu.

5 Q. Where do you currently work, Ms. Chu?

6 A. I currently work at Regeneron Pharmaceuticals in
7 Tarrytown, New York.

8 Q. And I want to come back and talk about how you got
9 there and your role. But just first, what is your job title at
10 Regeneron?

11 A. My current title is executive director of clinical
12 strategy and execution for ophthalmology.

13 Q. And what are your current responsibilities generally
14 in that role?

15 A. My responsibilities are that I oversee all of
16 ophthalmology clinical development alongside our therapeutic
17 area head. And that includes interacting with our research and
18 preclinical groups for molecules coming into the clinic as well
19 as the design, strategy, and execution of clinical trials.

20 Q. You mentioned just now clinical trials and clinical
21 development. Just so we're clear on what we're talking about,
22 what are clinical trials?

23 A. So clinical trials are the studies done in humans to
24 support bringing a therapeutic product to potential
25 commercialization.

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1 Q. So I want to back up now and talk a little bit about
2 how you got to where you are today. So can you give us a
3 little bit of background on your education.

4 A. Sure.

5 So I have a bachelor's of science in biology from Cal
6 Poly San Luis Obispo. And then I have a master's of science in
7 human nutrition from Columbia University.

8 Q. How did you come to work at Regeneron?

9 A. So at the end -- as part of my master's program, I
10 was required to complete thesis research. And I did that
11 research at St. Luke's Roosevelt Hospital in New York City and
12 was exposed to clinical research and clinical trials there.
13 They had an obesity clinical research unit.

14 And so I knew, coming out of my graduate program,
15 that I was interested in clinical research. I actually moved
16 back to California and was subsequently hired at Sequus
17 Pharmaceuticals as a clinical trial assistant.

18 Q. And where did you go from Sequus?

19 A. So from Sequus I subsequently worked for Purdue
20 Pharma as a regulatory compliance or clinical quality assurance
21 associate.

22 Q. And what was your next stop?

23 A. After that I went to a CRO, or a contract research
24 organization, called Barton & Polansky. And there I was a
25 clinical project manager helping to oversee the conduct of

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1 Phase IIIB clinical trials in HIV.

2 Q. So still doing clinical trial work at that point?

3 A. Absolutely.

4 Q. And from there what was the next stop in your career
5 path?

6 A. So after Barton & Polansky I was hired by GenVec.
7 They were a small gene therapy company based in Gaithersburg,
8 Maryland. And they did a lot of work in New York City with
9 their scientific founder at Cornell.

10 Q. What kind of diseases or disorders was GenVec looking
11 to treat?

12 A. So we had gene therapy products for both oncology
13 indications as well as a product that we were testing in
14 ophthalmology indications, specifically AMD at the time.

15 Q. And why did you ultimately leave GenVec?

16 A. So I was at GenVec for over four years. And towards
17 the end of my time there, there were some changes in the gene
18 therapy field that made it more difficult for the company to
19 stay funded. And we -- the company had to make some hard
20 decisions and laid off a number of people.

21 At that time I was not laid off, but it certainly
22 didn't portend for a positive future for the company. So I
23 started looking around for other opportunities at that time.

24 Q. Is that how you ultimately arrived at Regeneron?

25 A. Exactly. So I knew about Regeneron from mostly the

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1 oncology field, because at that time anti-VEGFs were presenting
2 brand-new data and were very much seen as a revolutionary
3 treatment. And so I knew that Regeneron had an anti-VEGF
4 product that they were developing as well as the fact that they
5 happened to be in New York, which was convenient.

6 Q. And just so we can put this kind of in time, what
7 year was it when you started with Regeneron?

8 A. I started with Regeneron in 2003.

9 Q. And what was your title at that point?

10 A. I was hired as a clinical trial manager.

11 Q. And what was your role at that point in 2003 when you
12 first started?

13 A. So primarily I was brought in to help implement and
14 execute the clinical trials. At that time we had mostly early
15 phase clinical trials. And having had experience in both
16 oncology and ophthalmology, I was a very good fit for the team
17 at the time. But my role quickly pivoted to being very much
18 focused on ophthalmology.

19 Q. And can you describe for the Court kind of how your
20 responsibilities at Regeneron have changed over the last two
21 decades in your time with the company.

22 A. Sure. So I've certainly -- my entire career at
23 Regeneron has been in ophthalmology. And, certainly, I have
24 been part of the Eylea development program really from the time
25 that it came from our preclinical group and entered the clinic.

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1 When I started at Regeneron, Regeneron was a small
2 company. We were only about 500 employees total. And in our
3 clinical and regulatory group, I think we were about 30 people
4 total. So everybody wore a lot of different hats. And I had
5 the great opportunity to be involved, really, from the very
6 beginning in discussions around development strategy as well as
7 had input into study designs, et cetera.

8 Q. Ms. Chu, do you have a medical degree or formal
9 medical training?

10 A. I do not.

11 Q. How is it that you're able to contribute to the
12 clinical research and development work at Regeneron without
13 that educational background?

14 A. Sure. So I have over 25 years of direct experience
15 in clinical development in various therapeutic areas but over
16 20 years of experience in ophthalmology and specifically in
17 retina clinical development.

18 Q. So I'd first like to discuss just a little bit
19 Regeneron's clinical development efforts for aflibercept for
20 the treatment of wet age-related macular degeneration. Is that
21 okay?

22 A. Sure.

23 Q. Just as some background to begin, can you remind me
24 what stage clinical trials did Regeneron ultimately perform of
25 aflibercept in wet AMD?

KAREN CHU - DIRECT

1 A. So we performed Phase I, Phase II, and Phase III
2 clinical trials in wet AMD.

3 Q. And what do Regeneron's Phase I clinical trials
4 entail in ophthalmology?

5 A. Yeah. So typically -- so with ophthalmology clinical
6 trials, our Phase I trials are relatively small. These are
7 considered first in human trials; so the primary purpose is to
8 get initial safety information.

9 So typically these trials would be less than 50
10 patients total, and we would be looking, as I said, to get
11 initial safety but also to do dose ranging and get additional
12 information around the kinetics of the drug and systemic
13 exposure to the drug.

14 Q. And what do Regeneron's Phase II ophthalmology trials
15 typically involve?

16 A. So Phase II trials are what we call proof-of-concept
17 trials. So these are the first trials where we're really
18 looking to get a confirmation of efficacy or biological effect.
19 And we're -- of course, we're always looking for additional
20 safety information. And typically Phase II trials tend to be a
21 bit larger, somewhere between, I would say, 100 to about 300
22 patients at the most.

23 Q. And how about Regeneron's Phase III ophthalmology
24 trials? What do those typically look like?

25 A. So Phase III trials are the pivotal trials that we

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1 plan to, if successful, hopefully submit to health authorities
2 to support a marketing application. And so these are trials
3 that are what we call powered for a statistical difference
4 between treatment groups. And they can typically be very
5 large, so on the order of hundreds to thousands of patients.

6 Q. Could you give us a sense of how long it typically
7 takes Regeneron to plan and execute its Phase III ophthalmology
8 trials?

9 A. So the planning for even the late phases of
10 development really begins very, very early in product
11 development. So even before we would bring a product into the
12 clinic, we would be looking at -- we would be laying out what
13 we think the clinical development plan would look like, and
14 that would include kind of a high-level review of Phase I,
15 Phase II, and Phase III clinical trials.

16 Obviously, as we conduct the clinical trials and
17 receive more information during development, we refine our
18 thoughts and our strategies around how we will move forward.
19 And so from the time that we would have that Phase II or
20 proof-of-concept data to the initiation of a Phase III
21 protocol, it would take somewhere between 18 months to a year.

22 Q. And how expensive is it for Regeneron to run a
23 Phase III ophthalmology clinical trial?

24 A. So our -- in my experience, our clinical trials
25 typically cost about 150,000 to \$200,000 per patient. So when

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1 you're talking about a trial on the order of, you know, 600 to
2 1200 patients, that can easily run in the hundreds of millions
3 of dollars.

4 Q. In your experience, does Regeneron typically disclose
5 publicly the details of its clinical trials or maintain those
6 details confidentially?

7 A. We're always very careful about ensuring that we have
8 confidentiality agreements in place, even when we're having
9 discussions with external experts about aspects of planning or
10 early, you know, decisions around indications to potentially
11 move into, et cetera.

12 And during the clinical trials all of the
13 investigators and their stuff operate under the clinical trial
14 agreements, which include a confidentiality clause.

15 Q. Now, are patients in Regeneron's clinical trials
16 subject to confidentiality agreements?

17 A. No, they are not.

18 Q. Have you ever heard of the term "investigator
19 brochure"?

20 A. Yes, I'm aware of that.

21 Q. Could you tell us what that is in your experience.

22 A. Sure. So the investigator brochure is a document
23 that summarizes all of the available data for that
24 investigational product. So it would detail important
25 information for an investigator to know, like the toxicology

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1 results, any safety information we have received from ongoing
2 or if completed clinical trials, as well as any information
3 from the class itself or what we know about the mechanism of
4 the drug.

5 Q. And do patients or subjects in Regeneron's clinical
6 trials get access to the investigator brochure?

7 A. No, they do not.

8 Q. Do patients in Regeneron's clinical trials know what
9 dosing regimen or arm of the trial they're in?

10 A. No. So, obviously, informed consent is a major
11 focus, and every patient who enters a clinical trial is
12 provided adequate time to ask questions and review the informed
13 consent form before agreeing to enter the trial. And we always
14 strive to put sufficient information into the informed consent
15 form so the patient understands the procedures and the design
16 of the study.

17 Typically, especially in Phase III trials, the
18 patients as well as the staff are masked to treatment
19 assignment or blinded to treatment assignment. So the patient
20 typically would not know what treatment assignment they were
21 receiving.

22 Q. Do patients in Regeneron's clinical trials know if
23 they're receiving -- in trials where a sham injection is
24 employed, do patients in those trials know if they're receiving
25 an actual injection as opposed to a sham injection?

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1 A. No, they do not. And the purpose of the sham
2 procedure is really to mimic as closely as possible without
3 actually piercing the globe, the intravitreal injection
4 procedure. So they're prepped in the same way and the needle
5 of the syringe -- or sorry -- the hub of the syringe is pressed
6 against the globe so the sensation is similar.

7 THE COURT: Counsel, if I could interrupt, and,
8 Ms. Chu, if this is outside your scope. So we're not talking
9 about a placebo. We're talking about a fake injection that
10 doesn't actually puncture the eyeball.

11 THE WITNESS: That's right.

12 THE COURT: Okay. All right.

13 THE WITNESS: If it helps you, I know --

14 THE COURT: None of this helps me. I'm still having
15 all manner of eyeball and contact fake discomfort. But go
16 ahead, ma'am. Sorry.

17 THE WITNESS: Well, I hope this will help you.

18 THE COURT: Thank you.

19 THE WITNESS: The way that these physicians complete
20 the intravitreal injection, the patient -- they certainly don't
21 come at the patient from right in front of their face with a
22 needle. So you -- typically, a patient is reclined in a chair,
23 and they prepare the injection behind the patient and they come
24 at them from behind so the patient really never has a chance to
25 see the syringe or the needle.

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1 THE COURT: Okay. Don't think that helped, ma'am,
2 but thank you.

3 Counsel, go ahead.

4 MR. GREGORY: I have the exact same question, Your
5 Honor.

6 THE COURT: The sneak attack sham injection.
7 Understood. Go ahead, Counsel.

8 BY MR. GREGORY:

9 Q. Ms. Chu, do patients in Regeneron's clinical trials
10 typically know the technical details of the product they're
11 being administered?

12 A. No. So the investigators brochure, obviously,
13 contains a high-level description of the product, but as we've
14 discussed, that's typically not provided to the patient.

15 Q. Do patients in Regeneron's clinical trials know the
16 formulation of the drug product they're being administered?

17 MS. MAZZOCHI: Objection, Your Honor. Calls for
18 speculation as to what the patients know.

19 THE COURT: Sustained.

20 BY MR. GREGORY:

21 Q. Does Regeneron provide information to the patients in
22 its clinical trials about the formulation of the drug product
23 they're being administered?

24 A. No, we do not.

25 Q. In the informed consent that is given to the patients

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1 as part of their participation in the clinical trials, it does
2 not contain that information, correct?

3 A. It does not.

4 Q. Do you recall a time frame in or around 2007 when
5 Regeneron was engaged in planning for its prospective at that
6 point Phase III wet AMD trials?

7 A. Yes. We actually began our development in DME
8 back -- all the way back beginning in 2004.

9 Q. What role did senior management play in those
10 development discussions around the Phase III trials?

11 A. Yeah. So as I've already mentioned, Regeneron was
12 and in many ways is still a small company, and so our senior
13 management has always been heavily involved in discussions
14 around the clinical development planning and strategy as well
15 as decisions around study design.

16 Q. Just for clarity, was it the -- what Phase III
17 planning began in 2004? Was it wet AMD? Was it DME? What
18 indications in that planning? What began then?

19 A. I mean, obviously, in 2004 we were already thinking
20 about development in DME, but in 2004 we were really focused on
21 what we felt was the initial indication or the priority
22 indication, which was neovascular AMD.

23 Q. What was Dr. Yancopoulos's typical role in those
24 discussions around Phase III wet AMD planning?

25 A. So Dr. Yancopoulos was heavily involved and certainly

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1 was part of many, many discussions related to the clinical
2 study designs and strategy, and ultimately he was the final
3 decision maker regarding aspects of the study design and
4 clinical development program.

5 Q. I'd like you to take a look at a document for me,
6 Ms. Chu. And you should have a binder in front of you, and
7 we're also going to put it up on the screen. But I'd like you
8 to take a look at PTX 0188.

9 Let me know when you have that in front of you.

10 A. Yes, I see that.

11 Q. And do you recognize this document?

12 A. Yes. This is an email from March 28, 2007, regarding
13 decisions that need to be made to facilitate the beginning of
14 the first AMD pivotal study.

15 Q. And I'd like you to take a look at item number --
16 just for clarity, you are a recipient of this email, right?

17 A. Yes, I am on this email as a recipient.

18 Q. It's dated March 28, 2007?

19 A. That's correct.

20 Q. And I'd like you to take a look at Item Number 2 in
21 the body of the email.

22 Can you please explain to the Court what was under
23 consideration at this time.

24 A. Yeah. So in this email we were planning on a
25 four-arm study with approximately 1,200 patients with the doses

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1 of .5 milligrams, 2 milligrams, and potentially 4 milligrams
2 with different intervals being considered, q4, q8, and q12.

3 Q. There hadn't been a decision yet on the exact dosing
4 interval?

5 A. At this time we had not made a final decision.

6 Q. Could you please take a look at Item Letter G at the
7 bottom of the email. Do you see that?

8 A. Yes, I see that.

9 Q. And so what is being discussed here?

10 A. So this was an action item for an internal meeting to
11 be set up; so that way we could make decisions -- have
12 discussions and make decisions about these elements that would
13 facilitate the finalization of the -- what we call the clinical
14 study concept document, which was the precursor to the clinical
15 protocol.

16 Q. And when was that meeting set for?

17 A. That was set for April 13th, 2007.

18 Q. Could you take a look back just briefly at that.

19 A. Oh, sorry.

20 Q. Just for clarity. The first line reads, "Kathleen to
21 set up a meeting next week, week of April 2nd."

22 A. Oh, sorry. The week of April 2nd.

23 Q. Let's look at DTX 227, which should also be in your
24 binder, and we'll also put it up on the screen.

25 Do you have DTX 227 before you, Ms. Chu?

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1 A. Yes, I see that.

2 Q. Do you recognize this document?

3 A. So this is an email from April 2nd, 2007.

4 Q. And you're a recipient of this email?

5 A. Yes, I am.

6 Q. And there's a -- the first line of the body of the
7 email reads, "Below is a summary of the decisions and actions
8 from the AMD Phase III program meeting," right?

9 A. Right.

10 Q. Could you please take a look at the decision bullet a
11 little bit further down the page and explain to us what
12 decision had come out of this meeting.

13 A. So we had made a decision about the study design and
14 the arms that would be included in the Phase III -- one of the
15 Phase III AMD studies, the 0605 study, which was the VIEW 1
16 study. And we were planning to include a Lucentis group as a
17 control, .5 milligrams aflibercept every four weeks,
18 2 milligrams every eight weeks after three initial monthly
19 doses, and a 2-milligram-every-four-week group.

20 Q. Ms. Chu, do you specifically recall how that decision
21 was made in this meeting?

22 A. I do not specifically recall.

23 Q. What was the typical practice at Regeneron for making
24 these type of clinical trial design decisions?

25 A. So typically the study team would be charged with

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1 coming to our senior management with proposals and any
2 supporting data or other aspects of the program that would
3 support our proposals, and then we would have a discussion
4 about it with senior management. And then ultimately a final
5 decision would be made about how to move forward.

6 Q. What was Dr. Yancopoulos's typical role in those
7 decisions?

8 A. Dr. Yancopoulos was very involved in the discussions
9 as well as in any analysis of data. He very often would ask
10 for additional data or additional analyses to be presented, and
11 he was ultimately the final decision about the study -- the
12 groups that went into the study.

13 Q. I want to direct your attention to the final action
14 item, the bottom of the email. It says, "Discussed proposed
15 development plan with Darlene Jody," and then it's Bob, George,
16 Peter.

17 Who was Darlene Jody?

18 A. Darlene Jody was with Bayer at the time. She was a
19 senior executive responsible for the collaboration that we had
20 with them for Eylea.

21 Q. Did Bayer make the Phase III trial design decision
22 that we just saw in the upper part of this email?

23 A. No, they did not. The nature of our collaboration
24 with Bayer was such that Regeneron held the final scientific
25 decision-making for the program. So while we would certainly

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1 have discussions with them and include members of their team
2 both at the team level as well as the senior management level
3 in our meetings and discussions about aspects of the clinical
4 development program, ultimately Regeneron had the final say.

5 Q. If Bayer had come up with a decision that we were
6 looking at in the upper part of the email, would the final
7 action item here have been discussed, proposed development
8 plan, with Bayer?

9 A. Well, they would probably have a set of minutes that
10 said they should discuss it with us.

11 Q. Okay. Let's take a look -- let's turn our attention,
12 actually, to the question of Regeneron's development of
13 aflibercept for the treatment of diabetic macular edema. Okay?

14 A. Sure.

15 Q. And I may slip from time to time and call diabetic
16 macular edema DME, but you'll understand what I'm talking
17 about, right?

18 A. Yes.

19 Q. Approximately when did Regeneron begin its clinical
20 development of aflibercept for the treatment of diabetic
21 macular edema?

22 A. Yeah. So like I already said, we actually began in
23 2004 with a study utilizing intravenous delivery of aflibercept
24 for the treatment of DME.

25 Q. And that was a Phase I study?

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1 A. Yes.

2 Q. Did you eventually also do a Phase I intravitreal
3 study?

4 A. We did. So we eventually did a small study with five
5 patients with intravitreal delivery.

6 Q. Did Regeneron perform Phase II studies in DME?

7 A. Yes. So we conducted the 0706, or DA VINCI study,
8 which was a Phase II study in diabetic macular edema.

9 Q. Did Regeneron perform or conduct Phase III clinical
10 studies in DME?

11 A. Yes. Our Phase III studies were called VIVID and
12 VISTA.

13 Q. I want to put another document before you. I want to
14 direct your attention to, actually, a pair of documents that go
15 together. One is PTX 3150 and the next is PTX 3151, both of
16 which, again, should be in your binder. And we'll put the
17 first of them up on the screen right now.

18 A. Okay.

19 Q. Do you recognize this document, 3150?

20 A. Yes. So this is an email from May 2nd, 2007, with a
21 high-level summary of a DME planning teleconference.

22 Q. Did you attend that DME planning teleconference?

23 A. Yes, I did.

24 Q. So I want to take a look now at the attachment to
25 PTX 3150. This will be PTX 3151.

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1 Do you recognize this document?

2 A. Yes. So this is a summary of the discussion at that
3 same teleconference.

4 Q. And I want to direct your attention up to the
5 attendees list at the top of the document here. Could you let
6 me know or tell me who the external doctors were who attended
7 this teleconference.

8 A. Sure. So Dr. Lloyd Aiello from Harvard University,
9 Neil Bressler from Wilmer Eye Institute, Quan Nguyen also from
10 Wilmer Eye Institute, and Dr. Jeff Heier from Ophthalmologic
11 Consultants of Boston.

12 Q. Did Regeneron have questions for those assembled
13 doctors about the nature of diabetic macular edema?

14 A. Yes, we did.

15 Q. And I want to take a look at the first bullet here,
16 the first item. Coming out of this call with these assembled
17 doctors, what was your understanding about the progression and
18 the nature of DME relative to, for example, wet AMD?

19 A. Yeah. So I think we understood that, first, this is
20 a very different eye disease because it stems from, obviously,
21 the underlying diabetes that these patients have; and we wanted
22 to know more about exactly how these patients are diagnosed,
23 treated, et cetera.

24 And out of this teleconference we had a better
25 understanding that DME is -- can be not only a slowly

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1 progressive disease but also one that fluctuates much more than
2 AMD.

3 So in AMD the typical course for patients was that,
4 within the year after diagnosis with neovascular AMD, patients
5 would precipitously lose vision and that vision could not be
6 regained. But in DME we understood that vision is often more
7 recoverable. And so it was a very different disease from that
8 perspective.

9 THE COURT: Yes, Counsel.

10 MS. MAZZOCHI: Your Honor, I think now we're starting
11 get to the point where Ms. Chu is offering the equivalent of
12 expert testimony. She's just expounding on DME generally, not
13 what did she know back at that time period. She's offered as a
14 30(b)(1).

15 THE COURT: Understood.

16 Stay within the lane of Ms. Chu's capacity as a
17 witness here, Counsel.

18 MR. GREGORY: Yes, Your Honor. My question was
19 specifically about her understanding coming out of this
20 meeting. I'll try to keep it to that narrow lane.

21 THE COURT: Understood.

22 BY MR. GREGORY:

23 Q. Ms. Chu, I want to direct your attention to the third
24 bullet on this page, and I want -- I'm asking some narrow
25 questions here, okay, with the Court's guidance in mind.

KAREN CHU - DIRECT

1 Did Regeneron pose to the assembled doctors on this
2 teleconference any questions about the treatment outcomes of
3 patients with DME?

4 A. Yes. So we were obviously very interested in the
5 current treatment landscape as well as their expectations
6 around what outcomes they could expect or anticipate with the
7 current treatments available, including laser and steroid.

8 Q. And, again, I want to be narrow here. What was your
9 understanding at the time, including coming out of this call
10 with these doctors, about those treatment outcomes?

11 MS. MAZZOCHI: Your Honor, I'm just going to object
12 as well to the relevance of this. We're all -- the questions
13 that are before the Court relate to the validity of these
14 patents with regard to the perspective of a person of ordinary
15 skill in the art. And to the extent she's been offered on
16 issues relating to conception or reduction to practice, again,
17 we don't think that it's been established that she has
18 knowledge on that.

19 But going through all this history is not really
20 relevant to any of the issues here. I'm concerned, again, that
21 Regeneron is trying to just -- actually, I'm not going to
22 predict what's going on in their heads.

23 I'm just going to object that it's not relevant to
24 the issues before the Court.

25 THE COURT: How is this line of questioning relevant,

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1 Counsel?

2 MR. GREGORY: Of course, Your Honor. While the
3 Federal Circuit has been very, very clear that the inventor's
4 path to the invention cannot negate the invention or prove
5 obviousness, the Federal Circuit has also been equally clear
6 that the inventor's efforts, the roads that they went down, the
7 roads that they did not go down, their understanding can be
8 relevant to, for example, the motivation to combine elements of
9 the prior art or whether there was a reasonable expectation of
10 success.

11 Ms. Chu is here talking about the clinical
12 development. Dr. Yancopoulos's invention occurred within the
13 context of the clinical development program. They didn't occur
14 in a vacuum. It was in the context of this program and
15 Regeneron's understanding of these disease states at the time
16 and of what was going on in the world at this time, and Ms. Chu
17 is providing some of that.

18 THE COURT: Understood. Overruled.

19 MR. GREGORY: Your Honor, I'll move on from this
20 document quite quickly.

21 BY MR. GREGORY:

22 Q. I want to look at Item Number 1 once more along with
23 an item from the -- I believe it's the third page of the
24 document. We put it up on the screen here.

25 I want to understand if Regeneron asked the doctors

KAREN CHU - DIRECT

1 that it assembled about the available DME treatment options at
2 this point in time.

3 A. Yes. So we absolutely had a discussion about
4 available treatments. And, you know, certainly, as I already
5 mentioned, laser and steroid were being used as treatments for
6 DME, and we also understood that the patient's underlying
7 diabetic status was something that was a focus for these
8 physicians as well.

9 Q. I have one more question about this document,
10 Ms. Chu. Can you look at -- I think it's the final page, Item
11 Number 5.

12 Do you see there's a question there or there's an
13 item about competitive landscape and a reference to Lucentis?
14 Do you see that?

15 A. I do see that.

16 Q. What is Lucentis?

17 A. So Lucentis is another anti-VEGF molecule that was
18 being developed by Genentech.

19 Q. And was Regeneron monitoring the status of Lucentis's
20 development?

21 A. Yes. We were very interested in the status as well
22 as their decisions around development with Lucentis.

23 Q. I want to move to a different document. This is
24 going to be DTX 8190, which again should be in your binder. I
25 will also put it up on the screen.

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1 A. Okay.

2 Q. Do you have DTX 8190 before you?

3 A. Yes, I do.

4 Q. Do you recognize this document?

5 A. Yes. So this is a summary of the EMEA's scientific
6 advice procedure that was requested by Bayer.

7 Q. And I want to look -- and Bayer was your
8 codevelopment partner at the time?

9 A. Correct.

10 Q. I want to take a look at the third page of the
11 document, and there's a sentence about midway down -- we have
12 it called up right here -- the sentence that begins "based on
13 this experience."

14 Do you see that sentence?

15 A. Yes, I do see that.

16 Q. First, just to be clear, whose position is being set
17 forth here? Is this Bayer's?

18 A. No. So this would be the joint position between
19 Bayer and Regeneron.

20 Q. And I just want to be very clear. The sentence
21 reads, "Based on this experience, we believe that the doses and
22 dosing intervals for VEGF Trap-Eye for Phase III in DME can be
23 selected based on the results of the Phase II study in patients
24 with AMD."

25 Do you see that?

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1 A. I do see that.

2 Q. To be clear, was it Bayer or Regeneron's position
3 that they could predict the success of a dosing regimen to be
4 employed in the Phase III trial solely on the basis of this
5 Phase II data?

6 MS. MAZZOCHI: Objection, Your Honor. Again, this is
7 attempting to elicit expert testimony. To the extent
8 Mr. Gregory said that this was going to be relevant to anything
9 on reasonable expectation of success, reasonable expectation of
10 success is assessed from the perspective of a person of
11 ordinary skill in the art. So this is not relevant to that
12 question.

13 If their expert wanted to rely on it because he
14 thought it was relevant to his opinion, he could have. He
15 didn't. So we don't need this -- so this witness's testimony
16 is simply not germane to that issue.

17 MR. GREGORY: Again, Your Honor, the inventor's path
18 can be reflective of, in support, a lack of reasonable
19 expectation of success and a lack of motivation to combine the
20 elements in the prior art. This is a Regeneron -- as she just
21 testified, a Regeneron and Bayer joint document that she saw at
22 the time. I'm asking her to clarify the meaning of this
23 sentence.

24 THE COURT: Understood. And we're going to hear from
25 experts, Counsel, presumably on this very point. Her testimony

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1 is not going to be credited with that respect. This strikes me
2 as background and factual information leading up to what we're
3 going to hear from the experts.

4 Objection overruled.

5 BY MR. GREGORY:

6 Q. I'm not sure if I actually got an answer to that
7 question; so I'm just going to repeat it.

8 Looking at this first sentence that reads, "Based on
9 this experience, we believe that the doses and dosing intervals
10 for VEGF Trap-Eye for Phase III and DME could be selected based
11 on the results of the Phase II study in patients with wet AMD."

12 But you had that sentence. My question was, to be
13 clear, was it Bayer or Regeneron's position that they could
14 predict the success of a dosage regimen employed in the
15 Phase III trial solely on the basis of the Phase II data?

16 A. So, obviously, with any scientific experiment there's
17 the possibility of failure. And although we understood that
18 DME, like neovascular AMD, is a disease driven by
19 overexpression of VEGF which causes the pathological
20 neovascularization, we also understood that DME was a very
21 different disease.

22 And so typically in our interactions with health
23 authorities, our approach is to ask questions around minimum
24 requirements. And so this was a question intended to frame
25 support for our proposal in the document but not one that was

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1 predictive of what we expected from the Phase III studies
2 certainly.

3 Q. I want to now shift gears and take a look at a new
4 set of documents. These are going to be PTX 3167 and 3168.
5 Again, it's a paper and an attachment that go together.

6 Will you please let me know when you have them in
7 front of you, Ms. Chu.

8 A. Yes, I have them in front of me.

9 Q. So do you recognize PTX 3167?

10 A. So 3167 is an email dated January 31st, 2008,
11 highlighting some scenarios for a meeting that would be held
12 the same day.

13 Q. And the first sentence says, "Enclosed are the DME
14 scenarios that the team has put together for today's meeting"?

15 A. Right. So there was an attachment with a PowerPoint
16 presentation intended to be presented and discussed at the
17 meeting.

18 Q. There's an acronym on this page, JSC. Can you tell
19 us what the JSC was.

20 A. So JSC stands for joint steering committee. And as
21 part of our collaboration agreement with Bayer, we had several
22 joint committees that were formed. The joint development
23 committee was charged with overseeing all development of Eylea
24 and included members from both Regeneron and Bayer. And the
25 joint steering committee was the senior-level committee that

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1 included members from both companies.

2 Q. I want to now look at the attachment. So this is
3 PTX 3168. And in particular I want to take a look at the
4 second page -- or the second slide.

5 This is a slide titled "DME Target Product Profile,"
6 right?

7 A. Yes.

8 Q. What is a target product profile at Regeneron?

9 A. So a target product profile is a document that we
10 typically put together early in development just highlighting
11 at a high level what we see as the sort of minimal as well as
12 target claims that we would like to strive for for our product
13 to be commercially viable or commercially successful.

14 Q. So to be clear, these TPPs -- these are a regularly
15 prepared type of Regeneron document?

16 A. Yes.

17 Q. And these are commercial documents?

18 A. Typically they're driven by commercial. Clinical
19 obviously has input in terms of the end points and
20 expectations, but this is typically charged -- the
21 responsibility of our commercial group.

22 Q. How many monthly loading doses were set forth in the
23 TPP at this point in time?

24 MS. MAZZOCHI: Again, Your Honor, she's talking
25 about -- she's talking about Regeneron documents, Regeneron's

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1 perspective. She's being offered in her 30(b)(1) capacity.
2 She's testified this is a joint collaborative document between
3 Regeneron and Bayer.

4 This is not relevant to any of the issues relating to
5 the commercial success or the motivation or any of the things
6 that Mr. Teagan identified. It's not even relevant to his
7 inventor's path because the cover email said that
8 Mr. Yancopoulos was not present at this meeting. So how can
9 this be in any way, shape, or form relevant to either
10 Dr. Yancopoulos's path or --

11 THE COURT: Commercial success.

12 MS. MAZZOCHI: -- commercial success.

13 THE COURT: Counsel?

14 MR. GREGORY: Your Honor, again, it's the path to the
15 invention. And this invention occurred in the context of this
16 broader clinical development program. There is no, I think,
17 dispute about that. All right? It was part of the clinical
18 development program that these inventions occurred in.

19 The path to that invention is relevant to both the
20 motivation to combine elements of the prior art as well as
21 reasonable expectation of success. The roads that Regeneron
22 did go down, the roads that it did not go down, the walls they
23 bumped their heads against, that all goes to those issues.

24 I'm looking at here Regeneron's path to get to five
25 loading doses. And as we see, there's no five loading doses on

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1 this page.

2 MS. MAZZOCHI: And, Your Honor, again, motivation,
3 reasonable expectation of success is assessed from the
4 perspective of the person of ordinary skill in the art based on
5 the prior art that was available at the time. These are
6 Regeneron's internal documents. That's completely irrelevant
7 to that question.

8 MR. GREGORY: Your Honor, I would point the Court to
9 *Micro Chemical v. Great Plains Chemical*, 103 F.3d 1538, which I
10 think is clear on this point.

11 THE COURT: Understood. Overruled.

12 MR. GREGORY: We can set this document aside.

13 BY MR. GREGORY:

14 Q. We've talked a little about Regeneron's planning for
15 its own clinical trials. I think you mentioned previously that
16 Regeneron was also monitoring the clinical trial work being
17 performed by the folks who were developing Lucentis.

18 Do you recall that?

19 A. Yes.

20 Q. And those companies that was Genentech and Novartis,
21 right?

22 A. Right. So Genentech had rights to Lucentis in the
23 United States and Novartis outside of the United States.

24 Q. Did Genentech and -- or let's frame it like this:
25 Was Lucentis approved for treatment of diabetic macular edema

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1 in 2010?

2 A. No. I believe they received their approval for DME
3 in 2012.

4 Q. And were they approved for -- was Lucentis approved
5 for the treatment of diabetic retinopathy in 2010?

6 A. No. That came subsequent to their DME approval.

7 Q. Was Lucentis being explored in clinical trials for
8 the treatment of DME in 2010?

9 MS. MAZZOCHI: Again, Your Honor --

10 THE COURT: Stop saying "again." What's the
11 objection?

12 MS. MAZZOCHI: I object that he hasn't established
13 this is her own personal knowledge. Again, she --

14 THE COURT: Understood. Sustained.

15 BY MR. GREGORY:

16 Q. Ms. Chu --

17 MR. GREGORY: May I try to lay a foundation, Your
18 Honor?

19 THE COURT: I would encourage you to do so if you
20 want an answer to that question ultimately, yes, sir.

21 MR. GREGORY: Thank you.

22 BY MR. GREGORY:

23 Q. Ms. Chu, were you monitoring -- you personally
24 monitoring the status of Lucentis's clinical development in
25 mid-2010?

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1 A. Yes. It was part of my role to understand what the
2 competitive landscape was.

3 Q. Did you have an understanding of -- I'm asking a
4 narrow question right now.

5 Did you have an understanding of what clinical trials
6 were -- of any clinical trials that were being performed with
7 Lucentis in 2010?

8 A. So the Phase III RISE and RIDE trials were ongoing as
9 well as, during that period of time, Novartis had a couple of
10 studies called the RESOLVE and RESTORE trials.

11 Q. And did you personally have knowledge of what the
12 dosing regimens were that were being tested in those trials in
13 2010?

14 A. So in RISE and RIDE, it was both .3 and .5 milligram
15 monthly compared to sham. And in the RESOLVE and RESTORE
16 trials -- in RESOLVE it was .3 and .5 milligrams with three
17 initial monthly doses with the ability to double the dose at
18 month one followed by prn dosing. And RESTORE
19 was .5 milligrams with three initial monthly doses followed by
20 prn .5 milligrams, three initial monthly doses followed by prn
21 plus laser photocoagulation. And the control in that group was
22 laser photocoagulation.

23 Q. Okay. I want to talk about what Regeneron was doing
24 at this same point in time. In mid-2010 what was
25 Regeneron's -- let me reframe the question.

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1 In mid-2010 was there a Regeneron Phase II trial
2 ongoing?

3 A. Yes. So the 0706, or DA VINCI, trial was ongoing in
4 2010.

5 Q. And in mid-2010 had Regeneron received any results
6 from the DA VINCI Phase II DME trial?

7 MS. MAZZOCHI: Again, Your Honor, can she please not
8 speak on behalf of Regeneron but on her own personal knowledge.

9 THE COURT: Sustained.

10 MR. GREGORY: Your Honor, I'm asking if the company
11 received it. I can reframe the question if defense counsel
12 would like.

13 THE COURT: Please.

14 BY MR. GREGORY:

15 Q. Ms. Chu, were you aware of any preliminary results
16 from the Phase II DA VINCI trial as of mid-2010?

17 A. So the DA VINCI trial was a year-long trial with a
18 week 24 primary end point. So at the beginning of 2010 we had
19 received data from the Week 24 primary end point, but the study
20 was ongoing through 52 weeks, or one year.

21 Q. Had you, personally, Ms. Chu, seen by mid-2010 mean
22 visual acuity gain data for the DA VINCI trial up through
23 Week 24?

24 A. Yes. So typically when we execute clinical trials,
25 once the patient has completed the final visit of interest and

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1 the data has been entered into the database, there's a process
2 we go through to clean the data and, quote/unquote, lock the
3 database, which is the initiation of the statistical analysis.

4 And then the output from the statistical analysis is
5 provided to the clinical group, where we review the detailed
6 data and typically summarize it in PowerPoint presentation
7 format.

8 Q. I want to skip ahead a little bit, then, from
9 mid-2010 to the fall. Let's look at PTX 3131 and PTX 3133.

10 Do you recognize this document -- or these documents,
11 Ms. Chu?

12 A. Yes. So this is an email dated October 6th, 2010,
13 circulating PowerPoint slides related to an upcoming program
14 strategy meeting for VEGF Trap-Eye, or aflibercept.

15 Q. And I want to take a look, then, at the attachment,
16 the slide deck. So this is PTX 3133. Can you please direct
17 your attention to page 11 of that deck.

18 A. Okay.

19 Q. Do you have an understanding at this point in the --
20 in October of 2010 as to what the planning was as to the design
21 of Regeneron's Phase III DME trial?

22 A. So at this time we were planning on a three-arm
23 study, 2 milligrams aflibercept every four weeks, 2 milligrams
24 every eight weeks after three initial monthly doses, compared
25 to macular laser photocoagulation.

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1 Q. Okay. And to be clear, your understanding at this
2 point in time was that Regeneron was not planning for a
3 five-loading-dose study?

4 A. That's correct.

5 MS. MAZZOCHI: Objection. She can't speak to what
6 Regeneron was thinking; she can only speak to her own personal
7 knowledge.

8 THE COURT: Sustained.

9 BY MR. GREGORY:

10 Q. Ms. Chu, I want to phrase this question very
11 narrowly. I want you to listen to my question. Okay?

12 Did you have an understanding -- you personally have
13 an understanding of what the planning was as of October 2010 as
14 to the number of loading doses in Regeneron's Phase III
15 clinical trial?

16 A. Yes. At this time we were still considering three
17 initial monthly doses followed by every eight weeks as one of
18 the dosing arms for the clinical trial.

19 Q. Ms. Chu, again, to reiterate, at this point in time
20 in October of 2010, how long had you had the Week 24 DA VINCI
21 data? Was that nine months at that point?

22 A. I believe we had received it in January of that year;
23 so we had had it for nine or ten months.

24 Q. Let's take a look next at PTX 3188.

25 Do you recognize this document, Ms. Chu?

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1 A. Yes. So this is a slide presentation from the joint
2 development committee to the joint steering committee.

3 Q. And I just forget if you provided this elaboration
4 already. So I apologize. I think you've told us what the
5 joint steering committee was.

6 What is the joint development committee?

7 A. Yeah. So, again, that's the joint committee between
8 Bayer and Regeneron responsible for the development decisions
9 for aflibercept.

10 Q. I want to take a look at -- let's just skip ahead
11 here to -- skip ahead here to page 4. There's a reference on
12 this page to the EMA. Do you know what the EMA is?

13 A. So that's the European Medicines Agency.

14 Q. And there's a -- the title here is "EMA - Outcome and
15 Consequences." I guess the title of the slide is "Health
16 Authority Feedback."

17 Do you see that?

18 A. Yes, I do see that.

19 Q. Okay. What was your understanding of what was being
20 discussed here?

21 A. Yeah. So at this time we were seeking health
22 authority feedback about our plans for DME development. And
23 the EMA had pointed out that they did not feel that our AMD
24 safety data could be extrapolated completely to the diabetic
25 macular edema population.

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1 Q. Let's jump to page 19 of this same deck.

2 And do you see the reference there again in the
3 middle of the page to the safety data?

4 A. Give me one minute.

5 Yes, I do.

6 Q. What was your understanding at this time as to EMA's
7 position on that?

8 A. So their position was that the diabetic population
9 was distinct from the neovascular AMD population, that this
10 is -- while a younger -- somewhat younger population, that they
11 also had several comorbidities and an increased -- so, for
12 instance, diabetics are more frequently hypertensive as well as
13 they have an increased risk of what we would term
14 thromboembolic events; so things like stroke and heart attack.

15 And we knew that VEGF inhibitors like aflibercept had
16 certain class effects, especially when delivered systemically,
17 that included increased blood pressure as well as an increased
18 risk for thromboembolic events. So this was a population that
19 we felt could be particularly vulnerable to systemic exposure.

20 Q. Let's next look at PTX 1028C. Let's put the first
21 page of this up on the screen for you here.

22 MS. MAZZOCHI: Your Honor, that last part of her
23 answer where she started off from diabetic hypertension through
24 what they thought, that's either getting into what Regeneron
25 thought or it's expert testimony.

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1 THE COURT: Understood. Motion to strike denied,
2 though.

3 Go ahead, Counsel.

4 MR. GREGORY: Thank you, Your Honor.

5 BY MR. GREGORY:

6 Q. PTX 1028C, which is up on the screen and also should
7 be in the binder, do you recognize this document?

8 A. Yes. So this a PowerPoint presentation of the
9 one-year data from DA VINCI.

10 Q. DA VINCI again, that's the Phase II DME trial?

11 A. That's right.

12 Q. And how would a document like this -- I think you may
13 have already talked a little bit on this subject, but how would
14 a document like this typically be prepared at Regeneron in your
15 experience?

16 A. Yeah. So as I mentioned -- so the process is
17 typically that once the last patient completes their -- that
18 last visit of interest, there's a process where the data is
19 entered into the database and any questions about the data are
20 resolved.

21 Once we lock the database, our statisticians then
22 begin their process of analysis. And from that comes a
23 detailed set of what we call tables, figures, and listings,
24 which really is the -- the raw data from the study as well as
25 any aggregate data or analyses that are performed.

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1 And so the clinical group would be charged with
2 reviewing those tables, figures, and listings and summarizing
3 that in this kind of PowerPoint presentation for disclosure and
4 discussion with management.

5 Q. And so it gets rolled up, then -- the initial set of
6 data gets rolled up through a series of steps into this type of
7 deck?

8 A. That's correct.

9 Q. What becomes of that broader underlying set of data?

10 A. The tables, figures, and listings become the basis
11 for the clinical study report which is eventually provided to
12 health authorities.

13 Q. And what, if anything, does senior management do with
14 that broader set of data at Regeneron typically?

15 A. So I think I already mentioned that our senior
16 management has always been heavily involved in the discussions
17 and decisions. And certainly when we would review this kind of
18 PowerPoint presentation with them, there would often be
19 questions that would require we would pull up raw data. They
20 certainly would have access to the tables, figures, and
21 listings. And frequently they would ask for additional
22 analyses, et cetera. So it was always a very lively
23 discussion.

24 MR. GREGORY: Your Honor, permission to approach.

25 THE COURT: Granted.

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1 BY MR. GREGORY:

2 Q. Ms. Chu, I've just handed you a sizable document
3 marked PTX 1170.

4 Do you recognize that?

5 A. So this appears to be tables, figures, and listings
6 from the DA VINCI study, the 0706 study.

7 Q. Do you recall when a decision was made about the
8 treatment arms to evaluate in Regeneron's eventual Phase III
9 DME trial?

10 A. I don't recall the specific date that a decision was
11 made.

12 Q. Do you recall the general time frame?

13 A. Yes, I do. It would have been the end of 2010 or
14 early -- very early 2011.

15 Q. And in the meeting that we were just looking at where
16 this deck -- the deck we were just looking at, do you remember
17 exactly when that meeting occurred?

18 A. I believe it was the beginning of December.

19 Q. Do you remember who ultimately made the decision
20 about the dosing regimens to be explored in the Phase III DME
21 clinical trial?

22 A. So it was ultimately George's decision to move
23 forward with the five initial monthly doses followed by q8.

24 Q. And George, that's George Yancopoulos?

25 A. Yes. Sorry. That's Dr. Yancopoulos.

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1 Q. Why do you remember that?

2 A. So part of the landscape in diabetic macular edema is
3 that these are patients that are not only more susceptible to
4 some of what we knew were the potential class effects of
5 anti-VEGF from a safety perspective, but they were also
6 patients that are at working age and have a high burden of
7 healthcare in general.

8 So the pressure was really to minimize the number of
9 doses. Especially in an investigational arm in a trial, we
10 were really seeking to minimize the treatment burden for these
11 patients. And members of the team disagreed with
12 Dr. Yancopoulos' decision, but it -- ultimately it was his
13 decision based on what he felt would optimize outcomes for
14 patients.

15 Q. Did the Phase III trials at Regeneron ultimately
16 conducted in DME, did those have names?

17 A. Yes. So they were called the VIVID and VISTA trials.

18 Q. And just for clarity, what treatment arms were
19 explored in those trials?

20 A. So both studies included a 2-milligram monthly
21 treatment group, a 2-milligram every-eight-week treatment group
22 after five initial monthly doses, and the control group was
23 laser photocoagulation.

24 Q. I want to talk very briefly about Regeneron's
25 development efforts around diabetic retinopathy if that's okay.

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1 A. Sure.

2 Q. Can we take a look at PTX 3332.

3 Do you recognize this document?

4 A. Yes. So this is a section from our supplementary
5 BLA, or biologics licensing application, for diabetic
6 retinopathy in DME.

7 Q. And there's a reference on -- actually, why don't we
8 go down to page 3 first. That's probably the easiest place to
9 look.

10 Do you see there's this heading "Summary of the
11 Requests for Breakthrough Therapy Designations"?

12 A. Yes, I see that.

13 Q. What's your understanding of what a breakthrough
14 therapy designation is?

15 A. So a breakthrough therapy designation is a relatively
16 new designation that the FDA allows for products that have
17 shown -- that are indicated for a severe disease and have shown
18 preliminary evidence of significant effect over standard of
19 care or available treatments.

20 And it allows many aspects of what we call fast-track
21 designation, which essentially facilitates more frequent and
22 more informal interactions with the FDA during your
23 development.

24 Q. What breakthrough therapy designation -- or what
25 indication did Regeneron seek a breakthrough therapy

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1 designation at this time?

2 MS. MAZZOCHI: Again, Your Honor, objection. In her
3 personal capacity, not on behalf of Regeneron.

4 THE COURT: Understood. But given her position and
5 testimony she's offered, I do believe this witness would have
6 personal knowledge about that. Overruled.

7 MR. GREGORY: Your Honor, I'll just -- we're coming
8 up to the end here. I have three questions left, I think.

9 THE COURT: Understood.

10 BY MR. GREGORY:

11 Q. For what indication did Regeneron seek breakthrough
12 therapy designation for aflibercept?

13 A. We were seeking a breakthrough therapy designation
14 for diabetic retinopathy broadly.

15 Q. Can you turn to page 43 of this document.

16 And embedded within this document we just have this
17 email here from Jennifer Woo.

18 Do you see that?

19 A. I do see that.

20 Q. And could you explain to us what's being discussed
21 here.

22 MS. MAZZOCHI: Objection, Your Honor. Foundation.
23 She's not on this email.

24 THE COURT: Sustained.

25 BY MR. GREGORY:

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1 Q. For clarity, Ms. Chu, let's look back to the first
2 page of the document.

3 Could you explain what this document is broadly
4 speaking.

5 A. Yes. So this is a section of the SBLA that would
6 summarize our interactions with the FDA leading up to the
7 filing.

8 Q. Did you review this document at the time?

9 A. Yes, I did.

10 Q. You're familiar with this document?

11 A. I am.

12 Q. The email that we were just talking about, that's not
13 a standalone email; it's an email that's included within this
14 section of the supplemental BLA, correct?

15 A. That's correct. So that was a communication between
16 our regulatory group and the FDA that was included as part of
17 this summary or interactions with the FDA.

18 MR. GREGORY: Your Honor, with your permission, I'd
19 like to examine her about that.

20 THE COURT: You may proceed, Counsel.

21 BY MR. GREGORY:

22 Q. Ms. Chu, could you look at page 43 again.

23 A. Sure.

24 Q. Could you explain to us what's being discussed here.

25 A. So this is in regards to a teleconference that we had

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1 to the -- with the FDA on August 21st, 2014, to discuss our
2 breakthrough application.

3 Q. And what did FDA do with your breakthrough therapy
4 designation application for the treatment of DR, diabetic
5 retinopathy?

6 A. They did not grant our breakthrough designation for
7 DR.

8 Q. And what was your understanding at the time as to the
9 rationale for that?

10 A. My understanding was that they did not consider the
11 evidence we had provided of patients achieving a
12 two-or-more-step improvement in diabetic retinopathy severity
13 in the VIVID and VISTA trials, which enrolled patients with
14 DME, as representative of the broader DR population.

15 Q. Did Regeneron ultimately pursue or forgo approval in
16 DR alone?

17 A. Yes, we did. We subsequently conducted an additional
18 Phase III trial called the PANORAMA trial in patients with
19 diabetic retinopathy without DME.

20 Q. And what treatment regimens did Regeneron test in
21 that trial?

22 A. In the PANORAMA trial we included 2 milligrams dosed
23 every eight weeks after five initial monthly doses,
24 2 milligrams dosed every 16 weeks after three initial monthly
25 doses and 1q8 interval, and the control group in that study was

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1 sham or observation.

2 Q. And so those are not exactly the same dosage regimens
3 that you tested in the Phase III DME trials, right?

4 A. The group that received five initial monthly doses,
5 then every-eight-week dosing, that was the same group as had
6 been used in the VIVID and VISTA studies.

7 Q. Was there an additional arm, though?

8 A. Yes. So there was the additional treatment arm with
9 the q16 dosing after the three initial monthly doses and 1q8
10 interval.

11 Q. What was your understanding of the basis for
12 including that additional treatment arm?

13 A. The basis was that again -- so patients with DME have
14 underlying diabetic retinopathy, but patients can have even
15 severe diabetic retinopathy and not have DME, and those
16 patients can have very good vision.

17 So again, the focus was really on minimizing the
18 treatment burden as well as minimizing the risk, especially for
19 the diabetic retinopathy patients that did not have immediate
20 vision loss.

21 MR. GREGORY: Thank you, Ms. Chu. I have no further
22 questions at this time, Your Honor. I may have some exhibits
23 to move into evidence before the witness leaves the stand, but
24 I'll wait till the end of cross-examination.

25 THE COURT: Understood.

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1 Counsel, you may proceed with cross.

2 MS. MAZZOCHI: Thank you, Your Honor.

3 May I proceed, Your Honor?

4 THE COURT: You may.

5 CROSS-EXAMINATION

6 BY MS. MAZZOCHI:

7 Q. Ms. Chu, I'm going to show you DTX 5385, exhibit
8 page 1.

9 MS. MAZZOCHI: I'm sorry, Your Honor. May we do the
10 ritual distribution of the binders?

11 THE COURT: Please.

12 BY MS. MAZZOCHI:

13 Q. Ms. Chu, I'm going to show you DTX 5385, exhibit
14 page 1, which is titled the "JDC Update to the JSC Clinical
15 Plan" dated January 26, 2011.

16 And you participated in that discussion, right?

17 A. I don't remember the specific meeting, but this is
18 the type of meeting that I would participate in.

19 Q. Let's go to the second page of the exhibit.

20 You can confirm that the JSC did include Bayer
21 employees, right?

22 A. Correct.

23 Q. And the JDC, which included Regeneron and Bayer
24 employees, endorsed running Study B?

25 A. Yes, I see that here.

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1 Q. Let me take you to the seventh page of DTX 5385.

2 This confirms that the choice of five loading doses for the DME
3 indication was a compromise of the joint development committee,
4 right?

5 A. Well, this indicates that it was a suggested
6 compromise.

7 Q. And it says five loading doses was the suggested
8 compromise for DME?

9 A. It does suggest that, but again, the caveat here is
10 that the -- this included commercial and market access
11 perspective as well.

12 Q. Okay. But whatever the case may be, five loading
13 doses was the compromise position with the JDC, right?

14 A. It was suggested, yes.

15 Q. Okay. And it says in parenthesis after five loading
16 doses, "equals one additional dose," right?

17 A. I see where it says that, yes.

18 Q. And your understanding that this five loading dose
19 compromise from the JDC meant just adding in one additional
20 dose at the 12-week mark, right?

21 A. So, again, the proposal that had been being discussed
22 was the same as what we had utilized in the AMD Phase III
23 trials, which was three initial monthly doses, so -- followed
24 by every eight weeks. So this did represent, at least in the
25 first year, an additional dose.

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1 Q. Right. And that additional dose was going to come at
2 the 12-week mark, right?

3 A. Correct.

4 Q. And one of the reasons why this was viewed as an
5 attractive compromise is because it would not have involved
6 changing the primary end point, which would have required a
7 substantial protocol amendment, true?

8 A. That's actually not true. So the primary end point
9 in these studies was a discussion point from the very beginning
10 because there were -- the EMA accepted a one-year primary end
11 point in Phase III studies with diabetic macular edema while at
12 this time the FDA required a two-year primary end point.

13 Q. Let's take a look at page 21 in the exhibit where
14 it's talking about Study B and loading doses. If we look at
15 the second dash under the heading "Operational aspects of a
16 potential change of number of loading doses," can you read what
17 it says, please.

18 A. So sorry. Do you just want me to read this?

19 Q. Yeah.

20 A. So the second main bullet is "Operational aspects of
21 a potential change of number of loading doses," subbullet,
22 "Protocol amendment required," subbullet, "Four or six loading
23 doses would result in a shift of the primary end point visit to
24 maintain the paradigm that efficacy should be determined four
25 weeks after the last injection in the 2q8 arm (equals

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1 substantial protocol amendment)."

2 Q. So we can agree, then, that one of the benefits of
3 the five loading doses as compared to four or six is that it
4 would not require a shift of the primary end point visits to
5 maintain the paradigm that efficacy should be determined four
6 weeks after the last injection in the 2q8 arm, which would have
7 been a substantial protocol amendment?

8 A. Well, these were design considerations, yes.

9 Q. Okay. Ms. Chu, let's take a look at PTX 3332,
10 exhibit page 16, the breakthrough therapy application that
11 Regeneron submitted to the FDA, dated July 14th, 2014, which
12 you discussed on your direct examination. And I'd like to
13 direct you to the last paragraph heading "Overall Summary of
14 Study Results."

15 Do you have that on screen?

16 A. Sorry. What page is this on?

17 Q. Exhibit page 16. Well, it will say 12 of 30 on the
18 bottom, but it's PTX exhibit page 16. It's on the screen in
19 front of you as well.

20 A. Yes, I see that section.

21 Q. The data that Regeneron relied on as the basis for
22 this application was the Phase III VIVID and VISTA studies,
23 right?

24 A. Correct.

25 Q. But neither the clinical trial protocol for the

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1 Phase III VIVID or VISTA studies are set forth in the '572 or
2 '601 patents that are at issue here, right?

3 A. I would have to look at the patents to be able to
4 answer that sufficiently.

5 Q. Do you recall being asked at your deposition, "If you
6 can take a look at the '601 patent, is the clinical trial
7 protocol for the Phase III VIVID or VISTA studies set forth in
8 any of the patent examples?"

9 You gave that same answer. And then after your
10 review you said, "So in my review of Patent '601, I do not see
11 a description of the VIVID or VISTA trials given as an
12 example."

13 Does that help to refresh your recollection?

14 A. Okay.

15 Q. Let me call up DTX 19, exhibit page 2.

16 You're a named inventor on this patent, true?

17 A. Sorry. Give me a minute.

18 Yes, I am a named inventor on this patent.

19 Q. So this is U.S. Patent Number 10,973,879?

20 A. Is that a question?

21 Q. Yes.

22 A. Yes, 973,879.

23 Q. Dr. Yancopoulos is not listed as a named inventor on
24 this patent, right?

25 A. No, he is not.

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1 Q. Let's go to DTX 19 at exhibit page 38, right-hand
2 column 2, lines 48 to 67. We've got that on the screen in
3 front of you.

4 A. Okay.

5 Q. Ms. Chu, can you confirm that in your patent, DTX 19,
6 lines 48 to 49, you stated that "The present invention provides
7 a method for treating diabetic retinopathy," right?

8 A. So our process at Regeneron is that we, as clinicians
9 and scientists, provide information to our intellectual
10 property attorneys for the purpose of patent applications and
11 documents.

12 Q. Ms. Chu, I'm going to say my question again.

13 In your patent, DTX 19, lines 48 to 49, you stated,
14 "The present invention provides a method for treating diabetic
15 retinopathy," right?

16 A. That is what the patent states.

17 Q. Okay. And if we go down a few more lines to the
18 description of the dosing regimen you consider to be part of
19 the present invention, can you confirm that dosing regimen (ii)
20 is listed as "3 or 4 or 5 monthly doses followed by one or more
21 secondary doses every 8 weeks, wherein the secondary doses
22 initiate 8 weeks after the final of the 3 or 4 or 5 monthly
23 doses and continues with a dose given every 8 weeks
24 thereafter"?

25 Do you see that?

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1 A. I do see that.

2 Q. And that's something that your '879 patent, DTX 19,
3 said was your invention, right?

4 A. That's correct.

5 Q. Okay. Let's go to the sixth exhibit page of DTX 19.
6 Do you have a Figure 1 there?

7 A. Sorry. What page?

8 Q. The 19th -- I'm sorry. It's the sixth page of the
9 exhibit, DTX 19.006, where Figure 1 appears.

10 A. Yes, I do see that figure.

11 Q. Does Figure 1 display a dosing regimen with what
12 could be called three monthly doses followed by doses every
13 eight weeks where the eight-week doses initiate after the final
14 of the three monthly loading doses and continue with a dose
15 given every eight weeks thereafter?

16 A. Sorry. Could you just restate your question.

17 Q. Sure. Looking at Figure 1, does that figure show a
18 dosing regimen with three monthly doses, or what could be
19 called three monthly doses, followed by doses every eight weeks
20 where the eight-week doses initiate after the final of the
21 three monthly loading doses and continue with a dose given
22 every eight weeks thereafter?

23 A. Yes. So my understanding of this figure is that
24 there's an initial dose given at baseline, followed by
25 secondary doses at -- it appears to be four and eight weeks,

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1 followed by a tertiary doses, I think, every eight weeks apart.

2 Q. And if we were to put an arrow at the 12-week mark in
3 your patent's Figure 1, that would be a dosing regimen that
4 would correspond to what we could call five monthly loading
5 doses followed by one or more doses every eight weeks, wherein
6 the eight-week dosing is initiated after the final of the fifth
7 monthly loading dose is given, right?

8 A. Yes. That would be a graphical representation of
9 that dosing regimen.

10 Q. You, at your deposition, did not identify George
11 Yancopoulos as the person who first came up with the idea of a
12 five-loading-dose regimen for diabetic retinopathy that we see
13 in Claim 18 of the '601 patent, right?

14 A. So as I mentioned previously, our process was that
15 the team was charged with bringing proposals for discussion and
16 decision-making by senior management; so I don't know who first
17 came up with that idea.

18 Q. But Dr. Yancopoulos did not have any input into the
19 particular methodology for the PANORAMA study, for example,
20 right?

21 A. He definitely did have input into the methodology for
22 the PANORAMA study.

23 Q. Let me bring -- let me have you take a look at
24 DTX 7212, exhibit page 0024, your deposition testimony. And
25 just to give you context, we'll start at line 17 of page 91 and

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1 we'll go over to page 92, line 6.

2 Starting at line 25, referring to Dr. Yancopoulos --

3 A. Sorry. I don't have a page 92.

4 Q. No. It'll be transcript page 92. So it's exhibit
5 page 24.

6 THE COURT: Ma'am, if you'll see, there's actually
7 four pages on each page. The upper right-hand corner will be
8 the second page number that counsel's referring to.

9 BY MS. MAZZOCHI:

10 Q. And we'll call it up on the screen for you as well.

11 The question was, referring to George Yancopoulos,
12 "And did he have any input into what this particular
13 methodology in the PANORAMA study was going to look like?"

14 And did you give the answer, "I don't recall the
15 specific meeting, but we most certainly would have discussed it
16 with him."

17 A. Yes. I think that's consistent also with our process
18 that I just described.

19 Q. But the day-to-day involvement was really more with
20 the clinical team, yourself and Dr. Vitti, right?

21 A. And Dr. Berliner, who is also on the patent.

22 Yes. I mean, as a clinical team, we're obviously
23 responsible for providing proposals around future development
24 and development strategies.

25 Q. You mentioned something about filing patent

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1 applications.

2 Was it your understanding that patent applications
3 would be filed on all of the methods that were going to be
4 tested by Regeneron in human Phase III clinical trials?

5 A. That was not my understanding. So, typically, we
6 would have discussions with our intellectual property attorneys
7 about the programs and planning and the decisions around what
8 patent applications were to be filed or made by them.

9 Q. Again, let me pull up your deposition testimony,
10 DTX 7212, page 34. Your testimony at lines 31:12 to 22.

11 Were you asked the question, "Was it Regeneron's
12 custom and practice to file patent applications on all of the
13 methods that it was going to test in human Phase III clinical
14 trials?"

15 And did you give the answer, "It's my understanding
16 that Regeneron always seeks to patent any novel inventive
17 aspects of both our -- of any aspect of our development
18 process."

19 Was that the question you asked and the answer you
20 gave?

21 A. That's the answer that I gave, but I don't think
22 that's inconsistent with the idea that there's a decision made
23 about what aspects of our development program is inventive and
24 possible to patent.

25 Q. But we can agree that Regeneron put a five monthly

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1 loading dose regimen followed by every-eight-week dosing for
2 diabetic retinopathy in both your '879 patent, saying it was
3 your invention, as well as in the '601 patent's Claim 18 and
4 19, right?

5 A. I understand that regimen appears in both patents.

6 Q. Okay. Ms. Chu, during your time at Regeneron, did
7 you also become aware of the Protocol T study that was
8 conducted by the Diabetic Retinopathy Clinical Research
9 Network?

10 A. Yes, I'm aware of that study.

11 Q. But that Protocol T regimen was not Regeneron's idea,
12 was it?

13 A. Well, the Protocol T study was conducted by the DRCR,
14 which is a collaborative group funded by the National Eye
15 Institute, and Regeneron did have input into the study design
16 and provided drug for the conduct of the study.

17 Q. Well, let's take a look at what I will designate as
18 DTX 9002 and exhibit page 1.

19 Can you confirm this is an email forwarding
20 Protocol T color handouts to Regeneron dated Saturday,
21 March 31st, 2012?

22 A. So I can see this is an email dated March 31st, 2012,
23 regarding Protocol T color handouts to Regeneron.

24 Q. Do you know based on -- given your capacity and your
25 involvement in clinical trials, whether Regeneron had ever

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1 given any input into the Protocol T protocol prior to this
2 date?

3 A. I'm not on this email, and I don't recall
4 specifically what date we had input into the Protocol T
5 protocol.

6 Q. Well, let's go to the eighth page of the exhibit.
7 And there is a slide that's titled "Visit/Treatment Schedule
8 Year 1, the 4:2:7 Guide."

9 Do you see that?

10 A. I see.

11 Q. Is this Protocol T regimen consistent with your
12 recollection?

13 A. With the Protocol T study design?

14 Q. Yes.

15 A. Yes. So I understand this to be the Protocol T
16 dosing regimens.

17 Q. And so here for aflibercept, they proposed a
18 mandatory four loading doses every four weeks at the start of
19 the regimen for Protocol T, right?

20 A. Yes. So this was a comparative study with three
21 different anti-VEGF molecules, and all three dosing groups
22 received four initial monthly injections.

23 Q. And then on weeks -- those monthly loading doses were
24 to be given on weeks 0, 4, 8, and 12, right?

25 A. That was the proposed schedule, yes.

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1 Q. Then Protocol T allowed for two required injections
2 if the patient hadn't reached success; but if they had, they
3 could skip a dose at their next four-week visit, right?

4 A. That was the dosing regimen outlined in the protocol.

5 Q. And, likewise, in the weeks after that, when the
6 patient showed up at their next four-week office visit, if they
7 had not reached success, they were dosed; if they had reached
8 success, they would skip and come back in four weeks, right?

9 A. Yes, that's correct. So they were essentially dosed
10 as needed during that period of time, but the visits were still
11 every four weeks.

12 Q. And that regimen would include an eight-week interval
13 then, right?

14 A. Well, not necessarily. I mean, obviously, each
15 individual patient was dosed based on the criteria outlined in
16 the protocol.

17 Q. Right. But this regimen permitted an eight-week
18 dosing regimen dosing interval, right?

19 A. Potentially. But, again, it wasn't specifically
20 stated that that was the intent.

21 Q. But -- and, likewise, this Protocol T could permit
22 for five monthly doses before any extended dosing interval,
23 right? Just depended on the characteristics of the patient, to
24 your understanding?

25 A. It could. But, again, it would be based on the

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1 individual patient status.

2 Q. And this Protocol T is the only dosing regimen you're
3 aware of where aflibercept was tested head-to-head with
4 ranibizumab and performed better, right?

5 A. Yes, that's correct.

6 Q. But this isn't the dosing regimen in the FDA-approved
7 labeling for Eylea, is it?

8 A. No, it is not. It's not the approved regimen for
9 ranibizumab either.

10 Q. Ms. Chu, let's put DTX 216 before you.

11 Can you confirm this is a March 21st, 2006, email
12 from Jesse Cedarbaum to you and others?

13 A. Yes, I see that this is an email dated March 21st,
14 2006, from Jesse Cedarbaum and I'm one of the recipients.

15 Q. And according to the email, the attachment is the
16 final version of the 0502 Part A abstract for the American
17 Society of Retinal Specialists, ASRS, meeting in the fall, yes?

18 A. Actually, the email states that this is the 0508
19 Part A abstract for ASRS.

20 Q. Well, if you take a look at the attachments line,
21 does it say 0502A ASRS attachments -- ASRS abstract?

22 A. Yes. The attachment was titled "0502A ASRS
23 Abstract."

24 Q. If you take a look at the second page of DTX 216,
25 does this confirm that you were an author on the abstract to

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1 present the results of the Phase I study of intravitreal VEGF
2 Trap in 2006?

3 A. Yes. So I was an author on this abstract of the
4 Phase I study in neovascular AMD.

5 Q. Right. And based on this description here of this
6 being the CLEAR-IT 1 study, this was the 0502 protocol, right?

7 A. Right.

8 Q. Not 0508?

9 A. Correct.

10 Q. And this CLEAR-IT 1 study is where Regeneron first
11 dosed aflibercept in humans intravitreally, right?

12 A. Right. So this is summarizing the dose escalation
13 portion of this study, which is where we dosed a small number
14 of patients across a range of doses.

15 Q. And Dr. Yancopoulos is not listed as a coauthor on
16 this study, is he?

17 A. He is not on this particular abstract, no.

18 Q. But you understand this study is found in Example 1
19 of the '572 and '601 patents?

20 A. Again, I'd have to review the patent to be sure.

21 Q. Well, maybe we can shortcut it. I'm happy to call up
22 your deposition testimony, page 169, lines 14 to -- actually
23 we'll do lines 13 to 17.

24 So this is exhibit page 43.

25 THE COURT: What page of the deposition again,

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1 Counsel?

2 MS. MAZZOCHI: It's deposition page 169.

3 THE COURT: Thank you.

4 BY MS. MAZZOCHI:

5 Q. And, Ms. Chu, did you confirm -- "So the study in
6 Example 1 was referred to as the CLEAR-IT 1 study. The study
7 in Example 2 was the CLEAR-IT 2 study."

8 Was that the testimony you gave?

9 A. Yes, but I had -- I was provided with the patents as
10 an exhibit at that time. So I'd be happy to look at the
11 patents now. Are they in my binder?

12 Q. Was that true testimony you gave at your prior
13 deposition?

14 A. Again, if I had the patents in front of me, I'd be
15 happy to take a look and confirm this.

16 Q. Well, let's go ahead and put up the '601 patent,
17 PTX 1, exhibit page 14, the '601 patent at Column 8, lines 3 to
18 27, which corresponds to Example 1.

19 Do you have that there on the screen?

20 A. I see it on the screen. Just give me a minute to
21 find it in the document.

22 Sorry. What page would it be on?

23 Q. Exhibit page 14.

24 A. Okay.

25 Q. So this is the CLEAR-IT 1 study, right?

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1 A. So Example 1 appears to be the CLEAR-IT 1 study, the
2 Phase I study in neovascular AMD, yes.

3 Q. And looking at the dose listed here in Example 1,
4 what was the volume injected into the eye in your 2005
5 CLEAR-IT 1 study? Was it 0.05 or 0.1 milliliters?

6 A. So at this time we were using 100 microliters
7 or .1 milliliters.

8 Q. At least the 4-milligram dose concentrations that
9 were administered in the study were formed at a 40 mg/mL
10 concentration, correct?

11 A. In this study, yes.

12 Q. Regeneron put exactly what amounts it was dosing in
13 its Phase I protocol documents, right?

14 A. Well, we certainly outlined the doses and dose volume
15 intended.

16 Q. Okay. Let me take a look at what I've marked as
17 DTX 9005.

18 Can you confirm that this is an April 5th, 2005,
19 email to -- that you were cc'd on from Sri Vuthoori?

20 A. Sorry. Did you say DTX 9005?

21 Q. Yes.

22 A. I don't have that in my binder.

23 Q. You should. It should be right before PTX 1.

24 A. Okay. I see it now. Sorry.

25 Q. Can you confirm that this is an email to you and

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1 others dated April 5th, 2005, from Ms. Vuthoori?

2 A. Yes. So this is an email from Sri Vuthoori, dated
3 April 5th, 2005, and I am a recipient of this email.

4 Q. If we look at the email attachment, can you confirm
5 that this is Regeneron's April 5th, 2005, protocol for the
6 intravitreal Phase I study, protocol VGFT OD 0502?

7 A. So this is what at the time we called a pass
8 document, which was basically a synopsis intended to be the
9 basis for the final protocol.

10 Q. But you're familiar with this document?

11 A. Yes. This is the type of document that we would have
12 written, again, to lead into the writing of the final protocol.

13 Q. Let's go to the 23rd page of the exhibit that
14 describes the clinical drug supply profile.

15 Do you have that on screen?

16 A. Yes, I see that.

17 Q. All right. And, again, this confirms that the
18 4-milligram doses were given at a concentration of 40 mg/mL in
19 the CLEAR-IT 1 clinical trial that you published in your
20 abstract in or about 2006?

21 A. Yes, in the 100 microliter volume.

22 Q. And Regeneron, according to this document, also
23 proposed having a percent overage in the vials of 30 percent,
24 right?

25 A. That appears to be in this document, yes.

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1 Q. And the total fill size was 1.2 milliliters with a
2 max withdrawable volume of 1 milliliter, right?

3 A. That's what's specified in this document, but I'm not
4 the manufacturing expert. So if you're asking me to confirm
5 that that's what was actually in the trial, I would defer that
6 to the expert.

7 Q. Well, this is what you were using to prepare the
8 protocol, right?

9 A. These were assumptions that were being used to
10 prepare the protocol, yes.

11 Q. Now, we've talked about the ASRS meeting in 2006, but
12 Regeneron also presented your CLEAR-IT 1 study at the ARVO
13 meeting in Ft. Lauderdale, right?

14 A. I don't recall, but that's typically one of the
15 meetings where we would seek to present data.

16 Q. And were you a named author on the abstract that was
17 presented at the 2006 ARVO meeting?

18 A. I don't recall specifically.

19 Q. Well, let's take a look at DTX 9003.

20 This is titled "Results of a Phase I,
21 dose-escalation, safety, tolerability, and bioactivity study of
22 intravitreal VEGF Trap in patients with neovascular
23 age-related macular degeneration."

24 Do you have that?

25 A. Yes, I see that.

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1 Q. All right. And you're a named author on that one?

2 A. Yes, I am.

3 Q. And this is referring to the CLEAR-IT 1 study?

4 A. Yes, this would have been the CLEAR-IT 1 study.

5 Q. And that ARVO meeting where CLEAR-IT 1 was presented
6 was held between April 30th and May 4, 2006, right?

7 A. I don't remember the exact dates, but that's the time
8 of year where it's typically held.

9 Q. Okay. Well, just to tie it up because I don't want
10 you to have to take my word for it, let me give you a document.
11 It should be in your binder. And I apologize. I think it's
12 the very last one that's entered in there. It's got the
13 designation DTX 9006.

14 I'll go to exhibit page 12, citation Number 56.

15 And is that referring to your abstract results of the
16 Phase I dose-escalation, safety, tolerability, and bioactivity
17 study of intravitreal VEGF Trap in patients with neovascular
18 age-related macular degeneration as something presented at the
19 annual meeting of the -- of ARVO between April 30th to May 4th,
20 Fort Lauderdale, 2006?

21 A. Yes. This appears to be a reference to that
22 abstract.

23 Q. Now, Ms. Chu, you indicated that Regeneron was
24 keeping some things secret, but I'd like you to -- when it came
25 to its clinical trial work, but I'd like you to take a look at

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1 DTX 4957.

2 Do you see that this is Regeneron's Form 10-K for the
3 prior year 2005?

4 A. I see that this is a Regeneron Form 10-K, yes.

5 Q. I'd like to direct your attention to this exhibit
6 page 5 in DTX 4957 and specifically under the heading "VEGF
7 Trap - Eye Diseases."

8 And we'll pull that up for you on the screen.

9 Do you see that?

10 A. Yes, I see that.

11 Q. All right. And do you see in the second paragraph it
12 says, "In February 2006, Regeneron announced positive
13 preliminary results from an ongoing Phase I dose-escalation
14 study of VEGF Trap-Eye"?

15 That was your ASRS abstract, right?

16 A. So I actually don't know exactly which meeting this
17 is referring to. February -- ASRS is typically held later in
18 the summer. But it has moved around over the years; so it
19 could be referring to the ASRS abstract.

20 Q. All right. Well, can we at least agree that your
21 CLEAR-IT 1 0502 protocol Phase I test results we just looked at
22 in DTX 9002, that Regeneron believed they had announced that --
23 those results at least as early as February 2006?

24 A. So in this 10-K it indicates that we announced
25 positive preliminary results from the ongoing Phase I

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1 dose-escalation study, which I understand to be the CLEAR-IT 1
2 study.

3 Q. And you also -- it was also reported that VEGF
4 Trap-Eye was delivered by intravitreal injection into the eye,
5 right?

6 A. Yes.

7 Q. And Regeneron reported in its 10-K that the patients
8 in your CLEAR-IT 1 study where you coauthored the abstract
9 received a high dose of VEGF Trap-Eye of up to 4 milligrams?

10 A. Right. So the design of the study was to test across
11 a range of doses, those -- some very low and some higher; but
12 yes.

13 Q. And that 4-milligram formulation was dosed as a
14 40 mg/mL formulation?

15 A. So I don't see that as part of this document.

16 Q. Right. But you know that it was?

17 A. The concentration used to dose the 4-milligram dose
18 in these studies was 40 mg/mL.

19 Q. And Regeneron described that dose as well tolerated
20 in its SEC 10-K filing, right?

21 A. We did describe it as well tolerated in this small,
22 early phase study.

23 Q. Right. And that was consistent with what you had
24 seen in that study, right?

25 A. Yes.

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1 Q. And if we take a look at the 51st page of the
2 exhibit, it indicates that this document had been signed off on
3 by your CEO, Len Schleifer, right?

4 A. Yes. I see that it indicates that Len Schleifer had
5 signed this document.

6 Q. Dated February 28th, 2006?

7 A. That's what it appears to be, yes.

8 MS. MAZZOCHI: Your Honor, I'm about to go into a
9 different set of topics. Would this be a good time for our
10 lunch break?

11 THE COURT: It probably is. Why don't we go -- let's
12 take a half hour. Let's pick back up at 12:45.

13 Ms. Chu, ma'am, because you're midstream on your
14 testimony, no one can talk with you about what you've said or
15 anything else. So you'll see folks flee from you in the
16 hallways. They're not being rude or discourteous; they're just
17 following the rules. But I wanted to make sure you understand
18 that.

19 They are permitted to feed you, however, and they are
20 required to feed you. But, otherwise, they can't interact with
21 you. But, ma'am, you can go ahead and step down, and we'll
22 resume with your testimony at 12:45.

23 So we'll see everyone at that point.

24 (A recess was taken from 12:18 p.m. to 12:58 p.m.)

25 THE COURT: Ms. Mazzochi, you may resume.

KAREN CHU - CROSS

1 MS. MAZZOCHI: Thank you, Your Honor.

2 BY MS. MAZZOCHI:

3 Q. Ms. Chu, Mr. Gregory took you to PTX 188 on your
4 direct examination, which was previously your deposition
5 Exhibit 225, to talk about that meeting referenced --
6 supposedly referenced in the email from April 2nd.

7 If you slide down just a little bit on the exhibit,
8 we'll put it in front of you, Item G, but let's keep all of
9 Item 2 up on the screen.

10 Who decided to put the q8 interval on the table for
11 this meeting?

12 A. I don't recall who specifically put the q8 interval
13 on the table for the meeting.

14 Q. Mr. Gregory also asked you about DTX 227, where you
15 indicated that some type of decision was made, but you don't
16 actually recall this specific meeting, right?

17 A. I don't recall this specific meeting.

18 Q. And you don't recall who actually assembled that
19 particular regimen with 2 milligrams q8 weeks with PIER
20 lead-in, dosed monthly for first three months, as one of the
21 arms to consider for the VIEW 1 Phase III clinical trial,
22 right?

23 A. I don't recall who specifically proposed that first,
24 but the final decision about the study design would have been
25 made by George.

KAREN CHU - CROSS

1 Q. Ms. Chu, unequivocally, you don't recall specifically
2 who proposed that dosing regimen, right?

3 A. I don't recall who first proposed it.

4 Q. Ms. Chu, are you aware that this document, DTX 227,
5 was not identified as a document that Regeneron thought related
6 to conception or reduction to practice for the '572 and '601
7 patent and Regeneron's discovery response?

8 THE COURT: Yes, Counsel?

9 MR. GREGORY: Objection, Your Honor. That's a
10 misrepresentation of our discovery responses.

11 THE COURT: Overruled. You can address it on
12 redirect.

13 Repeat your question, please, Counsel.

14 BY MS. MAZZOCHI:

15 Q. Ms. Chu, are you aware that this document, DTX 227,
16 was not identified as a document relating to conception and
17 reduction to practice for the '572 and '601 patent in
18 Regeneron's discovery responses?

19 A. I'm not an attorney; so I don't think I can
20 adequately answer your question.

21 Q. Do you know if you ever assisted in the preparation
22 of those responses?

23 A. Sorry. Which responses are you referring to?

24 Q. Sure. I'll put it up on the screen for you,
25 DTX 7001. And we've also got some hard copies, I believe, that

KAREN CHU - CROSS

1 we can pass out.

2 A. Sorry. Is this in your binder or --

3 Q. No. We're going to hand you a copy if we can.

4 MS. MAZZOCHI: Your Honor, may we approach?

5 THE COURT: You may.

6 MS. MAZZOCHI: Thank you.

7 THE COURT: They're fresh. They're still nice and
8 warm.

9 BY MS. MAZZOCHI:

10 Q. Ms. Chu, do you see this is titled "Regeneron
11 Pharmaceutical Inc.'s Objections and Responses to Defendants'
12 First Set of Interrogatories (1 to 17)" as DTX 7001?

13 A. I see that this document has that title, yes.

14 Q. Okay. And if you can turn to page DTX 7001, exhibit
15 pages 37 to 38.

16 A. Okay.

17 Q. Do you see there's a long list of documents there
18 that have numbers that say RGN-EYLEA-MYLAN and then followed by
19 a more specific number?

20 A. Yes, I see that beginning on page 37 and continuing
21 on page 38.

22 Q. All right. Will you accept my representation that a
23 document ending with the number -- with the Bates Number
24 RGN-EYLEA-MYLAN-00631182 is not found on that list?

25 A. Unless the Court wants me to take the time to review

KAREN CHU - CROSS

1 this whole list, I'll accept your representation.

2 THE COURT: And I do not, ma'am. The Court will
3 likewise accept that representation.

4 MS. MAZZOCHI: Thank you.

5 BY MS. MAZZOCHI:

6 Q. You describe this document, DTX 228, as the one where
7 Dr. Yancopoulos conveyed to Bayer the optimal designs for the
8 VIEW 1 and VIEW 2 trials, right?

9 A. I did not. I actually indicated that Dr. Yancopoulos
10 would have spoken with Darlene Jody about the plans.

11 Q. Let's go to your deposition transcript. It's
12 transcript page 287. I believe it's going to be DTX 7272.
13 Here, we've got it up on the screen for you.

14 And were you asked about DTX 228, the April 4th,
15 2007, email from George Yancopoulos to Darlene Jody -- strike
16 that. Let me start over.

17 Were you asked, "Sure. In your capacity as
18 Regeneron's 30(b)(6) witness, what's the significance of this
19 April 4th, 2007, email from George Yancopoulos to Darlene
20 Jody?"

21 And did you give the answer, "So this email from
22 George to Darlene Jody, who is a senior executive responsible
23 for the Bayer collaboration with us, is communicating the
24 Regeneron proposal and decisions around the optimal designs for
25 the VIEW 1 and VIEW 2 trials"?

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1 Is that the testimony you gave?

2 A. Yes.

3 Q. Okay. And also at your deposition, this document,
4 DTX 228, the April 4th, 2007, email from George Yancopoulos to
5 Darlene Jody, that document was identified by your legal
6 counsel to prepare you for your deposition, right?

7 A. I don't recall if this specific document was provided
8 to me in preparation for my deposition.

9 Q. That's fine. I know some time has passed. So let's
10 go back to your deposition transcript, then, DTX 7212. This is
11 exhibit page 73.

12 And starting around line 13, were you shown this --
13 were you asked the question, "This is an email dated Wednesday,
14 April 4th, 2007, from George Yancopoulos to Darlene Jody. Do
15 you have that?"

16 "A Yes. So I have Exhibit 228 dated
17 Wednesday, April 4th, 2007, with the subject
18 'Summary of Issues for Call, AMD P3 Planning'
19 from George Yancopoulos to Darlene Jody.

20 "Q Now, earlier in the deposition today
21 you referred to an email that you recalled seeing
22 that you discussed with George Yancopoulos. Was
23 this one of the emails?

24 "A Yes. This was the email I reviewed in
25 preparation for this deposition."

KAREN CHU - CROSS

1 Was that the testimony you gave?

2 A. Yes. It appears to be my testimony.

3 Q. Ms. Chu, let's go to PTX 3167, exhibit page 1, that
4 your counsel took you to. And according to the second-to-last
5 sentence in the top paragraph, the sentence that starts out,
6 "Unfortunately," do you see that on the screen?

7 A. Sorry. Can I just -- this is in the original binder,
8 right, not in your binder?

9 Q. Yes. So PTX 3167, exhibit page 1.

10 A. Okay.

11 Q. And while you have DME scenarios the team had put
12 together, you did note that, "Unfortunately, George, Len, and
13 Neil are unavailable today, but we can send them the final
14 recommendations after today's meeting."

15 Is that what's written in the email?

16 A. That's what's written in the email. It's also
17 consistent with our process of having team discussions before
18 presentation and discussion with senior management.

19 Q. But these ideas of using no more than three to six
20 monthly doses, if there was any decision made as to choose one
21 amongst them, that was not generated at that meeting attended
22 by -- it would not have been -- if it was generated at that
23 meeting, it was not one attended by Dr. Yancopoulos, right?

24 A. Again, it was the role of the team to prepare
25 proposals for discussion and decision by senior management.

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1 But Dr. Yancopoulos was, according to this email, not in
2 attendance at this meeting.

3 Q. Ms. Chu, I believe you also indicated on your direct
4 examination that you believe George Yancopoulos was responsible
5 for the five-loading-dose regimen. And I believe you pointed
6 to PTX 1028 and PTX 1170, that big, thick exhibit, as support
7 for that.

8 Do you recall that?

9 A. Yes.

10 Q. Do you also recall me asking you at your deposition
11 if your theory that George Yancopoulos made the decision about
12 the five loading doses was documented anywhere?

13 A. I don't recall that specific question.

14 Q. That's fine.

15 Let's pull up DTX 7212, exhibit page 21, which is
16 your deposition transcript pages 80 to 81. And feel free to
17 look at your prior answer just to get the context that we were
18 talking about, five loading doses, but I'd like to focus on the
19 question that starts at line 16.

20 Were you asked the question, "Right. Who decided
21 that the dosing was going to be for the first five injections
22 as opposed to three or four"?

23 "A My recollection is that George
24 Yancopoulos made that decision.

25 "Q Is that documented anywhere?

KAREN CHU - REDIRECT

1 "A I don't recall if there is specific
2 documentation of that."

3 Was that the testimony you gave?

4 A. Yes.

5 MS. MAZZOCHI: Your Honor, there's several other
6 places where I believe Ms. Chu testified inconsistently with
7 her prior deposition; but because you heard that yesterday, to
8 move things along, we'll save that for the posttrial findings
9 if that's all right.

10 THE COURT: Understood.

11 MS. MAZZOCHI: Thank you very much, Your Honor.

12 With that, I'll pass the witness.

13 THE COURT: Redirect, Counsel?

14 MR. GREGORY: Briefly, Your Honor.

15 REDIRECT EXAMINATION

16 BY MR. GREGORY:

17 Q. Hello again, Ms. Chu.

18 A. Hi.

19 Q. Defense counsel showed you DTX 7001. I think it was
20 a somewhat lengthy document. It's kind of collected together
21 with a binder clip. Do you have that in front of you?

22 A. Yes, I do.

23 Q. And this is Regeneron Pharmaceutical Inc.'s
24 objections and responses to defendants' first set of
25 interrogatories.

KAREN CHU - REDIRECT

1 Do you see that?

2 A. Yes. This document has that title.

3 Q. Now, defense counsel showed you the response to
4 Interrogatory Number 10 set forth on pages 37 and 38.

5 Do you recall that?

6 A. Yes.

7 Q. And do you recall her asking you whether a particular
8 document was within the list of the approximately 50 documents
9 identified on those pages?

10 A. I remember her asking me to agree with her assertion,
11 and I agreed.

12 Q. Defense counsel did not show you the interrogatory
13 itself, did she?

14 A. No.

15 Q. I want to direct your attention to page 36. And that
16 Interrogatory Number 10 at the bottom of page says, "For each
17 claim of each of the initial patents, identify (a) the date
18 that the claimed subject matter was first conceived and the
19 date it was reduced to practice, and the diligence leading to
20 such reduction to practice, and for each such date and
21 diligence, identify with particularity the documentary evidence
22 supporting that date or diligence and at least three persons
23 with any knowledge relating to that date and diligence."

24 Do you see that?

25 A. I see that.

KAREN CHU - REDIRECT

1 Q. I read that correctly?

2 A. Yes.

3 Q. You can set that aside.

4 Defense counsel asked you some questions about
5 DTX 228.

6 Do you recall those questions?

7 A. Let me just find the exhibit first.

8 Okay. Yes, I have that.

9 Q. Was DTX 228 the only email you reviewed to prepare
10 for your deposition in this case?

11 A. No, it was not. I reviewed several emails in
12 preparation for my deposition.

13 MR. GREGORY: No further questions, Your Honor.

14 THE COURT: Recross?

15 MS. MAZZOCHI: Nope. It's all in the record, Your
16 Honor. Thank you.

17 THE COURT: Ms. Chu, thank you so much. You can step
18 down.

19 MR. GREGORY: Your Honor --

20 THE COURT: Oh, no, no. You may not step down.

21 MR. GREGORY: We have just a few exhibits I think we
22 would move into evidence at this point.

23 THE COURT: Thank you, Counsel. I forgot about that.
24 Go right ahead. Slowly, please.

25 MR. GREGORY: Of course. And I'll ask defense

KAREN CHU - REDIRECT

1 counsel as well to make sure that I'm not reading any that are
2 already in evidence. I think I've done that filtration process
3 myself.

4 We would move PTX 3131, PTX 3133, PTX 3332, PTX 0188,
5 DTX 227, PTX 3150, PTX 3151, PTX 3167, and PTX 3168. We would
6 move those into evidence.

7 I believe additional documents we discussed were
8 DTX 8190, PTX 3188, and PTX 1028C, all of which I believe are
9 already in evidence.

10 THE COURT: Any objection or disagreement with that?

11 MS. MAZZOCHI: I would like to object to PTX 3151.

12 And the reason for that, Your Honor, is because this is the
13 lengthy list of -- they're basically hearsay statements from a
14 DME expert teleconference. So, again, I had no problem with
15 Ms. Chu discussing something that was in her personal
16 knowledge, but because, again, these are proffering supposed
17 expert opinions, I don't want to see them later on as being
18 proffered as this is what the experts thought or something
19 along those lines.

20 THE COURT: What is the purpose of offering 3151?

21 MR. GREGORY: Yes, Your Honor. It's PTX 3151. It's
22 not for the truth of the matter asserted; it's the Regeneron
23 and Ms. Chu's state of mind.

24 THE COURT: Understood. Objection overruled.

25 Any other objections other than 3151?

KAREN CHU - REDIRECT

1 MS. MAZZOCHI: I believe that's the only one, Your
2 Honor.

3 THE COURT: All right. Subject to that -- I'm sorry,
4 Counsel.

5 MS. MAZZOCHI: You did not do --

6 MR. GREGORY: I don't believe I showed those to
7 Ms. Chu.

8 MS. MAZZOCHI: Yes. Then we're good, Your Honor.

9 THE COURT: All right. Subject to that ruling on the
10 objection of 3151, each of those identified by counsel are
11 hereby admitted.

12 (PTX 3131, PTX 3133, PTX 3332, PTX 0188, DTX 227,
13 PTX 3150, PTX 3151, PTX 3167, and PTX 3168 were admitted.)

14 THE COURT: Any from the defense?

15 MS. MAZZOCHI: Yes, Your Honor. We have DTX 19,
16 DTX 216, DTX 4957, DTX 5385, DTX 9002, DTX 9005, DTX 9006,
17 DTX 7001, and PTX 3332.

18 I'm sorry, Your Honor. Hang on.

19 I might be -- told I might have gotten one of the
20 9000 numbers wrong.

21 9006, which was the drugs of the future article.

22 THE COURT: Any others, Counsel?

23 MS. MAZZOCHI: Nope. That's it.

24 THE COURT: Any objection to any of those from
25 plaintiff?

KAREN CHU - REDIRECT

1 MR. GREGORY: Your Honor, if you give me just a
2 moment to consult with my cocounsel?

3 THE COURT: Certainly.

4 MR. GREGORY: No objection, Your Honor.

5 THE COURT: Without objection, each of those will be
6 admitted.

7 (DTX 19, DTX 216, DTX 4957, DTX 5385, DTX 9002,
8 DTX 9005, DTX 9006, DTX 7001, and PTX 3332 were admitted.)

9 THE COURT: Anything further we require of this
10 witness, then?

11 MS. MAZZOCHI: Nothing from us, Your Honor.

12 MR. GREGORY: Nor from us, Your Honor. Thank you.

13 THE COURT: I now reextend my invitation to step
14 down, ma'am. Thank you very much. You can leave whatever
15 there. We will tidy up. Thank you.

16 MR. GREGORY: May I approach to remove the binders?

17 THE COURT: You may, yes. It's Ms. Chu's chance to
18 escape.

19 Regeneron may call its next witness.

20 MR. TRASK: Your Honor, Regeneron calls Dr. Kenneth
21 Graham.

22 THE COURT: Dr. Graham, sir, if you wouldn't mind
23 making your way all the way to the front of the courtroom.

24 You're going to pause here with Madam Clerk so she
25 can swear you in, then we'll ask you to take the witness stand

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1 over here to your left.

2 **KENNETH S. GRAHAM, PhD, PLAINTIFF'S WITNESS, SWORN**

3 THE COURT: Anticipating a request to approach and
4 distribute, so granted.

5 MR. TRASK: Thank you, Your Honor.

6 MR. RAKOCZY: William Rakoczy from Mylan and Biocon.
7 I'd like to get an objection on the record before this witness
8 begins, if I may.

9 THE COURT: Why don't we distribute materials, and
10 then when it's a little calmer and quieter, Mr. Rakoczy, the
11 floor will be yours again.

12 Mr. Rakoczy, sir.

13 MR. RAKOCZY: Yes, Your Honor. We object to any
14 testimony or proffered exhibits from this witness on invention
15 date. This goes back to our motion in limine.

16 THE COURT: Good thing I waited for calm and still,
17 Mr. Rakoczy.

18 MR. RAKOCZY: We object to any testimony or proffered
19 exhibits from this witness on invention date. This goes back
20 to our Motion in Limine Number 5, which I believe is in the
21 compilation of documents at Docket Number 449. This also goes
22 back to our interrogatories to Regeneron.

23 Interrogatory Number 10 asks for detailed information
24 on the alleged conception and reduction to practice of the
25 invention. We asked for Regeneron to identify with

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1 particularity all documents they would rely on and for
2 knowledgeable witnesses. We received a three-line response to
3 that. They cited no witnesses and cited one page of one
4 document.

5 And for the record, the interrogatory is at DTX 900
6 at page 36, and the response is at DTX 900 and page 37. So
7 this --

8 THE COURT: May I have a copy of that?

9 MR. RAKOCZY: Yes, Judge.

10 THE COURT: I don't believe I have that. If I do, I
11 apologize.

12 Mr. Rakoczy, you said that was Interrogatory
13 Number 10?

14 MR. RAKOCZY: Interrogatory Number 10, which is at
15 the bottom of page 36, and the response on the '865 patent is
16 in the middle of the page on DTX 900 at page 37, where it says
17 "with respect to the '865 patent" and it begins, talks about
18 the inventors conceived, and then it gives a Bates number
19 RGN-EYLEA-MYLAN-00475679. There is no witness identified.
20 There are no documents except, again, one page of one document.

21 Now, two nights ago, Your Honor --

22 THE COURT: What is that document, 475679?

23 MR. RAKOCZY: Your Honor, I believe that is DTX 3580,
24 also PTX 2275. It is a several-page document.

25 The other night I received a list of exhibits that

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1 they intended to go through with this witness which is -- I
2 don't know -- a couple feet high, two large binders, a lot more
3 than is cited in that interrogatory answer, and obviously,
4 Dr. Graham is not named in that interrogatory answer at all.

5 And this is exactly what we had feared and why we
6 filed Motion in Limine Number 5. So at the very least, Your
7 Honor, I want to put that objection on the record and also
8 would like to orally renew Motion in Limine Number 5 as well
9 for the very same reasons.

10 THE COURT: Understood.

11 What is Dr. Graham purportedly going to tell us,
12 Counsel?

13 MR. TRASK: Yes, Your Honor. So Dr. Graham is one of
14 the inventors on the '865 patent, and he's here to describe, in
15 large part, the work that he did leading to the inventions
16 described in the '865 patent.

17 This is, obviously, information about which he has
18 personal knowledge, experience himself.

19 THE COURT: He's been disclosed as a witness
20 presumably, correct?

21 MR. TRASK: Absolutely, Your Honor.

22 The point Mr. Rakoczy made about the Interrog 10
23 conception date, it's important to remember in context there
24 were other interrogatories that were propounded by Mylan
25 which -- to which Regeneron provided responsive information.

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1 Interrogatory 2 asked for documents regarding the
2 development efforts that led to the present formulation of
3 aflibercept. There's a range of documents disclosed in
4 response to that interrogatory.

5 Interrogatory 7 asks for documents underlying the
6 examples in the patent. There's a long list of documents
7 disclosed at page 27 of this interrogatory response.

8 So these are all -- all of the documents about which
9 Dr. Graham will be testifying today are documents that were
10 disclosed to counsel for Mylan and Biocon from essentially day
11 one of this case. They've been aware that Dr. Graham was an
12 inventor of this patent from day one of this case. They took
13 the deposition of Dr. Graham. They asked him about some of
14 these documents. They didn't ask him about other of these
15 documents. And it is routine in patent cases for inventors to
16 testify on the stand about the work they did leading to their
17 inventions.

18 THE COURT: Yes, Mr. Rakoczy.

19 MR. RAKOCZY: Your Honor, it is not routine to
20 testify about an invention date when you didn't respond to the
21 interrogatory on an invention date and you gave a three-line
22 answer citing one document and not identifying that witness as
23 someone who would testify about invention date. That is a
24 problem, and again, it's not routine.

25 We had no reason to believe Dr. Graham would testify

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1 about the invention date or earlier invention date because his
2 interrogatory doesn't identify him, and it certainly doesn't
3 identify all the documents that they've disclosed.

4 MR. TRASK: If I may, Your Honor.

5 THE COURT: Go ahead.

6 MR. TRASK: With respect to the invention date
7 question in particular, so the invention date, of course, is
8 keyed off of defendants' invalidity case. They bear the burden
9 of showing invalidity. And the prior art reference that
10 they've been relying on principally is this Dix reference.
11 That was filed in March -- on March 22, 2006.

12 And so responding to that case, we took the position
13 in this interrogatory response that the invention was conceived
14 no later than March 21, 2006. This is a responsive answer to
15 their asserted prior art.

16 Now, the facts you'll see, if Dr. Graham testifies,
17 are that work was done prior to that date, and he wants to
18 describe the work that he did leading to the invention.

19 But the position we took here was directly responsive
20 to the prior art that they've raised, and so Regeneron had no
21 need to prove up a priority date any earlier than the prior art
22 date on which Mylan and Biocon rely.

23 THE COURT: Understood.

24 Last word, Mr. Rakoczy. Go ahead.

25 MR. RAKOCZY: Your Honor, we could not have asked a

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1 clearer or more unambiguous interrogatory: Identify the date
2 of conception and reduction to practice; identify with
3 particularity the documents you will rely on; identify the
4 witnesses with knowledge you will rely on. And they answered
5 with none of that.

6 THE COURT: I agree. I'm going to hold the objection
7 in abeyance at this point given the totality of the
8 interrogatory responses, the fact that Dr. Graham's disclosed
9 as a witness. Defendants obviously had an opportunity to
10 depose him.

11 I do understand and appreciate the concerns,
12 Mr. Rakoczy, you raised with respect to the response provided
13 in Interrogatory Number 10 and the response thereto, but I'm
14 going to hold it in abeyance at this point finding, at least at
15 this point, there's not sufficient prejudice to preclude the
16 doctor from testifying about it. But I would certainly expect
17 and encourage that to be addressed in posttrial submissions at
18 this point with the distinctive prospect the Court not
19 accepting any of that testimony for the reasons you've
20 articulated.

21 MR. RAKOCZY: Thank you, Judge. And would Your Honor
22 prefer if I objected to each and every document?

23 THE COURT: As a matter of fact, I would not, sir.
24 I'll -- the subject area is noted and, I think, defined by our
25 conversation here, and we are certainly aware of it and mindful

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1 of it, addressing it in posttrial proceedings.

2 MR. RAKOCZY: Thank you, Judge. I just want to make
3 sure the objection is preserved. And I'll just assume I have a
4 continuing objection to all of these exhibits.

5 THE COURT: No, I understood. And I will
6 certainly -- that certainly works for me.

7 MR. RAKOCZY: Thank you, Your Honor.

8 MR. TRASK: Thank you, Your Honor.

9 THE COURT: Thank you, Counsel. You may proceed.

10 MR. TRASK: Thank you.

11 May I proceed, Your Honor?

12 THE COURT: You may.

13 MR. TRASK: Thank you.

14 DIRECT EXAMINATION

15 BY MR. TRASK:

16 Q. Dr. Graham, how are you?

17 A. I'm all right. How are you doing?

18 Q. Fine. Thank you.

19 Would you please introduce yourself to the Court.

20 A. My name is Kenneth Graham. Right now I live in
21 Pleasant Valley, New York. I've been an employee of Regeneron
22 Pharmaceuticals for 22 years and some months at this point in
23 time.

24 Q. What is your role at Regeneron, Dr. Graham?

25 A. So now I am a senior director in charge of one of the

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1 teams in formulation development; so we manage a suite of
2 products.

3 Q. And where are you from originally?

4 A. Well, I was born smack dab in the middle of
5 Pennsylvania in a little town called Bellefonte.

6 Q. Where did you do your undergraduate degree?

7 A. Actually, right down the road at Penn State
8 University, State College, Pennsylvania.

9 Q. What was your major?

10 A. Animal bioscience.

11 Q. And why did you study animal bioscience?

12 A. Well, my family has a farm in Schuylkill County. So
13 I grew up with animals and kind of was looking to be a large
14 animal veterinarian, and I read the James Herriot books and was
15 thinking I want to be a veterinarian and go that route.

16 Q. Did you continue there for a master's degree?

17 A. I did.

18 Q. What was your focus?

19 A. So my focus was actually -- the master's degree was
20 in veterinary science. What I was studying was a number of
21 diseases related to selenium and vitamin D. There's a disease
22 in sheep called white muscle disease, and when lambs are
23 deficient in selenium, they basically lose their ability to
24 walk, become paralyzed.

25 Q. After getting your master's degree at Penn State, did

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1 you go on to do a PhD?

2 A. I did.

3 Q. Where was that?

4 A. That's at the California Institute of Technology,
5 Caltech.

6 Q. What was your PhD thesis in?

7 A. So I was studying the way in which a specific class
8 of proteins bind DNA. So my thesis had a couple of parts. One
9 was what aspects of the protein molecule determine which
10 sequence in the DNA will bind. Another aspect was developing
11 what I refer to as a synthetic enzyme. So I was able to take a
12 part of a human serum albumin binding -- human serum albumin copper
13 binding domain and attach it to this protein that binds the
14 DNA, gamma-delta resolvase. It's the binding agent from that.
15 And then in the presence of nickel and an oxidizing agent, site
16 specifically cut the DNA in much the same way a restriction
17 enzyme does. And I also characterized that reaction doing some
18 kinetic isotope effects studies as well.

19 Q. And did you graduate with your PhD?

20 A. I did.

21 Q. And what did you do after you graduated?

22 A. So immediately after I graduated from my doctoral
23 degree, I went to work at a place called the Beckman Research
24 Institute - City of Hope. It's a private cancer institute that
25 was in Duarte, California, that has a research institute that's

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1 endowed by Beckman Institute. It's an arm of Beckman.

2 Q. How long did you remain at the Beckman Research
3 Institute?

4 A. About ten years.

5 Q. Where did you go after that?

6 A. After that I joined Regeneron.

7 Q. What was your first role at Regeneron, Dr. Graham?

8 A. So I was hired in to manage or supervise the
9 bioanalytical testing lab that was part of our pilot
10 manufacturing facility in Tarrytown, New York.

11 Q. And what was the first product you worked on at
12 Regeneron?

13 A. So the first product I worked on was something we
14 referred to as IL-1 Trap. It's now marketed as a compound
15 called Arcalyst.

16 Q. And what is that product used for?

17 A. So Arcalyst is a IL-1 inhibitor. It is used to treat
18 a disease called FCAS. It is basically an ultra-orphan or
19 orphan indication. There's maybe a thousand people in the
20 world that have this disease. And it works out to be an
21 allergy to the cold.

22 So people that have this disease, if they would walk
23 into an air-conditioned room like this courthouse, mild form,
24 they break out in hives; more severe, they break out in hives,
25 have joint pain; most severe, you know, they start having their

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1 hands and knees get twisted like you do with rheumatoid
2 arthritis. Quite a horrible, actually, disease.

3 I actually met a woman -- I don't know whether I can
4 call it fortunate or not, but my wife and I were waiting to go
5 see a movie, and we were talking and she made some comment
6 about Regeneron. And the woman a couple people behind us said,
7 "Oh, you work for Regeneron." And I said yes. And she
8 proceeded to tell me her story.

9 And she had the disease, both her kids had the
10 disease. And the way she described it, she said, "Prior to
11 your drug, I didn't have a life." Literally, that was her
12 quote. And, basically, she couldn't go out in the summer and
13 go into a theater or anyplace, had problems going outside in
14 the winter just because of the response to the cold.

15 Q. When did you first work on aflibercept, what is now
16 known as the active ingredient in Eylea?

17 A. So at the end of my first year at Regeneron in 2002,
18 the pilot manufacturing facility changed over from IL-1 track,
19 and we set up to work on our new molecule which we were calling
20 VEGF Trap at the time.

21 Q. And what was your contribution at that time to the
22 aflibercept project?

23 A. So in the bioanalytical lab we do in-process testing
24 of the product as it goes through the purification steps. We
25 also monitor some aspects of the product during bioreactor

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1 production.

2 So I set up methods that would be able to follow the
3 product through the purification strain and to ensure the
4 ultimate material that we got out of the bioreactor was of
5 suitable quality.

6 Q. And can you explain, Dr. Graham, how the aflibercept
7 material that you worked on was being purified within your
8 facility was first made?

9 A. Well -- so when you make a protein with CHO cells,
10 Chinese hamster ovary cells, in some ways -- this is going to
11 sound a little weird -- but it's like brewing beer. So you
12 have a big stainless steel vat. You put a bunch of things in
13 that the protein or the yeast -- or the cells or the yeast need
14 to grow.

15 You grow it up for a period of time. And when it's
16 ready, you take the material out of the vat. And in the case
17 of the aflibercept molecules, the cells are expressing the
18 protein into the solution. And you have a solution of
19 aflibercept, just like you have beer with a bunch of cells
20 floating in it like a cloudy IPA.

21 Then you take this through a series of purification
22 steps, and you remove the cell debris. You remove all the
23 unwanted stuff. And you end up with something that's a clear
24 solution and probably looks like more Coors Light.

25 THE COURT: Finally, something I understand. Thank

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1 you, Doctor.

2 MR. TRASK: Happy hour.

3 BY MR. TRASK:

4 Q. So just to be clear, the aflibercept that you were
5 saying is made by these cells, is it in solution from the very
6 beginning?

7 A. Yes.

8 Q. Okay. When you were doing this work on the
9 purification of aflibercept, were you in the formulation
10 development group at the time?

11 A. No. I was in pilot manufacturing.

12 Q. Did you join the formulation development group at
13 some point after that?

14 A. I did. In 2005 Regeneron was having some financial
15 problems. We started off by eliminating redundant functions,
16 one of which was the pilot manufacturing facility. And
17 ultimately they laid off more people beyond that. But I was
18 fortunate enough to be able to transfer into preclinical
19 development and formulation development at that time.

20 Q. And after joining the formulation development group,
21 when did you start working on formulations of aflibercept?

22 A. Probably within the first two, three months, tops.

23 Q. And what was your first project on aflibercept when
24 joining the formulation and development group at Regeneron?

25 A. So we had a formulation that was being tested for

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1 ophthalmic purposes. And that formulation in our formal
2 stability group, which is where our QC group monitors the GNP
3 product that is used for people, they started seeing particles
4 in the formulation.

5 And this is kind of a very serious thing. So I was
6 tasked with what -- why are we seeing these particles? What's
7 going on here? You know, this became an all-hands-on effort,
8 and everybody in the group focused in on this.

9 Q. Who were you reporting to at the time in the
10 formulation development group?

11 A. Dan Dix.

12 Q. And who did Dan report to?

13 A. Eric Furfine.

14 Q. Okay. And did you also work with someone named Kelly
15 Frye?

16 A. Yes. She was one of my colleagues.

17 Q. Are those the four people, including yourself, who
18 are named as inventors on the '865 patent?

19 A. They are.

20 Q. When you joined the formulation development group,
21 did you become aware of work that was previously done as part
22 of that group on formulating aflibercept?

23 A. So when I joined the group, there were several years
24 of research that had been conducted prior to arriving there. I
25 wanted to -- wanted to -- needed to go back, look at what was

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1 done so I could understand the types of things that had been
2 tested, what the results were. So I went through and reviewed
3 the previous stability studies and things that we had conducted
4 and in formulation development.

5 Q. Were all of the prior aflibercept formulations
6 intravitreal formulations?

7 A. No.

8 Q. What were some of the others used for?

9 A. So aflibercept was originally developed to treat
10 cancer. So it was -- the idea was it would stop tumors from
11 growing. So we had looked at IV, maybe some subcu routes, but
12 the predominant work was focused on IV.

13 Q. And when you were tasked with developing an
14 intravitreal formulation of aflibercept, did you consider using
15 the prior formulation for cancer for that purpose?

16 A. No. So the cancer formulation was designed to be a
17 concentrate that you would put into an IV bag, dilute out, and
18 give to a patient through an IV. So it had a really high
19 osmolality, like 1100, 1160 milliosmoles. It had a lot of
20 sucrose in it, 20 percent sucrose. And there was concerns that
21 sucrose can be toxic to the eye. Different buffer system.

22 Q. Now, when was it that you first attempted to develop
23 an improved intravitreal formulation of aflibercept?

24 A. Well, the improved version came after our first
25 version started to fail. And this was -- I'm sorry. I was

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1 going to say oh, crap, you know, now what do we do? because
2 everything is falling apart.

3 And it was pretty much, all right, we have to have
4 this trial -- these clinical trials to keep running. We have
5 to be able to dose the patients. What do we do?

6 So we started looking at the cause of what was
7 happening with the first formulation. We figured out -- or I
8 figured out that exposure to the shear stress going through the
9 tiny needle that's used for intravitreal injections was likely
10 causing the particles to form. And we began working on that,
11 really, mid of 2005, May time frame, I would say.

12 Q. Now, when you set out to develop an improved
13 intravitreal formulation of aflibercept, did you have any
14 objectives in mind relating to the stability of the
15 formulation?

16 A. So we wanted to ensure that the product had a minimum
17 two-year shelf life. We were looking to make the most stable
18 product possible; so we were concerned about having very pure
19 aflibercept to start with. That was a focus in the pilot
20 manufacturing, and then we wanted to sustain that.

21 Q. Did you have any objectives in mind regarding the
22 concentration of aflibercept in the intravitreal formulation?

23 A. So the desire was to have a -- I'm going to use the
24 words "high-concentration formulation." And we tested a range
25 of concentrations, but we didn't have a specific one in mind at

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1 that point.

2 Q. Were the objectives of having a formulation that
3 was -- had high stability and a high concentration, were those
4 compatible or in contention with one another?

5 A. Well, to put it simply, they're like opposites. So
6 if you have a lower concentration formulation, they tend to be
7 more stable. As you make the concentration higher, the
8 stability goes down. And this is because, at least with
9 aflibercept, the primary degradation pathway is molecules
10 coming together.

11 So it's just -- the more concentrated, the more
12 molecules, the greater the chance that they'll come together
13 and aggregate. You know, if you want to put it in an equation,
14 it goes up as the square of the concentration. So, you know,
15 you double the concentration, you go from 10 to 20, it's the
16 difference between a rate of 100 and a rate of 400 if I can
17 still do math.

18 Q. Why was it that you were aiming to develop a
19 formulation with a high concentration of aflibercept?

20 A. So this is for an injection into the eye. Based on
21 my experience when my mother was treated for AMD, an injection
22 into the eye is really traumatic. You know, even if you go
23 once a month, it takes a couple days out of the person's life.
24 There's a lot of risk associated with it. A lot of bad things
25 can happen. And we wanted to be able to have as long an

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1 efficacious range as possible.

2 Q. Now, if the goal was to get more drug into the
3 patient's eye, why couldn't we just use a lower concentration
4 formulation and inject more of it?

5 A. Well, the eye is a closed thing. It's kind of
6 like -- I don't know -- a ping-pong ball. You just have that
7 much volume in there. And when you go to inject it, you run
8 the risk of increasing the pressure. So you can't put a lot of
9 volume in it.

10 Based on what I understand to be the limits, you
11 know, you certainly don't want to inject more than 100
12 microliters. You know, 50 microliters is considered to be an
13 optimal injection.

14 MR. RAKOCZY: Objection, Your Honor. This witness
15 has not been qualified as an expert in ophthalmology or
16 intravitreal injections.

17 THE COURT: Understood. Sustained.

18 But you can continue. I recognize it's background
19 information.

20 MR. TRASK: Thank you, Your Honor.

21 BY MR. TRASK:

22 Q. So about -- can you just give the Court a sense for
23 how much is the volume that we're talking about here in these
24 formulations that would be injected.

25 A. So I don't know if you've ever played with the

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1 old-school glass eyedroppers in, like, elementary school or
2 high school chemistry. It's like one or two drops from one of
3 them.

4 Q. And did the fact that the formulation you were
5 developing would be injected intravitreally pose any challenges
6 to you from a formulation standpoint?

7 A. Okay. Yes. It did.

8 Q. What was that?

9 A. So we knew we had limited volume. We knew that it
10 was going to have to go through a very small needle. You know,
11 the small needle causes what's called shear stress or shear on
12 the drug. And that can be destabilizing to the drug. It can
13 cause the drug to, in the case of aflibercept, precipitate.

14 Q. What was the gauge of the needle that you understood
15 these formulations would be injected through?

16 A. 30-gauge.

17 Q. Did you bring demonstratives with you today to
18 illustrate these needles?

19 A. Yeah. We have a couple examples.

20 MR. TRASK: May I approach with those, Your Honor?

21 THE COURT: You may.

22 MR. TRASK: I'm going to hand up what has been marked
23 for identification as PDX 7.001. This is the 30-gauge needle.
24 And PDX 7.002, this is the 22-gauge needle. I'm going to be
25 very careful with these.

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1 THE COURT: I was going to say marshal services isn't
2 in here. Usually you don't get this close with a sharp object.

3 THE WITNESS: Well, it would take a lot of effort for
4 me to do any appreciable damage.

5 THE COURT: I'm pretty soft. I'd probably crumble
6 pretty quick.

7 THE WITNESS: I don't know. You don't look that soft
8 to me.

9 BY MR. TRASK:

10 Q. Dr. Graham, where did these demonstratives come from?

11 A. Actually, they came out of my lab.

12 Q. And can you explain to the Court what these are.

13 A. All right. So I grabbed the one that was labeled 02
14 out of the baggie. So this is a 22-gauge needle. So this is
15 the typical needle that is used -- or a typical gauge that this
16 is used to do an IV infusion is 22.

17 The other one -- I probably should have pulled both
18 of these out first so I don't stab anybody -- is a 30-gauge.
19 And the 30-gauge is what's typically used to inject somebody in
20 the eye. I don't know if you want to take a look at these.

21 THE COURT: I might as well.

22 MR. TRASK: For the record, there's nothing but water
23 in those needles, Your Honor.

24 THE WITNESS: Please don't stick yourself.

25 THE COURT: I promise I will not.

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1 All right. Thank you so much, Doctor. I'm going to
2 hand those back to you. Thank you, sir.

3 BY MR. TRASK:

4 Q. I'll let you put the caps back on those so we don't
5 have any inadvertent accidents.

6 A. That would be a good thing.

7 Q. And why was the size of the needle through which the
8 formulation would be injected relevant to your work as a
9 formulator, Dr. Graham?

10 A. All right. So I think I said that you encounter
11 something called shear when you go through the needle. What
12 shear is, it's basically like you run down a three-lane highway
13 and you slam into one lane. So everything kind of comes
14 together and bounces up on the walls as well. So the narrower
15 the needle gauge, the greater the amount of shear.

16 Q. Let's take a look at PTX 3327.

17 What is this document, Dr. Graham?

18 A. This is a presentation that I prepared some years
19 ago.

20 Q. Okay. And this document itself isn't dated. But if
21 we can take a quick look at PTX 3326, what is this document?

22 A. It's an email that I sent to Eric Furfine back in
23 April of 2006.

24 Q. And what is the first attachment indicated on this
25 email that you sent?

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1 A. KSG PCD talk, March of 2006.

2 Q. Okay. And which presentation is that?

3 A. The previous document you had up on the screen.

4 Q. Let's then turn back to 3327.

5 You said you yourself prepared this slide deck as
6 part of your work on --

7 A. Yes.

8 Q. -- Eylea -- rather, aflibercept intravitreal
9 injections?

10 A. I did.

11 Q. Let's look at page 44 of this document.

12 Did you prepare this slide, Dr. Graham?

13 A. I did.

14 Q. What does this slide show?

15 A. So what I did is I went back and did some
16 calculations to estimate the shear rate that the formulation
17 would experience when it went through different needle sizes.

18 Q. And if we look at the row labeled "One Second" under
19 "Time to Inject," what did the data show that you calculated
20 for a 22-gauge needle and a 30-gauge needle?

21 A. So for the 22-gauge needle, you've got about 16,000
22 reciprocal centimeters' worth of shear -- or not reciprocal
23 centimeters, reciprocal seconds. So shear is like a frequency.
24 It's seconds to the minus 1.

25 And then when you narrowed that needle gauge -- so

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1 you went down to the 30-gauge -- if you're going at the same
2 rate, that number jumps up to 370,000, about 20, 22 times more.

3 Q. So when comparing the amount of shear experienced by
4 a formulation through a 22-gauge needle versus the amount of
5 shear experienced when passing through a 30-gauge needle, about
6 how much higher is the shear with the 30-gauge needle used for
7 intravitreal injection?

8 A. Massively. I think I said 22 times, but it's a huge
9 difference.

10 Q. And how does that compare to the shear that's
11 experienced by the formulation during normal manufacturing
12 processes?

13 A. So one of the most shear-intensive or stressful parts
14 of the manufacturing process is when you take the formulation
15 through a diafiltration step. At that point you're pushing the
16 formulation up against a membrane with a great deal of force.
17 And that's only about 3,000 reciprocal seconds.

18 Q. So if a formulation is being manufactured and then
19 administered through a 30-gauge needle, what's the point in
20 time at which the formulation experiences the highest shear
21 rate?

22 A. Going through the 30-gauge needle.

23 Q. Now, can changes to the formulation lead to higher
24 shear stress?

25 A. Yes, they can.

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1 Q. How so?

2 A. So as the formulation protein concentration goes up,
3 the solutions become a little bit more viscous and you increase
4 the viscosity. That will increase the shear stress.

5 Q. What is viscosity, Dr. Graham?

6 A. All right. So this is -- the definition is the
7 resistance of a solution to flow. What that means --

8 THE COURT: To what, Doctor? I'm sorry.

9 THE WITNESS: To flow.

10 So what it means is if you take, like, a bottle of
11 water, you go to pour it. Water is 1 centipoise. It starts
12 immediately. You stop; it stops immediately. Take honey, go
13 to pour it, it takes a little while for the honey to start
14 going. Go to stop it, it takes a little while for the honey to
15 stop. Low viscosity/high viscosity.

16 BY MR. TRASK:

17 Q. Why is shear an issue when it comes to the handling
18 of formulations?

19 A. In the case of aflibercept, work that I did
20 identified that shear stress or shear caused the formulation to
21 form particles.

22 Q. And what's the process by which particles are formed?

23 A. So this is one of those things that it's kind of like
24 a spectrum of what you deal with. You have the individual
25 molecules in solution. You know, sometimes a couple slam

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1 together. Sometimes a couple more slam together. When you get
2 to the point you get enough of them stuck together, it falls
3 out of solution and you get a visible particle.

4 Q. Is this related to the concept of aggregation?

5 A. It is.

6 Q. And so what happens when proteins aggregate?

7 A. So if I'm talking about aflibercept, aflibercept
8 exists as what we call a native dimer. It's two of the same
9 protein strands that are hooked together. So if you take two
10 of those native dimers and they come together, that starts to
11 form aggregates or high molecular weight species.

12 Usually what happens first is you'll get to maybe
13 four or eight of these things come together. They stay in
14 solution. And then if it gets bigger, you know, you'll start
15 getting some of these things that show up as turbidity. So if
16 you look at smoke, smoke is particles. Do you see individual
17 smoke particles? No. You see the mass of them, but you can't
18 see one. So turbidity is the whole bunch of these little
19 things that are coming out now that you can't see individually
20 but you see as a group.

21 And then the next step -- or the next step can be
22 these things come together. And then it falls out of solution
23 and becomes something that you can see by your naked eye.

24 Q. From your perspective as a formulator, was the
25 formation of particles in an intravitreal formulation a bad

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1 thing?

2 A. It was an exceptionally bad thing. It's bad in any
3 formulation; but for the eye, it's very bad.

4 Q. Can you explain why that is.

5 A. So I think the eye being a closed system, whatever
6 you put in tends to stay in. You know, one aspect is there's a
7 drain in the back of the eye called the trabecular network.
8 And these particles have a chance to, if they move into that
9 area, plug the drain.

10 What happens when you plug the drain in the back of
11 the eye is you raise the pressure. And this is what happens in
12 glaucoma. So you can cause blindness.

13 MR. RAKOCZY: Objection, Your Honor. Again, the
14 witness has not been qualified as an expert in this area.

15 THE COURT: Understood. Sustained. The Court will
16 disregard that testimony.

17 Next question, Counsel.

18 BY MR. TRASK:

19 Q. I think you touched on this a moment ago, but was the
20 possibility of particle formation in an aflibercept formulation
21 just a theoretical concern to you?

22 A. No.

23 Q. Why not?

24 A. So we had gotten -- I don't know -- a year, year and
25 a half in to a clinical trial. And all of a sudden our

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1 clinical supplies were falling out of solution, forming
2 particles.

3 Q. If particles are forming in a formulation, what does
4 that mean about the formulation's stability?

5 A. That's bad.

6 Q. Now, you mentioned that there was a prior oncology
7 formulation for cancer.

8 A. Yes.

9 Q. What was the concentration in that formulation?

10 A. It was 25 mg/mL.

11 Q. Okay. So if Regeneron had already developed a stable
12 25 mg/mL aflibercept formulation, weren't you sure that you
13 could make a stable 40 mg/mL formulation as well?

14 A. No.

15 Q. Why not?

16 A. So increasing concentration leads to decreasing
17 stability. The challenges with aggregation or particle
18 formation, however you want to describe it, go up as the square
19 of the concentration.

20 Q. And when you set out to develop a 40 mg/mL
21 aflibercept formulation for intravitreal use, were you
22 reasonably sure that you could achieve such a formulation with
23 acceptable chemical and physical stability?

24 A. Certainly not when I'm sitting there staring at vials
25 of IVT1 with particles in it.

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1 Q. I'd like to now switch gears just a bit to some of
2 the analytical techniques that you used in your laboratory to
3 assess the stability of the formulations you were working on.

4 So first if we could take a look at the '865 patent.
5 This is PTX 2.

6 Is this your '865 patent, Dr. Graham?

7 A. Yes, it is.

8 Q. And you're the Kenneth Graham named on the face of
9 it?

10 A. I am.

11 Q. Let's look at Table 3 of this patent. What's shown
12 in Table 3?

13 A. So this is data from a stability study. The study is
14 VGFT-SS207.

15 Q. Okay. And I'd like to ask you about the headings of
16 the different rows here. Are these -- do these reflect
17 different analytical data on the formulation?

18 A. They do.

19 Q. Let's cover each of these just briefly. What is the
20 visual appearance analysis that was done here?

21 A. So visual appearance is simply how does the
22 formulation look in its container. You're looking to see if
23 you've got particles in it. Has it discolored? You know, what
24 does it look like?

25 Q. You mentioned turbidity a moment ago. Can you just

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1 briefly remind us about turbidity analysis.

2 A. All right. So turbidity, we use a machine to measure
3 that. And what we do is we look for a decrease in the amount
4 of light that goes through the sample. As the amount of light
5 drops, the signal goes up. You'll see we're at 00 here. This
6 is a -- not an absolute measure; this is corrected for the
7 first time we make the formulation. So we make it, we test it
8 immediately. And then after time we look at it again and see
9 if it's changing. So we subtract that zero value from the
10 value at the month where we measure it again.

11 Q. What is the pH analysis reported here?

12 A. It tells you the alkalinity or acidity of the
13 formulation. We look for no change.

14 Q. And the last two columns, percent VEGF Trap recovered
15 and percent VEGF Trap native configuration, what analytical
16 technique is used for those measurements?

17 A. Size-exclusion chromatography.

18 Q. Okay. And what does size-exclusion chromatography
19 measure?

20 A. So it's a sieving method, basically. So you have a
21 column. And it separates things -- the material in the column
22 separates things based on their size. Big stuff comes out
23 first, intermediate stuff kind of hangs around for a while, and
24 the small stuff comes out last.

25 Q. Now, over the course of your career at Regeneron,

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1 roughly how many size-exclusion chromatography analyses have
2 you run on aflibercept?

3 A. I don't know. 100,000. Tens of thousands. More
4 than I can count.

5 Q. And what does SEC tell you -- if I use SEC to refer
6 to size-exclusion chromatography, you'll understand that?

7 A. Yes.

8 Q. What does that technique tell you?

9 A. So SEC gives you an indication of the molecule in its
10 native state. So it tells you what percentage of the molecules
11 in that solution are hanging out as they're individuals. It
12 also tells you when the molecules start coming together and
13 have -- and form the soluble aggregates that I described
14 earlier.

15 Q. And now beyond the ones that we've just discussed
16 here from the example in the patent, did Regeneron use other
17 techniques for analyzing the formation of insoluble
18 particulates in formulations?

19 A. Yes, we did.

20 Q. Why did you need so many different analytical
21 techniques to understand aggregation and particle formation in
22 formulations?

23 A. Well, first off, they cover a range of sizes. So you
24 have techniques that are dialed in for each size of particle.

25 Secondly, the formation of particles in a formulation

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1 is very bad. You know, we talk about the stability of the
2 formulation. The problem is with these particles or
3 aggregates, it can cause the drug to become either inactive or
4 worse. In some cases it can lead to, you know, autoimmune
5 responses or immune responses to the drug.

6 MR. RAKOCZY: Objection, Your Honor. Again, he's not
7 qualified as an expert in that area.

8 THE COURT: Understood. Sustained. I'll disregard
9 that last portion of the testimony.

10 BY MR. TRASK:

11 Q. Let me just ask, Doctor, in the course of your duties
12 at Regeneron, do you meet with ophthalmologists to understand
13 their concerns regarding aflibercept formulations?

14 A. Yes, I have.

15 Q. And do you take into account the information you
16 learn from ophthalmologists in designing the formulations that
17 you've done as part of your invention and on other molecules as
18 well?

19 A. Yes, absolutely.

20 Q. Do you analyze particle formation using a technique
21 called HIAC, H-I-A-C?

22 A. We did, yes.

23 Q. Let's return to Exhibit 3327. And I'd like to look
24 at page 34 of this document now.

25 What is this page of the presentation, Doctor?

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1 A. So this is a -- kind of a section divider. So I was
2 talking about one topic and then I switched over to talk about
3 HIAC.

4 Q. Okay. And did you prepare this section of the
5 presentation as well?

6 A. Yes, I did.

7 Q. At the time you prepared these slides, who was the
8 in-house specialist in Regeneron's formulation development
9 group on the HIAC analysis?

10 A. That would be me.

11 Q. And did you actually perform the HIAC analysis in
12 this section of the slide deck?

13 A. Yes.

14 Q. Let's take a look at page 46 of the same exhibit,
15 3327. What's shown on this slide, Doctor?

16 A. So this is a summary table taking account the impact
17 of needle shear on a number of different protein formulations
18 and --

19 Q. And what -- I'm sorry.

20 A. Go ahead.

21 Q. What's shown -- the first row of the table is
22 highlighted in blue. What does that show?

23 A. So the one that's highlighted in blue is the clinical
24 oncology formulation that we had at the time. You'll note
25 there's a note on the backside of it that says 22-gauge needle.

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1 So what we did is we took the oncology formulation,
2 pushed it through the 22-gauge needle four times, and looked to
3 see how many particles we had when we began and after we did
4 it. And we showed that there were really no difference. You
5 know, it only went up a small amount.

6 Q. And what about the fourth line down that's
7 highlighted in red? What does that convey?

8 A. So the IVT1 formulation that we were looking at that
9 was forming particles, this is that formulation four times
10 through a 30-gauge needle. So in that case we got about a
11 tenfold increase in particles.

12 Q. And what about all of the rows below the fourth row
13 labeled "Formulations" numbered 2 through Number 9. What is
14 the information conveyed there?

15 A. So those are a series of different formulations that
16 we made seeking to come up with an improved ITV formulation.
17 What that data shows is our improved versions were all better
18 than the original. Some of them are better than each other.
19 But said that yes, we had demonstrated something that works
20 better.

21 Q. And let's turn to page 60 of this slide deck.

22 Are these some of the conclusions you drew from the
23 data we just looked at?

24 A. Yes.

25 Q. Can you explain what's conveyed in the first bullet

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1 point.

2 A. Well, the first one's pretty straightforward. The
3 small 30-gauge needle caused more shear than the bigger needle
4 and more particles.

5 Q. What about the third bullet point highlighted on the
6 screen?

7 A. So what that is is we had the improved IVT
8 formulations, those 9s that you were talking about. And
9 basically it showed that, compared to our original formulation,
10 we were at least three times better with the worst ones that we
11 were dealing with.

12 Q. And the fourth bullet point?

13 A. So it said that when we added polysorbate, we had
14 more resistance than when we added PEG.

15 Q. Okay.

16 We can take that down, please.

17 I'd now like to look at your '865 patent, again,
18 PTX 2.

19 Can we look at the provisional application date on
20 the face of the patent.

21 Doctor, what was the filing date of the provisional
22 application for your '865 patent?

23 A. June 16th, 2006.

24 Q. And were you involved in the preparation of that
25 provisional application?

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1 A. Yes, I was.

2 Q. What was your involvement?

3 A. So I supplied data and data tables to the attorney
4 who drafted the document.

5 Q. Were those the same data tables that appear in the
6 '865 patent itself?

7 A. The data is the same that appears in the patent, yes.

8 Q. And did you also review the provisional application
9 before it was filed on June 16th, 2006?

10 A. Yes, I did.

11 Q. And you're familiar with the contents of that
12 provisional application?

13 A. Yes, I am.

14 Q. All right. I'd like to ask you about some of the
15 internal work you did at Regeneron leading and relating to your
16 invention.

17 So first let's take a look at PTX 2293.

18 What is this document, Dr. Graham?

19 A. It's one of Regeneron's laboratory notebooks. It
20 looks like it belonged to Kelly Frye.

21 Q. And remind us. Who's Kelly Frye?

22 A. So she was one you of my colleagues. She worked in
23 the lab alongside of me.

24 Q. Does she have a PhD as well?

25 A. She does.

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1 Q. And she's your coinventor on the '865 patent?

2 A. Yes, she is.

3 Q. Did you review this lab notebook, PTX 2293, as part
4 of your role in Regeneron's formulation development group?

5 A. Yes, I did.

6 Q. You're familiar with its contents?

7 A. Yes.

8 Q. Let's turn to page 58 of this document. What's shown
9 on this page of the laboratory notebook?

10 A. So this is a protocol for a stability study. This is
11 Protocol Number 195.

12 Q. What is a stability study, Dr. Graham?

13 A. So a stability study is a collection of tests and
14 formulations or formulations containers and tests that we
15 assemble and conduct to look at the stability of a formulation.
16 The protocol's kind of like a contract in that it tells you
17 what you're going to test, what tests you're going to do, and
18 when you're going to do them.

19 Q. And what other types of documentation would be
20 associated with a stability study?

21 A. So typically we create what's called a pull schedule.
22 And the pull schedule outlines when we're going to do specific
23 thermal tests. So thermal tests basically put the formulation
24 in a refrigerator or a freezer, an oven. And, you know, you
25 say I'm going to come back three days, one month, six months,

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1 and check how it is.

2 Q. So if we look at the second paragraph shown on this
3 page of the exhibit, can you make out what's written there
4 highlighted in yellow?

5 A. It's getting to be a stretch; but yes, it says,
6 "There is a problem with the physical stability of VEGF Trap in
7 the current IVT formulation above 10 mg/mL, VEGF Trap.
8 Specifically, particulate is seen after high-concentration
9 formulations are pulled into a syringe and ejected into vials
10 or into a vial. Therefore, a more stable ITV formulation is
11 essential."

12 Q. Does this help explain why your group was researching
13 more stable intravitreal formulations of aflibercept?

14 A. Yes.

15 Q. What are the types of stress conditions that were
16 used in the stability studies your group ran?

17 A. It was dependent on the study. But, typically, we
18 would look at agitation stress. Agitation stress is you take
19 the container of the formulation and you put it on a lab scale
20 vortexer, which is like a paint shaker. And it just shakes it
21 up.

22 We would do thermal stress. So we would look at it
23 at a range of temperatures. Sometimes we would just use
24 accelerate and stress temperatures like 25, 37, and 45 to kind
25 of get an early read on what's going on.

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1 We'd also do freeze/thaw, is another one that we
2 would use.

3 Q. Let's take a look at the formulations that you tested
4 in this SS195 stability study. This is under the heading
5 "Procedure" on page 58 of PTX 2293.

6 Doctor, how many different formulations did you test
7 in this study?

8 A. There were five.

9 Q. And can you make out what is the makeup of the
10 Formulation Number 2 in the study?

11 A. Okay. So what we would do is we had a base
12 formulation which was common to all the formulations that are
13 being tested in the study. That's in the little snippet out
14 above. And that says that we used 10 millimolar
15 phosphate, .03 percent polysorbate 20, 40 mg/mL of VEGF Trap,
16 and the pH was 6.25.

17 In addition, that formulation also contained
18 40-millimolar sodium chloride and 5 percent sucrose.

19 Q. And does that Formulation Number 2 stand out to you
20 today, Dr. Graham?

21 A. It does.

22 Q. Why is that?

23 A. It's what ultimately became the commercial Eylea
24 formulation.

25 Q. And does this laboratory notebook also indicate when

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1 that formulation was first made?

2 A. Yes, it does.

3 Q. Let's turn to page 60 of PTX 2293.

4 What's shown here, Dr. Graham?

5 A. So this is the compounding record; so the mixing of
6 the formulation. And it's for Formulation Number 2 with a
7 specific lot number. And it was conducted on September 30th of
8 2005.

9 Q. To your knowledge, is this the very first time that
10 the formulation was made that is known today as the Eylea
11 formulation?

12 A. I believe it is, yes.

13 Q. And who made this formulation?

14 A. This was done by Kelly.

15 Q. Okay. And what was the date?

16 A. September 30th, 2005.

17 Q. Did your group test the stability of this formulation
18 that was run as part of Stability Study SS195?

19 A. Yes, we did.

20 Q. And what did you find?

21 A. We found it to be a very good stable formulation.

22 Q. Is there stability data for this same composition in
23 the '865 patent?

24 A. For the same composition in terms of the excipients,
25 yes, there is. It's for a different lot of material.

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1 Q. Do you recall which example in the '865 patent this
2 is?

3 A. So it's Stability Study 207, and I think it is
4 Example 3.

5 Q. And so as of September 30th, 2005, had you and your
6 coinventors made and tested the stability of the formulation
7 that eventually became the commercial Eylea formulation?

8 A. Yes, we did.

9 Q. Let's look at Example 1 of the '865 patent. You see
10 that on the screen, Doctor?

11 A. Yes, I do.

12 Q. Do you see that the formulation in Example 1 is
13 highlighted in yellow?

14 A. Yes, I do.

15 Q. What's the term VGFT-SS065 that's shown as part of
16 Example 1?

17 A. So that's our stability study number. The VGFT
18 identified the product. 065 is it's the 65th study we put up.

19 Q. Was there a protocol associated with this stability
20 study?

21 A. Yes, there was.

22 Q. Let's look at PTX 2292.

23 What's this document, Doctor?

24 A. It's one of Kelly Frye's notebooks.

25 Q. And are you familiar with that document?

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1 A. Yes, I am.

2 Q. How is it that you're familiar with this notebook?

3 A. I reviewed its contents when I joined the VEGF Trap
4 team.

5 Q. Let's turn to page 34 of the notebook.

6 What's shown on this page, Dr. Graham?

7 A. It says that the protocol for stability VEGF
8 Trap 065.

9 Q. And is there a date on this stability study protocol?

10 A. Yes, there is.

11 Q. Can you make out the date?

12 A. It was signed by Kelly on December 4th of 2003. I
13 can't make out the other signature.

14 Q. That's okay.

15 Let's look at the procedures section of this protocol
16 on page 34. What types of things were varied with respect to
17 the formulations studied in this stability study?

18 A. So a couple things. There were different buffers
19 used. We changed the concentration of sodium chloride. We
20 tested 50 and 100 millimolar. We tested polysorbate. We
21 tested PEG. We tested a couple of different concentrations of
22 sucrose.

23 Q. And what is Formulation Number 2 in this study?

24 A. Formulation Number 2 was a 50 mg/mL VEGF Trap
25 formulation with 10-millimolar phosphate, 50-millimolar sodium

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1 chloride, .1 percent polysorbate 20, and 5 percent sucrose.

2 Q. Let's compare this formulation, Formulation Number 2
3 in Stability Study SS065, with the formulation in Example 1 of
4 the '865 patent.

5 Do you see those both on the screen?

6 A. Yes, I do.

7 Q. Can you confirm whether or not the same formulation
8 is used in both of these documents?

9 A. They're identical.

10 Q. Does this formulation have a buffer?

11 A. Yes, it does.

12 Q. What's that?

13 A. 10-millimolar phosphate.

14 Q. Does it have an organic cosolvent?

15 A. Yes, it does.

16 Q. What's that?

17 A. Polysorbate 20.

18 Q. Can that also be called a stabilizer?

19 A. Yes, it can.

20 Q. Does it also have a stabilizing agent?

21 A. That would be 5 percent sucrose.

22 Q. Is the VEGF Trap referenced here in these
23 formulations aflibercept?

24 A. It is.

25 Q. And what's the concentration of VEGF Trap in this

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1 formulation?

2 A. 50 mg/mL.

3 Q. Did you do size-exclusion chromatography analysis on
4 this study?

5 A. Yes, we did.

6 Q. Let's look at PTX 1921.

7 Is this the SEC data for SS065?

8 A. Yes, it is.

9 Q. For Formulation Number 2 stored at 5 degrees C, what
10 was the starting percent native VEGF Trap percent?

11 A. It was 98.8 percent.

12 Q. And what was the value at three months stored at 5C?

13 A. 98.7 percent.

14 Q. And what about at six months?

15 A. 98.3 percent.

16 Q. What does that tell you about the percent native
17 conformation of this sample at two months at 5 degrees Celsius?

18 A. I would expect it to be greater than 98.7 percent.

19 Q. Why is that?

20 A. So when a protein aggregates, it's like rolling a
21 ball downhill. It goes -- the level of purity goes down. It
22 doesn't roll back up.

23 Q. Let's look at the bottom of this spreadsheet,
24 PTX 1921. Does this information tell you when the six-month
25 pull sample in Stability Study 065 was analyzed by SEC?

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1 A. Yes, it does. It says it was May 24th, 2004.

2 Q. Let's look back up at the Formulation Number 2 in
3 this spreadsheet. Now, you've said that this formulation
4 involved aflibercept at 50 mg/mL, right?

5 A. Yes, it does.

6 Q. What did this tell you about the percent native
7 conformation of 40 mg/mL formulation of aflibercept stored at
8 5 degrees Celsius for two months?

9 MR. RAKOCZY: Objection, Your Honor. Again, the
10 witness has not been qualified as an expert.

11 MR. TRASK: Your Honor, if I may, this is data from
12 his group that he would -- he testified he routinely relied
13 upon in performing the studies that led to the claimed
14 invention, and he testified that he's run over 100,000
15 size-exclusion chromatography analyses during his time at
16 Regeneron. He has personal knowledge of this data and relied
17 upon it in the course of developing the inventions.

18 THE COURT: Understood.

19 Counsel.

20 MR. RAKOCZY: Your Honor, that didn't have anything
21 to do with my objection. My objection is -- let me back up.

22 I'm not objecting that this formulation tested a
23 50 mg/mL. That's the whole point. That's what this is. The
24 question was asking for an opinion on how does that bear on a
25 40 mg/mL, a different formulation. That's asking for an expert

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1 opinion.

2 THE COURT: It is, Counsel. You need to reword that
3 question, please.

4 BY MR. TRASK:

5 Q. Okay. Doctor, what did you understand the percent
6 native conformation at 50 mg/mL reported in this table would
7 tell you about the percent native conformation of a 40 mg/mL
8 formulation of aflibercept at 5C for two months?

9 MR. RAKOCZY: Objection, Your Honor. It's the exact
10 same question.

11 THE COURT: It's not exact. It's close.

12 But I assume, Counsel, this is part of the work in
13 developing the ultimate formulation that results in the patent
14 at issue, correct?

15 MR. TRASK: Absolutely, Your Honor.

16 THE COURT: With that understanding, objection
17 overruled. Would you repeat your question, Counsel.

18 BY MR. TRASK:

19 Q. Dr. Graham, for the third time, I suppose, what did
20 you understand the percent native conformation at 50 mg/mL, as
21 reported in this data sheet, tell you about the percent native
22 conformation of a 40 mg/mL formulation of aflibercept stored at
23 5 degrees Celsius for two months?

24 A. Okay. So as the concentration of a formulation
25 increases -- at least as the concentration of aflibercept

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1 formulation increases, generally the rate of -- the rate of
2 aggregation goes up. So it's more concentrated, more crowded,
3 faster aggregation.

4 If you got a rate at 50 mg/mL, you can predict
5 reliably that the rate at 40 mg/mL is going to be less in the
6 same formulation.

7 MR. RAKOCZY: Objection, Your Honor. Again, that's
8 pure expert opinion predicting what would and would not happen.
9 That's for the experts.

10 MR. TRASK: I disagree, Your Honor. He's a scientist
11 talking about the work he did leading to the inventions claimed
12 in that patent being asserted in the suit. This is routine
13 testimony at patent trials.

14 THE COURT: I don't believe the word "routine" shows
15 up in the rules of evidence, but I understand the background
16 involved here. Objection overruled.

17 BY MR. TRASK:

18 Q. Did you view the results of this study as promising,
19 Dr. Graham?

20 A. Yes.

21 Q. Let's turn to Example 3 of your '865 patent, Doctor.
22 You see Example 3 on the screen?

23 A. I do.

24 Q. You see the formulation used in this study is
25 highlighted in yellow?

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1 A. Yes, it is.

2 Q. What is the term there, VGFT-SS207?

3 A. That is Stability Study 207, 207th study.

4 Q. That's another stability study you performed?

5 A. Yes.

6 Q. Let's look at PTX 1825, and I want to see page 85 of
7 this document.

8 Now, is this the protocol for Stability Study
9 VGFT-SS207?

10 A. Yes.

11 Q. This stability study is part of a larger document
12 that was produced in this case, all of which appeared to relate
13 to SS207.

14 Is this how the documentation for stability studies
15 was kept in the ordinary course of Regeneron's business?

16 A. So yes, it was. We kept what was called a study
17 file, and that collected all the paper. We also kept lab
18 notebooks as well.

19 Q. Okay. Let's turn to page 92 of this exhibit. Is
20 this the approval page for the stability study we just
21 discussed?

22 A. Yes, it is.

23 Q. Is that your signature on the page, Doctor?

24 A. It is.

25 Q. What does this page indicate your role was with

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1 respect to SS207?

2 A. It says that I was the study director.

3 Q. And what does the role of study director entail?

4 A. Well, that meant I was the responsible party. So I
5 had to ensure pulls were done as scheduled, make sure there was
6 staff assigned to do the analysis, do some of the analysis
7 myself, summarize the data, interpret the data, give readouts
8 to management in terms of what we had, prepare presentations.
9 Pretty much name it.

10 Q. And when did you sign this protocol, Dr. Graham?

11 A. On the 16th of January 2006.

12 Q. And so had you made the formulation that was tested
13 in SS207 prior to January 2006?

14 A. Yes. It actually was made the previous year, I think
15 in October of 2005.

16 Q. I'd like you to compare the formulation identified in
17 the study protocol for SS207 -- that's PTX 1825, page 85 --
18 with the formulation in Example 3 of the '865 patent. That's
19 PTX 2, page 8, Column 9.

20 Do you see those on the screen?

21 A. I do.

22 Q. Is the formulation that you studied in Stability
23 Study 207 the same as the one disclosed in Example 3 of the
24 '865 patent?

25 A. They're identical, yes.

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1 Q. Does this formulation have a buffer?

2 A. Yes.

3 Q. What's that?

4 A. 10-millimolar phosphate.

5 Q. Does it have an organic cosolvent?

6 A. Yes, it does.

7 Q. What's that?

8 A. .03 percent polysorbate 20.

9 Q. Is there a stabilizing agent?

10 A. Yes, there is.

11 Q. What's that?

12 A. 5 percent sucrose.

13 Q. And the VEGF Trap here is aflibercept?

14 A. Yes, it is.

15 Q. And what's the concentration?

16 A. 40 mg/mL.

17 Q. Let's turn to Table 1 of the SS207 protocol. This is
18 PTX 1825 at page 86.

19 You see that table on the screen?

20 A. I do, yes.

21 Q. Did this study involve testing the formulation
22 stability in different containers?

23 A. It did.

24 Q. Was a glass vial one of those containers?

25 A. So the glass vial was what's listed as Device

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1 Number 7.

2 Q. Okay. Was there a pull schedule for this stability
3 study as well?

4 A. Absolutely.

5 Q. Let's look at that. Page 172 of PTX 1825.

6 Is this the pull schedule for SS207?

7 A. Yes, it is.

8 Q. What was the two-month pull date for this study?

9 A. March 21st of 2006.

10 Q. And so what does that mean? What happened on that
11 date?

12 A. So this is for a 5-degree C condition. That meant on
13 the 21st analysts went in, removed the samples from the
14 5-degree, and began performing the tests that were outlined in
15 the protocol.

16 Q. And was size-exclusion chromatography one of the
17 tests performed on these samples?

18 A. Yes, it was.

19 Q. Let's look at PTX 2277 at page 15. This is a
20 spreadsheet produced in native format.

21 Does the spreadsheet shown in this document report
22 the SEC data for the glass vial Device Number 7?

23 A. It does.

24 Q. What did the SEC data show after two months' storage
25 at 5C?

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1 A. It showed that the percent native VEGF Trap is
2 99.18 percent or -- which rounds to 99.2 percent.

3 Q. What did that tell you about this formulation's
4 stability?

5 A. That it had good stability, yes.

6 Q. Let's look at the bottom of the same document.

7 Does this tell you when the size-exclusion
8 chromatography data was obtained for this sample at two months,
9 5 degrees Celsius in a glass vial?

10 A. Yes, it does.

11 Q. When was that?

12 A. So this is a different date format than what we had
13 been using earlier. We transitioned to going year-month-date;
14 so we had the whole list of things in the computer you could
15 find by year.

16 So 06 is 2006, 03 is March, and 20 is the 20th of
17 March.

18 Q. Was this the first time you'd made an aflibercept
19 formulation achieving at least 98 percent native conformation
20 after two months at 5C?

21 A. No, it wasn't.

22 Q. Had you done that sooner?

23 A. Yes.

24 Q. Did you analyze the stability in SS207 by more than
25 just size-exclusion chromatography?

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1 A. We did.

2 Q. Let's look at PTX 2278, page 9.

3 What type of data do we have here, Doctor?

4 A. This is turbidity or OD at 405.

5 Q. Does the column on the right report when the
6 turbidity analysis was performed for the 5C two-month sample in
7 a glass vial?

8 A. The two-month samples were analyzed on March 21st of
9 2006.

10 Q. And what were the results reported here?

11 A. So for the glass vial, the value was -- is
12 negative .003, which is reported as 0.00.

13 Q. And what did that tell you about this formulation's
14 stability?

15 A. It was stable. It was not changing from the initial
16 state.

17 Q. Did you analyze the pH of the samples in this study
18 as well?

19 A. We did.

20 Q. Let's look at page 10 of this document, again,
21 PTX 2278. Is this pH data?

22 A. Yes, it is.

23 Q. Can you tell when the pH was measured at the
24 two-month time point for the sample stored at 5 degrees Celsius
25 in a glass vial?

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1 A. March 21st of 2006.

2 Q. And is the pH result reported here a good one?

3 A. Yes, it is.

4 Q. What did it indicate to you about the stability of
5 the sample?

6 A. That the sample was stable.

7 Q. Let's turn back to the size-exclusion chromatography
8 data spreadsheet at PTX 2272. Now, you testified that there
9 was a two-month pull and a sample was analyzed at that time?

10 A. Yes.

11 Q. Was that the end of the study?

12 A. Oh, no.

13 Q. What happened?

14 A. So we wanted to understand how the formulation
15 performed at 5 degrees C over a number of years. So we
16 continued to pull samples monthly through six months. So we
17 had a three-, four-, five-, and six-month pull.

18 After that we pulled samples every three months,
19 which was 9, 12, 15, and 18. And then after 18 months, we went
20 every six months, which worked out to 24, about 31 months, and
21 then 36 months.

22 Q. And why were you testing the stability of this sample
23 at so many different time points?

24 A. So we were making decisions pretty much on the fly.
25 We had a lot of pressure to come up with what is going to go

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1 into the clinic, go into the patient. We were getting early
2 reads, and we were trying to confirm that yes, our projections
3 are right. And if by some quirk of fate something went wrong,
4 we would know it immediately and be able to course correct.

5 Q. Thank you, Doctor. And just for the record, I think
6 I may have misspoken. If I said PTX 2272, I meant to say
7 PTX 2277, the exhibit we're looking at with this data.

8 Turning now, Doctor, to Example 5 of your '865
9 patent, do you see that on the screen?

10 A. I do.

11 Q. And do you see the formulation that was tested in
12 this example?

13 A. Yes, I do.

14 Q. And there's a term here "VGFT-SS203." Is that
15 another stability study you ran?

16 A. That was the 203rd stability study.

17 Q. Let's look at that one. This is PTX 1860. Is this
18 the protocol for SS203?

19 A. It looks like it's a pull schedule, actually.

20 Q. I'm sorry. It's a pull schedule. Thank you.

21 If we turn to page 122 of this document, is this the
22 stability study protocol for this study?

23 A. That's the first page of the stability study
24 protocol.

25 Q. And this again was produced as part of a larger

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1 collection of documents relating to Stability Study 203. Is
2 this also how these documents were kept in the ordinary course?

3 A. Yes.

4 Q. Now, I'd like to -- I'd like for you to compare, if
5 you could, Doctor, the formulation investigated here in SS203,
6 page 122, of PTX 1860, with the formulation in Example 5 of the
7 '865 patent, PTX 2, page 8, Column 10.

8 Do you see those both on the screen?

9 A. I do.

10 Q. Are these the same formulations?

11 A. Yes, they are.

12 Q. Let's go back to the protocol, SS203. This is
13 PTX 1860, page 129. Is this the approvals page for the SS203
14 protocol?

15 A. Yes, it is.

16 Q. Is that your signature next to -- above study
17 director?

18 A. It is.

19 Q. Were you the study director for this?

20 A. Yes, I was.

21 Q. And when was this protocol approved?

22 A. The 19th of January 2006.

23 Q. All right. Let's turn back to the first page of the
24 protocol. This is page 122 of PTX 1860. What was the -- let's
25 turn to page 123, actually, with the Table 1 displayed.

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1 Was this a study that involved testing the
2 formulation in different containers?

3 A. It did.

4 Q. And were glass vials tested in this study?

5 A. Yes.

6 Q. Which device is that?

7 A. So it's Number 6.

8 Q. And if we look at page 8 of PTX 1860, what is this
9 document?

10 A. So this is the pull schedule for that study.

11 Q. And what does it tell you about the two-month 5C
12 sample pull date?

13 A. So it was scheduled to be pulled on the 12th of
14 February; and it actually was pulled on the 13th of February.

15 Q. Okay. And did you do size-exclusion chromatography
16 analysis in this study as well?

17 A. Yes, we did.

18 Q. Let's look at a spreadsheet marked as PTX 2238,
19 page 14. Is this the SEC data for the formulation in SS203
20 sorted 5C in a glass vial at different time points?

21 A. Yes, it is.

22 Q. What was the native conformation you found for the
23 vial at two months?

24 A. 99.2 percent.

25 Q. That's greater than 98 percent, of course?

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1 A. Yes, it is.

2 Q. What did that tell you about the formulation's
3 stability?

4 A. That it had good stability.

5 Q. Let's look at the bottom of this page. Does this
6 document also tell you when the size-exclusion chromatography
7 test was run?

8 A. Yes, it does.

9 Q. What does it say?

10 A. So 06, year, so 2006; 02, February; 14, 14th.

11 Q. If we could turn to page 156 of PTX 1860, is this
12 more data from the Stability Study SS203?

13 A. Yes, it is.

14 Q. What's shown here?

15 A. So it's the osmolality of the formulation.

16 Q. And what osmolality is reported here, Doctor?

17 A. 287.

18 Q. And what units are those?

19 A. Milliosmoles.

20 Q. And so is the formulation that was analyzed in SS203
21 an isotonic formulation?

22 A. No, it's not.

23 Q. What's your understanding of what's isotonic?

24 A. 300, 320, that range.

25 Q. And you said earlier that the formulation in SS203 is

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1 the same as the formulation reported in Example 5 of the '865
2 patent. Was that right?

3 A. Yes, it is.

4 Q. So what does that mean about the tonicity of the
5 formulation disclosed in Example 5 of the '865 patent?

6 A. So it's hypertonic, below iso-osmolar.

7 Q. Did you say hypo, H-Y-P-O?

8 A. H-Y-P-O.

9 Q. Now, I next would like to look at the disclosure of
10 your '865 patent, Dr. Graham. And I'd like to see if you can
11 confirm whether the data for the native conformation for the
12 stability studies we just reviewed are the same as the native
13 conformation data disclosed in the examples of your patent.
14 Okay?

15 A. Okay.

16 Q. Let's start by comparing the size-exclusion
17 chromatography data in Table 1 of your '865 patent -- this is
18 PTX 2, page 7, Column 8 -- with the SEC data from study SS065
19 for Formulation Number 2 at 5 degrees Celsius. This is
20 PTX 1921.

21 Do you see both of those on the screen?

22 A. I do.

23 Q. Do the SEC data in these two tables match?

24 A. They do.

25 Q. Next let's compare the SEC data in Table 3 of your

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1 '865 patent -- this is PTX 2, page 8, Column 9 -- with the SEC
2 data from your SS207 study for the glass vial stored at 5C.

3 Do you see those?

4 This is PTX 2277, page 15.

5 A. I see it.

6 Q. Do you see those on the screen?

7 A. Yes, I do.

8 Q. So the SEC data in these two tables match?

9 A. They do when you appropriately round the values in
10 the spreadsheet.

11 Q. And can you explain how the rounding works.

12 A. Yeah. It's very straightforward. If it's .5, it
13 goes up; if it's .4, it goes down. So -- or .5 or greater, .4
14 or less. So if it's 98.49, that becomes 98.5.

15 Q. And next I would like to compare the size-exclusion
16 chromatography data from Table 5 of your '865 patent, PTX 2,
17 page 8, Column 10, with the SEC data from the SS203 study for
18 the glass vial at 5C. This is PTX 2238, page 14.

19 Do you see those on the screen?

20 A. Yes, I do.

21 Q. Do the SEC data in these two tables match?

22 A. Yes, they do.

23 Q. Okay.

24 Let's take that down, please.

25 Now, we've been looking at your issued '865 patent up

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1 till now, right, Doctor?

2 A. Yes, we have.

3 Q. Were there earlier related patent filings that
4 preceded the '865 patent?

5 A. Yes, there were.

6 Q. And when did you first disclose the data in the '865
7 patent to the U.S. Patent Office?

8 A. We filed a provisional patent.

9 Q. And you testified earlier that you were involved in
10 the preparation of that provisional patent?

11 A. Yes.

12 Q. Is the data in the examples of your provisional
13 patent application the same as the data in the examples of the
14 '865 patent?

15 A. Yes, they are.

16 Q. Let's take a brief look at that.

17 Let's look at PTX 3249.

18 Do you recognize this document, Doctor?

19 A. This is the -- it looks like the title page for the
20 provisional filing.

21 Q. Okay. And let's compare a few of the examples and
22 data in your provisional application with the corresponding
23 examples and data in your '865 patent.

24 And before we do that, can we just zoom in on the
25 date on which this is filed on the bottom right.

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1 Does this show when the provisional application was
2 filed, Doctor?

3 A. June 16th of 2006.

4 Q. Okay. Let's first look at Example 1 from your
5 provisional application, PTX 3249 at page 17, with Example 1
6 from your '865 patent. This is PTX 2, page 7, Column 8.

7 Do you see both of those on the screen?

8 A. Yes, I do.

9 Q. How do those examples and data compare?

10 A. They're identical.

11 Q. Next let's compare Example 3 from your provisional
12 application, PTX 3249, pages 18 to 19, with Example 3 of your
13 '865 patent, PTX 2, page 8, Column 9.

14 You've reviewed both of these previously, Doctor?

15 A. I have.

16 Q. How do these examples and data compare?

17 A. They're identical.

18 Q. Next let's look at Example 5 of your provisional
19 application, PTX 3249, pages 19 to 20, with Example 5 of your
20 '865 patent, PTX 2, page 8, Column 9.

21 You've reviewed both of these previously?

22 A. Yes, I have.

23 Q. How do these examples and data compare?

24 A. They're identical.

25 Q. So to sum up on this point, then, are the data in

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1 examples -- in Examples 1, 3, and 5 of your '865 patent and
2 your provisional application the same as one another?

3 A. Yes, they are.

4 Q. And are those data also the same as the data that was
5 originally collected from your laboratory at Regeneron?

6 A. Yes, it is.

7 Q. Let's take a look at -- again at PTX 1825, page 172.
8 This is the pull schedule for Stability Study 207,
9 Doctor.

10 A. Okay.

11 Q. What is the two-month pull date for the 5C storage
12 condition?

13 A. March 21st, 2006.

14 Q. Of the various stability studies that you've
15 addressed during your testimony today, were any of the
16 two-month pull dates after March 21, 2006?

17 A. No.

18 Q. And so, Dr. Graham, in your view, had you conceived
19 of the inventions claimed in your '865 patent no later than
20 March 21, 2006?

21 A. Well, we first made it in September of 2005; but yes,
22 no later than March of 2006.

23 Q. Let's --

24 MR. RAKOCZY: Your Honor, I'd just again renew my
25 objection to make sure it's preserved.

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1 THE COURT: No. Understood. Preserved from my
2 perspective, certainly, Counsel, and will be addressed
3 presumably in posttrial submissions and in the Court's final
4 order.

5 MR. RAKOCZY: Thank you, Your Honor.

6 MR. TRASK: And just to note, Your Honor, that's the
7 same date that was in our interrogatory response, March 2006.

8 THE COURT: Yes. Thank you.

9 BY MR. TRASK:

10 Q. Let's look at the examples in your '865 patent. So
11 here we've tried to show on the screen many of the examples
12 from your '865 patent. I know it's a little too small to read.
13 But we've been discussing Examples 1, 3, and 5 up to this
14 point, right?

15 A. Yes.

16 Q. Are all of those liquid formulations in vials in
17 Examples 1, 3, and 5?

18 A. 1, 3, and 5 are all liquid formulations in vials,
19 yes.

20 Q. Are there also examples in your patent that involve
21 prefilled syringes and lyophilized formulations?

22 A. Yes, there are.

23 Q. So for purposes of your invention involving liquid
24 formulations in vials, what's more relevant, the examples
25 involving prefilled syringes and lyophilization or Examples 1,

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1 3, and 5?

2 A. So the most relevant is the examples in the vial.

3 Q. I'd also like you to compare, Doctor, the passage in
4 your '865 patent, PTX 2, at page 4, Column 2, lines 39 to 57,
5 with the passage in your provisional application at
6 paragraphs 7 and 8. This is PTX 3249 at page 11.

7 Do you see those two passages side by side on the
8 screen?

9 A. I do.

10 Q. Have you reviewed these passages previously?

11 A. Yes, I have.

12 Q. Can you confirm whether or not these two passages
13 convey the same information?

14 A. They do.

15 Q. All right. Let's turn back to your '865 patent once
16 more. Have you reviewed the section of your patent titled
17 "Related U.S. Application Data" on the face of the patent?

18 A. Yes, I did.

19 Q. Let's take a look at that in PTX 2.

20 Now, you are aware, of course, Doctor, that after
21 your provisional application was filed but before your '865
22 patent issued, there were nine intervening related patent
23 applications filed and issued naming you as an inventor?

24 A. Yes, I am.

25 Q. Have you reviewed each of those?

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1 A. Yes. I did.

2 Q. Did you determine in your review of those documents
3 whether or not each of those patents contains the same
4 disclosure as in your '865 patent at Column 2, lines 39 to 57,
5 and Examples 1, 3, and 5?

6 A. All of them contain the same examples, the exact same
7 data. Those paragraphs, although they appear on different
8 pages sometimes in slightly different formatting, are all
9 identical with respect to the words.

10 Q. Thank you, Doctor.

11 Now, were the aflibercept formulations that are
12 reported in your '865 patent the only ones that you tested for
13 stability?

14 A. No.

15 Q. Okay. How many did you make and test, just ballpark?

16 A. 40.

17 Q. I'd like to look at just a couple of those.

18 First, when you varied the ingredients in your
19 formulations, did you ever try stabilizing agents other than
20 sucrose?

21 A. Yes.

22 Q. What did you try?

23 A. We tried -- mannitol was one.

24 Q. Okay. Let's look at your '865 patent, PTX 2, at
25 Column 2, lines 45 or thereabouts. What does this passage of

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1 the patent convey in part?

2 A. It says that you might want to use mannitol as a
3 stabilizing agent.

4 Q. And did you, in fact, do a stability study on a
5 formulation with mannitol as the stabilizing agent?

6 A. We did.

7 Q. Okay. Let's look at PTX 2281 at page 1. What is
8 this document, Doctor?

9 A. This is the 208th stability study protocol.

10 Q. And did you run this study?

11 A. I did.

12 Q. Let's turn to page 2 of this document. This is the
13 mannitol-containing formulation you just referenced?

14 A. Yes, it is.

15 Q. And on page 2, does this indicate whether or not a
16 glass vial was tested as the container?

17 A. Container Number 7 was a glass vial, yes.

18 Q. Let's compare the formulation of Example 3 from your
19 '865 patent, PTX 2, Column 9, with the formulation of SS208,
20 which is PTX 2281, page 1.

21 Do you see these on the screen?

22 A. I do.

23 Q. How do these two formulations compare?

24 A. They're identical.

25 Q. Is the stabilizing agent identical?

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1 A. No. So the formulations are identical with respect
2 to every other component except one has sucrose and the other
3 has mannitol.

4 Q. Did this study involve testing the
5 mannitol-containing formulation by SEC?

6 A. Yes, it did.

7 Q. Let's look at PTX 2282 at page 14. Is this
8 spreadsheet the SEC data for SS208?

9 A. Yes, it is.

10 Q. And this is the glass vial at 5C?

11 A. Yes, it is.

12 Q. What was the percent native conformation as measured
13 by size-exclusion chromatography at 5C, two months' storage in
14 a glass vial?

15 A. 99.05.

16 Q. And is that -- that's greater than 98 percent?

17 A. Yes, it is.

18 Q. Did you do turbidity on this formulation as well?

19 A. Yes, we did.

20 Q. Let's look at PTX 2283, page 12.

21 What is this document?

22 A. So this is the data that was collected for turbidity
23 or optical density at 405.

24 Q. And what does it show for the turbidity of the
25 mannitol-containing formulation following storage at 5C for two

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1 months in a glass vial?

2 A. It shows that it was unchanged from the initial
3 measurement; so it's good stability.

4 Q. Now, in the course of your stability study work on
5 aflibercept formulations, did you also vary the amounts of
6 polysorbate 20?

7 A. We did.

8 Q. Let's look at PTX 2265, page 1.

9 What is this document, Dr. Graham?

10 A. This is the 205th stability study protocol.

11 Q. And what amount of polysorbate did you test here?

12 A. 0.06 percent.

13 Q. And if we look at page 2, Table 1, of PTX 2265, was a
14 glass vial tested in this study as well?

15 A. Yes, it was.

16 Q. Was that Device 7?

17 A. Yes, it is.

18 Q. Let's compare the formulation of the SS205 protocol
19 that we just looked at with the formulation of Example 5 of the
20 '865 patent, PTX 2, page 8, Column 10. How do these two
21 formulations compare, Dr. Graham?

22 A. So they have the same components. The difference is
23 that there is .03 percent polysorbate in Example 5
24 and .06 percent polysorbate in Study 205.

25 Q. Did you look at these -- this .06 percent

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1 polysorbate 20 formulation by size-exclusion chromatography?

2 A. Yes, we did.

3 Q. Let's look at PTX 2266, page 15. Is this the SEC
4 data for the glass vial at 5 degrees C?

5 A. Yes, it is.

6 Q. And what was the percent native conformation as
7 measured by SEC following storage in a glass vial for two
8 months at 5C for this formulation?

9 A. 99.0 percent.

10 Q. Did you run turbidity analysis here as well?

11 A. Yes, we did.

12 Q. Let's look at PTX 2267, page 17.

13 THE COURT: Counsel, once we go through this table,
14 if we're at a spot to take our afternoon break.

15 MR. TRASK: Absolutely, Your Honor.

16 BY MR. TRASK:

17 Q. Is this the turbidity data for the SS205 study?

18 A. Yes, it is.

19 Q. And what was the turbidity at 5 degrees Celsius for
20 two months in a glass vial?

21 A. It was unchanged from the initial measurement.

22 Q. Is that a good result?

23 A. Yes.

24 MR. TRASK: Okay. Happy to break at this point, Your
25 Honor, if you'd like.

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1 THE COURT: Why don't we go ahead and do that, then.
2 We're going to take ten minutes. We'll resume at 3:00, a
3 couple minutes after that.

4 Doctor, you haven't been in the courtroom; so this
5 may be a new speech for you. Because you're midstream on your
6 testimony, no one can speak with you in particular about your
7 testimony. So everyone would run the other way as opposed to
8 greeting you.

9 THE WITNESS: Sounds good.

10 THE COURT: You're welcome.

11 I just didn't want you to think that anyone was being
12 rude or discourteous to you. But you can go ahead and step
13 down, sir. But you're a man without a country for the next ten
14 minutes or so.

15 We'll see everyone in a few. Thank you.

16 (A recess was taken from 2:54 p.m. to
17 3:15 p.m.)

18 THE COURT: Apologies. That break ran over. We had
19 a cataclysmic user error with the Keurig coffee machine. That
20 was my user error. Don't worry. We're getting new carpet as
21 part of the great asbestos project. That's what we're telling
22 ourselves.

23 Counsel, you may proceed.

24 MR. TRASK: It doesn't show on the black robe.

25 THE COURT: That's the beauty of the black robe.

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1 Thank you, sir. Go right ahead.

2 MR. TRASK: Thank you.

3 BY MR. TRASK:

4 Q. If we could turn back to Stability Study 207 briefly,
5 Dr. Graham.

6 A. Sure.

7 Q. And if we look at PTX 2275. And, actually, this one
8 is not in your binder; so I'm going to hand up copies of this.

9 MR. TRASK: With the Court's permission?

10 THE COURT: You may.

11 BY MR. TRASK:

12 Q. Doctor, do you have PTX 2275 in front of you?

13 A. Yes.

14 Q. Okay.

15 And for the record, this is Bates-stamped
16 RGN-EYLEA-MYLAN-00475679. And it's a native Excel file printed
17 as a PDF.

18 Doctor, we previously discussed the two-month
19 5C-degree pull date in exhibit -- in Stability Study SS207.
20 Does this exhibit, PTX 2275, show the same pull date at two
21 months, 5 degrees C, that we discussed in connection with
22 PTX 1825 for Stability Study 207?

23 A. Yes, I believe it does.

24 Q. And for the record, what is the pull date at two
25 months, 5C, in Stability Study SS207?

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1 A. 21 March 2006.

2 Q. Okay. I'd also -- we can put that aside for the
3 moment.

4 I'd also like to discuss or revisit briefly in
5 connection with SS207, PTX 2277, page 15. And this --
6 actually, this is -- if we could look at the bottom of this
7 Excel spreadsheet.

8 So, Doctor, I think you testified about the date at
9 the bottom of this Excel spreadsheet, SS207, indicating when
10 the two months' SEC data was run?

11 A. Yes.

12 Q. Can you explain the date it was run and the
13 connection to the date shown at the bottom of this spreadsheet.

14 A. Okay. So this is a sequence number. What we do is
15 we start the sequence and we assign a date code to it. So 06
16 is 2006, 03 is March, 20 is the 20th of March. The F is the
17 system number or system identifier that we used.

18 So this sequence actually was started the day before
19 the samples were pulled. And we did that because we were
20 running standards and systems suitability, and we wanted to
21 ensure that we got all the standard system suitability, all
22 that done, and then allowed -- had a system that's all set,
23 ready to go, you walk in in the morning, you pull out your
24 samples, you put them on, and you run them that day. We didn't
25 want things drifting later and later. We just wanted to be set

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1 and primed and ready to go.

2 Q. Okay. So what was the date that you were getting the
3 size-exclusion chromatography analysis machine ready?

4 A. So the date we were getting it ready was the 20th,
5 which was the date before the pull.

6 Q. And that's March 20th, 2006?

7 A. Yes.

8 Q. And then what's the date on which you actually ran
9 the sample for 5 degrees C, two months?

10 A. They would have gone up on the 21st, the day they
11 were pulled.

12 Q. And that's March 21, 2006?

13 A. Yes.

14 Q. Okay.

15 We can take that down.

16 Thank you, Doctor.

17 Doctor, did you sit for a deposition in this case?

18 A. Yes, I did.

19 Q. Do you recall during your deposition counsel for
20 defendants showed you some internal Regeneron documents where
21 polysorbate was referred to as a stabilizing agent?

22 A. Yes, I did.

23 Q. During your work involving formulations of
24 aflibercept, did you sometimes call polysorbate 20 a stabilizer
25 or a stabilizing agent?

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1 A. Yes, I did.

2 Q. Did you also refer to polysorbate 20 as an organic
3 cosolvent in connection with that work?

4 A. Yes, I did.

5 Q. And did you also call polysorbate 20 at times a
6 surfactant?

7 A. Yes.

8 Q. Can you explain why you were using these different
9 labels?

10 A. So surfactant is kind of self-explanatory. It's the
11 chemical structure of the polysorbate.

12 Cosolvent is, you know, what we were using it for
13 within the formulation. And a cosolvent stabilizes the
14 formulation; so hence stabilizer or stabilizing agent.

15 Q. So would I be mistaken if I called polysorbate 20 a
16 stabilizing agent?

17 A. No, you would not be.

18 MR. RAKOCZY: Your Honor, I'm going to object.
19 Again, expert testimony. Also, he's offering opinions on
20 construction of claims. He didn't offer any of that before.
21 We're hearing this for the first time.

22 THE COURT: Counsel?

23 MR. TRASK: This is not in connection with the claim,
24 Your Honor. I'm referring to the documents that he prepared in
25 the course of his development of the invention.

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1 THE COURT: Well, let's stick to those actual
2 documents as opposed to what's his interpretation thereof.

3 Otherwise, sustained.

4 MR. TRASK: Thank you, Your Honor.

5 BY MR. TRASK:

6 Q. Let's look at PTX 672.

7 What is this document, Doctor?

8 A. So this is the pharmaceutical development section
9 that I wrote for Eylea.

10 Q. Section of what?

11 A. The BLA.

12 Q. Is this the Eylea BLA?

13 A. Yes.

14 Q. Okay. And you're familiar with this document?

15 A. Yes.

16 Q. It's a long document, 483 pages. What was your
17 specific involvement with this document?

18 A. I wrote it.

19 Q. The whole thing?

20 A. Yes.

21 Q. Okay. If we turn to page --

22 A. Sorry.

23 THE COURT: Understood, Doctor.

24 BY MR. TRASK:

25 Q. If we turn to page 26 of this document, Dr. Graham,

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1 did you write this section of the document as well?

2 A. I did.

3 Q. And what is this section of the document?

4 A. It is describing the choice of organic cosolvent and
5 the selection of the concentration for the formulation.

6 Q. If we look at the last paragraph on page 26 of
7 Exhibit PTX 672, do you see where it says polysorbate 20 was
8 selected as the organic cosolvent?

9 A. Yes. It says polysorbate 20 was selected as the
10 organic cosolvent because a lower concentration was required to
11 stabilize the VEGF Trap when subjected to agitation stress.

12 Q. Why did you call polysorbate 20 an organic cosolvent
13 in this document?

14 A. Because that's what I was using it for in the
15 formulation.

16 Q. And you understood, when you wrote this document,
17 that it would be submitted to the FDA?

18 A. Yes.

19 Q. And was it, in fact, submitted to the FDA?

20 A. Yes, it was.

21 Q. And this is an accurate statement?

22 A. Yes, it is.

23 Q. Okay.

24 We can take that down.

25 Now, when you were working to develop more stable

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1 intravitreal formulations of aflibercept, were you aware of
2 public information about other existing protein formulations?

3 A. Some, yes.

4 Q. And in the course of your work, did you ever consider
5 taking the aflibercept and just plugging it into a formulation
6 that had been used to stabilize a different protein?

7 A. No.

8 Q. Why not?

9 A. All right. So proteins are individuals. No two
10 proteins really behave exactly the same. They have different
11 likes and dislikes. So a formulation that works well for one
12 protein may not work well for another one. Things like pH
13 are critical. Choice of stabilizer can be critical.

14 MR. RAKOCZY: Again, objection, Your Honor. Again,
15 that's expert opinion testimony. He can testify about his
16 personal experience with aflibercept, but now he's venturing
17 into other proteins and what would and would not work.

18 THE COURT: That's sustained.

19 BY MR. TRASK:

20 Q. Moving on, when developing your invention, was
21 tonicity a consideration for you, Doctor?

22 A. To a degree.

23 Q. Okay. Can you explain that?

24 A. So we knew that we -- or thought that we did not want
25 to inject something that was 1,000 milliosmoles. We thought

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1 that could potentially be bad. But we weren't necessarily
2 concerned that we had to be exactly isotonic with the
3 environment. We figured we had wiggle room.

4 Q. And you testified earlier that Example 5 of your '865
5 patent was not an isotonic formulation; is that right?

6 A. That is correct.

7 Q. Did you nonetheless consider the formulation of
8 Example 5 to be a candidate formulation for intravitreal
9 injection?

10 A. Yes.

11 Q. Now, does -- the '865 patent on which you're named as
12 an inventor, does that identify which of the formulations it
13 discloses is the one that corresponds to Regeneron's Eylea
14 formulation?

15 A. No, it does not.

16 Q. Does it indicate anything about whether Regeneron
17 preferred one of those formulations over another?

18 A. Not that I've seen in the document, no.

19 Q. Were you permitted as a Regeneron employee to
20 publicly identify the formulation for Eylea before the Eylea
21 product was released onto the market?

22 A. I was not.

23 Q. And to your knowledge, prior to Eylea's launch, was
24 the formulation that you invented that eventually became the
25 commercial Eylea formulation ever publicly identified as

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1 Regeneron's commercial formulation?

2 A. Not to my knowledge, no.

3 Q. Now, you invented formulations of aflibercept that
4 have greater than 98 percent native conformation following
5 storage?

6 A. Yes.

7 Q. To your understanding at the time, did the FDA
8 require some degree of stability in the products that it
9 approves?

10 A. Yes.

11 Q. To your understanding at the time, did the FDA
12 require at least 98 percent native conformation for an approved
13 intravitreal product?

14 MR. RAKOCZY: Your Honor, I'm going to object to the
15 extent he's asking what the FDA did or didn't think, did or
16 didn't require.

17 MR. TRASK: He just testified that he wrote part of
18 the BLA --

19 THE COURT: Understood, but let's focus on his
20 understanding as to why or why not certain things might or
21 might not be included in there.

22 Overruled with that caveat.

23 BY MR. TRASK:

24 Q. Okay. Dr. Graham, when you were developing your
25 aflibercept formulations, did you understand that you needed to

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1 achieve at least 98 percent native conformation in order for
2 the product to be approved?

3 A. That would not have been an obligate requirement. We
4 needed a stable formulation. A stable formulation is supported
5 based on what your clinical experience is. We wanted the 98
6 percent or -- as pure as we could possibly get it because we
7 wanted the best possible product, you know, for the patient.
8 That was our goal.

9 Q. Now, is aflibercept a fusion protein, Doctor?

10 A. Yes, it is.

11 Q. Is aflibercept an antibody?

12 A. No.

13 Q. Are fusion proteins and antibodies the same thing?

14 A. No, they are not.

15 MR. RAKOCZY: Objection, Your Honor. Again, expert
16 testimony.

17 THE COURT: Sustained.

18 BY MR. TRASK:

19 Q. Okay. So one brief point to wrap up, Doctor.

20 You've been working as a scientific researcher for
21 about how long?

22 A. Well, 22 years at Regeneron, ten years at the City of
23 Hope, and then -- god -- since probably -- what? -- '81 at Penn
24 State. So what? 42 years, give or take.

25 Q. And of all the scientific work you've done over the

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1 course of your career, where did the inventions of the '865
2 patent rank?

3 A. Well, that's probably at the top of the heap.

4 Q. Why is that?

5 A. Well, I have a very personal story with respect to
6 Eylea. My mother suffered from wet AMD. I knew that my
7 grandmother, her mom, had gone blind. I didn't know why. Now,
8 my mom was a very, very private person. She never revealed
9 what was going on with her. She had basically gone blind in
10 one eye from the disease, and we didn't know this. And then
11 she started complaining about her eyesight. And then we
12 realized or learned, she finally fessed up, that she had the
13 disease in the other eye.

14 You know, she was getting regular doses of Lucentis
15 every month, but her vision was getting worse. My wife and I
16 were, like, trying to find every opportunity so she could see
17 my daughter, you know, get to see her at swim meets and get to
18 see her and spend time with her while she still could see her.

19 And by the time or before -- shortly before Eylea was
20 approved, her vision had gotten to 21/20, 21/40. She wasn't
21 driving anymore. You know, she was somebody that always liked
22 to do crossword puzzles and word things, couldn't see to do
23 those. So it was kind of very dire.

24 Eylea got approved. I had seen the clinical data and
25 thought, well, this looks better. I started having

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1 conversations with her ophthalmologist, which she didn't like
2 much, but I kind of was I'm not going to sit there and let you
3 go blind; I want to see if there's something we can do. I
4 suggested Eylea. I got back oh, these things are all the same.

5 I finally, in March of 2011, got to the point where I
6 stood and looked at him and said, okay, why are you sentencing
7 my mother to blindness? What we're doing right now is not
8 working. It's just getting worse. Can we just try something
9 better or different? If it doesn't work, we're no worse off.

10 And he agreed at that point to order the drug in.
11 She did her three loading doses. Her vision improved. She got
12 to the point where she was seeing 20/40. With eyeglasses, she
13 was driving again. She got to see Kendra grow up. And it
14 maintained her vision up until the last few months of her life.

15 You know, what can you do better than save your
16 mother's sight?

17 MR. TRASK: Thanks so much, Doctor.

18 Nothing further at this time.

19 THE COURT: Understood.

20 Cross?

21 MR. RAKOCZY: May we approach with some binders, Your
22 Honor.

23 THE COURT: You may.

24 MR. RAKOCZY: Good afternoon, Your Honor. William
25 Rakoczy for Mylan and Biocon.

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1 THE COURT: You may proceed, sir.

2 CROSS-EXAMINATION

3 BY MR. RAKOCZY:

4 Q. Good afternoon, Dr. Graham.

5 A. Good afternoon.

6 Q. Nice to meet you.

7 Dr. Graham, I'd like to start with DTX 722. And
8 we'll pull it up on screen, and it's also in your binder that
9 hopefully you were just handed.

10 A. Yes.

11 Q. I'd like you to look at page 1. You see this is an
12 email dated March 21st, 2006, correct?

13 A. Yes, I do.

14 Q. And it's from Kathleen DeWald to you?

15 A. Yes.

16 Q. Is that right?

17 And I'd like to go to the attachment at page 2. And
18 here you see a product composition, correct?

19 A. I do.

20 Q. It contains phosphate -- strike that.

21 And the formulation, under the "Product Composition"
22 heading, contains phosphate, NaCl, polysorbate 20, sucrose, and
23 40 mg/mL VEGF Trap, correct?

24 A. I do.

25 Q. And I'd like to focus on the first sentence of the

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1 paragraph above it. It states, "This is an unstable
2 formulation for VEGF Trap since there are minimal excipients
3 for intravitreal delivery and the formulation contains a high
4 concentration of VEGF Trap."

5 Is that right?

6 A. That is correct.

7 Q. Now, below that it actually goes on to caution that
8 the drug product should -- being held or stored at 25 degrees C
9 should be kept to a minimum during the manufacturing process,
10 correct?

11 A. Yes. I see those words on the page.

12 Q. And at temperatures above 25 degrees C -- strike
13 that.

14 Temperatures above 25C must be avoided, correct?

15 A. That's correct.

16 Q. And that this drug product should be held or stored
17 at less than minus 20 degrees C, correct?

18 A. I see that, yes.

19 Q. Now, I'd like to look at the table just below that.
20 And in this table we see polysorbate 20 identified as a
21 stabilizer as its function, correct?

22 A. Yes.

23 Q. It's not identified as a solvent, correct?

24 A. The description on the page says stabilizer.

25 Q. And the solvent in this formulation is the water or

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1 the water for injection, correct?

2 A. That is the description for water for injection on
3 the page.

4 Q. Now, let's take a look at one of your signed memos on
5 your ITV formulation.

6 Let's pull up DTX 737.

7 And here we see a signed memo from you dated
8 April 6th, 2006, correct?

9 A. Hang on. I'm trying to follow you.

10 Q. DTX 737. And I have it on the screen as well. We'll
11 go to page 2.

12 A. Yes, I see page 2.

13 Q. And you see your signature dated April 6th, 2006, at
14 the very top, correct?

15 A. Yes, I do.

16 Q. And this is entitled "40 mg/mL VEGF Trap for ITV in a
17 sucrose- and polysorbate-containing formulation," correct?

18 A. That is correct.

19 Q. Now, we see just below that the same cautionary
20 statements on storing the drug product.

21 Do you see that?

22 A. There are cautionary statements. They're not exactly
23 the same, though, no.

24 Q. It says the drug substance, formulated drug
25 substance, or drug product, the time it's held or stored at 25

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1 degrees C should be kept to a minimum during the manufacturing
2 process, correct?

3 A. That's the words on the page, that's correct.

4 Q. And, again, it cautions that temperatures above 25
5 degrees C must be avoided for this formulation, correct?

6 A. That is correct.

7 Q. And it says that this drug product formulation should
8 be held or stored at 2 to 8 degrees C, correct?

9 A. Well, yes, it says 2 to 8 degrees C on this page,
10 correct.

11 Q. Now, let's go down to the table below this as well.
12 And here again, we see that water is identified as the function
13 in the formulation -- or as the solvent in the formulation,
14 correct?

15 A. Well, WFI is identified as the solvent, yes.

16 Q. And that's water for injection; is that right?

17 A. That is correct.

18 Q. And the polysorbate 20, its function is identified as
19 stabilizer, correct?

20 A. Yes, it is.

21 Q. It's not the solvent, correct?

22 A. It's identified as stabilizer.

23 Q. And it's not the solvent in this formulation,
24 correct?

25 A. It's identified as a stabilizer.

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1 Q. My question is it is not the solvent in this
2 formulation? Is that right or is that not right?

3 A. Water is identified as the solvent in the
4 formulation.

5 Q. And water is the only solvent in this formulation; is
6 that right?

7 A. Water is what is identified as the solvent in the
8 formulation.

9 Q. Let's take a look at another one of your memos, DTX--
10 I believe the next one would be -- let me back up. I want to
11 stay on this one.

12 This particular memo does not have any stability data
13 for the formulation in it, correct?

14 A. If -- can you show me the whole screenshot of this.

15 Q. Yes. Can we pull up that whole page, DTX 737,
16 page 2.

17 A. Okay. So this document does not have stability data
18 associated with it. It's a recipe that was provided to the
19 manufacturing group so that they could formulate the material.
20 It's not -- it's not our common practice and has never been our
21 common practice to include stability data with a recipe.

22 Q. My question is simple. In this document there's no
23 stability data, no turbidity data, no native conformation data;
24 is that right?

25 A. That's correct.

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1 Q. Let's go to DTX 736. And we have another one of your
2 memos. Can you confirm for me on page 3 that you, in fact,
3 signed and dated this document April 21st, 2006; is that right?

4 A. Well, I see that on page 1 of 2 I signed it.

5 Q. And that is on page 3 of the exhibit; is that
6 correct?

7 A. Oh. I'm sorry. I didn't understand what you were
8 meaning by page 3.

9 Q. At the bottom you should see DTX 736.0003 of the
10 exhibit.

11 A. Yes, I do.

12 Q. And under the heading "Formulation," you see this
13 formulation contains phosphate, NaCl, polysorbate 20, and
14 40 mg/mL VEGF Trap, correct?

15 A. Yes.

16 Q. And we see similar cautionary statements in this memo
17 as well for the formulation; is that correct?

18 A. That is correct.

19 Q. The time that the drug product is held or stored at
20 25 degrees C should be kept to a minimum, correct?

21 A. During the manufacturing process, yes.

22 Q. And temperatures above 25 degrees C must be avoided,
23 correct?

24 A. Yes.

25 Q. And the drug product should be held or stored at 2 to

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1 8 degrees C, correct?

2 A. That's correct.

3 Q. And like the prior memo, there's no stability,
4 turbidity, or native conformation data in this particular memo;
5 is that right?

6 A. No. It's a recipe.

7 Q. Can we go to the formulation table at the second half
8 of this page. And here again, water for injection, or WFI, is
9 identified as the solvent; is that right?

10 A. That is correct.

11 Q. And polysorbate 20 is identified as the stabilizer,
12 correct?

13 A. Yes.

14 Q. Now, let's look at DTX 725 and look at the lead
15 formulation. And I want to focus in this exhibit first on the
16 email on page 1 which is dated May 8th, 2006, from Dr. Furfine
17 to you.

18 Do you see that?

19 It's in the middle of the page.

20 A. Yes, I do.

21 Q. And you see Dr. Furfine addresses you. He says,
22 "Ken, can you provide to Ellen the two formulations that we are
23 moving into the tox study." Correct?

24 A. Yes.

25 Q. And then you then responded in the email above this

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1 and you provided two formulations; is that right?

2 A. Yes, it is.

3 Q. And the formulation above is entitled the lead
4 formulation; is that right?

5 A. It is.

6 Q. That formulation contains phosphate, NaCl,
7 polysorbate 20, and sucrose, and 5 to 4 mg/mL VEGF Trap; is
8 that right?

9 A. That is what's written on the page, yes.

10 Q. And then there's a backup formulation as well,
11 correct?

12 A. Yes.

13 Q. Now, this email that you forwarded with the lead and
14 the backup formulation, you didn't provide any tox study
15 information in the email, correct?

16 A. No, I did not provide any tox study information.

17 Q. And that's because, as of the date of this email,
18 May 8, 2006, these are the formulations, the lead and the
19 backup, that were going to be moved into the tox study; is that
20 right?

21 A. So as of May 2006, I'm not sure if -- which tox study
22 this is referring to. There were a number of tox studies.
23 Looking at this and knowing Ellen's function, she's
24 pharmacokinetics; so she does PK studies. So she would be
25 looking at a range of these things possibly for an ongoing tox

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1 study. So I'm not sure what you're referring to.

2 Can you be more specific?

3 Q. Well, we can look at Dr. Furfine's email again in the
4 middle of the page. Dr. Furfine asked you to send her the
5 formulations --

6 A. Yeah.

7 Q. -- that you were moving into the tox study, correct?

8 A. Okay.

9 Q. All right. Let's look -- you mentioned the BLA. You
10 worked on and drafted parts of that, right?

11 A. Yes.

12 Q. Excuse me. The Eylea BLA, correct?

13 A. Yes.

14 Q. Let's pull up PTX 1519 and go to page 5. And this is
15 already in evidence. And here we see the description
16 composition of the drug product from the Eylea BLA, correct?

17 A. That is correct.

18 Q. And at Table 1 again we see polysorbate 20 identified
19 as a, quote, stabilizer agent, end quote, correct?

20 A. Yes. It's identified as a stabilizer agent in
21 Table 1 and I think maybe another table or two in the document.
22 But in the pharmaceutical development section, it was described
23 as a cosolvent.

24 Q. We're going to get to the -- I promise you we'll get
25 to the pharmaceutical development section next.

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1 Very quickly, though, the function here on Table 1 in
2 the Eylea BLA is identified as stabilizing agent, correct?

3 A. Yes.

4 Q. And the BLA does not identify polysorbate 20 here in
5 PTX 1519 as a solvent, correct?

6 A. Could you say that again, please.

7 Q. The Table 1 of the Eylea BLA here in PTX 1519 does
8 not identify polysorbate 20 as a solvent, correct?

9 A. That is correct. It's not identified as a solvent.

10 Q. And that's because polysorbate 20 has never been
11 considered to be a solvent, correct?

12 A. For our purposes, we've always used it as a cosolvent
13 or stabilizing agent.

14 Q. Let's pull up your deposition. You recall being
15 deposited in this case, correct?

16 A. Yes, I do.

17 Q. And you understand you were under oath during that
18 deposition, correct?

19 A. Yes, I was.

20 Q. And you swore to tell the truth?

21 A. I did.

22 Q. We're going to pull it up on screen, but it's also in
23 your binder, Dr. Graham, DTX 5103. And the exhibit is page 46
24 of the transcript. We're going to look at transcript page 179,
25 lines 19 to 25.

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1 A. Can you give me the DTX number again, please.

2 Q. Yes. DTX 5103.

3 A. Okay.

4 Q. At page 46. And I also have it on screen for you.

5 Were you asked this question; did you give this
6 answer?

7 "Q So I guess I'm not understanding why
8 Regeneron listed here in its BLA document,
9 Exhibit 738, that the function of polysorbate 20
10 is stabilizing agent and not solvent like water
11 for injection. Can you explain this?

12 "A Well, polysorbate 20 has never been
13 considered to be a solvent."

14 Was that the question you were asked and the answer
15 you gave?

16 A. Yes, they are.

17 Q. And that's a true answer, correct?

18 A. Yes.

19 Q. Now, I think you mentioned -- and I don't need to go
20 through it again, but there are other places in the BLA that
21 identify polysorbate 20 as a stabilizing agent, correct?

22 A. Yes.

23 Q. Well, let's pull up the pharmaceutical development
24 portion that you drafted, which I believe you testified was at
25 PTX 672.

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1 You recall that?

2 A. Yes.

3 Q. Now, you mentioned a portion of this document where
4 you called polysorbate 20 a cosolvent. I'd like to look at a
5 different portion of the same document you drafted. And let's
6 go to page 108 of PTX 672. And I'm going to look at Table 63,
7 I believe. You see Table 63, the document you drafted, is
8 entitled "Role of excipients in the IVT2 VEGF Trap-Eye
9 formulation," correct?

10 A. Yes.

11 Q. And we see polysorbate 20, excipient, the reason for
12 addition is identified as "stabilizing agent," correct?

13 A. That's correct.

14 Q. And it goes on to describe it as "increases stability
15 when agitated or subjected to freeze/thaw stress," correct?

16 A. That is correct, yes.

17 Q. I'd like to switch gears briefly and talk about one
18 of the other excipients you mentioned, which are buffers. Your
19 '865 patent only uses a phosphate buffer; is that right?

20 A. It describes a pH range. And the pH range tells
21 anybody that works in this field that there are a series of
22 compounds that you can use as a buffer.

23 Q. But it doesn't mention any other buffers by name
24 beyond phosphate, correct?

25 A. The phosphate is mentioned as -- by name as an

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1 example of a buffer.

2 Q. And matter of fact, you recall your counsel showed
3 you all those examples on the screen from your patent.

4 You remember that?

5 A. Yes.

6 Q. And they all used a phosphate buffer, correct?

7 A. All the examples used a phosphate buffer, yes.

8 Q. Now, in fact, you don't recall using a histidine
9 buffer to develop an intravitreal formulation of VEGF Trap
10 prior to the filing of your '865 patent application in 2006,
11 correct?

12 A. I don't believe that we did, no.

13 Q. In fact, your boss, who is Dr. Dan Dix; is that
14 correct?

15 A. Yes, my boss was Dan Dix.

16 Q. I think you know where I'm going here. Dr. Dan Dix
17 had Dr. Dan Dix nevers, right?

18 A. Yes, he did.

19 Q. And one his nevers was -- Dan Dix nevers, I believe
20 you said, things that you would never do, according to Dr. Dix,
21 is that you would never have a liquid formulation with a
22 histidine buffer; is that correct?

23 A. So Dan is quite a character. Unfortunately, he's
24 suffering from Parkinson's right now, but he had a list of
25 nevers. And one of the list of nevers he had is you would

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1 never use histidine in a liquid formulation. It was his
2 preference. He had lots of preconceived notions around things.

3 You know, I personally have used histidine buffer in
4 other formulations. And, actually, with one of the products I
5 developed subsequent to Eylea actually completely got rid of
6 all the Dan Dix nevers in one fell swoop with one approved
7 product. So he has those.

8 Q. Let's talk about Dan Dix nevers for aflibercept, not
9 other formulations.

10 A. Well, Dan Dix's nevers were for formulations, period.
11 They were not specifically for aflibercept.

12 Q. And you never used histidine with aflibercept,
13 correct?

14 A. I have used histidine with aflibercept.

15 Q. I believe you just told me that you never used
16 histidine to develop an aflibercept formulation prior to the
17 filing of your patent application.

18 A. Okay. You said prior to the filing of the patent
19 application. You just said I never used.

20 Q. And that's correct?

21 A. So the question is what time frame are you talking
22 about?

23 Q. Prior to your patent, you never used histidine to
24 develop an aflibercept formulation, correct?

25 A. If you're going with prior to the patent validation,

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1 no, I did not. After it, I did.

2 Q. And none of your patent examples, again, use a
3 histidine buffer?

4 A. That's there in black and white. Yes, that's
5 correct.

6 Q. All right. I'd like to talk about some of the
7 stability study documents, or SS documents, that you testified.
8 Do you recall that? We saw quite a few of them.

9 A. Yes.

10 Q. Before we do that, I'd like to pull up DTX 900,
11 pages 36 and 37, and I want to look at and show you a Regeneron
12 discovery response and ask you a couple questions about it if I
13 could, sir.

14 A. All right. Hang on a second. Let me --

15 Q. And we're going to put this on screen to make it
16 easy.

17 A. Well, the challenge is the screen is just a little
18 bit too far for the glasses, and this is a little bit too
19 close; so if I can get to the written document, I think I'll be
20 a little bit better.

21 Q. At the bottom of page 36, you'll see
22 Interrogatory 10. And in the middle of page 37, you'll see a
23 response with respect to your '865 patent.

24 A. And you said bottom of which page?

25 Q. Bottom of page 36 is Interrogatory 10.

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1 A. Okay.

2 Q. You see Interrogatory 10 asks, "For each claim of
3 each of the initial patents, identify (a) the date that the
4 claimed subject matter was first conceived and the date it was
5 reduced to practice, and (b) the diligence leading to such
6 reduction to practice, and for each such date and diligence,
7 identify with particularity the documentary evidence supporting
8 that date or diligence and at least three persons with any
9 knowledge relating to that date or diligence."

10 You see that?

11 A. I see those words on the page, yes, I do.

12 Q. And the response in the middle of page 37 on your
13 '865 patent says, "With respect to U.S. Patent Number
14 11,084,865" -- that's your patent, correct?

15 A. Yes.

16 Q. It goes on to say, "The inventors concede the
17 inventions in the asserted claims of the '865 patent no later
18 than March 21st, 2006, the date on which samples from Stability
19 Study 207 were analyzed after two months' incubation."

20 Do you see that?

21 A. Yes, I do.

22 Q. It cites one page for the record,
23 RGN-EYLEA-MYLAN-00475679. Do you see that?

24 A. Yes, I do.

25 Q. Have you seen this response before?

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1 A. No, I have not.

2 Q. It doesn't identify you as a person to have any
3 knowledge of the date of conception or reduction to practice,
4 correct?

5 A. I don't see my name on the page, but this is getting
6 into the realm of legal things. And if I'm not an expert on
7 intravitreal injections after seeing my mother receive over 90
8 some-odd injections, I can't possibly be an expert on something
9 that's a legal document without a law degree, I don't think.

10 Q. My question is much simpler.

11 You're not identified as a witness with knowledge in
12 this response, correct?

13 A. I don't see my name there.

14 Q. It identifies one page in Stability Study 207,
15 correct?

16 A. I see that it identifies the page. I'm not sure
17 what's on the page, but --

18 Q. And it does not identify all the other stability
19 studies you testified about, like the 065 study, the 203 study,
20 the 205 study. Those aren't mentioned here, correct?

21 A. No, I don't see them.

22 Q. As a matter of fact, you testified about more than
23 one page today, right? I saw dozens of documents you testified
24 about.

25 A. Yeah.

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1 Q. All right. Let's look at one of those. Let's start
2 with PTX 1825. And you recall this document, right?

3 This is the 207 study document.

4 A. Yes.

5 Q. Are you okay for short if I just go by the number,
6 the 207 study?

7 A. I think we can handle that.

8 Q. All right. So I want to start with the first page.
9 For the 207 study, we see Amendment 7.0 dated November 8, 2010;
10 is that right?

11 A. That is correct.

12 Q. Now, you know Michelle Looyenga, correct?

13 A. Michelle? What was the last name?

14 Q. Looyenga, L-O-O-Y-E-N-G-A.

15 A. Okay. It's Looyenga.

16 Q. Looyenga?

17 A. I'm sorry. The Loo threw me.

18 Q. My apologies. Looyenga. Did Michelle Looyenga help
19 make the invention in your '865 patent?

20 A. So Michelle was one of the members of the technical
21 staff that we had. She did help with study analysis. I think
22 she probably helped label some of the samples and things that
23 were put up.

24 Q. So did she help invent the formulation?

25 A. I would say no, she did not.

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1 Q. Let's take a look at one of her lab notebooks. And
2 then we'll jump back to 1825. But for a moment, let's jump to
3 PTX 2304.

4 And you see this is a Michelle Looyenga lab notebook,
5 correct?

6 THE COURT: Counsel, could I ask you to spell
7 Ms. Looyenga's last name for our record, please.

8 MR. RAKOCZY: Michelle, last name L-O-O-Y-E-N-G-A,
9 Looyenga.

10 THE COURT: Thank you. My apologies if I'm
11 mispronouncing that.

12 MR. RAKOCZY: No worries.

13 BY MR. RAKOCZY:

14 Q. And you see this is a lab notebook from Ms. Looyenga
15 dated March 9th, 2006, correct?

16 A. I do.

17 Q. Let's go to page 32 of PTX 2304. And here we see at
18 the top this is the protocol for the 207 study, correct?

19 A. Okay. You're on page what number?

20 Q. 32.

21 A. Okay. I'm trying.

22 Okay. So 32.

23 Q. I just want to confirm this is the 207 stability
24 protocol at the top, correct?

25 A. Okay. By page 32, you don't mean laboratory notebook

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1 page 32.

2 Q. No. I'm sorry, sir. I will always try to refer to
3 the exhibit number.

4 A. I'm sorry. I'm looking at the lab notebook, and I'm
5 going why are we talking about IV mixtures?

6 Q. If you look at the bottom, you see PTX 2304.0032?

7 A. Yes. 0032. All right. I'm getting there.

8 Q. Are you with me?

9 A. I am working on it. If my fingers would work. I'm
10 sorry.

11 Okay. I see 0032, yes.

12 Q. You see the protocol for the 207 study at the top on
13 the left, correct?

14 A. I do.

15 Q. And let's go to the bottom and look at the
16 signatures. And you see this was signed by Ms. Looyenga
17 March 3rd, 2006, correct?

18 A. So the laboratory notebook was signed by Michelle on
19 March 3rd, 2006. The protocol itself is not signed, however.

20 Q. And then it was witnessed August 22nd, 2006, correct?

21 A. Yeah, by Gareth Walsh, it looks like.

22 Q. Now, I want to jump back. And I'm sorry to put you
23 through that. Let's toggle back to PTX 1825. That's the very
24 large 207 document in your binder that you testified about.
25 Let's go to page 85.

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1 And you see here we have the purpose of the 207
2 study, correct?

3 A. And you said this is on page 85?

4 Q. Page 85 of PTX 1825, also on your screen.

5 A. Yes.

6 Q. And you see the purpose at the top is, "Determine the
7 stability of 40 mg/mL VEGF Trap in the polysorbate 20-based
8 intravitreal formulation when packaged in a prefilled syringe
9 with six different component combinations," correct?

10 A. Yep.

11 Q. Now, the test article was the prefilled syringe, and
12 the vial was the control in this study, correct?

13 A. So it goes on to say the stability of VEGF Trap, when
14 filled in grass vials, will serve as a control for the study.
15 So we were performing multiple pieces of work in one study.
16 One, we had the formulations. We wanted to see how they
17 perform in the vial.

18 The other thing is we were tasked with developing a
19 prefilled syringe and had to contract to somebody to fill a
20 prefilled syringe. Studies are a lot of work. So in one study
21 we have six syringes, one vial. Yes, we called the vial as a
22 control for the prefilled syringes because we expected, if
23 anything, the prefilled syringes would perform worse than the
24 vial.

25 Q. You understand the asserted claims in this case are

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1 all to a vial, right?

2 A. Yes.

3 Q. And so in this test, the 207 test, just so the
4 record's clear, the test article was the syringe and the
5 control was the vial, correct?

6 A. Yeah. The control for the syringe was the vial, yes.

7 Q. All right. Let's go to page 92 of the same document.
8 I just want to look at the signature at the bottom. It looks
9 like your boss Dan Dix signed this February 3rd, 2006, correct?

10 A. He signed it for the second time, yes.

11 Q. And this protocol was amended numerous times; is that
12 right?

13 A. Over the course of three years, yes, it was amended a
14 number of times. This, I think, if I look back at it, we
15 identified that there were a number of minor changes that
16 needed to be -- or the lead technician on the study felt needed
17 to be corrected.

18 One of them was we put up 39 vials instead of 42 that
19 we planned. So she initialed and dated the corrections on the
20 17th of January when she realized she was short items, signed
21 it. I signed it very shortly thereafter, and then Dan signed
22 off on the changes as well.

23 Q. Let's go to page 103. I just want to get the dates
24 of some of these amendments.

25 On page 103 we have Amendment 4.0 dated August 21st,

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1 2008, correct?

2 A. Which page number are you on?

3 Q. We're on page 103, on your screen as well.

4 A. Okay.

5 Q. And that amendment is dated August 21st, 2008,
6 correct?

7 A. That's the number in the upper left hand -- or
8 right-hand corner, yes.

9 Q. And the first amendment -- I'm sorry -- the latest
10 amendment, it's on the first page of the exhibit, page 1. And
11 that was Amendment 7.0 all the way up to November 8, 2010,
12 correct?

13 A. Yes.

14 Q. Now, let's go to page 137 and look at some of the
15 data. On 137 at the top you see we have analysis of VEGF Trap
16 by visual inspection, correct?

17 A. Hang on.

18 Yes.

19 Q. And if we look under vial under 5 degrees C, we can
20 see at .5 months the technician wrote filamentous particle and
21 one small particle, correct?

22 A. That is correct.

23 Q. Particles are not good, right?

24 A. Well -- so in this case, these were hand-filled vials
25 in our lab. And we were used to getting extraneous particles

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1 from filaments and fibers. And we had a scoring system that
2 allowed a certain number of particles to be present.

3 This is totally different than GNP product, which is
4 produced in a clean room in an environment that ensures no
5 particles from dust and whatever else is floating around in
6 your lab that's in there.

7 Q. I just asked if particles are bad. And I recall you
8 testifying --

9 A. Particles are bad.

10 Q. Particles are "kind of a serious thing" and "very
11 bad."

12 That's what you said, right?

13 A. That's true.

14 Q. And there are particles in this formulation, correct?

15 A. Yes.

16 Q. Let's look at another one. Let's go to page 142 of
17 the same exhibit at the top. And we see some more visual
18 inspection data. You see that?

19 A. Uh-huh.

20 Q. And for 5 degrees C. And here we see in several
21 places the technician noted small particle, filamentous
22 particle, small particles, particles, correct?

23 A. Yes.

24 Q. Particles all over the place. That's very bad,
25 correct?

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1 A. Well, so -- let's see. This is 2007. You're looking
2 at Syringe Number 1, Syringe Number 2, Syringe Number 3, and
3 Syringe Number 5, if I have the right page, 142. So this is
4 syringes, and this isn't the vial.

5 Q. So this doesn't count? The syringe data doesn't
6 count?

7 A. Well, you know, we're talking about a vial in the
8 patent. One of the things that is a concern, when you move a
9 formulation from a vial into a prefilled syringe, is you
10 encounter a lot of different materials that are not in the
11 vial. So syringes have silicone oil either sprayed or baked on
12 the inside of them. Some syringes -- well, glass syringes have
13 tungsten, and tungsten can cause proteins to precipitate. So
14 it's kind of two different environments.

15 Q. I just want to get it straight.

16 You took us through a dozen studies showing us
17 prefilled syringe data. And so I'm looking at prefilled
18 syringe data that's got particles all over the place. And
19 you're saying that's not relevant to the stability of the vial?

20 A. A vial is a very different environment.

21 Q. So all that syringe data we looked at would not be
22 relevant to the stability of the vial, correct?

23 A. I would assess my stability with things in the vial.
24 If it's unstable in a syringe, doesn't mean it's unstable in a
25 vial. They're different beasts.

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1 Q. All right. Let's go to page 14 of this same exhibit
2 and look at some additional data.

3 And the first thing I want to note on this page, here
4 we have the 207 study data for 5 degrees C. And it's dated --
5 can you tell me, what's that date at the top?

6 A. Which page are you on?

7 Q. We're on page 14 of PTX 1825.

8 A. Okay. So on the screen here, if I'm seeing it right,
9 it looks like the 28th of August 2008.

10 Q. August 28th, 2008, at the top, correct?

11 A. Yes.

12 Q. Now, there are no dates in this table on when exactly
13 the testing was conducted, correct? At least none that I can
14 see.

15 A. So that would be captured at the end with the
16 sequence information.

17 Q. We'll get there. But on this table right here, this
18 doesn't say when this testing was conducted?

19 A. No. I don't see it on the table at all, no.

20 Q. And I see a syringe column but not a vial column,
21 correct?

22 A. Yes. So the reason why you see a syringe column --
23 everything had a syringe column, but that's Device Number 1.

24 Q. I'm just asking do I see a syringe column and not a
25 vial column. That's all I'm asking. Your counsel can ask away

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1 whatever else he wants.

2 A. Okay. Well, you see a syringe column, and it's
3 Device Number 1, which was a syringe.

4 Q. All right. Let's go to page 68 of the same document.

5 And here we see analysis of VEGF Trap by OD at
6 405 nanometers, correct?

7 A. That is correct.

8 Q. So I'll call this OD405 data for short. And at two
9 months, you see the data that's been highlighted?

10 A. Uh-huh.

11 Q. And all this data, it ranges from .047 through about
12 .0 -- 0.053, correct?

13 A. That is correct.

14 Q. And it's all been crossed out and rewritten, correct?

15 A. Yeah. It looks like there were two entries there.

16 Q. Now, let's jump to page 111 of this same document --
17 and let me back up.

18 You said that the way this document is compiled, this
19 is the way that it was kept in the normal course of business?

20 A. So this is a file. It is called a study folder. It
21 collected all the loose paper from the stability study. And
22 things went in. Sometimes things went in in the middle;
23 sometimes things went in the end.

24 Q. Because it kind of looks like a dog's breakfast, like
25 someone threw everything in the air and then just recompiled

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1 it?

2 A. Well, I wouldn't say that they threw it in the air.
3 It was like, I'm stuffing it in, I've got it, I'm stuffing it
4 in, I've got it. You know, that's kind of the way it was done.

5 Q. All right.

6 A. Is it a good way to do it? Well, we have better ways
7 now, but --

8 Q. Let's jump to page 111 of the same exhibit, PTX 1825.
9 And here we see Amendment 5.0 --

10 A. Yeah.

11 Q. -- to the 207 study dated August 19th, 2008, correct?

12 A. That is correct.

13 Q. And I'd like to look at the second paragraph. And
14 you see it states that, "Variability between HPLC systems and
15 HPLC column lots over time may cause variability in purity
16 results between samples run at discrete points in time."

17 Do you see that?

18 A. Yes, I do.

19 Q. And the next sentence continues that "This may impact
20 the ability to confidently identify trends in data which have
21 been processed on different systems and across a wide spectrum
22 of time," correct?

23 A. That is correct.

24 Q. All right. I'd like to switch gears if I could.

25 You testified about your provisional application. Do

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1 you recall that?

2 A. Yes.

3 Q. I want to look at just a couple quick things
4 hopefully. Let's go to PTX 3249. I believe it's already in
5 evidence. And this is your provisional application you were
6 looking at during your direct testimony. And I'd like to go to
7 page 11.

8 THE COURT: I'm sorry, Counsel. What page was that
9 again?

10 MR. RAKOCZY: PTX 3249 at page 11.

11 THE COURT: Thank you.

12 THE WITNESS: Looks like you're having trouble with
13 this too.

14 BY MR. RAKOCZY:

15 Q. I'd like to focus on paragraph 8 starting the third
16 line. You see it describes an ophthalmic formulation.

17 Do you see that?

18 A. You're on which page?

19 Q. I'm on page 11.

20 A. Yeah.

21 Q. Paragraph 8. And the third line down describes an
22 ophthalmic formulation comprises about 40 to 50 mg/mL of the
23 VEGF antagonist Sequence ID Number 4.

24 Do you see that?

25 A. Yes, I do.

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1 Q. So that's disclosing a range of concentrations, 40 to
2 50 mg/mL, correct?

3 A. It lists a range of 40 to 50 mg/mL, yes.

4 Q. It's not describing 40 mg/mL, correct?

5 A. It's listing a range. What that plays out in the
6 patent, I'm not an attorney; so I'm not going to try and
7 interpret that one.

8 Q. Well, my question is simple. This formulation is
9 describing a range, 40 to 50 mg/mL?

10 A. Yes.

11 Q. Not 40 mg/mL, correct?

12 A. That is what I see on the page. There's a range of
13 40 to 50 mg/mL.

14 Q. Now, let's look down on the same page, the next line.
15 You see it describes a range of "0.01 to 3 percent
16 polysorbate."

17 Do you see that?

18 A. Yes, I do.

19 Q. So that is not 0.03 percent polysorbate 20, correct?

20 A. It is a range that encompasses 0.03 percent
21 polysorbate.

22 Q. So that range covers 0.03 percent. Is that what
23 you're saying?

24 A. No. All I'm saying is, mathematically, 0.03 percent
25 falls in between 0.01 and point -- and -- not .3 -- and

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1 3 percent. Interpreting the claim would be something that an
2 attorney would need to do.

3 Q. Under that rationale, 40 mg/mL falls within 40 to
4 50 mg/mL aflibercept, correct?

5 A. Mathematically, yes, it does.

6 Q. Now, this range on screen, 0.01 to 3 percent
7 polysorbate, is different from a range of 0.03 to .1 percent
8 polysorbate 20; is that right?

9 A. Okay. Say that again.

10 Q. The range on screen, 0.01 to 3 percent polysorbate,
11 is different from 0.03 to .1 percent polysorbate 20; is that
12 right?

13 A. The ranges that are described -- in that case, the
14 ranges are different.

15 Q. Now, let's go take a quick look at paragraphs 11 and
16 12. And these, unfortunately, bridge pages 11 and 12 of the
17 same exhibit.

18 And do you see here it discloses 0.03 percent
19 polysorbate; is that right?

20 A. It says 0.03 percent polysorbate, yes.

21 Q. And that is different from a range of 0.03 to
22 0.1 percent polysorbate; is that right?

23 A. If you're asking me within the context of the patent,
24 that's something I would need an attorney to answer.

25 Q. I'm just asking about the number. The number

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1 0.03 percent polysorbate is not 0.03 to 0.1; is that right?

2 A. Well, all right. If I'm not talking about a patent
3 and I'm talking about math --

4 THE COURT: He's just asking about the specific
5 document, Doctor.

6 THE WITNESS: About the specific document?

7 If this is about the document, this is a patent; so I
8 don't feel that I'm the appropriate person to answer that.

9 BY MR. RAKOCZY:

10 Q. So you're not qualified to opine or testify about
11 patents, correct?

12 A. I can tell you about my invention. I can tell you
13 about the work that I've done. If -- and you're looking at
14 what I believe are claims within the patent or a summary of the
15 invention. By the time you're getting down to the very
16 specific meaning, you know, is 0.03 to 1 the same as 0.03, I'm
17 getting to the point where I'm sorry, I'm not an attorney.

18 Q. So when you were -- I'm sorry, sir.

19 When you were comparing with your counsel the text in
20 the provisional application compared to your '865 application,
21 you weren't interpreting any of that; you were just telling us
22 whether the words were the same or not. Is that right?

23 A. So I was looking to see if there was drift or change
24 in the words. I was looking to see if the data was correct.
25 And as near as I could tell, when I laid the documents down

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1 beside one another and looked at them, the words were the same.

2 Q. But you weren't interpreting those words, correct?

3 A. I was looking to see if the words were the same.

4 Q. All right. Let's jump back to some of your stability
5 studies. And I want to start with the 205 study which is at
6 PTX 2265. And it's on screen.

7 Do you see that?

8 A. Okay. Yes.

9 Q. And the 205 study, I want to look at the formulation.
10 And this formulation in the 205 study was phosphate, NaCl,
11 polysorbate 20, and 40 mg/mL of VEGF Trap, correct?

12 A. Phosphate, NaCl, polysorbate 20, and 40 mg/mL VEGF
13 Trap, yes.

14 Q. Now, there's no sucrose in this formulation, correct?

15 A. That is correct.

16 Q. There's no sugar or sugar alcohol stabilizer in this
17 formulation, correct?

18 A. There is not.

19 Q. You're aware all asserted claims require a sugar
20 stabilizer?

21 A. I'm not sure that that is the case. I don't know.

22 Q. You don't know whether the asserted claims require a
23 stabilizer?

24 A. So that would be a question for my lawyer.

25 Q. Okay. Did you look at the asserted claims in

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1 preparation for your testimony today?

2 A. I read through them, yes.

3 Q. Did you ask anybody what the asserted claims were?

4 A. Actually, I don't recall specifically asking to go
5 through the details of the asserted claims.

6 Q. All right. Let's look at another study. I want to
7 very briefly touch on the 065 study.

8 If we could pull up PTX 3266. That may be the wrong
9 exhibit. No, there it is.

10 I just want to confirm. In the 065 study, all the
11 formulations were 50 mg/mL concentration of aflibercept; is
12 that right?

13 A. That is my recollection, yes.

14 Q. And I think you testified earlier you understood that
15 all the asserted claims are to 40 mg/mL aflibercept, correct?

16 A. I believe that I may have made a statement to that
17 effect, yes.

18 Q. So I just want to be clear, then. We can consider
19 the 40 and the 50 mg/mL concentrations equivalent in your view?

20 A. No. They're different.

21 Q. They're different. Okay.

22 All right. I'd like to pull up one of your slide
23 decks, which is PTX 3314. It should be in your binder. We'll
24 pull it up on screen as well. You see this is entitled "ITV
25 Review and Summary," correct?

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1 A. Yes.

2 Q. And this was attached to an email at PTX 3313 from
3 Jennifer Carrier dated March 14th, 2006. So we'll pull that up
4 and confirm it.

5 If we could please see PTX 3313.

6 And you see the email at the top dated March 14th,
7 2006, from Jennifer Carrier. Do you see that?

8 A. Yes, I do.

9 Q. And she's attaching an ITV review and summary, March
10 14th, 2006, laptop presentation, correct?

11 A. Yes.

12 Q. All right. Let's jump back to the presentation. I
13 want to go to page 7. And here we see at the top the title of
14 the slide is "VEGF Trap ITV, the next steps," correct?

15 Do you see that?

16 A. Yes.

17 Q. And the first step or the first bullet is "a more
18 stable ITV formulation was and is desired," correct?

19 A. Yes.

20 Q. And it says "because due to demonstration of
21 instability to vortex in various syringe stresses," correct?

22 A. Yes.

23 Q. And then let's look at the next page, 8. Here you
24 say that you're going to use stability analysis tools to
25 identify superior formulations, correct?

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1 Do you see that?

2 A. Okay. I see two assays. I guess, yes, that is the
3 meaning of what is on the page, yes.

4 Q. Now, I want to very briefly jump to page 22 of your
5 presentation. And here we have some data at 5 degrees C.

6 Do you see that?

7 A. I'm working on it.

8 Okay. 5 degrees C, yes.

9 Q. And you see in the left-hand column you have the
10 formulations, right?

11 A. Yes.

12 Q. And the F2 formulation is the 40 mg/mL VEGF Trap
13 containing 0.03 percent polysorbate 20, correct?

14 A. So yes. It contains -- it's listed as having those
15 components, yes.

16 Q. And then for the length of stress at 5 degrees C, we
17 have one month and five month, correct?

18 A. Yes.

19 Q. And at one month, the native VEGF Trap was less than
20 98 percent, correct?

21 A. So at one month, the native VEGF Trap was 97.9. But
22 I'm not sure what the full composition of this formulation is
23 based on what I'm seeing here. I know it's from Stability
24 Study 191, which I would need that detail to know the actual
25 composition.

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1 Q. I'm just asking if Formulation 2 at the one month was
2 below 98 percent VEGF Trap native. Correct?

3 A. It was. It started out below 98 percent.

4 Q. All right. Let's jump to PTX 3312. And I think you
5 testified about this document, correct, the update on ITV
6 syringe stability studies?

7 A. 3312?

8 Q. Yes.

9 A. No. I think I testified about a different document,
10 but this might have been in my deposition.

11 Q. This is yours as well, correct? It's entitled
12 "Update on ITV Syringe Stability Studies"?

13 A. It's mine and Dan's, yes.

14 Q. By Dr. Dix and yourself, dated March --

15 A. That is correct.

16 Q. I'm sorry. I'll start over.

17 This is one of your presentations along with Dr. Dix
18 dated March 16th, 2006; is that right?

19 A. Yes, it is.

20 Q. Let's go to page 2 of your presentation. And here it
21 says that "studies ongoing, examining the stability of the
22 following formulations," correct?

23 A. That is correct.

24 Q. And at the bottom we see two of the formulations
25 where the studies were ongoing are Formulations 8 and 9?

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1 A. Yes.

2 Q. And both of those are the 40 mg/mL which contains
3 0.03 percent polysorbate; is that right?

4 A. That is correct.

5 Q. Now, let's go to page 27 of this same exhibit. And
6 am I correct? Does it say that the VEGF Trap in the oncology
7 formulation is threefold more stable than the current ITV
8 formulation? Is that right?

9 A. Which page are you on?

10 Q. On page 27.

11 A. Okay. I'm going to lose my mind because I keep
12 looking at the document page and not your page number. I
13 apologize.

14 Q. They're the same on this one. Slide 27 is page 27.

15 A. Yeah, it is. That's pretty good. I'm going wow.

16 So you said the oncology formulation is approximately
17 threefold more stable than the current ITV?

18 Q. Yes. Is that right?

19 A. That's a fair statement, yes.

20 Q. All right. Just a couple more, Dr. Graham.

21 I'd like to go to PTX 3327. And I believe I was
22 mistaken before, but I believe you did testify about this slide
23 deck entitled "Travels through two stability-indicating
24 assays," correct?

25 A. Yes, I did.

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1 Q. And I believe you said this was dated in March or
2 April of 2006, correct?

3 A. I've seen enough dates right now, I'll take the
4 record's word for that. But yes.

5 Q. I'd like to go to page -- sorry. Let's go to page 46
6 and look at formulations listed here.

7 A. Page 46?

8 Q. Yes.

9 A. At least I only have one set of page numbers this
10 time.

11 Q. Are you there?

12 A. I am.

13 Q. And this one you see has total number of particles
14 500 nanometers or larger in 1 mL formulation; is that right?

15 A. That is correct.

16 Q. And if we look near the bottom, Formulations 8 and 9
17 are both 40 mg/mL concentration and they both contain 0.03
18 percent polysorbate.

19 Do you see that?

20 A. Yes.

21 Q. And unstressed, each of these particles -- strike
22 that. Let me back up.

23 I apologize, Your Honor. It's getting late.

24 Unstressed, each of these formulations had over
25 60,000 particles 500 nanometers or larger, correct?

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1 A. Yes, they did.

2 Q. Particles are very serious and very bad, correct?

3 A. They are serious and bad, yes.

4 Q. And when stressed, they each contained over 300,000
5 particles, correct?

6 A. Yes. They increased, yes.

7 Q. I apologize. I forgot to ask about one other study,
8 and then I promise you we're going to leave the studies.

9 Let's jump to PTX 1860, different exhibit.

10 And this is the 203 study. You remember mentioning
11 that, correct? And I want to jump to page 130 and look at the
12 formulation.

13 A. So the exhibit is?

14 THE COURT: You said 1860, Counsel?

15 THE WITNESS: I don't see that.

16 BY MR. RAKOCZY:

17 Q. PTX 1860. Oh, it's in your original binder. I
18 apologize.

19 THE COURT: The other book, Doctor.

20 THE WITNESS: Thank you.

21 BY MR. RAKOCZY:

22 Q. I want to go to PTX 1860, page 130. And I just want
23 to confirm the test article formulation.

24 A. 130.

25 Q. Do you see it?

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1 A. Okay. So --

2 Q. I'm looking at the test article on page 130. It's on
3 screen.

4 A. So you're saying the document is PTX and the page is
5 0130?

6 Q. I believe it's page 130 of PTX 1860. It's on screen
7 as well.

8 A. All right. Now I'm really confused. You said it was
9 the other notebook. Oh, you mean not this other notebook; the
10 other notebook.

11 THE COURT: Yes, Doctor. Yes.

12 THE WITNESS: Don't give me more than two notebooks
13 at a time or I'm in trouble. Okay. And you are on page 130?
14 BY MR. RAKOCZY:

15 Q. Yes. And I want to confirm that the test article in
16 this study did not contain sucrose or another sugar stabilizer;
17 is that right?

18 A. Let me get to 130.

19 So ask your question. I'm there.

20 Q. I just want to confirm the test article -- and we
21 have it on screen -- did not contain sucrose or another sugar
22 stabilizer; is that correct?

23 A. There is no sucrose in the formulation.

24 Q. Now, you testified quite a bit today about the
25 40 mg/mL aflibercept concentration formulations, correct?

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1 A. Yes.

2 MR. RAKOCZY: I have a couple more exhibits, Your
3 Honor. May I approach?

4 THE COURT: You may.

5 BY MR. RAKOCZY:

6 Q. I'm going to give you two more exhibits, Dr. Graham.

7 A. Thank you.

8 Q. All right, Dr. Graham. Let's start with the first
9 one, DTX 4121. We're going to pull it up on screen as well.

10 Do you see this is United States Patent Application
11 Publication Number U.S. 2006/0217311.

12 Do you see that?

13 A. I do.

14 Q. It's entitled "VEGF Antagonist Formulation."

15 Do you see that?

16 A. Yes.

17 Q. And the inventors are two of your colleagues, Dr. Dix
18 and Dr. Frye, correct?

19 A. That is correct.

20 Q. And do you see the file date in the middle of the
21 page, filed March 22nd, 2006, correct?

22 A. Yes, I do.

23 Q. And I want to look below that to the column where the
24 heading "Related U.S. Application Data" -- date -- or data.
25 I'm sorry. It's at the top right hand of the page. My fault.

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1 Do you see in the right "Related U.S. Application
2 Data," correct?

3 A. Yes.

4 Q. And it says, "Provisional Application
5 Number 60/665,125 filed on March 25th, 2005," correct?

6 THE COURT: Yes, Counsel?

7 MR. TRASK: Your Honor, objection. This is outside
8 the scope of the direct examination. This is a document that
9 was never shown to the doctor during his direct examination.
10 And, in fact, it's a document that defendants didn't rely on at
11 this point.

12 MR. RAKOCZY: Your Honor, he testified repeatedly
13 about the 40 mg/mL concentration. This is a U.S. patent
14 publication disclosing 40 mg/mL concentration that I'd like to
15 address with the witness.

16 THE COURT: Overruled.

17 BY MR. RAKOCZY:

18 Q. Let's turn to exhibit page 3, paragraph 17. And I
19 want to go to the ninth line down. And you see in the middle
20 here the document describes "A 40 mg/mL prelyophilized
21 solution."

22 Do you see that?

23 A. So you're on page 3?

24 Q. Paragraph 17.

25 A. And a 40 mg/mL prelyophilized solution. Yes, I see

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1 that.

2 Q. Now let's look at paragraph 36 on page --

3 A. So --

4 Q. -- 5.

5 A. -- you know, a prelyophilized solution is not a
6 formulation.

7 Q. Sir, I was just asking whether it disclose a 40 mg/mL
8 concentration in a prelyophilized --

9 A. It is a prelyophilized solution, but that's never
10 designed to be a -- I'm sorry. I'm looking at the science.
11 And I don't understand how a lyophilized solution or
12 prelyophilized solution matches up with a liquid formulation at
13 the same concentration. It's two different things.

14 Q. Sir, I'm just asking did your boss Dr. Dan Dix
15 disclose a "40 mg/mL prelyophilized solution" in that
16 paragraph?

17 A. That is what's in there, yes.

18 Q. So let's go to paragraph 36, which is on page 5. I
19 want to look at the last sentence. And here you see Dr. Dix
20 describes, "An example of a pharmaceutically acceptable liquid
21 formulation comprises a VEGF-specific fusion protein antagonist
22 in a pharmaceutically effective amount of buffer, a cosolvent,
23 and one or more stabilizers."

24 Do you see that?

25 A. Yes. That's what's written on the page.

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1 Q. Now, I want to compare this to the provisional
2 application which is the second document I handed you, which is
3 DTX 8149.

4 I'm sorry. I misspoke.

5 This document, the provisional, is DTX 8194. It's
6 the second --

7 A. I think we had you. Even with the dyslexia, it was
8 good. That one, I followed.

9 Q. All right. And do you see in the right-hand upper
10 corner we have a stamp? You see that? You see the stamp says
11 "Application 60/665,125."

12 Do you see that in the upper right-hand corner?

13 A. Yes. That's what it looks like.

14 Q. Now, let's go to page 10 of this document, page 34 --
15 paragraph 34. I'm sorry. Here we see that same heading. You
16 see stable liquid formulations, correct?

17 A. So page 10?

18 Q. Paragraph 34. We have a paragraph entitled "Stable
19 Liquid Formulations," right?

20 A. All right. I'm doing it to myself again, following
21 the document pages, not the exhibit pages. Went too far.

22 Okay. Paragraph 34.

23 Q. And you see this -- we see the same sentence, the
24 last sentence, starting, "An example of a pharmaceutically
25 acceptable liquid formulation comprises a VEGF-specific fusion

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1 protein antagonist in a pharmaceutically effective amount, a
2 buffer, a cosolvent, and one or more stabilizers," correct?

3 A. So you're saying the last sentence, correct?

4 Q. Yes.

5 A. Yes, that's what it says.

6 Q. I want to jump to the claims very quickly on page 12.

7 And can you confirm for me Claim 7 is directed to a
8 stable liquid formulation of Claim 1 comprising 1- to
9 10-millimolar phosphate buffer, 1- to 10-millimolar citrate,
10 25- to 150-millimolar NaCl, 5 to 30 percent sucrose, 10 to 50
11 mg/mL of a fusion protein, at a pH of about 6 to 6.5; is that
12 right?

13 A. This is Claim 7?

14 Q. Yes.

15 A. Yes, that's what's written on the page.

16 Q. Just a couple more quick questions, sir.

17 Let's go back to page 8 of the same exhibit,
18 DTX 8194 -- I'm sorry -- page 5. I'm doing it as well.

19 Page 5, paragraph 8, of DTX 8194.

20 A. Doesn't that mean it's time to quit?

21 THE COURT: It's airborne contagious.

22 BY MR. RAKOCZY:

23 Q. Okay. I promise.

24 A. So you're going with paragraph 8?

25 Q. Yes.

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1 A. Okay.

2 Q. And here at paragraph 8 we see a prelyophilization
3 formulation of the invention.

4 Do you see that?

5 A. Yes.

6 Q. And then it also at the end of the paragraph says the
7 polysorbate may also be present, for example, as
8 polysorbate 20, correct?

9 A. Yes.

10 MR. RAKOCZY: Can you give me one moment, Your Honor?

11 THE COURT: Certainly.

12 BY MR. RAKOCZY:

13 Q. A couple more quick items, Dr. Graham.

14 Let's go back to the prior exhibit. So can you
15 switch for me again to the first one I handed you, DTX 4121.
16 Let's go to page 5. And in the right-hand column you see
17 Tables 1 and 2.

18 A. Yes.

19 Q. And Tables 1 and 2 in the titles, you see they
20 reference Stability Study 65?

21 Do you see that?

22 A. Yes, I do.

23 Q. That's one of the stability studies that you worked
24 on that we talked about earlier today and that you talked about
25 on your direct, correct?

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1 A. Yes, it is.

2 Q. So you're not an inventor on this patent, correct?

3 A. That is correct.

4 Q. But that's your stability study?

5 A. Well, I helped it along after I joined the group, but
6 my contributions to the patent were other things. I mean, I
7 ran all the 200 through 207 studies, conducted the shear
8 studies. So yeah, I'm not an inventor on that.

9 Q. All right. Last question, Dr. Graham. And I want to
10 refer to the formulations in your '865 patent.

11 If an ophthalmologist administered the formulation
12 from your '865 patent but without the aflibercept, would that
13 be a safe and effective medicine for treating eye diseases?

14 A. Did you -- would you say that again. I'm sorry.

15 Q. Yes.

16 If a doctor administered the formulation from your
17 '865 patent but without the aflibercept, would that be a safe
18 and effective medication?

19 A. I would not expect so.

20 MR. RAKOCZY: All right. Pass the witness, Your
21 Honor.

22 THE COURT: Thank you.

23 Redirect, Counsel?

24 MR. TRASK: Thank you, Your Honor.

25 THE COURT: Why don't we take five.

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1 You're still off limits for folks to speak with you,
2 but you can step down. We'll take a quick five-minute break
3 and finish the doctor's testimony.

4 THE WITNESS: Thank you.

5 (A recess was taken from 4:44 p.m. to
6 4:51 p.m.)

7 THE COURT: Counsel, you may proceed.

8 MR. TRASK: Thank you, Your Honor.

9 REDIRECT EXAMINATION

10 BY MR. TRASK:

11 Q. Dr. Graham, do you have the binder in front of you
12 that defense counsel handed up?

13 A. Yes.

14 Q. Could we turn to Exhibit DTX 900 in that binder.

15 I'd like to turn to page 37 of that document.

16 And if we could zoom in on the paragraph that starts
17 "with respect" -- actually, "Subject to the foregoing general"
18 and then following paragraph.

19 Doctor, do you see that on the screen?

20 A. Yes, I do.

21 Q. Do you remember defense counsel made a bit of a show
22 about the fact that your name is not identified in this
23 interrogatory response served by Regeneron?

24 A. Yes.

25 Q. Do you see that this document refers to the '865

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1 patent and it says the inventors conceived the inventions?

2 Do you see that?

3 A. Yes, I do.

4 Q. Who are the inventors of the '865 patent?

5 A. Well, that would be Dan Dix, Eric Furfine, Kelly
6 Frye, and myself.

7 Q. Thank you, Doctor.

8 Do you remember you were asked on cross whether
9 polysorbate 20 is a solvent?

10 A. Yes, I was.

11 Q. Is a solvent the same as a cosolvent?

12 A. No.

13 MR. RAKOCZY: Objection, Your Honor. Calls for
14 expert testimony.

15 MR. TRASK: Your Honor, he asked this exact question
16 and tried to impeach the witness about whether polysorbate is a
17 solvent, and I'm just following up on what the doctor
18 understands that to mean.

19 THE COURT: The examination was more what do the
20 papers indicate. Sustained.

21 BY MR. TRASK:

22 Q. Let's turn to the same binder, PTX 2304. That's P as
23 in plaintiff, PTX.

24 A. PTX, not --

25 Q. Correct.

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1 A. Okay. Yes. I see that.

2 Q. And if we could turn to page 32 of that document.

3 Are you there?

4 A. I'm trying to read it on the screen, but I'm going to
5 have to struggle. What was the number again?

6 Q. It's okay. If you can see it on the screen, just a
7 quick question. If you want it, it's PTX 2304.

8 A. 23 -- PTX 23 -- okay. Good with it on the screen.
9 What's your question?

10 Q. So the question, Doctor, is do you remember when
11 counsel for Biocon and Mylan pointed to the signature by your
12 colleague Michelle Looyenga in the bottom left of this page?

13 A. Michelle Looyenga, yes.

14 Q. Can we turn to the next page of this document,
15 PTX 2304, page 33.

16 And do you see that there's a page at the bottom
17 where -- it's not the signature block, but right above that
18 there's a signature line for study director?

19 A. Yes, I do.

20 Q. Now, that's not signed, but this is Stability
21 Study 207, right?

22 A. Correct.

23 Q. Who was the study director for Stability Study 207?

24 A. That would have been me.

25 Q. Let's look at PTX 1825, page 85.

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1 A. Yes, I see that.

2 Q. I'm sorry. Wrong page. Page 137. Sorry about that.

3 And do you remember -- I'll let you get there.

4 A. Okay. I can see this one on the screen.

5 Q. Do you remember when counsel for Biocon and Mylan

6 asked you about the entry under 5C at .5 months that says, I

7 think, clear, one filamentous particle. Do you see that?

8 A. Yes.

9 Q. Does that indicate to you that this formulation is
10 unstable?

11 A. No, not necessarily.

12 Q. Why is that?

13 A. So the filamentous particle, those are typically
14 items that come from the tech's wipes, the things that we use
15 in the lab as part of the routine operations. If it had said
16 one proteinaceous particle, then I might have been concerned.
17 But the subsequent vial also showed clear, no precipitate. And
18 having a particle is not a failure by our definitions.

19 Q. Thank you, Doctor.

20 If we could look in the same exhibit, page 111. And
21 I'm looking at the second paragraph on this page.

22 A. Okay. Variability between HPLC systems and HPLC
23 columns.

24 Q. Yeah. Are you there?

25 A. Yeah.

KENNETH S. GRAHAM, PHD - REDIRECT

1 Q. Do you remember you were asked questions by counsel
2 for Biocon and Mylan about the variability regarding HPLC?

3 A. Yes.

4 Q. Is this referring to SEC or HPLC?

5 A. So this says HPLC in terms of what it's being
6 described.

7 Q. Is that the same as SEC?

8 A. Not necessarily, no.

9 Q. Okay. With respect to SEC, size-exclusion
10 chromatography, do you consider that to be a good assay for
11 analyzing the stability of aflibercept formulations?

12 A. Okay. It is a very good assay. It's what I like to
13 call the sentinel assay.

14 Q. What do you mean when you say SEC is the sentinel
15 assay?

16 A. So it's the one that shows something going wrong,
17 typically, before anything else. You know, unless we have
18 major problems, generally we don't see particles, generally we
19 don't see increases in turbidity; but we always do see some
20 level of change in HPLC.

21 Q. So, Doctor, then, if you had only one assay by which
22 you could analyze the stability of a formulation containing
23 aflibercept, what assay would you choose to use?

24 A. I would use SEC.

25 Q. Let's look at PTX 3314, page 22.

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1 Do you remember being asked for counsel by Biocon and
2 Mylan about the data under percent native VEGF Trap in this
3 exhibit --

4 A. Yes.

5 Q. -- for Formulation 2?

6 A. Yes.

7 Q. And counsel pointed out that the percent native VEGF
8 Trap at that condition was 97.9.

9 Do you remember that?

10 A. Yes.

11 Q. Was the starting percent data of VEGF Trap -- what
12 was the starting percent native VEGF Trap with this material?

13 A. So it was 97.6.

14 Q. And what does that tell you about the stability of
15 this material?

16 A. Well, so generally you have variation in your assay,
17 but you don't go up in purity. So I started off at 97.6 plus
18 or minus .1, .2, ended up at 97.9 plus or minus .2. It shows
19 that there's really no change. It says that the stability is
20 good. The fact that I started out below 98 percent, you know,
21 I would never expect to -- if I start out below, I never would
22 expect to come back up two.

23 Q. And so what does this data tell you as a formulation
24 scientist? If you had started with material that was above 98
25 percent, what would you end up with?

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1 MR. RAKOCZY: Objection, Your Honor. That's asking
2 for opinion testimony and a prediction.

3 MR. TRASK: This is the very slide that counsel asked
4 him about. I'm just asking him to explain the meaning of it,
5 Your Honor.

6 MR. RAKOCZY: He's asking him to predict something
7 that's not on the slide, Your Honor.

8 THE COURT: Understood.

9 Sustained.

10 BY MR. TRASK:

11 Q. Let's turn to Exhibit 3327, please.

12 And we'll look at page 46. Now, do you remember when
13 counsel for Biocon and Mylan asked you about the last two rows
14 of this table, Formulations 8 and 9?

15 A. Yes.

16 Q. And they pointed out that there was an increase in
17 the number of -- I don't remember if it was aggregates or
18 particles shown in this data?

19 A. I think they used the words "particles."

20 Q. How does -- can you explain how the HIAC analysis
21 works that was done to generate this data?

22 A. So this is kind of an internally controlled
23 experiment in that you start off by measuring the formulation
24 and you look at whatever the base level is. Then you subject
25 it to stress and you look for a change.

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1 The bigger the change -- you know, that -- large
2 changes are not good. Small changes are to be expected. You
3 know, there's more to the story that isn't necessarily entirely
4 captured here, but what can happen is you not only get more
5 particles but you get bigger particles.

6 In comparison, if we look at all these formulations
7 and we say, okay, how do their performances compare? 8 and 9
8 are probably two of the top ones. I mean, 8 started out fairly
9 low, went up a little bit. 9 started out at 100,000 and went
10 up.

11 You know, really, the only formulations that are on
12 there that start out significantly lower are ones that are
13 lower protein concentration. There's a couple 10 mg/mL. And,
14 you know, they're down in the 30 thousands. You know, it
15 basically says that these are stable to the stress or more
16 stable to the stress more directly than everything else that's
17 on that page.

18 Q. Thank you. Can we turn to 3312, please, page 27.

19 Do you remember when counsel for Biocon and Mylan
20 asked a question about the fourth bullet down on this slide
21 comparing the oncology formulation stability to the "current
22 ITV formulation"?

23 A. Yes.

24 Q. What is the current ITV formulation here?

25 A. So that was what we had referred to as ITV1. It was

KENNETH S. GRAHAM, PHD - REDIRECT

1 a formulation that contained 40 mg/mL aflibercept,
2 135-millimolar sodium chloride, and 0.1 percent PEG 3350.

3 So it was the formulation that we were seeing the
4 issue with particulate formulation.

5 Q. Okay. Can we look at DTX 4121, please.

6 I believe this is one of the loose-leaf documents
7 that counsel handed you. And I would like to look at page 3,
8 paragraph 17.

9 Do you see that, Doctor?

10 A. I'm doing the wrong page number thing again; but yes,
11 I do.

12 Q. So do you remember when counsel asked you a question
13 about this statement in this document, 40 mg/mL prelyophilized
14 solution?

15 A. Yes.

16 Q. Is a prelyophilized solution an ophthalmic
17 formulation?

18 A. It is not.

19 Q. Why not?

20 A. Well, a prelyophilized solution is designed to have
21 the drug remain stable solely --

22 THE COURT: One second, Doctor.

23 Yes, Counsel?

24 MR. RAKOCZY: Objection, Your Honor. This is calling
25 for expert testimony.

1 THE COURT: It is. It is. Sustained.

2 MR. TRASK: In that event, nothing further, Your
3 Honor. We do have exhibits to move in unless, obviously,
4 there's further from defense counsel.

5 THE COURT: Understood.

6 Recross?

7 MR. RAKOCZY: Depending on the exhibits, I may have
8 none, Your Honor.

9 THE COURT: Let's take the exhibits first, then.
10 Keep our fingers crossed.

11 One second, Doctor, if you'll bear with us. Just
12 housekeeping stuff.

13 THE WITNESS: Okay.

14 THE COURT: Thank you.

15 Slowly counsel, but go ahead.

16 MR. TRASK: Thank you very much, Your Honor.

17 PTX 3327, PTX 3326, PTX 2293, PTX 2292, PTX 1921,
18 PTX 1825, PTX 2277, PTX 2278, PTX 1860, PTX 2238, PTX 3249,
19 PTX 2281, PTX 2282, PTX 2283, PTX 2265, PTX 2266, PTX 2267,
20 PTX 2275, and PTX 672.

21 MR. RAKOCZY: I apologize. That was going too fast
22 for me, Your Honor. Can I compare?

23 THE COURT: Please. Compare notes.

24 MR. RAKOCZY: Your Honor, as you can imagine, I need
25 to preserve an objection for a lot of these. I'll try to do

1 them in order.

2 No objection to PTX 672.

3 We object to PTX 1825, PTX 1860, PTX 1921, PTX 2238,
4 PTX 2265, PTX 2266, PTX 2267, PTX 2275, PTX 2277, PTX 2278,
5 PTX 2281, PTX 2282, PTX 2283, PTX 2292, PTX 2293, PTX 3326,
6 PTX 3327.

7 And our objections are as I stated before, Your
8 Honor, based on our motion in limine Number 5.

9 THE COURT: Understood. The Court will receive those
10 conditionally, subject to addressing -- the parties have the
11 opportunity to address those issues raised earlier in posttrial
12 briefing. The Court will obviously address it in its findings
13 of fact and conclusions of law.

14 MR. TRASK: Just for the record, Your Honor, we
15 disagree with the objection. We think these documents were
16 adequately disclosed during discovery and there's no basis for
17 their objection here.

18 THE COURT: Understood.

19 MR. RAKOCZY: I have a few to move in, Your Honor.

20 THE COURT: One second.

21 Are those all from Regeneron's standpoint?

22 MR. TRASK: That's all, Your Honor.

23 THE COURT: All right. Subject to that condition,
24 the exhibits previously identified by counsel are deemed
25 admitted.

1 (PTX 3327, PTX 3326, PTX 2293, PTX 2292, PTX 1921,
2 PTX 1825, PTX 2277, PTX 2278, PTX 1860, PTX 2238, PTX 3249,
3 PTX 2281, PTX 2282, PTX 2283, PTX 2265, PTX 2266, PTX 2267,
4 PTX 2275, and PTX 672 were admitted.)

5 MR. RAKOCZY: And then we move to admit DTX 4121,
6 DTX 8194, DTX 737, DTX 900.

7 And, Your Honor, I have several PTXs I'm not sure.
8 They may already be in. Can I look at these overnight and then
9 I can wrap it up in the morning?

10 THE COURT: Yeah. That would be fine.

11 MR. TRASK: Then with respect to those documents,
12 Your Honor, I'll just note again that DTX 4121 is a document
13 that plaintiffs had never relied on here. It wouldn't be
14 appropriate for them to rely on that document by their experts
15 or anyone else in this case.

16 But I understand that there's kind of been an
17 agreement reached here where documents used on cross will come
18 in. And on that basis, I understand the document will be
19 admitted.

20 THE COURT: Understood.

21 Any other objections or concerns with the list from
22 defendant?

23 MR. TRASK: No, Your Honor.

24 THE COURT: Those will all be deemed admitted pending
25 closure of some PTX that may or may not have been in evidence.

1 (DTX 4121, DTX 8194, DTX 737 and DTX 900 were
2 admitted.)

3 THE COURT: May the good doctor step down?

4 MR. RAKOCZY: With that, I have nothing further for
5 Dr. Graham. Thank you.

6 THE COURT: Sir, you may step down. Thank you. You
7 can leave all the binders and whatnot there. We'll tidy up.

8 THE WITNESS: Do you want the syringes?

9 THE COURT: No. Water or not. No, never mind. I'll
10 take the Fifth on what I was going to ask.

11 THE WITNESS: Don't go there. Now, these have been
12 promised to Rene, so --

13 THE COURT: We receive those.

14 MR. TRASK: I don't think those are being received.

15 THE COURT: I thought they were simply demonstrative,
16 purely demonstrative.

17 Thank you, sir. Those are all yours.

18 Counsel, any progress on looming or remaining
19 exhibits from Dr. Stewart's examination?

20 No, sir. Go right ahead. I'm sorry.

21 MR. RAKOCZY: We'll have to get back to you in the
22 morning about Dr. Stewart along with Dr. Graham. We'll clean
23 that up.

24 THE COURT: Let's have a logistics discussion. What
25 are we down to from Regeneron's standpoint in terms of witness

1 presentation?

2 MR. BERL: Your Honor, we still have Dr. Csaky to
3 call as well as Dr. Trout. In all candor, Your Honor, we're
4 evaluating how the evidence comes in. And it's possible that
5 we may not proceed with an additional witness. It's not clear
6 that, in our view, we need to advance commercial success. And
7 that last witness, Dr. Manning, was solely related to
8 commercial success. And we are looking at the evidence. But
9 it's quite possible that we may not, in fact, call Dr. Manning,
10 which would end the case before that.

11 THE COURT: Would we finish Dr. Csaky and Dr. Trout
12 tomorrow?

13 MR. BERL: I don't think that's likely.

14 MR. RAKOCZY: And, Your Honor, if I could just add,
15 whether Dr. Manning comes, it makes a huge difference because
16 we have the last witness, Dr. Hofmann. And so we -- it would
17 be nice to know sooner rather than later for witness logistics
18 just so we don't have him standing around here for no reason.

19 MR. BERL: Obviously, we are looking at that. We'll
20 analyze the transcript. We will tell them as soon as we've
21 made a decision. But that would end the trial presumably with
22 Dr. Trout. Mr. Hofmann, I think is their commercial success
23 witness who responded to Dr. Manning. So, obviously, no
24 Dr. Manning, no Mr. Hofmann. And we would be done subject to
25 their trying -- oh, sorry. I've just been reminded we have

1 very short videos as well. I think it's no more than half an
2 hour at most.

3 THE COURT: Are those the experts in dispute at this
4 point?

5 MR. BERL: Yes.

6 THE COURT: Okay. Any other sticky notes? Okay.

7 All right. When is -- I'm sorry. Is it Mr. or
8 Dr. Hofmann?

9 MR. RAKOCZY: Mr. Hofmann.

10 THE COURT: What are Mr. Hofmann's travel plans?

11 MR. RAKOCZY: Well, we were having him stick around
12 to be the last witness on Friday. So depending on what happens
13 with Dr. Manning, whether they're going to stipulate commercial
14 success is out of the case and then we could potentially do
15 something about Mr. Hofmann. But we'll need that information
16 so we can evaluate what's left of his anticipated testimony, if
17 anything.

18 THE COURT: Understood.

19 Any idea, Counsel, when the decision on Dr. Manning
20 might be in the offing?

21 MR. BERL: We hope tonight, but tomorrow at the
22 latest.

23 THE COURT: Okay. All right. Yeah, as soon as a
24 decision is made on that, if you wouldn't mind communicating
25 that so that Mr. Hofmann can make alternative arrangements if

1 he's not going to take the stand.

2 MR. BERL: Absolutely.

3 THE COURT: Okay. All right. Anything else we need
4 to take up today, then?

5 MR. BERL: Not from Regeneron, Your Honor.

6 MR. RAKOCZY: Nothing from Mylan and Biocon, Your
7 Honor. Thank you.

8 THE COURT: Well, let's resume at 9:00 a.m. tomorrow
9 with a renewed interest in being as efficient as possible.

10 Everyone have a wonderful evening.

11 (Proceedings concluded at 5:17 p.m.)

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CERTIFICATE

I, Cindy L. Knecht, Registered Professional Reporter and Official Reporter of the United States District Court for the Northern District of West Virginia, do hereby certify that the foregoing is a true and correct transcript of the proceedings had in the above-styled action on June 21, 2023, as reported by me in stenotypy.

I certify that the transcript fees and format comply with those prescribed by the Court and the Judicial Conference of the United States.

Given under my hand this 21st day of June 2023.

/s/Cindy L. Knecht

Cindy L. Knecht, RMR/CRR
Official reporter, United States
District Court for the Northern
District of West Virginia