UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AMGEN INC.,

Petitioner,

-vs-

ALEXION PHARMACEUTICALS, INC.,

Patent Owner.

Deposition of of ARTURO CASADEVALL, M.D., Ph.D.

New York, New York

Friday, January 24, 2020 - 8:30 a.m.

Reported by:

S. Arielle Santos

Job No.: 26639

DEPOSITION of ARTURO CASADEVALL, MD, PhD, before S. Arielle Santos, Certified Court Reporter, Certified LiveNote Reporter and Notary Public.

DATE: January 24, 2020
TIME: 8:30 A.M.
LOCATION: 1185 Avenue of the Americas
New York, New York

APPEARANCES:

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TARA RAHEMBA - In-House Counsel, Alexion

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ARTURO CASADEVALL, MD, PhD

(Whereupon Arturo Casadevall, MD, PhD is Sworn In.)

EXAMINATION

BY MS. STERLING:

Q Good morning, Dr. Casadevall.

My name is Deborah Sterling, I will be taking your deposition today.

A Good morning.

Q Can you please state your full name for the record.

A Arturo Casadevall.

Q Thank you.

Do you understand you are here today to provide testimony relating to declarations that you provided as part of three different inter partes review proceedings?

A I understand that I am here to provide testimony regarding the three declarations that I provided.

Q Okay.

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Do you understand that your testimony will be recorded and the transcript will be made public?

A I understand that my testimony will be recorded and it will be made public.

Q Okay.

MR. DIAMOND: Sorry. Assuming there's not any confidential information that comes up and is allowed in the transcript, I am not aware of any right now, of course, we would reserve the right to make -- put the transcript under seal if there were some reason at some point to do so.

MS. STERLING: Of course, as would we.

MR. DIAMOND: Okay.

BY MS. STERLING:

Q Do you understand that you are testifying today under oath and under penalty of perjury?

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A I understand that I am testifying under oath and under penalty of perjury.

Q That means you are here to testify truthfully and accurately to the best of your ability regarding the opinions and information you have set forth in your declarations.

Do you understand that?

A I am here to testify accurately and truthfully.

Q Is there any reason you can't testify accurately and truthfully today?

A Not to my knowledge.

Q Okay.

Dr. Casadevall, I don't plan on playing word games with you. I plan on using straightforward English words and sentences. If you don't understand a question I'm asking, please ask me for clarification and I will try to rephrase or restate it in a way that you understand.

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Is that okay?

A Yes.

Q If you answer my question, I am just going to assume you understood the question.

Is that fair?

A (Nodding Head) That is fair.

Q Okay.

You notice we have a court reporter here today, I am sure. Because the court reporter is transcribing our conversation, I am going to do my best to try not to speak over you and I would ask that you give me the same courtesy because it's very difficult to transcribe two conversations at once.

Does that make sense?

A That makes sense.

Q Okay.

I will also ask you give audible answers; so shaking or nodding a head is not going to come forward on

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the transcript. I need you to use audible answers.

Is that okay?

A I will provide audible answers.

Q Thank you.

MR. DIAMOND: I will provide audible objections.

MS. STERLING: Of course.

MR. DIAMOND: Per request.

BY MS. STERLING:

Q I am going to try to take a break roughly every hour, just for everyone's sanity in the room. And if you need a break at any other time, please let me know and I will do my best to accommodate it. I will just ask if there is a question pending, that you answer the question before we take that break.

Is that okay?

A Yes.

Q Okay.

I am going to hand you

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three -- actually, before we start. I see you have already got documents in front of you.

What are those documents?

A These documents are three declarations relating to Case IPR 2019/00741, related to US patent number 9,732,149; Case Number IPR 2019/00740, related to patent 9,718,880; and Case Number IPR 2019/00739, related to patent 9,725,504.

(Whereupon a Recess Commenced at 8:42 a.m. and Testimony Recommenced at 8:44 a.m.)

BY MS. STERLING:

Q So I believe you just explained what the three documents are in front of you.

Are those clean versions of your declarations or do they have any notes on them?

A (Reviewing.) Clean versions

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of my documents.

Q Okay.

I am going to ask you to set those aside for a moment and I am going to give you some documents.

MR. DIAMOND: And of course, at any time during the deposition today, feel free to look at any documents that you need to answer any of counsel's questions.

BY MS. STERLING:

Q Particularly just documents I put in front of you today, please.

A Yes.

MR. DIAMOND: And of course, these documents that are in front of you as well are available for you to look at if you want.

MS. STERLING: I will ask you to work from the documents that I'm working from today.

MR. DIAMOND: Counsel, he can look at those documents too.

MS. STERLING: Fine.

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BY MS. STERLING:

Q Just when we are on this point, when counsel objects, you are still obliged to answer the question. I just want to make sure you understand that, unless your counsel instructs you not to answer the question, and then I will hear from your counsel as to why counsel is giving you that instruction.

So in other words, even if your counsel objects today, you have to answer my question, unless your counsel instructs you not to answer.

Do you understand that?

A I understand that.

Q I am going to give you three documents. They are each previously labeled ALXN2002.

There you go, sir.

They are each labeled ALXN2002, but they are each from different proceedings --

MR. DIAMOND: Before you ask

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questions, I want to get the documents.

MS. STERLING: I am not asking any questions, Evan. Just give us a minute, we are handing the documents over.

MR. DIAMOND: You hand the documents over and then you start talking about them. Great.

BY MS. STERLING:

Q Dr. Casadevall, I have given you three documents; in the bottom right-hand corner you will see they are each labeled ALXN2022.

Do you see that?

A Yes.

Q So one of them in front of you will be for IPR 2019/00739.

Do you see that one?

A I see that one.

Q Okay.

And another one in front of you will be for IPR 2019/00740.

Do you see that one?

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A I see that one.

Q Okay.

Third one in front of you is for IPR 2019/00741.

Do you have that one as well?

A I have that one.

Q Okay.

So let's start with the one that is labeled for IPR 2019/00739.

A I have it.

Q You have that one in front of you?

A Yes.

Q Okay.

And this one is for the '504 patent.

Do you agree?

A (Reviewing.)

Q The patent number is on the front of the document, if that's helpful.

A Oh, yes.

Q Okay.

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Do you recognize this document?

A This document is a copy of a declaration.

Q Okay.

It's your declaration in IPR 2019/00739, correct?

A It is a copy of my declaration in IPR 2019/00739.

Q Okay.

Is your signature page in there, just to confirm that it is your declaration? I believe it is on the page following 149.

A (Reviewing.) My signature is down here.

Q Perfect. Okay.

Did you prepare this declaration yourself?

A I prepared this declaration with the help of counsel.

Q How much time did you spend preparing your declaration?

A I have not added up all the

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hours but it will be in the dozens of hours.

Q Dozens; two dozen, ten dozen?

A I cannot recall.

Q You can't give me a ballpark?

A I cannot give you a ballpark. It would be -- it's certainly I would say more than ten.

Q Is it more than 50?

A I cannot -- I cannot recall without looking in my records.

Q Would it be more than a hundred?

A I cannot recall without looking in my records.

Q More than 500?

A I think 500 would have been -- I cannot recall actually. I mean, I would have to look at my records and look how much time I spent.

Q Sitting here today, dozens

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is the closest you can come to an estimate for how much time you spent preparing this declaration?

MR. DIAMOND: Objection to form.

THE WITNESS: You know, I -- I give you more than ten hours.

BY MS. STERLING:

Q Okay.

Are you aware of any errors in this declaration that we are looking at?

A On re-reading them, I have found several typos.

Q Okay.

Can you point me to those typos?

A Oh, God --

MR. DIAMOND: Just for the record, here, I think the versions of Dr. Casadevall's declarations --

MS. STERLING: Adam, I'm asking the witness questions.

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MR. DIAMOND: I am talking right now.

For the record, the versions of Dr. Casadevall's declarations that you handed him are binder-clipped, loose pages. The versions that Dr. Casadevall had in front of him before are bound versions.

So you know Dr. Casadevall, feel free to look at any version of your declaration you feel is most convenient for you in answering counsel's questions.

THE WITNESS: Counsel, I don't have it marked for me to find those typos. I would have to read the document again and reading this document takes me a couple of hours.

BY MS. STERLING:

Q So sitting here today, you recall that you have some typographical typed errors in your

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declaration; is that fair?

A Right. It didn't change the content of the meaning; they are just typos.

Q Okay.

So there's nothing here today that you would like to correct in your declaration; is that fair?

MR. DIAMOND: Objection to form. Mischaracterizes the witness' testimony.

THE WITNESS: I stand by my declaration.

BY MS. STERLING:

Q Let's look to the declaration that you have in front of you for IPR 2019/00740.

Can you find that one?

A 00740. (Reviewing.) I have it.

Q And that's for US patent number 9,718,880 which I will call the '880 patent today.

A I see.

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Q Okay.

Do you recognize this document?

A (Reviewing.) I recognize this document as my declaration.

Q Okay.

So it's your declaration in IPR 2019/00740, correct?

A (Reviewing.) It's my declaration in IPR 2019/00740.

Q Good.

Is that your signature page, I believe it is following page 145 in this declaration?

A (Reviewing.) That is my signature page.

Q Okay.

Did you prepare this declaration yourself?

A I prepared this declaration with the help of counsel.

Q If I ask you how much time did you spend preparing this declaration, will you give me the same

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answer as before?

A I will give you the same answer as before.

Q Okay.

Are you aware of any errors in this declaration?

A There may be a few typos but they don't substantially change the meaning of what is there. I stand by the words in the declaration.

Q Okay.

Is there anything you would like to correct in your declaration today?

A There was nothing I would like to correct in the declaration today.

Q Let's look at the third declaration that's in front of you; that one is for IPR 2019/00741.

Do you have that one?

A I have in front of me IPR 2019/00741.

Q And that's for US patent

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number 9,732,149 which I will call the '149 patent; is that fair?

A That is for Patent Number 9,732,149 and I agree that we can call it '149.

Q Thank you.

Did you prepare this declaration yourself?

A Yes, with the help of counsel.

Q And how much time did you spend preparing this declaration?

A Same -- same answer as I gave you before.

Q Okay.

Are you aware of any errors in this declaration?

A There may be some typos.

Q Is there anything you would like to correct in this declaration?

A No.

Q Having written and assuming recently read this declaration -- these declarations, you are probably

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aware that there's significant overlap between the three; is that fair?

MR. DIAMOND: Sorry, objection to form.

THE WITNESS: I think there are some -- the arguments that are made are similar in the three declarations.

BY MS. STERLING:

Q Okay.

Just for the ease of today's conversation, I am going to work from the '504 declaration and ask you questions about that declaration predominantly.

So if I point you to a paragraph in your declaration, I am pointing you to the '504 declaration.

Do you understand that?

A I understand we will be working from the '504 declaration.

MR. DIAMOND: And again --

MS. STERLING: Evan.

MR. DIAMOND: -- feel free.

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MS. STERLING: Evan, this is my deposition. You can object and you cannot instruct the witness. This is my deposition.

MR. DIAMOND: I am going to be clear and I don't think you will disagree, counsel, that the witness is entitled to look at any of his declarations or any documents, for that matter, in front of him today that he feels he needs to answer any questions. I think it will be improper instruction.

MS. STERLING: Stop coaching your witness.

MR. DIAMOND: I am not coaching the witness. I am making sure the record is clear.

BY MS. STERLING:

Q Dr. Casadevall, if I want to talk about any specific paragraphs in your '880 declaration or your '149 declaration, I will take you to those

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declarations and point you to those paragraphs; is that fair?

MR. DIAMOND: Objection. It's an improper instruction.

THE WITNESS: I understand that we are going to be working from the '504 declaration. If you want to talk to me about the other declarations, we are going to have to go to those documents.

BY MS. STERLING:

Q Okay.

Did you perform any literature searches preparing your declarations?

MR. DIAMOND: Objection to form.

THE WITNESS: I concentrated primarily in the documents and the references that were -- they are in. I do not recall any particular literature references in preparation of this document.

BY MS. STERLING:

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Q I'm sorry, I didn't hear your answer.

A I do not recall any particular literature for this document.

Q I asked if you performed any literature searches in preparing your declaration.

MR. DIAMOND: Objection to form.

THE WITNESS: I performed no literature searches in preparing my declaration.

BY MS. STERLING:

Q How much time did you spend preparing for your deposition today?

A I have not added up the hours but we will be looking in excess of 30 hours.

Q I am going to ask you some questions about preparing for your deposition. Please understand I do not intend to ask you to disclose any confidential information or any

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discussions -- the substance of discussions with your attorneys.

Do you understand that --

A I understand.

Q -- before I ask these questions?

Did you meet with anyone to prepare for today's deposition?

MR. DIAMOND: You can answer that yes or no.

THE WITNESS: Yes.

BY MS. STERLING:

Q Who did you meet with in preparation for this deposition?

MR. DIAMOND: You can say who, if you recall.

THE WITNESS: I met with the legal team headed by Evan Diamond.

BY MS. STERLING:

Q Can you recall the specific people you met with?

A I met with Julia and I met with another lawyer known as Gerard, and another lawyer known as Vanessa.

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I do not recall their last names.

Q Were these meetings in person or by phone?

A They were meetings in person and there have been conversations by phone.

MR. DIAMOND: Again, just to be clear, counsel is not asking for the substance of any of these conversations.

THE WITNESS: Right.

BY MS. STERLING:

Q How long did you meet with the people that you just mentioned?

A I met -- I met three days from seven to eight hours each day. That would have been last Friday, last Monday, and yesterday.

Q Okay.

Did you review any documents in preparing for your deposition?

MR. DIAMOND: You can answer that yes or no.

THE WITNESS: Yes.

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BY MS. STERLING:

Q Which ones?

A I reviewed the documents, I reviewed my depositions, and I reviewed the patents, and I reviewed the literature that was cited.

Q When you say "the literature that was cited," what are you referring to?

A I am referring to the citations in these declarations, as well as in the appendices.

MR. DIAMOND: For the record, since we don't have video, the witness was indicating to his three declarations when he was answering that question.

MS. STERLING: I am looking at the transcript and it's also in front of you, I am sure, Evan.

BY MS. STERLING:

Q Earlier you said you reviewed your depositions.

What depositions are you

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referring to?

A I meant declarations.

Q Okay.

So just to clarify, is it fair to say you reviewed your declarations, the patents, and the literature that's cited in your declarations?

A I reviewed my declarations, the patents, and the literature that is cited in the declarations.

Q You have an Appendix B in your declaration, right?

A Yes (Reviewing.)

Q Is this the listing of references that you were just referring to?

MR. DIAMOND: Objection to form. Mischaracterizes the witness' testimony.

THE WITNESS: This is a list of the references but there may be references in here that are not included in here.

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BY MS. STERLING:

Q When you are saying there are references in here that are not included in here, what are the two "heres" in your --

A I did not --

MR. DIAMOND: Please, let her finish her question and then also leave me time to object before you answer, that way the court reporter can get the best record.

Sorry, what was your question again?

BY MS. STERLING:

Q My question was, you had "here" and "here" in your answer. I just want to know what those "heres" are?

A The here is the declaration.

Q Okay.

The second?

A There is a second here which is Appendix B.

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And there may be references in the body of the declaration that are not in Appendix B, although to my knowledge, the stuff cited in Appendix B is what is in the declaration.

Q Okay.

So are there any documents you considered in formulating your opinions that are not listed in Appendix B or not cited otherwise in your declaration?

A I -- formulation of my declaration, I relied on my own knowledge, I relied on what I know. But there are no specific documents that we -- that I can point to you that I considered in the -- for the preparation of this declaration, apart from the documents listed in B and that may be cited in the body of the declaration.

Q Okay.

Do you know Barnard Trout?

A Barnard --

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Q Trout, T-R-O-U-T?

A I do not recall that name.

Q Are you aware Dr. Trout submitted a declaration in this proceeding?

A I -- I don't know.

Q So is it fair to say, then, you didn't review Dr. Trout's declaration?

A I don't -- can you show me Dr. Trout's declaration. You know, I reviewed a lot of documents and it is possible that if I saw it, I would be able to recall it.

Q So you just told me that the documents you reviewed and relied upon are in Appendix B or otherwise cited in your --

A That's right.

Q -- and you're now telling me you reviewed a lot of documents and you can't recall maybe what they are?

MR. DIAMOND: Objection to form.

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THE WITNESS: Well, there are a lot of documents in B.

BY MS. STERLING:

Q Is Dr. Trout's declaration listed in your Appendix B?

A I don't know. I would have to look.

Q Please, go ahead.

MR. DIAMOND: If it's easier for you, if you are going to use those copies of the declarations, you can remove the binder clips or move them --

MS. STERLING: Evan, please, you should have had these conversations with your witness before the deposition started. The trial guide is pretty clear that you are using one-word objections and objections only. Please stop instructing your witness.

MR. DIAMOND: Gosh, I didn't know you were going to give the

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witness documents that are extremely burdensome to open up.

THE WITNESS: (Reviewing.) Would you point out to me where it is because I cannot locate Dr. Trout in this -- in Appendix B.

Let me see (Reviewing.) I don't see Dr. Trout's declaration in Appendix B.

BY MS. STERLING:

Q Okay.

So is it fair to assume, then, you did not review Dr. Trout's declaration?

MR. DIAMOND: Objection to form.

THE WITNESS: I do not recall right now Dr. Trout's declaration. I may have reviewed it but I do not recall it.

BY MS. STERLING:

Q Had you reviewed it, would you have listed it in Appendix B?

MR. DIAMOND: Objection to

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form.

THE WITNESS: The documents in Appendix B are those that are cited. I reviewed what was in Appendix B and I reviewed the references cited herein.

BY MS. STERLING:

Q You are not -- did you review other documents aside from Appendix B and whatever else may be cited in your declaration?

A I reviewed what was cited in the declaration and I do not recall specific document that I reviewed outside of these documents.

Q Okay.

Have you had any contact with Dr. Trout in connection with this proceeding?

A I do not believe I know Dr. Trout.

Q Okay.

Do you know Michel Nussenzweig?

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A Yes, I do know Michel Nussenzweig.

Q Are you aware Dr. Nussenzweig submitted a declaration in this proceeding?

A Yes.

Q Did you review Dr. Nussenzweig's declaration?

A I reviewed his declaration.

Q When did you review his declaration?

A Maybe a month ago.

Q Did you review it before you signed your declaration in these proceedings?

A I do not recall Nussenzweig being in Appendix B.

Q That wasn't my question.

My question was --

A No, because that's very important, right? Because if it's in Appendix B, that would be related to my signature.

I know that I reviewed

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Nussenzweig's declaration but I cannot tell you the -- I do not recall the exact date.

Q If you had reviewed Dr. Nussenzweig's declaration and you're relying on any content in Dr. Nussenzweig's declaration, would you had cited it in Appendix B?

MR. DIAMOND: Objection to form. Calls for speculation.

THE WITNESS: If the declaration from Nussenzweig was relevant to the case and to the declaration, it would have been cited.

BY MS. STERLING:

Q Have you had any contact with Dr. Nussenzweig in connection with this proceeding?

A I have had no-contact orders with Dr. Nussenzweig in connection with this proceeding.

Q How do you know Dr. Nussenzweig?

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A I know Dr. Nussenzweig because he is a person in the field. He's a well-known immunologist and we were students together at NYU, both in the MD-PhD program.

Q Do you know Daniel Bazarko?

A Who?

Q Daniel Bazarko, B-A-Z-A-R-K-O?

A No.

Q Are you aware that Mr. Bazarko submitted a declaration in this proceeding?

A I remember the name -- yes, I remember seeing that name and I remember looking at the document.

Q Do you recall when you looked at Mr. Bazarko's declaration?

A It would be roughly -- it would be a while ago.

Q Can you give me --

A No, let's say more than a month.

Q More than a month.

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Fewer than six months?

A Well, I became involved with this in the spring so it would have to be in that period of time.

Q Okay. So you reviewed Mr. Bazarko's declaration.

Do you recall if you reviewed it before you signed your declarations?

A I do not recall the date.

Q If Mr. Bazarko's declaration was relevant to your opinions in your declaration, would you have cited it in Appendix B?

MR. DIAMOND: Objection to form.

THE WITNESS: (Reviewing.) I think if Dr. Bazarko's declaration would have bared on the arguments that we have here, it would have been cited in Appendix B.

BY MS. STERLING:

Q In preparing for your

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deposition, did you review documents that are not cited in Appendix B or otherwise cited in your declaration?

A I did not review documents that were not in Appendix B or not cited in the declaration.

Q But you just told me you reviewed some declarations, correct, not cited in Appendix B --

A No, I --

MR. DIAMOND: Sorry, please -- let her finish her question and then give me chance to object.

Objection to form. Mischaracterizes the witness' testimony.

THE WITNESS: I said to you that I have read the Bazarko declaration. I said to you if it had been cited -- if it was relevant to these cases, it would have been cited in here.

BY MS. STERLING:

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Q So you did not review either the Bazarko declaration or the Nussenzweig declaration in preparation for your deposition?

MR. DIAMOND: Objection to form.

THE WITNESS: I went -- I went through --

MR. DIAMOND: In answering any questions about preparing for your deposition, just, please, I caution you not to reveal the substance of any communications that you had with counsel.

THE WITNESS: I think the Nussenzweig I know I definitely reviewed in preparation. And I think the Bazarko one probably been seen also.

But if you asking me yes or no, I do not recall exactly when or the content at this point.

BY MS. STERLING:

Q Correct me if I am wrong, I

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believe you just said you reviewed the Nussenzweig declaration in preparation for the deposition.

Is that accurate?

MR. DIAMOND: Objection to form. Mischaracterizes.

THE WITNESS: I reviewed the declaration prior to the deposition.

BY MS. STERLING:

Q Did you review any documents cited in the Nussenzweig declaration?

A No, I do not believe -- I do not believe I read -- I did not review -- well, I do not recall what was cited in the deposition. If you want me to answer that, you have to give me the deposition and we can look at the references and then we can match the references with those in Appendix B.

Q I believe you said deposition twice in that answer.

Are you referring to --

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A I'm sorry, I am not a lawyer. Declarations, depositions. This is stuff that's normal to you but to me you are going to have to bear with -- and please correct me and I will come back to you and be correct.

This is a deposition. These are declarations. I know.

Q Okay.

I just want to make sure we are talking about the --

A I know. It's -- this is the deposition.

Q Okay.

If I catch any of these errors, I will try to help you correct them, okay?

A Thank you. Thank you.

Q You're welcome. Okay.

Dr. Casadevall, as I mentioned, we are going to be working predominantly off the '504 declaration. I want to make sure that is the one in front of you. And you

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know, if you prefer, you can use the one with the spiral binding, if that's your preference. I just ask if you are going to --

A It is my preference, it's easier to open.

Q That's totally fine with me. I would like to see those documents first.

MS. KOLIBACHUK: We have another copy.

MR. DIAMOND: And you can also -- feel free to inspect those but we also have copies for you also.

MS. STERLING: I would like to note for the record that these declarations have been modified solely to insert tabs noting where Appendix A and Appendix B begin. Other than that, these are the same declarations, I believe, that are the exhibits in the declaration --

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MR. DIAMOND: That's our understanding as well.

MS. STERLING: Let me finish.

MR. DIAMOND: Sure, I wanted to say that's our understanding.

MS. STERLING: Okay.

BY MS. STERLING:

Q Do you have the declaration for the '504 patent in IPR 2019/00739 in front of you, Dr. Casadevall?

A I have my declaration for patent the '504 patent in front of me.

Q Okay. Let's turn to page 11. Let me know when you're there.

A (Reviewing.) I am on page 11.

Q Okay.

You have a header there, header V, Legal Standards.

Do you see that?

A I see header Legal Standards.

Q Okay.

ARTURO CASADEVALL, MD, PhD

So this section entitled Legal Standards, it starts here on page 11, and paragraph 32, and it spans through paragraph 47 -- yes, it spans through paragraph 47.

Do you agree?

A (Reviewing.) Paragraph, not page.

Q Yes.

A (Reviewing.) Yes, I agree it spans from 32 to 47.

Q Okay.

Let's look at paragraph 35. First sentence in that paragraph says, I understand that a document may "incorporate by reference" the disclosure of another document.

Do you see that sentence?

A I see the sentence, I understand that a document may incorporate by reference the disclosure of another document.

Q From where did that understanding come?

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Did it come from counsel for Alexion?

A It was explained to me -- yes, it was explained to me by counsel.

Q Okay.

Similarly, in paragraph 36, the second sentence says, "I understand a document does not anticipate just because it refers to a molecule or formulation that is later revealed to be the one claimed."

Do you see that sentence?

A I understand a document does not anticipate just because it refers to a molecule --

(Whereupon a Discussion is Held Off the Record.)

THE WITNESS: I understand a document does not anticipate just because it refers to a molecule or formulation that is later to be -- that is later revealed to be the one claimed.

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BY MS. STERLING:

Q Again, is it fair to assume this understanding came from counsel from Alexion?

A That understanding came from counsel.

Q Is it fair to say throughout this legal standards section that your understandings came from counsel for Alexion?

I understand you are not an attorney, so did these understandings come from counsel from Alexion?

A The understandings in the legal section between paragraph 32 and paragraph 47 came from counsel.

Q Okay.

Let's look at paragraph 50, it's on page 16.

Let me know when you're there.

A I am here.

Q Okay.

So we don't do it twice, do

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you want to read the first sentence into the record for me.

A "I understand that the '504 patent reflects the work of Alexion scientists in developing SOLIRIS as a safe and effective treatment for paroxysmal nocturnal hemoglobinuria (PNH)."

Q From where did that understanding come?

A That understanding came from my review of the patent.

Q Let's turn to paragraph 134. It's on page 68, if that's helpful.

A (Reviewing.) I am at paragraph 134.

Q The second sentence there that begins, "I understand..."

Can you read that sentence into the record, please?

A "I understand that SOLIRIS was the first antibody with a heavy chain of its kind containing a hybrid of sequences from both IgG2 and IgG4

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constant regions to be clinically tested in humans and that Alexion was the first to show that such an antibody could be safe and effective when administered to human patients."

Q From where did that understanding come from?

A From reading the documents, reading the patent and this sentence cites AMG1033 at 1257 to 58.

Q The next sentence says, "I also understand that SOLIRIS was the first FDA-approved product containing Alexion's uniquely-engineered heavy chain constant region."

Do you see that sentence?

A I see that sentence which is read: "I also understand that SOLIRIS was the first FDA-approved product containing Alexion's uniquely-engineered heavy chain constant region."

Q From where did that understanding come?

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A From my review of the documents and if they are involved, they are cited in Appendix B.

Q Can you recall any specific document that helped you with this understanding?

A (Reviewing.) I can't recall a specific document to cite on this.

Q Let's turn to paragraph 140.

Why don't you go ahead and read the first sentence of paragraph 140 into the record for us.

A "I understand from Dr. Balthasar's deposition that he admits key facts contrary to his position regarding POSA's understanding of eculizumab as of March 15, 2007."

Q From where did that understanding come?

A From reading Dr. Balthasar's deposition.

Q The transcript from the deposition?

A I had a copy of the

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transcript of the deposition.

Q When did you read the copy of the transcript from the deposition, do you recall?

A Sometime in the fall.

Q Let's turn to paragraph 154, please.

A I am at paragraph 154.

Q Perfect.

The last sentence of that paragraph begins, "I understand the use of an antibody..."

Are you there?

A I see it.

Q Can you read that sentence into the record.

A "I understand that the use of an antibody in clinical trials by itself is insufficient to disclose the antibody sequence. And so this does not change my opinion that a full length sequence of eculizumab was not publicly available prior to March 15, 2007."

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Q From where did that understanding come?

A That understanding comes from my experience. It comes from reviewing the documents.

Q Can you point me to any documents that tell you the use of an antibody in clinical trials by itself is insufficient to disclose the antibody sequence?

A I don't understand your question.

Q You say, "I understand that the use of an antibody in clinical trials by itself is insufficient to disclose the antibody sequence."

Do you see that in that sentence?

A I see that.

Q You just said that understanding came from documents that you reviewed.

A It came from my experience. That's what I said first. And then I

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said from documents that I reviewed. And my experience includes taking antibodies to clinical trials, seeing IRB documents, things like that.

Q I'm asking you about documents that you reviewed that you mentioned.

Can you point me to any documents that show that the use of an antibody in clinical trials by itself is insufficient to disclose the antibody sequence?

A I don't have -- I cannot recall a document that states that in particular.

Q Let's go to paragraph 216, please. It's on page 113.

A (Reviewing.)

Q Let me know --

A 216?

Q Yes, 216 on page 113.

A Yes.

Q You're there?

A Yes.

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Q Can you read the first sentence in to the record, please?

A "Further, I understand that Alexion has obtained to full amnio acid sequence of the" -- parenthesis -- "5G1.1 antibody of Evans from the HB-11625 hybridoma."

MR. DIAMOND: Just for the record, I think you said parenthesis but the document has quotation marks.

THE WITNESS: Quotation marks. Quotation marks.

BY MS. STERLING:

Q From where did that understanding come?

A That came from -- the document -- document ALXN2075 at 2.3, which was a report -- which is GenScript final report, Antibody Full Length Sequencing of Hybridoma 5.1 T175, Order Number U856UEK140-1 November 15, 2019.

Q Let's look at paragraph 281,

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please. If it's helpful, that's on page 146. Let me know when you're there.

A (Reviewing.) 281?

Q Paragraph 281. Yes.

A Yes.

Q Can you read paragraph 281 into the record?

A I understand that SOLIRIS is -- "I understand that since its approval, SOLIRIS has been commercially successful with over 1 billion in US sales each year in each of these three years."

Q Okay.

From where did that understanding come?

A I do not recall exactly where the reference is for the 1 billion in US sales.

Q Based on your answer, are you saying it's in a reference somewhere?

A I don't -- like I said,

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there's no reference here so I do not recall exactly where that comment came from or that statement came from, but it is my understanding and I stand by it, that is.

Q Where did the understanding come from, that's what I am trying to understand?

A Like I said, I don't recall exactly where it came from but it is my understanding that it is a very successful drug.

Q Specifically, you are talking about commercial success, right?

A I am talking commercial success of SOLIRIS.

Q But you are not sure from where you obtained this information?

MR. DIAMOND: Objection to form.

THE WITNESS: I do not recall where I obtained the information for the 1 billion.

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BY MS. STERLING:

Q So you haven't given us any information that we can go to and verify that, correct?

MR. DIAMOND: Objection. Sorry, objection. Mischaracterizes the witness' testimony.

THE WITNESS: I do not recall where I got the information for the one billion.

BY MS. STERLING:

Q Okay. Let's go back to your legal principles section.

I am going to focus on the anticipation part that's at paragraphs 36 to 40. Let me know when you're there.

A (Reviewing.)

Q I apologize, your anticipation actually starts at paragraph 34. I think I may have said 36.

MR. DIAMOND: So we are

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turning to paragraph 34?

MS. STERLING: Yes.

MR. DIAMOND: Okay.

BY MS. STERLING:

Q So you agree with me this is a section entitled, Standards for Anticipation?

A This section is Standards for Anticipation.

Q In paragraph 40 of that section you say, "I have also been informed by counsel that to anticipate a claimed invention, a prior art reference must be 'enabled' such that a POSA could make and use the claimed invention without undue experimentation."

Do you see that sentence?

A "I have been informed by counsel to anticipate a claimed invention, a prior art reference must be 'enabled' so that a POSA could make and use the claimed invention without undue experimentation."

Samsung Bioepis Exhibit No. 1101
Samsung Bioepis Co., Ltd. v. Alexion Pharmaceuticals, Inc., IPR2023-00998
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Q The next sentence you say: "I understand that the PTAB will consider the following factors in assessing whether a disclosure requires undue experimentation." And then you list eight factors.

Do you see that sentence?

A I see that sentence.

Q You say "the PTAB will consider the following factors."

Did you consider those factors in preparing your declaration?

MR. DIAMOND: Objection to form.

THE WITNESS: This section was -- as I stated, was provided -- legal standards were provided to me by counsel.

BY MS. STERLING:

Q I understand that the legal standards were provided to you by counsel.

I am trying to understand, did you apply them to your analysis

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here in your declaration?

A I applied these legal standards to my analysis in this declaration.

Q Okay.

In your consideration of anticipation, did you do this analysis that you are saying the PTAB will consider?

A In my analysis I consider what a POSA would have known prior to March 15, 2007, and that includes the eight items that you have there.

Q Where did you set forth your analysis based on these eight factors in your declaration?

A I don't understand your question.

Q I believe you just told me that you did consider these eight factors in your analysis in your declaration.

Is that fair?

A Yes, I considered those

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eight.

Q Where did you set forth that analysis in your declaration?

MR. DIAMOND: Objection to form.

THE WITNESS: I considered it as I read through the Balthasar deposition, and I considered it and when -- when I analyzed what a POSA would have known prior to March 15, 2007.

BY MS. STERLING:

Q Okay.

As part of your analysis regarding anticipation, did you consider whether any prior art reference of record was enabling using these eight factors?

A I considered whether any prior art -- any prior reference was enabling -- yes.

Q And you used these eight factors?

A I used these factors. They

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may not all apply to the same reference. But, yes, all of them, but they have to apply.

Q Can you show me where you have applied these eight factors in your declaration?

MR. DIAMOND: Objection to form.

THE WITNESS: I cannot show you but I can tell you a POSA prior to March 15, 2007, could not have generated eculizumab without experimentation, guidance.

The process of working examples, knowing the nature of the invention, considering the state of prior art, the relative skill in the art of predictability or unpredictability of the art.

BY MS. STERLING:

Q Yes. So I'm asking where have you discussed these factors in your declaration.

Do you discuss them anywhere

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other than in paragraph 40?

A The issues of anticipation are mentioned in the declaration. We would have to look for them but I cannot give you an exact page number right now.

MR. DIAMOND: We have been going close to an hour now, good time for a break.

MS. STERLING: No, I have a few questions then we can take a break.

THE WITNESS: I want to take a break.

MS. STERLING: I am in the middle of a question, can we finish this question?

MR. DIAMOND: Counsel, you are not in the middle of a question you had a question and answer.

MS. STERLING: I started talking and then you spoke up.

MR. DIAMOND: No, you were

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not.

Dr. Casadevall would you like to take a break?

THE WITNESS: I would like to take a break.

MR. DIAMOND: Okay. Taking a break.

MS. STERLING: Okay. We are off the record.

(Whereupon a Recess Commenced at 9:34 a.m. and Testimony Recommenced at 9:49 a.m.)

BY MS. STERLING:

Q Welcome back, Dr. Casadevall.

During the break, did you talk with your counsel about any substance of your deposition?

A No.

Q Before the break, we were looking at paragraph 40 in your declaration and I am looking at the eight factors that you have listed

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there.

Do you recall that?

A I recall that.

Q So I was asking you, is there anywhere in your declaration where you set forth your analysis of these eight factors.

Is there?

MR. DIAMOND: Objection to form. Asked and answered.

THE WITNESS: I think the eight factors are considered in my opinion, of course.

BY MS. STERLING:

Q So where do you discuss these eight factors other than here in paragraph 40?

A Well, you can look at for the nature of invention and you can see -- and for example, when you look at -- page 55, a POSA of March 15, 2007, would have understood eculizumab to be an IgG isotype humanized antibody, the nature of the invention

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would have been considered.

Q And where are you looking at on page 55?

A Page 55, Section 5.

Q So you're telling me the invention here is an IgG4-isotype humanized antibody?

MR. DIAMOND: Objection to form.

THE WITNESS: I am saying that eculizumab would have been understood to be an IgG4-isotype humanized antibody.

BY MS. STERLING:

Q And that is the nature of the invention here, an IgG4-isotype humanized antibody?

MR. DIAMOND: Objection to form.

THE WITNESS: You asked me to show you an example and I gave you an example where I would consider the nature of the invention. But this statement

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here is eculizumab was considered to be an IgG4-isotype humanized antibody prior to March 15, 2007.

BY MS. STERLING:

Q I am trying to understand how that explains the nature of the invention.

So you are saying the nature of the invention here is an IgG4-isotype humanized antibody?

A The nature of the invention that for which this case is, is SOLIRIS.

Q Okay.

Where else have you discussed -- SOLIRIS is eculizumab, right?

MR. DIAMOND: Objection to form.

THE WITNESS: Could you repeat the question?

BY MS. STERLING:

Q SOLIRIS is eculizumab, correct?

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A SOLIRIS is the name -- the name by which it is marketed. Eculizumab is the name of the antibody.

Q Is the nature of the invention the only factor you can point me to a discussion of?

A Well, we can go through the -- for example, the mechanism of action of SOLIRIS.

Looking at page 21, Section C. I would have considered the quantity of experimentation necessary, the amount of guidance presented, the presence -- an absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, and the predictability/unpredictability of the art, and the breadth of those claims.

Q And where did you set forth that analysis for the board?

A The analysis -- the

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conclusions to that analysis are set forth in my deposition -- in my declaration.

Q But I am trying to figure out where they are so we can review them.

A Well, you know, you can ask me -- like I said, I pointed to you two examples and I told you what I considered for those examples and we can go page by page, but I don't know if that's what you want to do.

Q So wherever it is you set forth these eight factors, how have you weighed them -- or did you weigh them?

Let's start there.

Did you weigh them?

MR. DIAMOND: Objection to form.

THE WITNESS: I did not weigh -- I did not weigh them in the sense of putting weight on them. But I considered them and

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they -- my understanding is to consider them together.

BY MS. STERLING:

Q So you did not weigh them, is what you are saying?

MR. DIAMOND: Sorry. Objection to form.

THE WITNESS: Can I ask what you mean by "weigh them"?

BY MS. STERLING:

Q Did you give one more weight than another one?

For example, did you give Factor 1 more weight than Factor 5?

A No, I took them in total. I took them in total. I considered them all together. I did not pick one out and give it more weight than the other.

Q So my understanding is you're telling me you discussed each of these factors throughout your declaration; is that fair?

A What -- what I have in my

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declaration is an analysis that in some cases may -- in some cases may focus more on one factor than the other. All eight factors were considered throughout the declaration.

Q Okay.

I would like to know where you have done this enablement analysis with regard to anticipation and giving us your analysis on enablement here.

A I don't understand your question.

Q So to anticipate, I am looking at paragraph 40.

You have an understanding from counsel that to anticipate a claimed invention a prior art reference must be enabled.

Do you see that in your paragraph 40?

A Yes.

Q And you understand that the PTAB is going to follow -- or consider these eight factors in that analysis.

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I'm asking you where have you performed this analysis in your declaration --

A So I.

Q -- to come to conclusion of enablement?

MR. DIAMOND: Please give counsel time to finish her question so the court reporter can get the questions and answers down.

THE WITNESS: I apologize.

BY MS. STERLING:

Q It's quite all right.

A So I will give you -- I will give you -- first of all, I will give you one example.

Consider a POSA prior to March 15, 2007, having by some magical way or some way of clairvoyance the sequence of eculizumab. I would basically have considered the quantity of the experiment necessary to enable the invention; they would have to do

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clinical trials, they would have to do a lot of scientific work, the amount of guidance presented, the presence of actual working examples, there being no prior working exams, the nature of the invention, what does it do, the state of the prior art, what would have known beforehand, how are patients treated beforehand, the relative skill of those in the art, the predictability/unpredictability of the art, and the breadth of those claims.

So, that's an example.

Q Yes. And I'm asking where you put this analysis together to weight these factors and come to a conclusion of enablement or lack thereof.

I am just not seeing it anywhere in your declaration.

MR. DIAMOND: Counsel, I object to your characterization. You can ask the question anyway

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you want but don't testify.

BY MS. STERLING:

Q I am asking you to point it to me in your declaration.

A Why don't we look at page number 1, Claims 1-3 and 7-10 of patent '504 -- so let's look at -- let me see.

Let's look at page 91. So if you look at the claims 1 and 3 and 7-10 of the '504 patent were not anticipated by Hillmen.

Well, you look at the claims and you look at the publication of Hillmen and you see that Hillmen refers to the Thomas reference which is -- and you would have concluded that eculizumab is a humanized IgG4.

That would be an example of how this would have been done.

Q I'm asking you to point me to an analysis of enablement here in this section.

You have taken us to Section

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6 -- 7(b).

Point me to enablement analysis where you weigh those factors in this section, please?

A (Reviewing.) I will take you to page 119.

Q Actually, you took us to Section B. I'm asking you about that first and then we can move on to somewhere else.

MR. DIAMOND: Counsel, it's not appropriate for you to interrupt the witness while answering.

Dr. Casadevall, can you please continue your testimony.

MS. STERLING: I would like you to answer the question I have asked. Evan, please stop.

MR. DIAMOND: Counsel, we will call the Board if you interrupt the witness.

MS. STERLING: Let's do that. Let's go off the record.

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We are going to call the board.

(Whereupon a Recess Commenced at 10:00 a.m. and Testimony Recommenced at 10:01 a.m.)

BY MS. STERLING:

Q Let's go back on the record. Thank you.

Dr. Casadevall, you had taken us to Section 7(b), and I asked you to point me where in that section -- because when -- let me rephrase that.

You took us to 7(b) because you said there would be a discussion of your enablement analysis there. And I asked you to point me to your discussion of your enablement analysis in this section.

Can you please do so?

A Can you tell me what page are we at?

Q You had directed us to page 91, Section 7(b), Entitled Claims 1 to

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3 and 7 to 10 of the '504 patent --

A Perhaps I didn't understand your question.

Q That's okay.

A Because what I answered you was how you take a look at these claims and then you match them with the eight criteria previously, and I gave you an example of how I did it.

Q But I'm asking you to point me to that example. And you took us to this section which is paragraph 174 to 184, and said this was an example.

I'm asking you to point me to where in these paragraphs that you directed us to that you did an enablement analysis.

A Well, let's look at 177. "I understand from counsel that, for a document to anticipate a patent claim, every element of the patent claim needs to be disclosed in at least one document, either expressly, as stated in the document, or inherently,

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meaning that that base on what is stated in the document itself, a POSA prior to March 15, 2007, would know the claimed invention was necessarily disclosed by that document."

There is no document that gives you eculizumab and the sequence. That's an example.

Q So you are saying this is a factor from your eight factors for your enablement analysis?

A I said that based on my understanding of your question, this my answer.

Q Which factor of the eight does paragraph 178 go to?

A What factor? I don't understand your question.

Q We are discussing the eight factors that you set forth for enablement analysis in your paragraph 40.

A (Reviewing.)

Q Do you recall that's what we

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are discussing right now?

A Yeah. But for example --

Q So I'm asking you -- let me point us to paragraph 177, as an example of your analysis for those eight factors. I'm asking you which of the factors are reflected in paragraph 177.

A (Reviewing.) All eight factors will have to be reflected. You will note the quantity of experimentation -- you would know the quantity of experimentation necessary, the amount of guidance presented, the presence of absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, and the predictability -- predictability or unpredictability of the art and breadth of the claims.

Q And you're telling me that paragraph 177 reflects your analysis of those eight factors?

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A Paragraph 177 states that for a document to anticipate a patent claim, every document needs to be disclosed in one document. And you can take those eight factors and you can -- you can -- you can apply them to any document.

Q I'm sorry.

Where does paragraph 177 say you can take those eight factors and apply them to any document?

A It's not stated -- it is not stated in paragraph 177.

Q Okay.

But 177 is where you take me to for an analysis of those eight factors; that's an example?

A Paragraph 177 is an example.

Q Okay.

You were wanting to look at a different example, earlier you were pointing me to somewhere else in your declaration.

Would you like to take me

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there?

A I don't recall which one it was because I was interrupted and brought back to this one.

Q Well, this is the one we were talking about at the time and you needed to answer the question that was pending.

So you can't recall anywhere else in your declaration where you discuss these eight factors?

A The declaration -- the words in the declaration, the analysis in the declaration considers all eight factors.

Q And where does it show how you weighed those factors and did your enablement analysis?

A I -- as I answered previously, I did not assign weight to the factors. I considered the factors in total.

Q Okay. Let's look at paragraph 42 of your declaration.

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A (Reviewing.)

Q It's on page 14, if that's helpful.

A (Reviewing.) Yes.

Q This is in the section entitled, Standards for Obviousness, correct?

A That is in the section -- paragraph 43 is in the Section B, Standard for Obviousness.

Q What is your understanding of obviousness?

MR. DIAMOND: Just to make sure, you asked for 42 or 43? I want to make sure we are looking at the right paragraph. I think you said 42, he might have said 43. I want to make sure.

MS. STERLING: When I look at a specific paragraph, I will point that out.

BY MS. STERLING:

Q What is your understanding of obviousness?

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A My understanding of obviousness is as laid out in the declaration.

"I have been informed by counsel that to establish obviousness, Amgen must show that the claimed invention as a whole would have been obvious to a POSA prior to the date on which a claimed invention was invented without the benefit or hindsight knowledge.

"I have been informed that for the purposes of this proceedings, the relevant date of invention or priority date is March 15, 2007, the earliest filing date for the '504 patent."

Q Okay.

In paragraph 42, you have been informed by counsel that the board will consider three factors in determining this obviousness analysis.

Do you see that paragraph?

MR. DIAMOND: Objection to

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form. Mischaracterizes the document.

THE WITNESS: I have been informed by counsel that the board will consider the following factors in determining whether Amgen has met its burden to establish invalidity based on obviousness: 1, the scope and content of the prior art; 2, differences between the prior art and claims at issue; 3, the level of ordinary skill in the art; and 4, objective evidence of non-obviousness.

BY MS. STERLING:

Q Is it fair to say that you, yourself, considered these factors in your analysis on obviousness?

A I considered these factors in my analysis.

Q You have been retained as an expert consultant in this case; is that accurate?

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A I have been retained as an expert -- yes, a consultant. I don't know what the exact legal term is, but I think that's close enough.

Q Okay.

So in paragraph 23 of your declaration, it's on page 8. Let me know when you're there.

A 23. (Reviewing.)

Q You say, "I am an expert in the design, development, evaluation, and testing (including biological and physicochemical analysis) of monoclonal antibodies for use in human clinical therapy, including humanized monoclonal antibodies."

Do you see that?

A Counsel, sorry. I thought -- I was looking at paragraph 23. Can you direct me to the correct paragraph.

Q I am reading from paragraph 23.

A I see but you began at, I am

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an expert...

Q Yes, in design development. Yes.

A But you began -- that's why I missed it.

Q Okay.

But you'd agree that's what paragraph 23 says?

A I would add to it, "As reflected by my education and experience as discussed above and further reflected in my curriculum vitae..."

And the part that you read -- I would read it back just to make sure that it's correct.

"I am an expert in design, development, evaluation, and testing, including biological and physicochemical analysis of monoclonal antibodies for use in human clinical therapy, including humanized monoclonal antibodies. I was also an expert in this field prior to

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March 15, 2007. A copy curriculum vitae is attached to this declaration as Appendix A."

Q Do you want to finish with the exhibit number to complete the sentence?

A Exhibit Number ALXN2023.

Q Okay.

Do you have an MD and PhD?

A I have an MD and a PhD.

Q As an MD, was your fellowship in infectious diseases?

A My fellowship was in infectious diseases.

Q Have you ever treated any patients for hematological disorders?

A Infectious disease doctors treat everyone who gets an infection, that would include many patient with hematological disorders.

Q Have you ever treated a patient with hematological disorders?

A For hematological disorders?

Q Yes.

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A I have treated them for infectious diseases.

Q But have you treated them for hematological disorders?

A Your question -- I asked you -- you began by asking me about infectious diseases. I am an expert in infectious disease.

Q I asked if your fellowship was in infectious disease --

A My fellowship was in infectious diseases.

MR. DIAMOND: Allow counsel to finish her question and give me a chance to object.

THE WITNESS: I apologize.

MR. DIAMOND: Ask your question.

BY MS. STERLING:

Q It's an awkward proceeding. It's an awkward present conversation.

So have you ever treated any patients for hematological disease?

A Have I -- the answer is yes.

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When I was a resident at Bellevue Hospital, we often had patients with hematological diseases and I would have been a physician at the time.

Q Have you ever treated a patient for PNH?

Is it okay if I call --

A Yes, PNH.

Q Have you ever treated a patient for PNH?

A I was thinking about that. I can't recall a specific patient, but it is possible that among the thousands of patients that I saw in my training, that there would have been a patient with PNH.

Q When you say the thousands of patients that you saw in your training, when was -- what is the training you were referring to?

A I was an intern at Bellevue Hospital between 1985 and 1986. I was then a resident at Bellevue Hospital between '95 -- '86 and '88, and then I

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did my fellowship infectious diseases between '88 and '92.

Q If I am understanding you correctly, and if I am not, please correct me, you say you may have treated patients with PNH during your training and that would span the years 1985 to 1992.

Is that accurate?

A If I treated patients with paroxysmal nocturnal hemoglobinuria for a hematological disorder, it would have been during my residency; that is, '85 to '88.

Q '85 to '88, okay.

And if you were to treat any patients for PNH in that time frame, do you recall what treatment you may have used?

A There was no specific treatment. It was supportive.

Q What do you mean by "supportive"?

A It means you could not

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address the underlying conditions or the underlying disease; that if they become anemic, you would give them transfusions and that you treated the symptoms of the disease.

Q So these were treatment options for a patient with PNH in this time frame, '85 to '88 that you mentioned?

A That is to the best of my recollection, yes.

Q Okay.

Were you aware of eculizumab before being retained for this case?

A I had heard about the antibody but -- but I had heard about it. I have seen it because it's often listed in review articles as a clinically used antibody.

Q Okay.

Do you have any experience in marketing therapeutic antibodies?

A No -- well, the only experience that I have had has been

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when there have been market analysis of antibodies that I have been involved in developing.

Q You have done that --

MR. DIAMOND: And just before -- I want to caution the witness. I don't know if any of this gets into any third-party confidential information. If anything -- you know, any research you have done does get into third-party confidential information, just let counsel know because I don't think she wants you to --

THE WITNESS: Yeah, I --

MS. STERLING: Before you start, that's totally accurate. I don't want you to divulge -- if you are under any confidentiality to any companies you have done research with, I don't want you to divulge that to me.

I am looking generally what

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aspects you are involved in.

THE WITNESS: So --

BY MS. STERLING:

Q I will ask the question.

I believe you mentioned you were involved in market analysis of antibodies.

Could you please explain generally without divulging confidences what that analysis entails?

A Yes. So I will give you my experience with developing anti-cryptococcal antibodies that came from my laboratory. These antibodies, what the market analysis was done, people look at the number of cases of cryptococcus, the number of doses that would be needed to treat it, the potential charge of -- the cost of making it, the cost of selling it, the likelihood that it would be used, the competing -- competing therapies; was there therapy, was there not therapy

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available.

So those were factors on it. But I will state that I am not an expert in market analysis. My expertise is, as defined in this declaration -- yeah, declaration -- and so I am speaking, you know, from some distance as to how this process goes.

Q Okay.

Let's turn to paragraph 96 in your declaration it is on page 40, if that's helpful.

A I have it.

Q Why don't you take a second and read it to yourself so you're oriented in the discussion.

A (Reviewing.)

Q You can feel free to read paragraphs around it, too, if that's helpful.

A I have read the paragraph.

Q Okay.

In this paragraph, you are

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referring to the convention of referring to early stage antibodies by reference to the original mice hybridoma and mice antibody from which they are developed.

Is that fair, generally?

MR. DIAMOND: Objection to form.

THE WITNESS: When you see an alphanumeric such as 5G1.1 that often refers to the hybridoma from which it was developed.

BY MS. STERLING:

Q Okay.

That answered my next question which was, 5G1.1 is an example of this type of naming convention you are referring to, right?

A It involves the context.

Q In this context -- in the context of this declaration, the 5G1.1 nomenclature that you are referring to, it's an example of that convention

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of referring to the original mice hybridoma.

Is that accurate?

MR. DIAMOND: Sorry. Objection to form.

THE WITNESS: You can see other examples here where humanized 5G1.1 or h5G1.1 is used or 5G1.1 is used alone. So it depends on the context of how it is written.

BY MS. STERLING:

Q Okay.

You state here, "Alexion identified the '5G1.1' hybridoma as producing the '5G1.1' mice antibody, and often referred to the humanized antibodies and fragments derived from the 5G1.1 antibody as 'humanized 5G1.1' or 'h5G1.1.'"

Do you see that?

A I see that.

Q I believe we are on the same page.

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5G1.1 is what Alexion has identified as being related to the hybridoma producing the 5G1.1 mice antibody, and there may be other letters or numbers or words associated with that 5G1.1 to further clarify.

Is that fair?

MR. DIAMOND: Objection to form.

THE WITNESS: I think you have to read it in context. I think that looking at an alphanumeric, you cannot conclude unless you see the rest of the sentence.

And I point out there are multiple references at the end of that sentence that would have provided context for how those antibodies were labeled.

BY MS. STERLING:

Q So what does humanized 5G1.1 convey to a POSA --

MR. DIAMOND: Objection.

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BY MS. STERLING:

Q -- as you have used it in this sentence as one of your examples?

MR. DIAMOND: Objection to form.

THE WITNESS: Humanized 5G1.1, in the context of Thomas, would mean to me an IgG4.

BY MS. STERLING:

Q Okay.

But would it also convey more generally a humanized version of the 5G1.1 mice -- original mice antibody?

A You have to be more specific. The word generally is a problem.

Q So -- we are going to get into specifics. I am trying to start at a higher level, if that's okay with you.

When you see humanized 5G1.1, without getting into specifics of sequence or portions, would this

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convey to a person of ordinary skill in the art that we are looking at a humanized form of the antibody 5G1.1, the original mice hybridoma? Just generally.

MR. DIAMOND: Objection to form.

THE WITNESS: I think generally would tell you you have a humanized 5G1.1. But whether it refers to your Alexion antibody, you would need to put it in context. You would need to see what reference it is.

BY MS. STERLING:

Q Okay. And those are questions I am going to get to.

The h5G1.1 that is your next example here.

Does that H also imply or express humanized --

MR. DIAMOND: Objection to form.

BY MS. STERLING:

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Q -- under this conventional nomenclature?

A In the field, the H can refer to human. It can refer to humanized. It could refer to even another sort of nomenclature. But I think that I would have to look at the reference and then I could tell you what the H means.

Q Do you recall just off the top of your head if you have any references referring to a human 5G1.1?

A I used it as an example. I did not recall the references in that case. I use it as an example that an H could be -- could be a human, for example, to distinguish it from a mouse, IgG1, some investigators may write H5G.1, others may write m5G.1. But I do not have reference for you off the top of my head.

Q But I believe you also said h5G1.1 could be humanized 5G1.1, depending on the context.

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A Well, in the context Thomas, 5G.1 has been humanized to an IgG4, constant region.

Q Okay.

5G1.1 is an antibody that binds human complement component C5; is that accurate?

MR. DIAMOND: Objection.

Now that the question got interrupted for the clarification of the reporter, could you read the whole question again so we can hear it.

BY MS. STERLING:

Q Is 5G1.1 an antibody that binds human complement component C5?

MR. DIAMOND: Objection to form.

THE WITNESS: It depends on the context.

BY MS. STERLING:

Q What context are you looking for?

A The context will be the rest

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of the sentence and the reference at the end.

Q So you're telling me 5G1.1 may not be an anti-C5 antibody?

A I am telling you that 5G1.1 -- you will have to know the context in what -- in what form it is as to whether it would bind a complement component of C5 or not.

Q Are you aware of any references here that talk about 5G1.1 as something other than an anti-C5 antibody?

A I am not aware of those references but you cannot conclude from 5G1.1 that it binds complement component 5.

Q When you say you can't conclude from 5G1.1, are you just considering that number and those letters in isolation -- or those numbers and that letter in isolation?

A I am considering the multiple times that this alphanumeric

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is being used in the documents cited in this declarations, in which in some cases it has been referred to in one -- in one type and in others -- being referred to something else. You have to look at the context to know what you're looking at.

Q So you're telling me there are documents of record that tell us that 5G1.1 is not a C5 anti -- anti-C5 antibody?

A I didn't say that. What I am saying is that you cannot conclude that it binds 5G1.1, based on -- stating it as such.

Q So you're telling me when Alexion's discussing 5G1.1 as it's antibody and discussing it as anti-C5 antibody, you would still see if you see 5G1.1 in those documents, you are not convinced that it's an anti-C5 antibody?

MR. DIAMOND: Objection to form.

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THE WITNESS: I would have to read the sentence in the context for me to make a conclusion as to whether that antibody bound 5G1 or not.

BY MS. STERLING:

Q So you're telling me a person of ordinary skill in the art, knowing about Alexion's 5G1.1 would in some situations not consider that antibody to be an anti-C5 antibody?

MR. DIAMOND: Objection to form. Asked and answered.

THE WITNESS: Which Alexion 5.1 are you referring to?

BY MS. STERLING:

Q Let's talk about the 5G1.1 in the patent.

MR. DIAMOND: What patent?

MS. STERLING: At issue here, the '504 patent.

THE WITNESS: Can I see the patent?

MS. STERLING: Yes, you may.

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BY MS. STERLING:

Q I am handing you what's been previously marked AMG101 [sic]. It is the '504 patent.

A (Reviewing.)

I am looking for a reference.

MR. DIAMOND: Just to be clear, there's no question pending right now; am I correct, counsel?

MS. STERLING: That's correct. There's no question pending.

MR. DIAMOND: Wait for counsel to ask you a question before you answer anything.

THE WITNESS: (Reviewing.)

BY MS. STERLING:

Q Actually, let's look at a different document. You can set the patent aside.

I am going to hand you what's been previously marked as AMG1021.

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A (Reviewing.)

Q This is a document entitled, Eculizumab Alexion, and it lists Mariana Kaplan as the author.

Do you see that?

A I see Eculizumab Alexion with Mariana Kaplan as the author.

Q Okay.

On that first page, in right-hand column, there's a box at the start of the column.

Do you see that --

A (Reviewing.)

Q -- box?

A Yes.

Q Okay.

And that box lists the originator, Alexion Pharmaceuticals, Inc.

MR. DIAMOND: Objection to form.

THE WITNESS: It states -- the words that are stated is originator, Alexion

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Pharmaceuticals, Inc.

BY MS. STERLING:

Q Yes.

And the next line says, Status Phase II Clinical.

Do you see that?

A I see Status Phase II Clinical.

Q And then the next entry is, Indication: Dermatological disease, glomerulonephritis, nephritis, pemphigus --

A Pemphigus.

Q -- pemphigus, psoriasis, rheumatoid arthritis, systemic lupus, erythematosus.

Do you see that?

A I see Indication: Dermatological disease, glomerulonephritis, nephritis, pemphigus, psoriasis, rheumatoid arthritis, systemic lupus, erythematosus.

Q Okay.

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And then the Action: Complement cascade inhibitor.

Do you see that?

A Complement cascade inhibitor.

Q Do you see the biotechnology line: Monoclonal antibody humanized?

A I see the biotechnology line: Monoclonal antibody humanized.

Q And then there's a line that says synonyms.

Do you see that line?

A I see the line synonyms.

Q Okay.

And there we see 5G1.1, h5G1.1, C5 complement inhibitor (Alexion), and h5G1.1 scFv.

Do you see those entries?

A I see those entries.

Q Below that there's a CAS registry database for 5G1.1 entry.

Do you see that?

MR. DIAMOND: Objection to form.

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THE WITNESS: I don't know what a CAS database registry is.

BY MS. STERLING:

Q Okay.

So here we are seeing mentions of 5G1.1.

Would you agree in this context, the 5G1.1 and the various variations of it that are mentioned here would be considered to be C5 complement inhibitor monoclonal antibodies?

MR. DIAMOND: Objection to form.

THE WITNESS: I would have to read the context of the question. To me, these are different molecules.

BY MS. STERLING:

Q Are you familiar with -- these are different molecules but do they connote an anti-C5 monoclonal antibody to you?

MR. DIAMOND: Objection to

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form.

THE WITNESS: The 5G1.1 is often referred to -- is a mouse antibody that is a C5 complement inhibitor.

BY MS. STERLING:

Q Okay.

You would agree that a person of ordinary skill in the art would have understood that prior to March 2007?

MR. DIAMOND: Objection to form.

BY MS. STERLING:

Q Right?

A A POSA at that time would have been very confused by the word synonyms; for these molecules are not synonyms.

Q Okay.

But my question was more in March 2007, a person of ordinary skill in the art would have understood that 5G1.1 can refer to a mice monoclonal

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antibody that's a C5 complement inhibitor, right?

A I think in March -- prior to March 2007, March 15, 2007, a person skilled -- a POSA, would have found references of 5G1.1 as a murine antibody that is a complement C5 inhibitor.

MR. DIAMOND: For the record murine is M-U-R-I-N-E, antibody.

BY MS. STERLING:

Q Let's go back to your declaration, paragraph 97. It's right across the page from where we just read.

A 97?

Q 97, yes.

A Paragraph 97?

Q Paragraph 97.

A I have it.

Q The second sentence of that paragraph, you talk about terminology indicating that isotype of a humanized antibody and you give two examples.

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Your examples are hG -- sorry -- h5G1.1, HuG4, and the second one is h5G1.1, HuG2/G4?

Do you see that?

A I see that.

Q What does the HuG4 in your first example mean?

A Human constant region 4.

Q What does the HuG2/G4 in your second example mean?

A It's vague. It would -- it would suggest IgG2 or 4, but it would give you no information at all in the structure.

Q You are saying it would suggest IgG2 or 4?

A It's a vague statement. You basically -- if you have human G2, you know is human IgG2. If you have a human IgG4, you know it is. But when you put that slash in there, you don't know what you have.

Q And you're telling me a person of ordinary skill in the art in

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March 2007 wouldn't have known what this was?

A I think a person of -- a POSA at the time would have looked at that and seen that it may have components of G2 and G4. But for all you know, it could have been another terminology. This is not a -- this is not a precise way of expressing a structure.

Q Let's go over to paragraph 102.

A Paragraph 102?

Q 102.

A (Reviewing.)

Q First sentence there, it says, "Accordingly, I agree with Dr. Balthasar's deposition testimony that a POSA as of March 15, 2007, would have understood that the term "eculizumab" referred to a single unique antibody with a single defined structure and primary amino acid sequence, not a class or genus of

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antibodies."

Do you see that sentence?

A I see that sentence.

Q So it's your opinion that before March 2007, the term "eculizumab" refers to one and only one single unique antibody with a single defined structure and primary amino acid sequence?

A It's my opinion that prior to March 15, 2007, the term "eculizumab" refers to one antibody with one defined structure.

Q In the previous paragraph you talk about INN and USAN names in the last sentence.

Do you see that sentence?

A (Reviewing.) Yes, I see the sentence.

Q Okay.

You say, "Generally, these names, these INN/USAN names with respect to humanized monoclonal antibodies would refer to one and only

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one specific antibody as defined by its unique primary amino acid sequence."

Do you see that?

A Yes.

Q Is eculizumab the INN name for SOLIRIS?

MR. DIAMOND: Objection to form.

BY MS. STERLING:

Q Is eculizumab an INN name?

A Eculizumab is the name that was given once it was in further development. And it would have meant the -- and eculizumab, when you look in the context of Thomas, you would have seen that it is a humanized IgG4.

Q I am just asking you simply is eculizumab under the INN naming convention, is that the name that was given to this unique sequence?

MR. DIAMOND: Objection to form.

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THE WITNESS: I can only answer by saying that eculizumab would have known as Thomas IgG4, humanized IgG4.

BY MS. STERLING:

Q You're telling me eculizumab is not an INN name for this antibody?

MR. DIAMOND: Objection to form.

THE WITNESS: Eculizumab is the entity defined by Thomas as an IgG4 humanized antibody.

BY MS. STERLING:

Q So is eculizumab a name under the INN naming convention or not?

A (Reviewing.) Under the INN naming convention, a humanized monoclonal antibody, which eculizumab would have been known as an human IgG4, would have referred to a specific molecule.

Q So is eculizumab the INN name -- is eculizumab an INN naming

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convention name or is it not?

Or can you not tell me? That's fine. If you say you don't know, that's fine as well.

MR. DIAMOND: Objection to the form.

THE WITNESS: You know, I would have to review this to make sure that the entities in INN are -- will match the conditions.

But I go back to the thing that eculizumab is one entity and eculizumab was, prior to March 15, 2004 [sic], known as a humanized IgG4.

BY MS. STERLING:

Q Okay.

Why don't we give you Exhibit Number 2046, that's been previously marked, for the record.

This is the guidelines on the use of International Non-Proprietary Names, or INNs for pharmaceutical substances.

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Do you see that title?

A Yes.

Q Are you familiar with the INN naming convention?

A I have seen this document before.

Q I am not asking about the document.

Just in general, the INN naming convention, are you familiar with it?

A I am familiar with -- I am familiar with the naming of antibodies. As to whether it is particularly identical to the INN convention, I cannot -- I don't know.

Q Okay.

But you discuss the INN guidelines in your declaration, correct?

A I -- I discuss the INN guidelines in my declaration.

Q And in fact, you cite to this document in your declaration at

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paragraph 1000?

MR. DIAMOND: Paragraph 1000.

MS. STERLING: Sorry, paragraph 100.

MR. DIAMOND: Paragraph 100. Okay.

BY MS. STERLING:

Q Do you see that?

A I stand by what I wrote here. "A POSA would have understood that this INN/USAN names with respect to humanized monoclonal antibodies would refer to one and only one specific antibody as defined by its unique primary structure and sequence."

Q Okay.

And then in paragraph 101, you go through these naming conventions.

Do you see that?

A Paragraph 101.

Q Yes.

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A Under the non-proprietary name existing in 2007, monoclonal antibodies all received the suffix -mab, and humanized monoclonals would have been -zumab --

MR. DIAMOND: Dr. Casadevall, if you can read slower so the court reporter can get the testimony.

THE WITNESS: I'm sorry.

"Under the non-proprietary naming system that existed in 2007, monoclonal antibodies all received the suffix -mab, and humanized monoclonal antibodies in particular were given the suffix -zumab." Alexion document ALXN2045 at 1210, ALXN2046 at 27.

BY MS. STERLING:

Q Okay.

Your next sentence explains that antibodies modifying the body's immune response were given the additional naming element L-I, or li,

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before the suffix, correct?

A That is correct.

Q And you say, Accordingly, an immunomodulatory humanized monoclonial antibody would end with the suffix '-lizumab' and then it would be given a unique arbitrary prefix, e.g., and you've given the example of ("ecu-").

A Right.

Q Would you agree with me that based on this naming convention and your testimony here, that eculizumab would be the naming -- a naming convention under the INN proprietary name standards or guidelines?

A Under the text of my declaration, eculizumab has been named under that naming convention since it modify -- since it inhibits complement C5 cleavage, it will meet the criteria of an immunomodulatory monoclonal humanized monoclonal antibody.

Q And when are antibodies given -- I believe you actually tell

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us when antibodies are given their INN name in paragraph 99.

You say -- let me know when you're there.

A 99.

Q Okay.

The second sentence: "A POSA would have understood that after a specific humanized monoclonal antibody with single unique sequence had progressed into clinical development, it may be assigned non-proprietary name by authorities, including INN and USAN, e.g., eculizumab."

Do you see that?

A "A POSA would have understood that after specific humanized monoclonal antibody with single unique sequence had progressed into clinical development, it may be assigned non-proprietary name by authorities, including INN and USAN... e.g., eculizumab." Is how the

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sentence ends?

A "...for example, eculizumab." Yes.

Q So once the antibodies are given these names, these antibodies have a single unique sequence; is that correct?

MR. DIAMOND: Objection to form.

THE WITNESS: I think once the antibodies are given a unique name, they are understood to have, as noted in paragraph 101, a specific antibody as defined by its unique primary amino acid sequence.

BY MS. STERLING:

Q Okay.

So setting aside whether or not you knew what that sequence is, for a person of ordinary skill in the art, before March 2007, seeing the word eculizumab and person of ordinary skill in the art would understand it

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would be in this context, right.

So a person of ordinary skill in the art, prior to 2005 [sic], seeing the word eculizumab, they would know that that was an antibody that had a single unique sequence; is that fair?

MR. DIAMOND: Sorry. Counsel, you said prior to 2005.

MS. STERLING: Sorry, 2007.

MR. DIAMOND: Ask the question again. I just want to make sure the record is clear.

BY MS. STERLING:

Q Dr. Casadevall, is my question unclear aside from the 2005, 2007?

A It was not clear and the date is critical.

Q Okay. So let's start again.

A person of ordinary skill in the art -- and you understand who that is for these proceedings, correct? Okay.

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A Yes.

Q A person of ordinary skill in the art seeing the term "eculizumab" in context, prior to March 2007, would they have understood that eculizumab would have had a single defined unique amino acid sequence?

MR. DIAMOND: Objection to form.

THE WITNESS: It's a very long question.

What I can tell you is that if you see eculizumab in the literature, you would have concluded that it is a humanized IgG4 as cited by Thomas.

BY MS. STERLING:

Q My question was, based on these INN naming conventions -- we are going to get to Thomas, don't worry and I will let you talk about Thomas as much as you want.

Under these INN naming

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conventions, seeing the word eculizumab, would a person of ordinary skill in the art have understood that to have a single unique sequence?

A You see, once the name is assigned, it is understood to be only one specific antibody as defined by its unique primary amino acid sequence.

Q Okay.

So if you were using eculizumab at a clinical trial, you would understand that that eculizumab being used in that clinical trial has a single specific antibody defined by a unique primary amino acid sequence?

MR. DIAMOND: Objection to form. Lack of foundation.

THE WITNESS: In a clinical trial, you would know that you are using it. But I don't think you -- you don't know -- you know they are using eculizumab and you know that it's an antibody that is

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defined by its unique primary amino acid sequence.

BY MS. STERLING:

Q Okay.

And just while you have document 2046 in front of you, on page 27 there's a heading, Monoclonal Antibodies about two-thirds way down the page.

Do you see that?

A (Reviewing.) Excuse me, can you repeat the question.

Q I said on page 27 there's a header about two-thirds down the page that says, Monoclonal Antibodies.

Do you see that?

A Right here. Yes, I see it.

Q Okay.

And this then gives a scheme for common stems that's being developed for naming monoclonal antibodies; is that fair?

A Yes.

Q So the general stem is -mab,

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that's point 1.

Do you see that?

A General stem is -mab.

Q Okay.

And the point 2 gives sub-stems for the source of the product.

Do you see that?

A Sub-stems for the source of the product, I see that.

Q And then humanized version is -zu.

Yes?

A Human will have a -u.

Q Humanized I asked for -- humanized is -zu.

Correct?

A Oh, I see at the bottom humanized would be -zu.

Q Do you see a sub-stem that is -za anywhere here in this list?

MR. DIAMOND: Objection to form.

THE WITNESS: Do I see a

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what? I don't understand your question.

BY MS. STERLING:

Q Do you see a -- okay.

So there's a human sub-stem which is -u.

Do you see that?

A I see that.

Q There is a rat sub-stem which is an -a.

Do you see that?

A I see that.

Q There is a hamster sub-stem which is an -e.

Do you see that?

A I see that.

Q There is a primate sub-stem which is an -i.

Do you see that?

A I see that.

Q There is a mice sub-stem which is an -o.

Do you see that?

A Yes.

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Q There is chimers sub-stem which is -xi.

Do you see that?

A I see that.

Q And then there's humanized which is -zu.

Do you see that?

A I see that.

Q Are any of these sub-stems -za?

MR. DIAMOND: Objection to form.

THE WITNESS: Are any of these -- I guess -- I am missing something.

Can you tell me -- can you repeat your question?

BY MS. STERLING:

Q We have a sub-stem for human that's -u.

A That's right.

Q Is that -u or is it -za?

MR. DIAMOND: Objection to form.

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THE WITNESS: A what?

BY MS. STERLING:

Q -za?

A What is Zed-A?

Q The two letters Zed-A -- in American Z-A, I guess.

MR. DIAMOND: Can you ask the question again.

MS. STERLING: That was the answer, What is -za? I answered his question.

MR. DIAMOND: You answered --

BY MS. STERLING:

Q Do you understand what I am saying when I say the letters Zed-A?

A No, I actually don't understand your question.

Q Do you understand what I am saying when I say the term, the letters Zed-A?

A Zed-A?

Q Yes.

A Like Z-A?

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Q Yes.

A Well, there is no letter called Zed. There is a letter called Z.

Q I'm sorry, in my country there is. Let me try to translate to American.

Z-A --

A Z-A.

MR. DIAMOND: Wait. What is the question?

BY MS. STERLING:

Q Are you comfortable with Z than Zed?

A I don't -- I did not what Zed means.

Q Okay.

So you will have to agree with me -- I am just going to tell you, where I come from Zed is the equivalent of Z here in America. So I will use the American version of Z for this question.

In this list of sub-stems,

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do you see the letters -za as a sub-stem?

A I do not see the letters -za.

Q Okay.

And to be clear, when I was asking you about -zu you could understand that I was talking about the humanized -zu here?

A -zu stands for humanized.

Q Okay.

MR. DIAMOND: We have been going about an hour now.

MS. STERLING: I was going to say it's a good time for a break before we launch to a new topic. Ten minutes, please.

MR. DIAMOND: More or less.

(Whereupon a Recess Commenced at 10:53 a.m. and Testimony Recommenced at 11:20 a.m.)

MS. STERLING: Back on the record.

ARTURO CASADEVALL, MD, PhD

BY MS. STERLING:

Q Dr. Casadevall, did you talk to your counsel about the substance of your deposition testimony during the break?

A No.

Q In your declaration, let's turn to pages 58 to 60. And we are still on the '504 declaration until I tell you otherwise.

A (Reviewing.)

Q So on these pages you include Table 1 which is references to eculizumab as Thomas's humanized IgG4 antibody.

Do you see where we are?

A Yes.

Q I would like to discuss a couple of papers in this table that you refer to.

I am going to hand you what's been previously marked as AMG1005, that's the Bell reference. It's the top row of the table on page

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59.

A (Reviewing.)

Q So it is a published patent application and it lists Leonard Bell as the first inventor and Russell Rother as the second inventor on the face page.

Do you see that?

MR. DIAMOND: Objection to form.

BY MS. STERLING:

Q Do you need me to repeat the question?

A Please.

Q Okay.

This document AMG1005, it's a published patent application and it lists tow inventors; the first one is Leonard Bell, the second one is Russell Rother on the first page?

Do you see that?

A Yes.

Q Do you still have your copy of the '504 patent that I gave you

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earlier?

A (Reviewing.) I have it.

Q Okay. Good.

Do you see the inventors listed on the first page of the '504 patent?

A Leonard Bell, Russell Rother, and Mark Evans.

Q Leonard Bell and Russell P. Rother are overlapping inventors between this Bell publication and the '504 patent, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: (Reviewing.) Leonard Bell and Russell Rother are listed as inventors in both applications.

BY MS. STERLING:

Q Okay.

I am going to call this Exhibit 1005 Bell for our discussion, okay?

Do you recognize Bell?

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A I recognize Bell.

Q You relied on it in your declaration, correct?

A I relied on it in my declaration.

Q Okay.

So you are familiar with Bell?

A I am familiar with Bell, I read it.

Q When was the last time you read it?

A Within the past month.

Q Do you know Leonard Bell?

A No.

Q Do you know Russell Rother?

A No.

Q Okay.

In your table, you point to -- again, I am on your table in your declaration, on page 59, the top column -- top row is your entry for Bell.

Do you see that?

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A I see that.

Q You cite to Bell on paragraph 0052. It's in your left-hand column.

Do you see, "You say Bell AMG1005 at paragraph 0052."

A Okay.

Q Let's go to that paragraph.

So that paragraph, if you look at the top of the page, it's on page 5 --

MR. DIAMOND: So --

MS. STERLING: We are in Bell, Dr. Casadevall.

MR. DIAMOND: Are you asking about paragraph 52 in Bell?

MS. STERLING: Yes.

THE WITNESS: Yes, I am sorry.

MR. DIAMOND: You're asking him to turn to 52 in Bell.

MS. STERLING: I can instruct the witness like you, Evan.

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MR. DIAMOND: He was confused.

MS. STERLING: Evan, it's my deposition.

MR. DIAMOND: Take all the time you need to do that, I suppose.

BY MS. STERLING:

Q Dr. Casadevall, are you looking at the Bell reference, AMG1005?

A I am looking at the Bell reference.

Q Can you turn to paragraph 52.

A I am now in paragraph 52.

Q Okay.

It's a pretty lengthy paragraph but you have provided us an excerpt from that paragraph in your table in the right-hand column. Correct?

A Yes.

Q Okay.

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So in that excerpt that you have given us, it talks about methods for the preparation of h5G1.1-mAb, h5G1.1 scFv and other functional fragments of h5G1.1. And it says that methods for the preparation were described in US patent number 6,355,245. And you inserted Thomas here, just a shorthand for the full quote that's provided in patent 52.

Is that fair?

MR. DIAMOND: Objection to the form.

BY MS. STERLING:

Q Did you not insert Thomas here in square brackets to replace the full-length cite?

MR. DIAMOND: Are you withdrawing the prior question or is that the new question?

BY MS. STERLING:

Q Did you insert Thomas in square brackets here to replace the full cite that's provided in paragraph

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52 of AMG1005?

A Let me find it.

(Reviewing.)

Q If it's helpful, it's at the top of the right-hand column. You will see your sentence bridging.

A Top of the right hand.

Q Starts at the very bottom of the left-hand column and bridges over to the right-hand column.

A Method for the preparation --

Q Yep.

A -- of h5G1.1 monoclonal antibody h5G1.1 scFv and other functional fragments of h5G1.1 are described in US patent number 6,355,245 and inhibition of complement activity by humanized anti-C5 antibody and single chain FB Thomas, et al, Molecular Immunology Volume 33 Number 17/18, pages 1389 and 1401, 1996.

Q Last sentence in that paragraph says, "The antibody

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h5G1.1-mAb is currently undergoing trade name eculizumab."

Do you see that?

A "The antibody h5G1.1-mAb currently undergoing clinical trials than the trade name eculizumab."

Q So when you repeat the sentence I just read to you, is that you agreeing that you see the sentence there?

I want to be clear that's what your answer means.

MR. DIAMOND: Objection to the form.

THE WITNESS: I am reading the text of the question because I want to be accurate.

BY MS. STERLING:

Q I understand that.

But when I ask you do you see that sentence there, and you read it back to me, is that your acknowledging that sentence is there?

MR. DIAMOND: Objection to

Samsung Bioepis Exhibit No. 1101
Samsung Bioepis Co., Ltd. v. Alexion Pharmaceuticals, Inc., IPR2023-00998
Page 144

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the form mischaracterizes the witness' testimony.

THE WITNESS: When I read you back the sentence it is exactly what is stated there. And those are the words, last sentence of paragraph 52.

BY MS. STERLING:

Q Okay.

So based on the sentence and person of ordinary skill in the art reading this sentence, would they associate the term h5G1.1-mAb with the tradename eculizumab?

MR. DIAMOND: Objection to form.

THE WITNESS: What a person would associate would be the earlier reference to Thomas because that is the context by which you read that sentence.

BY MS. STERLING:

Q So you're telling me based on this sentence a person of ordinary

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skill in the art would not associate the term h5G1.1-mAb with the tradename eculizumab?

A A POSA at the time would associate h5G1.1 with the earlier reference that cites Thomas and with the tradename eculizumab.

Q Okay. Let's look at the document Brekke, that's in the bottom row of that column on that table we are looking at on page 59. I am going to get you that document.

I am handing you what's been previously marked AMG1019. It's entitled, Therapeutic Antibodies for Human Diseases at the Dawn of Twenty-First Century, and lists first author Ole Henrik Brekke.

Do you see that?

A Yes (Reviewing.)

Q I am going to call this document Exhibit 1019 Brekke for our discussion, okay.

This is the same Brekke that

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you cited to in your table on page 59?

A (Reviewing.) Yes, it is the 2003 reference.

Q Okay.

Do you recognize this article?

A Yes.

Q When was the last time you reviewed Brekke?

A Within the past month.

Q Okay.

Do you know Ole Henrik Brekke?

A No.

Q In your table in the left-hand column, you point us to Brekke AMG1019, page 56.

Do you see that?

A I'm sorry, Brekke at 56?

Q Yes.

Let's turn to Brekke Exhibit 1019, page 56.

A We are on page 56?

Q Yes. That is the page you

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cite us to -- you direct us to, correct?

A Right (Reviewing).

Q We are on page 56 of Brekke, Dr. Casadevall.

A Oh.

Q And you can turn back in your declaration to the table that we are looking at on page 59.

A I'm sorry, I'm confused.

Q Yes, I can see that. Let's start again.

We are looking at your declaration on page 59.

A Yes.

Q There's the last entry on that page, you point us to Brekke at page 56.

A Yes.

Q So keep your declaration open there.

And let's now turn to Brekke page 56 where you point us to.

A I'm sorry, counsel. I am

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confused, because Brekke doesn't have a page 56, unless you want --

Q I can see page numbers here on the bottom left-hand corner.

A I am so sorry. I was looking at the --

Q Understood.

A At the 1 on the bottom.

Okay. 56 (Reviewing).

Q So I believe your quote that you point us to in your table on page 59, comes from somewhere close to the bottom of the left-hand column on that page 56. It's one, two, three, four, five, six, seven lines up.

A (Reviewing.) I see.

Q And it starts, Eculizumab (5G1.1).

Do you see that sentence?

A I see that sentence.

Q Okay. That is the quote that you have taken from Brekke and provided in your table on page 59 in your declaration, correct?

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A (Reviewing.) Eculizumab 5G1 Alexion Pharmaceuticals -- it's a humanized monoclonal antibody that prevents the cleavage of human complement component C5 into its pro-inflammatory component.

Yes, that is the quote. Reference 31.

Q So Brekke, in this quote, discusses eculizumab and in parenthesis afterwards provides us with 5G1.1 Alexion Pharmaceuticals, correct?

A In this quote -- in this quote has eculizumab followed by 5G1.1 Alexion Pharmaceuticals.

Q So a person of ordinary skill in the art reading this would associate eculizumab with 5G1.1 from Alexion Pharmaceuticals, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: A POSA reading this in the year 2003, would have

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gone to reference 31, to understand what this antibody is.

BY MS. STERLING:

Q How about in the year 2007? You said 2003. I just want to be clear we are talking --

A The paper was 2003.

Q Okay. So a person of ordinary skill in the art reading this in 2003 --

A So any POSA prior to March 15, 2007, reading this article will have concluded that the -- that the identity of this needs to go to reference 31 which is Thomas.

Q But they would also understand that eculizumab is associated with the term 5G1.1, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: I don't think they would have understand that.

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When you read this, you go to the authority. The authority in this case is reference 31.

BY MS. STERLING:

Q So you're telling me no one would associate, before March 2007, the word eculizumab with nomenclature of 5G1.1?

MR. DIAMOND: Objection to form. Asked and answered.

THE WITNESS: You're asking me about nobody. I have no way of knowing who is nobody.

BY MS. STERLING:

Q You're telling me a person of ordinary skill in the art would not have associated the word eculizumab with the name 5G1.1 prior to March 2007.

Is that what you are telling me?

A What I am saying is a POSA would have read this reference -- would have read this sentence and if

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it was interested in eculizumab, would have gone to 31.

Q But based on your testimony I am trying to understand you, are you saying they would not have associated eculizumab with 5G1.1?

A What I am saying is that they would have gone to the reference because that is the authoritative part of the sentence.

Q You won't even -- so you're telling me they would ignore the parenthesis after the word eculizumab and go straight to Thomas?

Is that what you are saying?

MR. DIAMOND: Hold on. Let her finish the question.

Objection to form.

THE WITNESS: I am not saying that they would ignore my question. I am saying that a POSA at the time would have gone back to the reference to try to understand what eculizumab is.

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BY MS. STERLING:

Q But would they have associated the term "eculizumab" with 5G1.1?

MR. DIAMOND: Objection to form. Asked and answered.

THE WITNESS: I don't -- I think they would have gone back to the -- this is a review article. This is a secondary source. You go back to the primary source. The primary source is Thomas.

BY MS. STERLING:

Q You can't tell me, sitting here today, that a person of ordinary skill in the art would have associated the word eculizumab with 5G1.1?

MR. DIAMOND: Objection to form. Asked and answered.

THE WITNESS: I think your question is too broad.

BY MS. STERLING:

Q I am looking at the sentence that says eculizumab (5G1.1).

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A I think a POSA at the time would have read the sentence, would have seen 5G1, would not know what that means, and would go straight into 31 to try to understand what eculizumab is.

Q So you're telling me a person of ordinary skill in the art would not have understood that 5G1.1 was associated with eculizumab?

A I think they would have seen that number. But to make a conclusion, especially when the source is a secondary reference, you go to the primary literature, and the primary literature is Thomas.

Q Okay.

Let's look back at your table in your declaration, page 58. You have several entries in your table as well. The first one is a reference Hillmen 2004 and it's AMG 1074.

Do you see that entry in the first row?

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A I see that entry.

Q I am going to hand you what's been previously marked as Exhibit 1004.

That document is a journal article entitled, Effect of Eculizumab on Hemolysis and Transfusion Requirements in Patients with Paroxysmal Nocturnal Hemoglubinuria. And it lists first author Peter Hillmen.

A I see that.

Q I am going to refer to Exhibit 1004 as Hillmen, just for purposes of this discussion, okay?

A Yes.

Q Do you recognize Hillmen?

A I recognize Hillmen.

Q And you rely on it in your declaration at page 58, correct?

A I relied on it in my declaration on page 58.

Q You are familiar with Hillmen?

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A I am familiar with Hillmen.

Q When was the last time you reviewed Hillmen?

A Within the past month.

Q Do you know Peter Hillmen, the first listed author?

A No.

Q Do you know any of the authors listed here?

A Claire Hall, Judy Marsh, Modupe Elebute, Michael Bombara, Beth Petro, Matthew Cullen, Stephen Richards, Scott Rollins, Christopher Mojcik and Russell Rother.

No, I do not know any of these authors.

Q So back to your table in your declaration, you point us to Hillmen at page 553 in your declaration.

A Yes.

Q Let's turn to page 553 in Hillmen and AMG1004.

And I believe the quote that

ARTURO CASADEVALL, MD, PhD

you have in your table in your declaration comes from the left-hand column of that page, and roughly about two-thirds down there's a paragraph that starts, "Eculizumab is a recombinant humanized monoclonal antibody."

Do you see the paragraph?

A I see the paragraph, "Eculizumab is a recombinant humanized monoclonal antibody that was designed to block the activation of terminal complement components."

And it gives references 14 and 15.

Q And based on your declaration -- and you can confirm this in the document -- reference 15 is the Thomas document you keep referring to, correct?

A Reference 15 -- reference 15 is the Thomas document.

Q Okay.

While you're on that page

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that you are on, I believe you're looking at page 559 for the listing of references, correct?

A I am looking at page 559.

Q Okay.

Can you see at the end of the text of the reference there's a box of smaller text on the right-hand column on that page?

MR. DIAMOND: A box?

MS. STERLING: An excerpt, a chunk of text.

THE WITNESS: You mean up here?

BY MS. STERLING:

Q Yes.

A I see the text -- I see the text.

Q Okay.

We see here that text reads, Funded by Alexion Pharmaceuticals," correct?

A I see that the study was funded by Alexion Pharmaceuticals.

ARTURO CASADEVALL, MD, PhD

Q You see in the next paragraph, Dr. Hillmen reports serving as consultant to Alexion Pharmaceuticals, correct -- and receiving grant support from the company, correct?

A The text says, "Dr. Hillmen reports serving as consultant to Alexion Pharmaceuticals and receiving grant support from the company."

Q You know to save time of me reading it and then you reading it, why don't you read that paragraph into the record for us.

A Happy to.

"Drs. Rollins, Mojcik and Rother, Mr. Bombara and Ms. Petro report having equity ownership in Alexion Pharmaceuticals. And Dr. Rollins and Rother have assigned to Alexion Pharmaceuticals their inventions made as employees of the company and have received no royalties from Alexion for these inventions.

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Dr. Rollins receives royalties for inventions that he made before becoming an employee of Alexion."

Q So based on this paragraph or these two paragraphs, is it fair to say that Alexion is associated with this publication?

MR. DIAMOND: Objection to form.

THE WITNESS: My reading of this paragraph is that Alexion funded the study.

BY MS. STERLING:

Q And you don't take away from the second paragraph that certain authors are employees of Alexion?

MR. DIAMOND: Objection to the form.

THE WITNESS: The paragraph states -- it has a lot of details, and this has to be parsed, but I will not draw conclusions hear except that the study was funded by Alexion Pharmaceuticals.

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BY MS. STERLING:

Q Okay.

Would you agree that Dr. Hillmen serves as consultant or reports serving as a consultant to Alexion Pharmaceuticals, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: The statement reports Dr. Hillmen reports serving as a consultant to Alexion Pharmaceuticals. But the way that it is written, it could have been in the past, could have been in the present; you can't get much out of that.

BY MS. STERLING:

Q Okay.

You don't consider "serving" as present term?

MR. DIAMOND: Objection to the form.

THE WITNESS: I read it as "report serving." "Report

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serving" could be read as the past.

BY MS. STERLING:

Q Okay.

It says, "Drs. Rollins, Mojcik and Rother, Mr. Bombara and Ms. Petro report having equity ownership in Alexion Pharmaceuticals."

Would you read that as present tense?

MR. DIAMOND: Objection to form.

THE WITNESS: (Reviewing.) I would -- "Drs. Rollins, Mojcik and Rother, Mr. Bombara and Ms. Petro report having equity ownership in Alexion Pharmaceuticals."

Again, it is vague whether it is the present or the past.

BY MS. STERLING:

Q How about: "Doctors Rollins and Rother have assigned to Alexion Pharmaceuticals their inventions made

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as employees of the company."

Would that connote to you that Doctors Rollins and Rother either are or were at this point Alexion Pharmaceutical employees?

MR. DIAMOND: Objection to form.

THE WITNESS: All I can get from this is that Dr. Rollins and Rother have assigned to Alexion Pharmaceuticals inventions made as employees of the company and have received no royalties from Alexion for these inventions.

BY MS. STERLING:

Q Okay.

On the first page, on the left-hand side there's a box or a paragraph an excerpt of text.

Do you see that?

A This one?

Q Yes.

Tells you the papers from certain places.

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A Right.

Q One of those places is Alexion Pharmaceuticals, Cheshire, Connecticut. That's about halfway through the paragraph.

Do you see that?

MR. DIAMOND: Objection to form.

THE WITNESS: (Reviewing.)

Can you repeat your question.

BY MS. STERLING:

Q We are looking at this paragraph of text on the left-hand side on the first page of the paper together, correct?

A Correct.

Q Okay.

That paragraph starts with from -- it tells you who the paper is from, and there are a list of various entities. About halfway down that paragraph, one entity listed is Alexion Pharmaceuticals in Cheshire, Connecticut.

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Do you see that?

MR. DIAMOND: Objection to form. Compound.

THE WITNESS: Alexion Pharmaceuticals, Cheshire Connecticut is listed in the box.

BY MS. STERLING:

Q Okay.

Would that have informed a person of ordinary skill in the art that Alexion was associated with this paper?

MR. DIAMOND: Objection to the form.

THE WITNESS: It would have only -- it would have only informed someone in the art that those people, MPB, BEP, SAR, CFM, RPR, are associated in some way with Alexion.

BY MS. STERLING:

Q Okay.

Those people, based on those initials, if we look at the authors,

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MPB, would it be fair to conclude that is Michael P. Bombara?

A Since that is the only set of initials that fits, I would agree that's Michael P. Bombara.

Q Okay.

BEP, those initials, would we conclude that's Beth E. Petro?

A Yes.

Q SAR. Would a person reading this conclude that could be Scott A. Rollins?

A Would be Scott A. Rollins, the only initial that's match.

Q Okay. The initials CFM, would a person reading this paper conclude that was Christopher F. Mojcik?

A Christopher F. Mojcik is the only initials that match CFM.

Q And then RPR, the last set of initials, would you agree a person of ordinary skill in the art reading this would have associated those

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initials with Russell P. Rother?

A Russell P. Rother would be associated with RPR.

Q Okay.

So based on this, we can conclude that those authors are with Alexion Pharmaceuticals in Cheshire, Connecticut; is that fair?

MR. DIAMOND: Objection to form.

THE WITNESS: I don't think you can conclude that. These individuals may have left the company. This work -- this work reflects work that was done. You cannot conclude anything about dates from looking at that.

BY MS. STERLING:

Q But Alexion Pharmaceuticals is associated with these names in this paper, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: Alexion

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Pharmaceuticals is associated with these names in this paper but it doesn't tell you anything about dates.

BY MS. STERLING:

Q Let's -- this was published in 2004, correct?

A It was published in 2004.

Q Okay.

And in 2004, this listing of authors in the paragraph that tells you where those authors are from, multiple authors are listed as being from Alexion Pharmaceuticals.

Would you agree with that?

A I don't agree that they are listed as being from Alexion Pharmaceuticals. They are listed with Alexion Pharmaceuticals, but I -- in 2004, these individuals could have left the company. This could reflect the past.

I don't think you can make any conclusion regarding what the

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association was on February 5, 2004.

Q Okay.

So then we are saying Hillmen 2004 is not associated with Alexion; that's your conclusion?

MR. DIAMOND: Objection to form.

THE WITNESS: I did not say that. What I said was that you cannot -- that you cannot make an association with time. So you don't know from that heading whether they are associated with the company at that time.

BY MS. STERLING:

Q So you're telling me based on this paragraph that we have looked at on page 1, and the repeated mentions of Alexion -- I'm sorry, page 1. Let me be clearer.

The document page 552 of the reference, so this paragraph that we looked at on page 552 and the repeated mentions of Alexion in the paragraph

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we looked at 559, you're telling me a person of ordinary skill in the art would still not associate this paper with Alexion Pharmaceuticals?

MR. DIAMOND: Objection to form.

THE WITNESS: I am saying that based on what we have read that this study is funded by Alexion; these people have some association -- these people are associated in a sentence with Alexion but you cannot infer that this is -- at what time this happened, whether it's a concurrent, the past or the past.

BY MS. STERLING:

Q Is it common when you're reciting where work comes from with multiple groups that you would recite authors no longer associated with that group, still associated with that group?

MR. DIAMOND: Objection to

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form. I am also going to object to this entire line outside the scope of the direct testimony. I don't know what this relates to.

THE WITNESS: I will answer as follows with my own experience.

BY MS. STERLING:

Q Okay.

A I was arborized in College of Medicine up to 2015. Since then, I have been at Johns Hopkins.

Work that traces in some ways to people who are associated with Einstein, may be published in the year 2-20. But those people may no longer be there.

So the bottom line is, what you have is names associated with a company. You cannot infer the relationship from looking at that.

MR. DIAMOND: Counsel, before you continue this line of questioning, maybe we want to take a break and you can explain it.

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Can you explain how this is within the scope or relates to the scope of the direct testimony per the PTAB rules?

MS. STERLING: This is a document that your witness has relied on. I am trying to understand his take on the document.

MR. DIAMOND: This is a document you introduced. I just don't understand what -- I mean, happy to take a break and you can explain to me. I want to make sure if I have an objection or not, and maybe there's not. If you can explain to me, but I don't understand.

MS. STERLING: I am trying to understand the information a person of ordinary skill in the art would have taken away from this document that Dr. Casadevall relies in his declaration and

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quotes from.

MR. DIAMOND: I still don't understand how --

MS. STERLING: You don't have to understand my questions, Evan.

MR. DIAMOND: Let me put it this way. I am going to maintain an objection to this entire line of questioning and reserve the right to strike it as outside the scope of the direct testimony without counsel providing any further explanation.

I will be happy, if you can provide some explanation on the record or at a break and maybe convince me otherwise. But right now I don't see how any of this is within the scope of anything that's at issue from either party.

MS. STERLING: Not your --

MR. DIAMOND: Particularly the line of questioning regarding

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which authors are from where. But again, if you can explain it, I'm happy to reconsider that.

MS. STERLING: Now you're done with that particularly lengthy speaking objection.

MR. DIAMOND: It's not a speaking objection. It's actually the rules and what allows you to be here and ask questions or not and I am happy to discuss that further with you.

MS. STERLING: Sure.

BY MS. STERLING:

Q The next entry in your table is Hill 2005, Exhibit AMG1047.

Do you see that?

A Hill 2005 Exhibit 1047 from Amgen, I see that.

Q Okay.

I am going to hand you what's been previously marked Exhibit 1047.

A (Reviewing.)

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Q This is a document entitled, Sustained response and long-term safety of eculizumab in paroxysmal nocturnal hemoglobinuria, with first author Anita Hill.

Do you see that?

A I see that.

Q So at the very bottom of this page, in the left-hand column, under the line, the last paragraph says, "Several of the authors (JC, CFM, RPR) are employed by Alexion."

Do you see that?

A (Reviewing.) "Several of the authors (JC, CFM, and RPR) are employed by Alexion."

MR. DIAMOND: Again, I am going to object to this line of questioning as to who and who wasn't employed by Alexion as outside the scope of direct testimony, pending any explanation from counsel for Amgen otherwise, and of course, reserve the right

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to object to any use of this testimony and replies or anything else as outside the scope of anything that Amgen introduced in its petition.

Again, if you have something else to say about that, I will be happy to hear it.

BY MS. STERLING:

Q Author CRM, would you agree that would be Christopher F. Mojcik?

A Christopher M. Mojcik matches the initials CFM.

Q You said Christopher M. Mojcik.

A F -- Christopher F. Mojcik matches initials CFM.

Q Okay.

And RPR, do those initials match author Russell P. Rother?

A RPR matches Russell P. Rother.

Q Okay.

So this document tells you

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at the bottom of the page was published October 2005, correct?

A It was published in October 2005.

Q Okay.

It says in present tense, Several of the authors are employed by Alexion.

Do you see that?

MR. DIAMOND: Same objection regarding to the scope of the direct testimony.

MS. STERLING: Understood.

THE WITNESS: It says that the date is October 2005. It says, in the present tense, are employed by Alexion. But that date may not reflect that paragraph because this paper was submitted for publication on May 25, 2005 -- submitted, no, on February 9, 2005.

And so we don't know how that statement which uses the

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present term "are," relates to October 1st, 2005, or to the February 9, 2005.

BY MS. STERLING:

Q So you would say -- do you read your articles before they are submitted if you are an author?

MR. DIAMOND: Objection to form. You are asking about this article?

MS. STERLING: No. I am asking about his own articles. That's why I said, do you read your articles. Listen to the question, Evan.

BY MS. STERLING:

Q Dr. Casadevall, when you write an article, do you read it before you submit it?

MR. DIAMOND: Objection to the form and generally outside the scope of the direct testimony. I mean, that question.

THE WITNESS: Every paper

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that have been submitted under my name is read by me. But there is often a huge difference between when I read it and publication, depending on the review process, depending how long it take to do it.

BY MS. STERLING:

Q So based on that, this paper was submitted on February 9, 2005.

You would agree with that?

MR. DIAMOND: Objection to the form.

BY MS. STERLING:

Q You have already testified to that, correct?

A It was submitted -- states here it was submitted February 9, 2005.

Q Okay.

So at least at February 9, 2005, several of the authors were employees of Alexion, correct?

MR. DIAMOND: Objection to

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form. Objection to scope.

THE WITNESS: I don't think you can conclude that. You don't know when several of the authors are employed by Alexion was written.

BY MS. STERLING:

Q Okay.

It has to have been written sometime before October 2005 when the paper was published, correct?

I mean, it can't be added to the paper after it's published?

MR. DIAMOND: Allow counsel to finish her question which I didn't hear now.

Can you say the question again.

MS. STERLING: You have realtime in front of you.

MR. DIAMOND: I couldn't hear the question. He cut you off. I want to make sure the witness doesn't speak over your

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question.

MS. STERLING: Evan, leave us alone.

MR. DIAMOND: Ask your question.

MS. STERLING: I have already asked the question. You keep interrupting like this, I told you we will call the board and we will.

MR. DIAMOND: We can talk about the scope, too.

MS. STERLING: Happy to.

Could you read the question back to the witness, please.

(Whereupon the Question is Read Back.)

THE REPORTER: I mean, it can't be added to the paper after it's published?

MR. DIAMOND: Objection to form.

BY MS. STERLING:

Q I am just going to -- that

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wasn't the full question.

A When things are printed, at the time of printing it appears you cannot add it on that. But you can always add a correction later on or something like that.

Q Is there an indication on this paper that there was a correction made?

A You would not know from this paper.

Q You're telling me once a paper is published if it's updated or modified, that's not noted anywhere?

MR. DIAMOND: Objection to form.

THE WITNESS: It depends. Some -- some papers, for example, PubMed, would have -- may have a correction. So when you look at the paper, they give you the correction and the reference. But I don't know what the practice was in 2005, and some corrections may

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not make it into PubMed. But, you know...

BY MS. STERLING:

Q You cite all these papers in this table that's on page 58 through 60, because these references either cite to Thomas or they cite to the document that, in turn, cites to Thomas.

Is that fair?

MR. DIAMOND: To be clear, I am no longer objecting to the scope now that you are talking about the declaration. So go on.

THE WITNESS: So as stated in my declaration, all the citations that are there are -- that are listed there cite to Thomas.

BY MS. STERLING:

Q Okay.

I am going to hand you a copy of Thomas previously marked as Exhibit 1023.

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A (Reviewing.)

Q Is this the same Thomas that you refer to --

A This paper --

Q -- in your declaration?

A -- is the paper that I refer to in my declaration.

Q Let's look at the abstract of Thomas.

Thomas talks about -- multiple entries that have 5G1.1 in them in the abstract.

Would you agree to that?

MR. DIAMOND: Objection to form.

THE WITNESS: The alphanumeric 5G1 appears multiple times in the abstract.

BY MS. STERLING:

Q Okay.

So those examples are 5G1.1 --

MR. DIAMOND: Objection to the form.

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BY MS. STERLING:

Q I am not finished with the question.

Those examples are 5G1.1, h5G1.1 scFv, intact humanized h5G1.1, humanized h5G1.1, murine 5G1.1.

Do you see those examples in the abstract?

MR. DIAMOND: Objection to the form.

THE WITNESS: I see the things that you have read. I see monoclonal antibody 5G1.1, humanized 5G1.1, regions of 5G1.1, humanized h5G1.1, humanized h5G1.1, and murine 5G1.1.

BY MS. STERLING:

Q Does Thomas mention eculizumab anywhere?

A Thomas does not mention eculizumab anywhere.

MS. STERLING: Okay.

We are about to start a new topic. Would it be a good time to

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break for lunch, Dr. Casadevall, or would you like to continue?

THE WITNESS: I am happy to break.

MS. STERLING: Okay.

MR. DIAMOND: You want to do the lunch break now?

MS. STERLING: (Nodding Head).

(Whereupon a Recess Commenced at 12:05 p.m. and Testimony Recommenced at 12:56 p.m.)

MS. STERLING: Back on the record.

BY MS. STERLING:

Q Dr. Casadevall, did you talk about the substance of your deposition with your counsel during the break?

A No.

Q You still have your declaration in front of you for the '504 patent?

A I have the declaration in

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front of me.

Q Okay.

And let's go to paragraph 108, please.

A 108?

Q Yes.

So generally, in paragraphs 108 through paragraphs 118, you discuss a series of publications that address whether constant regions can impact antigen binding properties; is that fair?

Take a chance to look through these paragraphs to see if it's fair.

MR. DIAMOND: Objection to form.

THE WITNESS: This section, those paragraphs deal with changes to amino acid sequences, including in the constant region can significantly impact the binding safety and efficacy of therapeutic antibodies.

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BY MS. STERLING:

Q Okay.

I am going to hand you a document that's been previously marked as Exhibit 2013.

A (Reviewing.)

Q It's entitled, Isotype can affect the fine specificity of an antibody for a polysaccharide antigen; and has first author Gary McLean.

Do you see that?

A I see the author.

Q I am going to refer to this Exhibit 2013 as McLean for our discussion, okay?

A Yes.

Q Do you recognize this paper?

A Hm?

Q Do you recognize this paper?

A This paper was published by my laboratory.

Q Okay.

And you discuss this paper in paragraph 109 of your declaration,

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correct?

A Correct.

Q In paragraph 109 you stated that, McLean reported comparing the binding specificity of chimeric antibodies, and then those antibodies contain specific constant regions. And you list them as IgA, IgG1, 2, 3, 4, and IgM.

Do you see that?

A Yes.

Q Okay.

Does McLean disclose any experiments relating to testing a human hybrid IgG2, IgG4 constant region?

MR. DIAMOND: Objection to form.

THE WITNESS: McLean reports the testing of mouse-human chimeric antibodies.

BY MS. STERLING:

Q Are any of those mice chimeric -- sorry, which antibodies

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did you say?

A McLean reports the testing of mouse-human chimeric antibodies based on the murine monoclonal antibody 18B7.

Q Do any of those antibodies tested in McLean have a human hybrid IgG2-IgG4 constant region?

A None of those antibodies have a hybrid IgG2-IgG4 constant region.

Q Is it fair to say McLean does not disclose any experiments relating to testing an antibody that has a human hybrid IgG2-IgG4 constant region?

MR. DIAMOND: Objection to form.

THE WITNESS: I disagree. The message of McLean is that the constant region can have an effect on the specificity of an antibody; therefore, it would imply that if you change the constant region and

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make it a hybrid, that you are going to be -- you will not be able to predict what happens.

BY MS. STERLING:

Q Please point me to the experiments in McLean that relate to testing an antibody having a human hybrid IgG2-IgG4 constant region?

A None of the experiments in McLean relate to experiments involving a human hybrid IgG2-IgG4 antibody.

Q You can set that document to the side.

I am going to hand you a document that's been previously marked Exhibit 2014.

A (Reviewing.

Q This document is entitled, Complementarity, specificity and the nature of epitopes and paratopes in multivalent interactions.

First author is Neil Greenspan.

Do you see that?

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A I see that.

Q I am going to call Exhibit 2014, Greenspan for our discussion, okay?

Do you recognize this Greenspan paper?

A I recognize the Greenspan paper.

Q Okay.

You discuss it in paragraph 110 of your declaration, correct?

A (Reviewing.) 110, yes.

"For example, in 1995, Greenspan and Cooper published an article describing how IgG3 monoclonal antibodies had been observed to more effectively bind target antigens than IgG1, IgG2B monoclonal antibodies or, IgG3-derived Fab fragments with the same variable sequences. Alexion -- or ALXN2014 at 227.

Q Does Greenspan provide any experiments relating to testing an antibody with a human hybrid IgG2-IgG4

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constant region?

MR. DIAMOND: Objection to form.

THE WITNESS: Greenspan -- Greenspan describes how the changing of the constant region affects defined specificity. In this paper, there are no experiments on a hybrid human IgG2-IgG4 antibody.

BY MS. STERLING:

Q I am going to hand you what's been previously -- you can put that to the side.

I am going to hand you what's been previously identified Exhibit 2011.

A (Reviewing.)

Q This is a journal article entitled, Can immunoglobulin CH1 constant region domain modulate antigen binding affinity of antibodies.

And has a first author of

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Otto Pritsch.

Do you see that?

A I see the article.

Q Okay.

I am going to call this Exhibit 2011 Pritsch in our discussion, okay?

A Yes.

Q Do you recognize this paper?

A Yes.

Q And you discussed Pritsch in paragraph 111 of your declaration, correct?

A Yes. It states, in 1996, Pritsch, et al., published a study comparing the binding activity of two antibodies with identical variable region sequences in either IgG or IgA isotype -- the authors found in spite of sharing identical variable domain sequences having identical light chain constant domains and recognize overlapping epitopes on the antigen, both antibodies significantly differed

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in their affinity for the target antigen.

Q Does Pritsch provide any experiments relating to testing an antibody that has a human hybrid IgG2-IgG4 constant region?

MR. DIAMOND: Objection to form.

THE WITNESS: Pritsch is one of the articles that sites how the constant region can affect defined specificity and that is the background.

BY MS. STERLING:

Q Can you point me to experiments or any report in Pritsch of an antibody having a human hybrid IgG2-IgG4 constant region?

A Pritsch does not have experiments containing IgG1 or IgG2 hybrid constant regions.

Q My question related to IgG2-IgG4 constant domains.

Does Pritsch report --

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A Sorry, I made a -- I misspoke.

Pritsch does not contain any experiment related to hybrid antibody containing the CH2 or CH4 hybrids domains.

Q You can set that to the side.

I am going to hand you what has been previously marked as Exhibit 2008.

A (Reviewing.)

Q This is a journal article entitled, Human constant regions influence the antibody binding characteristics of mouse-human chimeric IgG sub classes, with first author N. McCloskey.

Do you see that?

A I see that.

Q You discuss this paper in paragraph 112 of your declaration, correct?

A Yes.

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Q Okay.

So you are familiar with this paper?

A I am familiar with this paper.

Q Okay.

Does McCloskey provide any experiments relating to testing an antibody with a human hybrid IgG2-IgG4 constant region?

MR. DIAMOND: Objection to form.

THE WITNESS: McCloskey thought that despite having the same variable region sequences, human antibodies of different IgG subclasses which bind the same antigen have been shown to differ in functional affinity.

BY MS. STERLING:

Q Can you point me to any data in McCloskey that relates to a human -- sorry -- that relates to an antibody having a human hybrid

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IgG2-IgG4 constant region?

MR. DIAMOND: Objection to form.

THE WITNESS: (Reviewing.) In McCloskey there are no experiments involving an IgG2-IgG4 hybrid monoclonal antibody.

BY MS. STERLING:

Q You can set that to the side.

I am going to hand you a document that's been previously marked as Exhibit 2009.

A (Reviewing.)

Q This is a journal article entitled, The immunoglobulin heavy chain constant region affects kinetic and thermodynamic parameters of antibody variable region interaction with antigen, and lists Marcela Torres as the first author.

Do you see that?

A I see that.

Q This is another publication

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from your lab, correct?

A That is correct.

Q So you are familiar with this publication?

A I am familiar with this publication.

Q Okay.

You discuss this publication in paragraph 113 of your declaration, correct?

A Yes.

Q Does this Exhibit 2009 provide any experiments relating to testing an antibody that has a human hybrid IgG2-IgG4 constant region?

MR. DIAMOND: Objection to form.

THE WITNESS: In this paper, as well as the papers that we have discussed previously, the message is that the constant region could affect antibody binding and specificity.

There are no experiments in

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this paper dealing with IgG2-IgG4 hybrids. But the message is that if you change the constant region and you do something to the constant region, you could be affecting binding.

BY MS. STERLING:

Q But there's no data in Exhibit 2009 that relates to monoclonal antibodies having a human hybrid IgG2-IgG4 constant region correct?

MR. DIAMOND: Objection to form. Asked and answered.

THE WITNESS: The concept that is included in this paper will include a gamma 2-gamma 4 antibody, even though there is no direct data on gamma 2-gamma 4. Because the principle is that if you change the constant region and you alter it in some way, the outcome is unpredictable.

BY MS. STERLING:

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Q There's no mention in this paper of experiments looking at an antibody with an IgG2-IgG4 hybrid constant region, correct?

A There is no experiment dealing with hybrid IgG2-IgG4, but the concept, the constant region can affect the variable region, supersedes any combination that you want to do. So the message is included.

Q Okay. You can set that aside.

I am going to hand you what's been previously marked as Exhibit 2040.

A (Reviewing.)

Q This is a reference entitled, Variable-region-identical antibodies differing in isotype demonstrate differences in fine specificity and idiotype. Again, first author is Marcela Torres.

Do you see that?

A I see the paper,

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Variable-region-identical antibodies differing in isotype demonstrate differences in fine specificity and idiotype, by Marcela Torres.

Q This is another publication that you are listed on, correct?

A This is another publication from my laboratory.

Q So you are familiar with this Exhibit 2040, correct?

A I am familiar with exhibit -- with this paper.

Q You cite it in paragraph 113 of your declaration, correct?

A 113?

Q Yes?

A Reviewing.) Yes, I cite it in paragraph 113.

Q Does Exhibit 2040 provide any experiments relating to testing an antibody with a human hybrid IgG2-IgG4 constant region?

MR. DIAMOND: Objection to form.

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THE WITNESS: The paper reports that when you change the constant region, you alter fine specificity and idiotype. And this is a general principle that would apply to all changes. Although IgG2 and IgG4 are not included specifically in this paper, the constant would apply to them.

BY MS. STERLING:

Q What are the constant regions compared in this paper?

A IgG1, IgG2A, IgG2B and IgG3.

Q You have to agree with me none of those are human hybrid IgG2-IgG4, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: The antibodies that were studied in the paper were not hybrids of IgG2-IgG4, but they were -- they show that when you change the constant region,

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you change a key qualities of the antibody as measured by fine specificity and idiotype, and establish a concept that is broader and will encompass any IgG2-IgG4 construction.

BY MS. STERLING:

Q You can set that aside.

I am going to hand you another exhibit, previously marked Exhibit 2039.

A (Reviewing.)

Q This is a reference entitled, Exchanging murine and human immunoglobulin constant chains affects the kinetics and thermodynamics of antigen binding and chimeric antibody autoreactivity. Again, first author Marcela Torres.

Do you see that?

A I see you that you have handed me the paper, Exchanging murine and human immunoglobulin constant chains affects the kinetics and

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thermodynamics of antigen binding and chimeric antibody autoreactivity, by Marcela Torres.

Q Again, this is a publication from your lab, correct?

A This is a publication from my laboratory.

Q So you are familiar with this paper?

A I am familiar with this paper.

Q You discuss Exhibit 2039 in paragraph 113 of your declaration, correct?

A (Reviewing.) I'm sorry, what paragraph?

Q 113.

A 113.

Q Yeah.

A (Reviewing.) This paper is discussed in paragraph 113 of the declaration.

Q When was this paper that's Exhibit 2039 published?

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A December 2007.

Q So it wasn't published until after March 15, 2007, correct?

A It was not published until after March 15, 2007.

Q So a person ordinary skill in the art would not have been able to read this paper prior to March 2007, correct?

A A person -- the paper would not have been published; therefore, a POSA would not have seen the paper.

Q You can set that aside.

I am going to hand you reference previously marked Exhibit 2012.

A (Reviewing.)

Q It's a paper entitled, Can isotype switch modulate antigen-binding affinity and influence clonal selection. First author, Otto Pritsch.

Do you see that?

A Can isotype switch modulate

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antigen-binding affinity and influence clonal selection, by Otto Pritsch.

Q Do you recognize this paper?

A Yes.

Q And you discuss this paper in paragraph 114 of your declaration, correct?

A Yes.

Q Does this Pritsch paper, Exhibit 2012, provide any experiments relating to testing an antibody having a human hybrid IgG2-IgG4 constant region?

MR. DIAMOND: Objection to form.

THE WITNESS: This paper reports that when you change the isotype, it will modulate the antigen-binding activity and fits within the concept that if you change the constant region, you have unpredictable effects.

As to whether IgG2/4 hybrid was included in this paper, the

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answer is -- (Reviewing.) -- the answer is no. But the concept would apply to IgG2-IgG4 hybrid since the principle is the same.

BY MS. STERLING:

Q But just to be clear, there's no experiments relating to testing an antibody with a human hybrid IgG2-IgG4 constant region reported in Pritsch Exhibit 2012?

MR. DIAMOND: Objection to form. Asked and answered.

THE WITNESS: The paper reports set of antibodies which include IgM, IgA, IgG1, IgG2 and IgG4. It does not include a hybrid of IgG2-IgG4.

BY MS. STERLING:

Q You can set that one to the side, please.

I am going to hand you an exhibit that's been previously marked 2010.

A (Reviewing.)

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Q It's a reference entitled, IG constant region effects on variable region structure and function, and lists first author Alena Janda.

Do you see that?

A Yes.

Q You're also listed as an author here, correct?

A The paper is, IG constant region effects on variable region structure and function, by Alena Janda, and it is a paper from my laboratory.

Q When was this paper published?

A February '16 -- 20 -- I'm sorry, February 2016.

Q So this paper was not published until after March 15, 2007, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: This paper was published February 2016, which is

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after March 15, 2007.

BY MS. STERLING:

Q Okay. You can set that one aside. Thank you.

I am going to hand you a new document that's been previously marked as Exhibit 1007.

A (Reviewing.)

Q This is a US Patent. It's Patent Number 6,355,245, listing first inventor Mark Evans.

Do you see that?

A (Reviewing.) I see US Patent 6,355,245 listing Mark Evans as the first named inventor.

Q Are you familiar with this document?

A (Reviewing.) I am familiar with this document.

Q I am going to refer to this Exhibit 1007 as Evans during our discussion of it. Is that okay?

A It's okay with me.

Q Okay.

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So let's look at example 11 of Evans. It starts at column 42. The columns are at the top of the document.

Let me know when you're there.

A (Reviewing.) Example 11?

Q Yes.

A Page 43?

Q Column 42, page 43.

A I am here.

Q I am going to refer to column and line numbers. So just for clarity, the column numbers are at the top of the document and down the center of the document there are line number increments of five.

I am going to use that to point you to various places in this document.

Is that okay?

A Yes.

Q If you need clarity, let me know.

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A I will let you know.

Q Okay.

So this example 11 is entitled, Construction and expression of recombinant mAbs; is that correct?

A Construction and expression of recombinant mAbs.

Q And mAbs is shorthand for monoclonal antibodies, correct?

A Sure.

MR. DIAMOND: Objection to form.

THE WITNESS: The term "mAbs" generally refers to monoclonal antibodies.

BY MS. STERLING:

Q Okay.

So here in this example, just read that first paragraph. This example --

MR. DIAMOND: Sorry, go on. I want to see if there is a question pending.

BY MS. STERLING:

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Q In this example, in this first paragraph, says, "Recombinant DNA constructions encoding there are recombinant mAbs comprising 5G1.1 CDRs are prepared by conventional recombinant DNA methods, including restriction fragment subcloning and overlapping PCR procedures."

Do you see that?

A "Recombinant DNA constructions encoding there are recombinant mAbs comprising 5G1.1 CDRs are prepared by conventional recombinant DNA methods, including restriction fragment subcloning and overlapping PCR procedures."

Q Okay.

And then the next sentence tells you that the resulting recombinant mAb encoding DNAs include, and it has a list of 18 constructs that continue over the next few columns to the start of column 45.

Would you agree?

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MR. DIAMOND: Objection to form.

THE WITNESS: The next paragraph says, One encoding a non-humanized murine scFv designated 5G1.1M1, scFv (SEQ ID NO:7) --

BY MS. STERLING:

Q I don't mean to interrupt you. I think you're looking at different place from where I pointed you to.

I pointed you to the next sentence after the one we just read. And that sentence says, "The resulting recombinant monoclonal antibody encoding DNAs include..." and then it lists 18 constructs.

MR. DIAMOND: Objection --

BY MS. STERLING:

Q I want you to confirm that for me.

MR. DIAMOND: Objection to form.

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THE WITNESS: (Reviewing.)

It states that the resulting recombinant monoclonal antibody, including DNA or mAb including DNA include...

BY MS. STERLING:

Q And then after that it lists 18 constructs over the next few columns, if you can look at that and confirm.

MR. DIAMOND: Objection to form.

THE WITNESS: (Reviewing.)

The patent is ambiguous because these are fragments and the introductory sentence talks about monoclonal antibody.

BY MS. STERLING:

Q Okay.

So these constructs are fragments; is that a fair description of the constructs?

MR. DIAMOND: Objection to form.

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THE WITNESS: I would have to go through them, but they are -- they are designated S, single chain, Fv. That would be one single chain.

Single chain Fd, chimeric light chain. Chimeric Fd. Humanized Fd, as in David;

(6), including a humanized Fd, as in David;

Humanized (CDR grafted and framework sequence altered) light chain designated 5G1.1 VL+KVL 56;

One encoding a humanized (CDR grafted, not framework alerted) light chain designated 5G1.1;

One encoding humanized (CDR grafted not framework altered) light chain designated 5G1;

One encoding humanized (CDR grafted, not framework altered) Fd designated 5G1.1 VH+IGHRLD (SEQ ID NO:16);

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One encoding humanized (CDR grafted) scFv designated 5G1.1 scFv DO12, (SEQ ID NO:17);

(12) when encoding a humanized (CDR grafted and framework sequence altered) scFv designated 5G1.1 scFv;

One encoding a humanized (CDR grafted) scFv designated 5G1.1 scFv DO12B, (SEQ ID NO:21);

One encoding a humanized (CDR grafted) scFv designated 5G1.1 scFv DO12C, (SEQ ID NO:22);

One encoding a humanized (CDR grafted) scFv designated 5G1.1 scFv --

I will repeat.

One encoded a humanized (CDR grafted) scFv designated 5G1.1 scFv, DO12D (SEQ ID NO:23);

One encoding a humanized (CDR grafted and framework sequence altered) scFv designated 5G1.1 scFv CO13 (SEQ ID NO:24);

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One encoding a humanized (CDR grafted and framework sequence altered) sc designated 5G1.1 scFv CO14 (SEQ ID NO:25);

And, one encoding a humanized (CDR grafted and framework sequence altered) scFv designated 5G1.1 scFv CO15 (SEQ ID NO:26).

So the first 26 items -- I'm sorry, the first 18 items are all fragments.

BY MS. STERLING:

Q Okay.

Some of those fragments are humanized 5G1.1 scFv fragments, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: Some of those are fragments are described -- are encoding a humanized CDR grafted scFv designated 5G1.1 scFv DO12D.

BY MS. STERLING:

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Q Okay.

So I am going to take you through some of these constructs. Let's start with construct 2. Okay?

MR. DIAMOND: Objection to the characterization.

BY MS. STERLING:

Q Is there a term you prefer me to use when I point you to these numbered --

A I think 2 is fine.

Q Can I call it construct 2; is that fair?

MR. DIAMOND: Objection to form.

THE WITNESS: It's not a construct 2. It's -- 2 is the list -- listed. I think if you are going to call it something, I would call it by the proper name.

BY MS. STERLING:

Q Okay.

So I am going to point you to number 2 which is, a humanized (CDR

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grafted) scFv designated 5G1.1 scFv CB (SEQ ID NO:8).

Do you see that?

A Sequence number?

Q 8.

A 8. I see one encoding a humanized (CDR grafted) scFv designated 5G1.1 scFv CB (SEQ ID NO:8).

Q Then in this number 2 that we are looking at provides: CDR L1, CDR L2, CDR L3. And I point you toward where the amino acid residues are for those CDR regions.

Do you see that?

MR. DIAMOND: Objection to form.

THE WITNESS: It states CDR L1 is amino acid residues 26 to 36 of SEQ ID NO:8; CDR L2 is amino acid residues 52 to 58 of SEQ ID NO:8; CDR L3 is amino acid residues 91 to 99 of SEQ ID NO:8; CDR H1 is amino acid residues 152

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to 161 of SEQ ID NO:8; CDR H2 is amino acid residues 176 to 192 of SEQ ID NO:8; H3 is amino acid residues 225 to 237 of SEQ ID NO:8.

BY MS. STERLING:

Q CDR L1, CDR L2 and CDR L3, that's mentioned in this number 2, would a person of ordinary skill in the art understand those to be complementarity determining regions in the light gene of this scFv?

A When you see L, it usually refers to light. Yes.

Q And when we -- when a person of ordinary skill would see CDR H1 and CDR H2, and last entry just says H3, would a person of ordinary skill in the art understand those to be the CDR -- CDRs in the heavy chain, 1, 2, and 3?

MR. DIAMOND: Objection to the form.

THE WITNESS: A person of

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skill in the art would have known that there is uncertainty on how to define CDRs.

So it would have taken those numbers but it would not have been sure as to what CDRs they really referring to.

BY MS. STERLING:

Q What other CDRs would they be referring to aside from CDR1, 2, and 3 in the heavy chain here?

A A POSA at that time would have known there are two -- at least two general ways to describe a CDR; one is known as Kabat method and the other is known as Chothia method. And those methods differ on the ends of the CDR or what is included. And a POSA reading this paragraph would not know where -- what CDRs is being referred to.

Q A POSA reading CDR H2 would not understand that it's referring to CDR2 in the heavy chain of this scFv

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in number 2?

MR. DIAMOND: Objection to form.

THE WITNESS: I think person reading CDR2 would have looked at this and say, well, those are the CDRs that they define. But a person knowledgeable in the field would have looked at this data much more carefully than just taking those numbers from there.

BY MS. STERLING:

Q So even though Evans tells you that the specific amino acid residues in the CDR regions, you don't think that's informative enough --

MR. DIAMOND: Objection.

BY MS. STERLING:

Q -- to a POSA?

MR. DIAMOND: Sorry. Objection to form. Mischaracterizes.

THE WITNESS: Evans doesn't tell me what kind of method they

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use to establish the ends of the CDRs.

BY MS. STERLING:

Q But Evans just gives you the amino acid residues that Evans considers to be CDR regions in either the light chain or heavy chain, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: A POSA -- a POSA would have looked at this and know there's ambiguity on where the CDRs begin and end for both the heavy and the light chain.

BY MS. STERLING:

Q So that's twice you have said this patent is ambiguous, correct?

A I didn't say the patent is ambiguous.

MR. DIAMOND: Objection to form.

BY MS. STERLING:

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Q I'm sorry.

You said example 11 -- twice you said example 11 has been ambiguous; is that correct?

MR. DIAMOND: Objection to the form. The witness' testimony stands as it is.

THE WITNESS: I said that the CDR as listed, the POSA would be cautious on assigning those numbers to the CDRs.

BY MS. STERLING:

Q Even though Evans tells you expressly the amino acid residues that Evans associates with the CDR regions?

MR. DIAMOND: Objection to form.

THE WITNESS: Evans is defining some CDRs here. A POSA would have looked at the data and would have looked at it with caution because a POSA would have known that CDRs -- the boarders are defined differently depending

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on the method.

BY MS. STERLING:

Q But Evans has defined its borders, right?

Because Evans gives you the amino acid residues, for example, CDR H3 of 225 to 237 SEQ ID NO:8.

Do you see that?

MR. DIAMOND: Objection to form.

THE WITNESS: I see that. But I also say to you that a POSA or somebody -- a POSA -- we have defined a POSA would have read that and come across some -- with degree of ambiguity as to what CDR method they are using to label -- to make those assignments.

BY MS. STERLING:

Q But the assignments are finally labeled, regardless of the method used to get there; Evans has described amino acid residues to the CDR regions provided here in number 2,

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correct?

A Evans has stated -- has said of light chain and heavy chain CDRs. They are listed here with numbers.

A POSA would have read this, would have seen the numbers, and would have known that there is ambiguity on how you define a CDR based on the Chothia and Kabat methods.

Q Okay.

But let's look at why Evans chose to define Evans' regions. Okay? We will focus on that.

Evans provides CDR H3 of amino acid residues 225 to 237 of SEQ ID NO:8.

Do you see that?

MR. DIAMOND: Objection to form. Mischaracterizes.

THE WITNESS: I'm sorry, are we still on number 2?

BY MS. STERLING:

Q Yes.

A Where are you at now?

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Q The very last entry, H3 is amino acid residues 225 to 237 of SEQ ID NO:8.

A A POSA would have read that and known that Evans define it as 225 to 237. But a knowledgeable -- a knowledgeable individual would have looked at that and said, you know, those are the boundaries that Evans gives me, but CDRs are defined with some variability depending on the method. So...

Q Okay.

I am going to point you to column 5 in Evans. And I am going to direct you to line 25. So again, look for the numbers between the two columns, look for 25.

There's a paragraph that starts, "There are two definitions of CDR location are currently in general use in the art."

Do you see the paragraph that starts with that sentence?

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A (Reviewing.) I see the paragraph that starts with that sentence.

Q Okay.

About halfway down that paragraph there's a sentence that starts, "As used herein, the terms..." And then it lists some terms.

Do you see that sentence?

A "As used herein, the terms VL CDR1, VL CDR2, VL CDR3, VH CDR1, VH CDR2 and VH CDR3 refer minimally to the region of overlap between the regions designated for each CDR by each of these two definitions, and maximally, to the total region spanned by the combination of regions designated for each CDR by each of these two definitions."

Q Okay.

So Evans has explained what Evans means by these terms in the '245 patent.

Do you agree?

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A I disagree. I think this is -- there is -- the POSA would have been confused by the term "refer minimally to the region of overlap between the regions designated for each CDR by each of these two definitions."

Q So you're telling me Evans is ambiguous as to how it's using these terms?

MR. DIAMOND: Objection to form.

THE WITNESS: I am saying that as I would read this, the words that the POSA would not have come across with a clear way in which this CDRs were defined because it's referring minimally to the region of overlap between this region's designated for each CDR by each of the two definitions, and maximally to the total region spanned by the combination of regions designated

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by each CDR by each of these two definitions.

That is a mouthful and difficult to understand exactly what the definition is here.

BY MS. STERLING:

Q So a person of ordinary skill in the art reading Evans would not have understood what Evans is referring to when it talks about CDR H1 or CDR -- VH CDR3, a person of ordinary skill in the art would not have understood Evans' definition nor any of the reported constructs in Evans.

Is that what you are telling me?

MR. DIAMOND: Objection to the form. Asked and answered.

THE WITNESS: I disagree with the premise of your question.

A POSA at the time would have read this as Evans' definitions of CDRs, but would

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have had some uncertainty as to whether these are the actual CDRs in these -- in this fragments.

BY MS. STERLING:

Q So you're telling me a person of ordinary skill in the art would have had uncertainty as to what Alexion's patent was teaching the public?

MR. DIAMOND: Objection to form.

THE WITNESS: I did not say that. I said that person -- a POSA at the time would have uncertainty as to where the boundaries are for this CDRs based on two definitions, based on the wording of the sentence.

BY MS. STERLING:

Q So even though Evans itself puts amino acid residue boundaries on these CDRs in these numerical scFv constructs we are discussing, you are telling me there's still uncertainty

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as to what that means?

MR. DIAMOND: Objection to form.

THE WITNESS: A POSA would have read that and concluded that that's how Evans is defining the CDRs. But a POSA would have known that there is uncertainty in the science on how you define a CDR, and would have been cautious with those numbers.

BY MS. STERLING:

Q But Evans, in his own patent -- do you understand a patentee can be its on a lexicographer?

MR. DIAMOND: Objection to form. Calls for legal conclusion.

MS. STERLING: I'm asking if he has an understanding. He can answer yes or no whether he does.

BY MS. STERLING:

Q Do you have an understanding on that legal concept?

MR. DIAMOND: Objection.

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THE WITNESS: On what legal concept?

BY MS. STERLING:

Q That a patentee act as his or her own lexicographer?

A I have no idea --

Q Okay.

A -- about this concept.

Q Okay.

So even though I am -- I am going to go back -- Evans has told you how Evans is using these terms in his paper, you are saying that's still confusing and ambiguous; is that fair?

MR. DIAMOND: Where are we looking now? Are we in column 5?

MS. STERLING: Column 5. Keep up.

MR. DIAMOND: Objection to form. Asked and answered.

THE WITNESS: What I have said, and I will repeat it again, is that Evans provides a set of amino acids that Evans is calling

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the CDRs.

A POSA at the time would have seen those numbers and known that there is ambiguity in the beginnings and the ends of CDRs, as evident by the fact that the field was working with two definitions.

BY MS. STERLING:

Q Okay.

Let's focus on -- you said Evans provides a set of amino acids that Evans is calling the CDRs. Let's focus on those sets of amino acids, please.

MR. DIAMOND: Objection. Mischaracterizes the witness' testimony.

MS. STERLING: I read it exactly back from the record. Thank you, Evan.

MR. DIAMOND: You read a partial statement.

BY MS. STERLING:

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Q Number 2, Evans says, CDR H3 is amino acid residue to 25 to 237 of SEQ ID NO:8.

MR. DIAMOND: Objection.

BY MS. STERLING:

Q This is what Evans is calling it's CDR H3, correct?

MR. DIAMOND: Objection to form.

BY MS. STERLING:

Q We are back in column 43.

MR. DIAMOND: Why don't you ask the question again once he's back on 43.

THE WITNESS: I am back in 43.

MR. DIAMOND: Can you ask the question again.

BY MS. STERLING:

Q Evans says in this number 2, that Evans CDR H3 gives us an amino acid residue group. Okay?

So Evans says H3 is amino acid residues 225 to 237 of SEQ ID

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NO:8.

Do you see that?

MR. DIAMOND: Objection to form.

THE WITNESS: I see the patent says that H3 is amino acid residues 225 to 237 of SEQ ID NO:8.

BY MS. STERLING:

Q Okay.

Amino residues 225 to 2347, is that a 13 amino acid residue --is that 13 amino acids in residues 225 to 237?

MR. DIAMOND: Objection to form.

THE WITNESS: 225, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, those numbers will correspond to 13 amino acids. But this is -- what has been listed here, a POSA at the time would have looked at those numbers with great deal of caution because the

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boundaries of CDRs are uncertain depending on how you define them.

BY MS. STERLING:

Q Okay.

Let's look at number 11. It starts at the bottom of column 43 and extends over to column 44.

The end of number 11, it is the second and third line on column 44, Evans -- sorry. Let me start with what number 11 is.

Evans says it's one encoding a humanized (CDR grafted) scFv designated 5G1.1 scFv DO12 (SEQ ID NO:17). And Evans lists at the end of the paragraph CDR H3 is amino acid residues 225 to 237 of SEQ ID NO:17.

Do you see that?

MR. DIAMOND: Objection to form. Compound.

THE WITNESS: Evans is listing a different fragment. Evans is using the same numbering to refer to CDR H3. CDR H3 is

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amino acid residues 225 to 237. A POSA at the time would have read this and would have been very cautious in the interpretation of where the CDRs are because it was known by a POSA that there's uncertainty in how you call the ends.

BY MS. STERLING:

Q Evans himself says, CDR H3 is amino acid residues 225 to 237 of SEQ ID NO:17.

Is 225 to 237, a 13 amino acid stretch?

MR. DIAMOND: Hold on, counsel. You just testified. That's not a question. Okay. Ask questions. What is your question?

BY MS. STERLING:

Q Is amino acids 225 to 237 of SEQ ID NO:17, a 13 amino acid stretch?

MR. DIAMOND: Objection to form.

THE WITNESS: As I counted

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with my fingers, the numbers 225 to 237 would represent 13 amino acids.

BY MS. STERLING:

Q Number 12 is another fragment: One encoding a humanized (CDR grafted and framework sequence altered) scFv designated 5G1.1 scFv CO12 (SEQ ID NO:20).

And at the end of that entry, H3 is amino acid residues 225 to 237 of SEQ ID NO:20.

Do you see that?

MR. DIAMOND: Objection to form.

THE WITNESS: At the end of this paragraph I see the wording H3 is amino acid residues 225 to 237 of SEQ ID 20. And --

(Whereupon a Discussion is Held Off the Record.)

MS. STERLING: Finish, please.

THE WITNESS: H3 is amino

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acid residues 225 to 237 of SEQ ID NO:20.

BY MS. STERLING:

Q Okay.

You would agree 225 to 237 is a 13 amino acid stretch of that sequence ID number, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: I would say that when you list 225 to 237 and you count them in your fingers, the number is 13.

BY MS. STERLING:

Q Okay.

So if you see an entry of amino acid residues 225 to 237, you would consider that to be a 13 amino acid stretch?

MR. DIAMOND: Objection to form.

THE WITNESS: But it would not -- but I would not accept that this is necessary -- a POSA would

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not accept that this is necessarily H3 domain. This is a domain that's been labeled in the patent. But the CDR domain requires -- will require more knowledge.

One of the problems with all of this is that these are all fragments. CDRs by Chothia and Kabat were defined from antibodies.

So there's uncertainty built on uncertainty on these numbers. A POSA would have known that, and would have been very cautious in taking any of these antibodies at face value -- any of these numbers at face value.

BY MS. STERLING:

Q So you're telling me each of these fragments that we are discussing 1 through 18 here, you said you would require more knowledge than what is provided here to understand these

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fragments; is that correct?

MR. DIAMOND: Objection to the form.

THE WITNESS: I am saying that from what is written here, I accept that Evans has written H3 with the residues 225 to 237. But a POSA would have been very cautious looking at that number and accepting that as the CDR H3.

BY MS. STERLING:

Q Okay.

That goes for any of the 18 we're looking at, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: We would have to look at each one carefully. But we already looked at them and they are antibody fragments. None of these is an antibody.

BY MS. STERLING:

Q For the fragments that we are looking at your testimony applies

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across them, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: No, I think if you want we can discuss all 18 one at a time.

BY MS. STERLING:

Q Let's look at 13, that is the next one.

A Okay.

Q 13 is, one encoding a humanized (CDR grafted) scFv designated 5G1.1 scFv DO12B (SEQ ID NO:21).

And at the end again, we see H3 is amino acid residues 225 to 237 of SEQ ID NO:21.

Do you see that?

A I see that at the very end, H3 is amino acid residues 225 to 237 of sequence ID 21.

Evans is referring by H3 to a CDR3, but the point is that a POSA at this time would have looked at this

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data and would have a great deal of caution when accepting these numbers as the boundaries for CDR -- for CDR3, particularly when these are antibody fragments.

Q But you would agree with me that amino acid residues 225 to 237 of SEQ ID NO:21 is a 13 amino acid stretch?

A I would agree with you that when you list 225 to 237, by counting, it involves 13 amino acids.

Q Let's move on to number 14 then.

That is, one encoding a humanized (CDR grafted) scFv designated 5G1.1 scFv DO12C, and that's SEQ ID NO:22.

Again, at the end, H3 is amino acid residues 225 to 237 of SEQ ID NO:22.

Do you see that?

MR. DIAMOND: Objection to form.

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THE WITNESS: I see that at the end H3 is amino acid residues 225 to 237 of SEQ ID NO:22.

A POSA reading this would have read that as whatever was listed and would have had great caution in interpreting that information as being the boundaries of the CDR3.

BY MS. STERLING:

Q But you would agree with me that amino acid residues 225 to 237 of SEQ ID NO:22 is a 13 amino acid stretch?

A It's a 13 amino acid -- yeah, 225 to 237 will involve 13 amino acids.

Q Number 15 is, one encoding a humanized (CDR grafted) scFv designated 5G1.1 scFv DO12D (SEQ ID NO:23). And at the end of that entry it says, H3 is amino acid residues 225 to 237 of SEQ ID NO:23.

Do you see that?

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MR. DIAMOND: Objection to form.

THE WITNESS: I see that the ends of the sentence reads, H3 is amino acid residues 225 to 237 of SEQ ID NO:23.

BY MS. STERLING:

Q You would agree with me that amino acid residues 225 to 237 of SEQ ID NO:23 is a 13 amino acid stretch?

MR. DIAMOND: Objection to the form.

THE WITNESS: I read -- I read this as if you have residues 225 to 237, you are -- let me count again -- 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37 -- 13 amino acids.

BY MS. STERLING:

Q Okay.

Number 16, one encoding a humanized (CDR grafted and framework sequence altered) scFv designated 5G1.1 scFv CO13, which is SEQ ID

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NO:24. At the end of that entry we see, H3 is amino acid residues 225 to 237 of SEQ ID NO:24.

Do you see that?

MR. DIAMOND: Objection to the form.

THE WITNESS: I see that the last phrase of the last sentence says that H3 is amino acid residues 225 to 237 of SEQ ID NO:24.

But a POSA reading this would have been very cautious with this definition of H3 based on the ambiguity of defining CDRs depending on Chothia and Kabat.

BY MS. STERLING:

Q But you would agree with me that amino acid residues 225 to 237 of SEQ ID NO:24 is a 13 amino acid range?

MR. DIAMOND: Objection to the form.

THE WITNESS: I would agree with you that H3 amino acid

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residues 225 to 237, that if you count on your fingers, adds up to 13.

BY MS. STERLING:

Q Okay.

For number 17, one encoding a humanized (CDR grafted and framework sequence altered) scFv designated 5G1.1 scFv CO14, SEQ ID NO:25. And at the end of that entry it states, H3 is amino acid residues 225 to 237 of SEQ ID NO:25.

Do you see that?

A I see the last sentence that there is a phrase at the end that states, H3 is amino acid residues 225 to 237 of SEQ ID NO:25, which a POSA would have read with great caution because a POSA would have known that defining CDR3s is ambiguous depending on which -- which formulation you are using.

Q But you would agree with me that amino acid residues 225 to 237 of

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SEQ ID NO:25 is a 13 amino acid range?

A I would agree with you that when you have the sentence that states amino acid residues 225 to 237, by counting by my fingers, will be 13 amino acids.

Q Okay. One more construct.

18, one encoding a humanized (CDR grafted and framework sequence altered) scFv designated 5G1.1 scFv CO15 (SEQ ID NO:26). And at the end of that entry, H3 is amino acid residues 225 to 237 of SEQ ID NO:26.

MR. DIAMOND: I will object to counsel's testimony in the preamble of that question.

THE WITNESS: What I -- since there's an objection, I will read number 18.

One encoding a humanized (CDR grafted and framework sequence altered) scFv designated 5G1.1 scFv CO15 (SEQ ID NO:26) wherein CDR L1 is amino acid

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residues 26 to 36 of SEQ ID NO:26, CDR L2 is amino acid residues 52 to 58 of SEQ ID NO:26, CDR L3 is amino acid residues 91 to 99 of SEQ ID NO:26, CDR H1 is amino acid residues 156 -- I'm sorry, 152 to 161 of SEQ ID NO:26, CDR H2 is amino acid residues 176 to 192 of SEQ ID NO:26, H3 is amino acid residues 225 to 237 of SEQ ID NO:26.

BY MS. STERLING:

Q Okay.

You would agree with me that amino acid residues 225 to 237 of SEQ ID NO:26 is a 13 amino acid stretch, correct?

A I would agree with you that when you have amino acid residues listed as 225 to 227 [sic] it counts to 13 amino acids.

MR. DIAMOND: Counsel, we have been going over an hour, would it be a good time for a

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break?

MS. STERLING: It could be a good time for a break or I believe I have two or three more questions on Evans if you can --

MR. DIAMOND: I need a break myself, if that's all right.

MS. STERLING: Let's take one for you, Evan.

MR. DIAMOND: I appreciate it. It's been over an hour.

(Whereupon a Recess Commenced at 2:01 p.m. and Testimony Recommenced at 2:26 p.m.)

MS. STERLING: Let's go back on the record.

BY MS. STERLING:

Q Dr. Casadevall, during the break did you discuss the substance of your deposition testimony with counsel?

A No.

Q Okay.

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Before we took the break we were looking at Evans Exhibit 1007.

Do you still have that in front of you?

A Yes, I have everything in front of me.

Q You were looking at example 11.

A Okay.

Q Which begins on column 42, page 43.

Do you have that in front of you?

A Example 11 starts in column 43.

Q Page 43, column 42.

A 11?

Q I am pointing to example 11.

A Oh, sorry.

Q It's on column 42.

A (Reviewing.) Okay.

Q It spans over multiple columns.

But you recall this was the

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example we were discussing about before the break, correct?

A It was the example we were discussing before the break.

Q Okay.

In column 45, which is still example 11.

A Yes.

Q Starting around line 24, there's a paragraph that starts, "In accordance with the invention..."

Do you see that paragraph?

A I see the paragraph that begins, "In accordance with the invention..."

Q Okay.

Would you like to read that for us in the record, slowly?

A In accordance with the invention, match pairs of the variable regions, e.g., a VL and a VH region of the various antibody molecules, Fds and light chains described above may be combined with constant region

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domains by recombinant DNA or other methods known in the art to form full-length antibodies of the invention. Particularly, preferred constant regions for this purpose are IgG constant regions which may be altered or constructed of a mixture of constant domains from IgGs of various subtypes, example, IgG1 and IgG4.

Q So in this passage, Evans is telling us the variable regions and described above can be made into full-length antibodies by combining those variable regions by constant region domains; is that fair?

MR. DIAMOND: Objection to form.

THE WITNESS: I think Evans is stating that the fragments -- because Evans deals only with fragments -- may be combined with -- with constant regions to form full-length antibodies of the invention.

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BY MS. STERLING:

Q Evans, in this paragraph, says that can be done so by recombinant DNA or other methods known in the art.

Do you agree?

MR. DIAMOND: Objection to form.

THE WITNESS: (Reviewing.) In accordance with the invention, matched pairs -- matched pairs of the variable regions, example, a VL and a VH region of the various antibody molecules, Fds, and light chains described above may be combined with constant region domains by recombinant DNA or other methods known in the art to form full-length antibodies...

BY MS. STERLING.

Q ...of the invention.

A ...of the invention.

Q So Evans continues to say that, "Particularly preferred constant

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regions for this purpose are IgG constant regions."

Do you see that?

A Are IgG constant regions.

Q Evans tells us those IgG constant regions may be unaltered or constructed of a mixture of constant domains from IgGs of various subtypes.

Do you see that?

MR. DIAMOND: Objection to form.

THE WITNESS: I see that it says, Particularly preferred constant regions for this purpose are IgG constant regions, which may be unaltered, or constructed of a mixture of constant domains from IgGs of various subtypes, example, IgG1 and IgG4.

BY MS. STERLING:

Q So a constant region that was constructed of a mixture of constant domains from IgGs of various subtypes, that would be a hybrid IgG

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constant domain, correct?

MR. DIAMOND: Objection to form.

THE WITNESS: It would depend how you define hybrid. I think -- I think that I would read this as a mixture of constant domains from IgGs of various subtypes.

It doesn't use the word hybrid and that's just not here.

BY MS. STERLING:

Q What does the word mixture convey to a person of ordinary skill in the art in this paragraph?

A A POSA would have read this as taking pieces of the constant regions and putting them into -- that would take of various subtypes. But a hybrid is a very specific term.

For example, I can read this and say that it would take a piece of IgG1, a piece of IgG2, a piece of IgG3 and end up with a multi -- an antibody

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that is very different.

Q So one example of the mixture of constant domains from IgGs you've just given us a piece of IgG1, a piece of IgG2 and a piece of IgG3; is that correct?

MR. DIAMOND: Objection to form.

THE WITNESS: I used those examples to -- as an example when you asked me for the purpose -- for particularly preferred constant region for this purpose are IgG constant regions which may be unaltered, or constructed of a mixture of constant regions of IgGs of various subtypes.

BY MS. STERLING:

Q Would another example of a mixture of constant domains from IgGs of various subtypes be some from IgG2 and some from IgG3?

MR. DIAMOND: Objection to the form.

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THE WITNESS: What I think what they are saying is that that you will take -- that you will take a mixture of constant domains and assemble them in some way.

It doesn't say anything about hybrids and it's just what it says.

BY MS. STERLING:

Q Okay. You can set Evans aside.

I am going to go back to your declaration, Exhibit 2022, and we are going to stay with the declaration in IPR 2019/00739 for the '504 patent.

Is that the one you have in front of you?

A Yes, I have the 00739 in front of me.

Q Okay.

Let's turn to page 142.

MR. DIAMOND: Page 142?

MS. STERLING: Yes.

MR. DIAMOND: Okay.

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BY MS. STERLING:

Q On that page there's a header, header 2, SOLIRIS fulfilled a long-felt, unmet need for a treatment of PNH which others failed to satisfy.

Are we on the same page?

A Sorry. I am now, yes.

I am in that page.

Q Okay.

What standard did you use to formulate your opinion on long-felt need that you provide here in this section?

A (Reviewing.) A long-felt, unmet need is a need for which the -- you lack -- A therapy for the effective treatment of PNH.

Q So is your testimony here in this section, that it's necessary for a therapeutic to be sold to the general public or prescribed to the general public for a long-felt need to be met by that therapeutic?

MR. DIAMOND: Objection to

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form.

THE WITNESS: To have a long-felt, unmet need, I don't think the criteria of selling it to the public is necessary. For example, the government could make it and give it to necessary people and you will still have a long-felt, unmet need.

BY MS. STERLING:

Q So you are saying it's not necessary for a therapeutic to be prescribed to the public for a long-felt need to be met by that therapeutic.

Did I understand you correctly?

MR. DIAMOND: Objection to form.

THE WITNESS: It's not what I said.

BY MS. STERLING:

Q Okay.

A What I said was, you asked

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me whether it was necessary to sell it to the public to fulfill a long-felt, unmet need. And my answer was that the act of selling did not come into that long-felt, unmet need.

Q Okay. Let me ask the question again, then.

Is it your testimony that it's necessary for a therapeutic to be prescribed to the general public for long-felt need to be met?

A This statement, a general public, is itself vague. The general public does not have PNH. The people who have PNH are the patients.

Q Okay.

Is it then your testimony, then, that it's necessary for a therapeutic to be prescribed to a patient in need of that therapeutic in order for a long-felt need to be met by that therapeutic?

MR. DIAMOND: Objection to form.

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THE WITNESS: It doesn't have to be prescribed. It can be given.

BY MS. STERLING:

Q Who would give it?

A You know, we are in the middle of a Coronavirus outbreak. Imagine this takes over, we are susceptible to the Coronavirus outbreak. There is not a long-term but definitely an unmet need. It could be that the government gives out antivirals.

Q Okay.

So then is it your testimony we would need the government to give a therapeutic to patients in the need of that therapeutic for the therapeutic to meet a long-felt need?

A It's my opinion that you need an entity to give it out. You have patients who need it, they cannot produce it themselves. So you are going to need someone to give it to

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them; whether it is a company, whether it is a non-profit, whether it is a government.

Q So it's your opinion that you need an entity to give a therapeutic to a patient who needs that therapeutic in order for that therapeutic to meet a long-felt need; is that accurate?

MR. DIAMOND: Objection to form.

THE WITNESS: If you have a long-felt, unmet need, you will need something to alleviate the long-felt, unmet need, someone has to provide this material.

BY MS. STERLING:

Q I am trying to understand what you would consider having to be done or performed in order to meet the long-felt need. So let me ask another question.

Are you testifying that a long-felt need can only be met by a

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therapeutic once that therapeutic is approved by FDA, for example?

MR. DIAMOND: Objection to the form.

THE WITNESS: You know, I think approval is a regulatory part of the process. But a long-felt, unmet need, which is what we are talking about, undefined and vague, could be met, for example, drugs are given before they are approved. I forgot what the term is.

But oftentimes before approval, they are available to patients who need them. And so approval isn't necessarily an absolute requirement for unfelt -- for a long-felt, unmet need. Compassionate use is the term.

BY MS. STERLING:

Q Okay.

So would a publication of a successful clinical trial indicate to

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a person of ordinary skill in the art that the therapeutic in that clinical trial could meet a previously unmet need for a therapeutic?

MR. DIAMOND: Objection to form. Lack of foundation.

THE WITNESS: A drug that does well in a clinical trial would be a very encouraging compound as to whether it fulfills a long-felt, unmet need, is -- that is a subsequent criteria.

BY MS. STERLING:

Q What would you need -- what subsequent criteria would you need to know whether that drug that does well in the clinical trial would meet a previously unmet need?

MR. DIAMOND: Objection to form.

THE WITNESS: Can you rephrase the question because I am getting a little confused.

BY MS. STERLING:

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Q Okay.

I am going to read your answer back to you from the transcript.

You say: A drug that does well in a clinical trial would be a very encouraging compound as to whether it fulfills a long-felt need that is a subsequent criteria.

So I was asking you to help me understand what you meant by subsequent criteria. So here is my question again.

What subsequent criteria would you need to know, to know whether that drug that did well in the clinical trial would meet a previously unmet need?

MR. DIAMOND: Objection to form. And to the extent you misread the witness' testimony.

THE WITNESS: Could you tell me -- what you read back to me was what I said.

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BY MS. STERLING:

Q Yes.

MR. DIAMOND: Well, actually counsel, it wasn't, and the record will show that but go on and ask your question.

THE WITNESS: Okay. So please repeat the question.

MS. STERLING: Why don't we ask the court reporter to read the question again, if that's Okay.

Sorry, we are reading your answer back to you, not the question.

(Whereupon Answer is Read Back.)

THE REPORTER: A drug that does well in a clinical trial would be a very encouraging compound as to whether it fulfills a long-felt, unmet need, is -- that is a subsequent criteria.

BY MS. STERLING:

Q So that was the answer you

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gave me, and I am trying to understand what you meant by subsequent criteria.

A Subsequent criteria would be post-trial monitoring. You want to know that there are no long-term effects. That would be an important subsequent criteria.

Q So you would need -- you're telling me a person of ordinary skill in the art would need post-trial monitoring before a person of ordinary skill in the art could consider whether the therapeutic at issue would be able to meet a long-felt need?

MR. DIAMOND: Objection to form.

THE WITNESS: You asked me what other criteria would be needed, and I said that it is standard that all clinical trials include post-trial surveillance, because side effects could happen later and this is why drugs get recalled.

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BY MS. STERLING:

Q So you're telling me a therapeutic could not meet a long-felt, unmet need until there's been post-trial surveillance and you're confident the drug is not going to have side effects later?

MR. DIAMOND: Objection to form.

THE WITNESS: I disagree to your formulation because you could have a long-felt, unmet need, you could have a clinical trial that is highly successful, the reagent can be licensed, and you still have to have post-trial surveillance.

BY MS. STERLING:

Q So at which point in those events that you just recited to me would the therapeutic had been considered to meet a long-felt need, in your opinion?

MR. DIAMOND: Objection to

Samsung Bioepis Exhibit No. 1101
Samsung Bioepis Co., Ltd. v. Alexion Pharmaceuticals, Inc., IPR2023-00998
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form.

THE WITNESS: For patients with PNH, it would have -- it would have become a fulfilled long-felt, unmet need when it was available for them.

BY MS. STERLING:

Q And what would have made a therapeutic for PNH available to patients?

MR. DIAMOND: Objection to form.

THE WITNESS: It would have to -- it would have to do well in the clinical trial. It would have to be produced. It would have to be -- would be available to them from their physicians.

BY MS. STERLING:

Q And would this be by a physician prescribing the therapeutic to the PNH patient?

MR. DIAMOND: Objection.

BY MS. STERLING:

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Q Is that how the physician would provide this to the patient?

MR. DIAMOND: Objection to form.

THE WITNESS: You know, the decision on what is a prescription drug, not a prescription drug, I don't know how that is made so I don't know.

BY MS. STERLING:

Q Okay.

Paragraph 273 of your declaration, it's in the same section on page 143, you discuss treatments for PNH in that paragraph. Correct?

A In that paragraph 273 -- (Reviewing) -- states, "Prior to SOLIRIS, there were no drugs directed to regulation of the body complement system to treat PNH. Symptoms of PNH hemoglobinuria, dark urine caused by periods of acute hemolysis (paroxysms), chronic and potentially disabling fatigue, dysphasia,

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recurrent pain, severe anemia, severely impacted patients' quality of life. References AMG1004 at 6, AMG1047 at 2559, AMG 1012 at 1234, ALXN2049 at 122). Patients could also experience life-threatening clots or thrombosis. AMG1004 at 6, AMG1047 at 2559, AMG 1012 at 1234, ALXN2049 at 12. Because there were no drugs directed to a regulation of complement. As to treatment of PNH patients were forced to rely on other potentially invasive therapies, that could only address individual symptoms of the disease such as blood transfusions. See AMG1004 at 6, AMG1047 at 2559, AMG, 10-12 at 1234.

Q So you say in that last line on page 143, "There were therapies that could address individual symptoms of the disease such as blood transfusions."

Those therapies were available to patients with PNH prior

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to March 2007? Sorry, that therapy.

MR. DIAMOND: Objection to form.

THE WITNESS: Prior to the availability of SOLIRIS, the treatment of this disease was, as I used the word supportive previously, to mean that you could not do anything about the underlying disease; you had to treat the symptoms. The disease evolved the lysis of red blood cells, that results in anemia. Anemia is treated by blood transfusions.

BY MS. STERLING:

Q So what -- so -- then potential therapy for PNH prior to March 2007, would have been a blood transfusion; is that fair?

MR. DIAMOND: Objection to form.

THE WITNESS: That would not have been a therapy for PNH. It

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would have been to treat the symptoms. There is a difference.

BY MS. STERLING:

Q Were there any other therapies available prior to March 2007 that would treat the symptoms of PNH aside from the blood transfusions we just discussed?

A That is the only one I cited. I am not a hematologist and I was not treating patients around that time, so I don't know if there were other supportive measures that were used.

Q Okay.

Do you still have the '504 patent in front of you somewhere? Don't put your declaration aside, we are going to come back to it.

A '504 patent.

Q Let's turn to column 6. In column 6, you will see a header to Overview.

Do you see that?

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A (Reviewing.) Yes.

Q Okay.

So that recites, "The present disclosure relates to a method of treating paroxysmal nocturnal hemoglobinuria, ('PNH'). More specifically, to improving certain aspects of quality of life which are incurred in PNH patients and other hemolytic diseases in mammals."

Do you see that sentence?

A I see the sentence.

Q Do you know whether blood transfusions improved certain aspects of the quality of life of patients with PNH?

A Blood transfusions treat anemia. Anemia is associated with weakness, difficult breathing. Therefore, the blood transfusions would have improved certain aspects of the quality of life which are impaired in patients with PNH.

Q Okay. You can set the '504

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patent aside.

We are going to return to your '504 declaration. We are going to go to the next section, Section 3, that's on page 146.

Let me know when you're there.

A I am on 146.

Q Okay.

So in this Section 3, you provide your opinions about the commercial success of SOLIRIS, right?

A SOLIRIS is a commercial success.

Q Did you perform an independent analysis to determine whether SOLIRIS is a commercial success?

MR. DIAMOND: Objection to form.

THE WITNESS: What do you mean by "independent analysis"?

BY MS. STERLING:

Q Did you perform your own

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analysis to determine whether SOLIRIS is a commercial success?

MR. DIAMOND: Objection to form.

THE WITNESS: I still don't know what analysis you want me to do.

BY MS. STERLING:

Q How did you conclude SOLIRIS is a commercial success?

A There are documents citing that this -- that this drug got praises and it is my understanding that this drug is a commercial success.

Q What prices was the drug given?

A I have no idea. I do not know what price you sell that.

Q So you said there are documents citing --

A Oh, you mean prices. Prices. Yes, there are industry praise.

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Q That is a separate section.

A Right.

Q Okay.

We are talking about the commercial success.

A Right.

Q So I'm asking you what analysis you did to come to your conclusion that SOLIRIS is a commercial success?

A I did not do an analysis based on drugs. I am a scientist. I am not an economist or an accountant. To me, SOLIRIS is a commercial success based on what I know from being -- from being alive and being in the field.

Q And what is it that you know from being alive and being in the field that informed you as to whether SOLIRIS was a commercial success?

A Well, as I mentioned in the deposition [sic], that other companies are trying to develop biosimilars or

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equivalent drugs; therefore, the companies would not be trying to develop this if this was a financial failure.

Q So is that your analysis as to how you came to the conclusion that SOLIRIS is a commercial success?

MR. DIAMOND: Objection to form.

THE WITNESS: I think that's how -- that's one of the indicators by which I form my opinion. The other way in which I form my opinion is that this drug has been on the market at least for a decade, and is a success; therefore, I think that in the -- you know, to me that is a commercial success.

BY MS. STERLING:

Q So when you say the drug is on the market and a success, therefore, it's a commercial success, I am trying to understand what helps

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you get to the conclusion that it's a commercial success.

Was it merely the approval of the drug?

MR. DIAMOND: Objection to form.

THE WITNESS: You know, the idea of a commercial success is to some degree subjective because what may be a commercial success to one company, may not be a commercial success to another.

What I can tell you is that this drug brought to patients a brand new option for treating it; that the drug has been out there for over a decade; and that other companies have been trying to develop similar drugs. And to me, as I put it all together, from a physician with no training in economics and no training in accounting, that reads to me as a financial success.

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BY MS. STERLING:

Q Okay.

In that section that's entitled, Industry Praise, Section 4, it's on page 147.

Let me know when you're there?

A Industry praise.

Q Okay.

What analysis did you do to reach your conclusions about industry praise?

A I read -- I read the items that are cited here. I also understand that Alexion has received several significant awards honoring the groundbreaking nature of this development and introduction of SOLIRIS, including the Prix Galian USA 2008 award for best biotechnology product. And the Prix Galian France 2009 award for the most innovative drug for rare disease. And it cites LX -- LX -- ALXN2020 and ALXN2021.

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Q Are you familiar with these Prix Galian awards?

A I am not familiar with this awards but I can tell you that -- that they -- the fact that this compound received those awards must be significant.

Q Do you know what criteria goes into deciding who gets those awards?

A I do not know how the awards are selected.

Q Okay.

Your next section begins -- Section 5, and it's entitled, Copying. And it starts at paragraph 285.

Do you see that?

A I see 285, Section 5, Copying.

Q Okay.

And you're copying section spans through paragraph 287, would you agree?

A I agree.

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Q What standard did you use to reach your conclusions on copying?

A I -- you know, I think copying is a form of -- to me, copying is to challenge a patent to develop a similar type of drug, if not the same type of drug. That's to me is my standard of what copying means.

Q So what analysis did you perform to determine that other companies are seeking to copy or have already copied eculizumab?

A The information that I used to arrive at that conclusion is that Amgen is challenging this patent and that two other companies, Samsung Bioepis and Generium are seeking to copy or have already copied eculizumab, which is known today is a uniquely engineered antibody.

Q So your conclusion because Amgen challenged these patents in an IPR, that that is evidence that Amgen has copied these patents?

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MR. DIAMOND: Objection to form. Mischaracterizes the witness' testimony.

THE WITNESS: All I -- you asked me what evidence and I said to you that we are in the middle of a deposition challenging a patent, and why would you be challenging this patent. And to me, I interpret this as Amgen is -- wants to develop a similar product together with this other companies that are listed here.

And this is why we are -- and incidentally, this is evidence of commercial -- commercial success. If this had been a failure, I don't think they would be trying to develop the same type of compound.

BY MS. STERLING:

Q So you included copying in your analysis of commercial success in order to arrive at your conclusion

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regarding commercial success; is that fair?

MR. DIAMOND: Objection to form.

THE WITNESS: When I said to you commercial success, I said to you I am not an economist, I am not an accountant. I go with the big picture of this drug. It's been in the market for 10 years. It met an unmet need in patients with PNH and now we are in the middle of a deposition where one company is challenging a patent.

And I put -- I put this all together, as a non-expert, I am not here as an expert on financial success or economics to conclude that this is a financial success.

BY MS. STERLING:

Q But correct me if I am wrong, you still give a conclusion that SOLIRIS is a commercial success; is that fair?

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A My deposition [sic] says, SOLIRIS is a commercial success. SOLIRIS was approved by the FDA on March 16, 2007. So we have 13 years into this, for the treatment of patients with PNH reduced hemolysis, cites three references.

I understand that since approval, SOLIRIS commercially successful with over a billion in US sales each year, in each of the last 3 years. In my opinion, the commercial success of SOLIRIS is directly linked to the claimed invention of the '504 patent.

As I explained in Section VII.F.1 above, the invention of claims 1 to 10 of the '504 patent is coextensive with the clear therapeutic benefits of SOLIRIS that are highly valued by physicians and their patients suffering from PNH.

Q So I realized you read your declaration to me.

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Is this your opinion that SOLIRIS is a commercial success?

A The declaration reflects my words. If the words state SOLIRIS is a commercial success, that reflects my opinion and my words.

Q So I am trying to still understand what went into your analysis to make the conclusion that SOLIRIS is a commercial success.

MR. DIAMOND: Objection to form. Asked and answered.

THE WITNESS: What went into -- into my analysis -- well, first of all, as I said to you, I am not an expert in economics, accounting, or pharmaceutical economics. And -- but I am -- I am a physician in the field and I've seen drugs do well and I've seen drugs fail and here we have a drug that has been around for 13 years which -- which met an unmet need, and I will conclude

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this is a commercial success.

MS. STERLING: I thought we have been going about an hour. Why don't we take a break, if that's okay.

MR. DIAMOND: Sounds good.

(Whereupon a Recess Commenced at 3:05 p.m. and Testimony Recommenced at 3:28 p.m.)

MS. STERLING: Back on the record.

BY MS. STERLING:

Q Dr. Casadevall, did you have any discussions about the substance of your deposition with counsel during the break?

A No.

MS. STERLING: Okay.

With that, we have no further questions for you today on your cross-examination part of this proceeding. So thank you for your time.

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MR. DIAMOND: So we will take a break to see if we have any questions and -- I don't think it is going to go more than 10, 15 or so.

(Whereupon a Recess Commenced at 3:28 p.m. and Testimony Recommenced at 3:41 p.m.)

MR. DIAMOND: We have no further questions at this time. We are done.

(Whereupon Testimony Concluded at 3:41 p.m.)

A C K N O W L E D G E M E N T

STATE OF _____

COUNTY OF _____

I, the undersigned, hereby certify that I have read the transcript of my testimony taken under oath in my deposition; that the transcript is a true and complete and correct record of my testimony, and that the answers on the record as given by me are true and correct.

_____

ARTURO CASADEVALL, MD, PhD

Signed and subscribed to before me

This _____ day of _____, 20__.

_____

Notary Public

C E R T I F I C A T E

I, S. Arielle Santos,
Certified Shorthand Reporter,
Certified LiveNote Reporter do hereby
certify:
That prior to being examined, the
witness named in the forgoing
deposition, was by me duly sworn to
testify the truth, the whole truth,
and nothing but the truth.
That said deposition was taken before me
at the time and place set forth and
was taken down by me in shorthand and
thereafter reduced to computerized
transcription under my direction and
supervision, and I hereby certify the
foregoing deposition is a full, true
and correct transcript of my shorthand
notes so taken.
I further certify that I am neither
counsel for nor related to any party
to said action nor in anywise
interested in the outcome thereof.

_____

S. Arielle Santos

*** ERRATA SHEET ***

CASE: Amgen Inc., Petitioner
v. Alexion Pharmaceuticals, Inc

DATE: January 24, 2020 REF: 26639

WITNESS: Arturo Casadevall, M.D., Ph.D.

PAGE/LINE	CHANGE	REASON

_____

Arturo Casadevall, M.D., Ph.D.

Subscribed and sworn to before me

this ____ day of _____, 20__.

_____

Notary Public

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