IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

BAYER HEALTHCARE LLC,

Plaintiff

v.

BAXALTA INCORPORATED, BAXALTA US INC., and NEKTAR THERAPEAUTICS,

Defendants.

C.A. No. 16-1122(RGA)

J. Caleb Boggs Courthouse
844 N. King Street
Wilmington, Delaware

Friday, February 1, 2019
8:46 a.m.
Trial Volume V

BEFORE: THE HONORABLE RICHARD G. ANDREWS, U.S.D.C.J.

APPEARANCES:

MORRIS NICHOLS ARSHT & TUNNELL LLP
BY: RODGER D. SMITH, II, ESQUIRE

-and-

SIDLEY AUSTIN LLP
BY: BRADFORD J. BADKE, ESQUIRE
BY: KEVIN J. O'BRIEN, ESQUIRE
BY: SONA DE, ESQUIRE
BY: CHING-LEE FUKUDA, ESQUIRE
BY: CAROLINE BERCIER, ESQUIRE
BY: GWEN STEWART, ESQUIRE
BY: LAUREN KATZEFF, ESQUIRE

For the Plaintiff

APPEARANCES CONTINUED:

RICHARDS LAYTON & FINGER, P.A.
BY: FREDERICK L. COTTRELL, III, ESQUIRE
BY: KELLY FARNAN, ESQUIRE

-and-

HAUG PARTNERS
BY: EDGAR H. HAUG, ESQUIRE
BY: ANGUS CHEN, ESQUIRE
BY: RICHARD KURZ, ESQUIRE
BY: PORTER FLEMING, ESQUIRE
BY: ELIZABETH MURPHY, ESQUIRE
BY: GEORG REITBOECK, ESQUIRE
BY: ERIKA SELLI, ESQUIRE

For the Defendants

*** PROCEEDINGS ***

THE COURT: All right. Good morning, everyone. Please be seated.

So I got the letter about the defendant's obviousness combinations. It looks sufficient to me so the request of the plaintiff's bar or otherwise to do something to which you're planning to do, I'm overruling that objection. All right.

MR. CHEN: Thank you, Your Honor.

THE COURT: So on the defendant's motion on the judgment as a matter of law, basically I'm going to do the following. On the issue of the Doctrine of Equivalents, I'm going to reserve judgment on that.

On indirect infringement by Nektar and willful infringement by Baxalta, I'm going to grant the defendant's

motion. In my view there has been nothing shown that would allow for the state of mind requirements for either of those to be met. And other than that, I'm going to deny all of the defendants' judgment as a matter of law motions.

I think those -- so I think that's what I had on my plate. What would you like to discuss this morning?

MS. DE: Good morning, Your Honor. How are you?

THE COURT: Good morning, Ms. De.

MS. DE: We have one issue that the defendants have raised, but let me frame it for you. And the issue deals with Dr. Russell, he is our PEGylation expert. He is going to be testifying today in response to some of the things that I imagine we'll be hearing this morning.

THE COURT: Yes.

MS. DE: In the course of this case when we first wanted to put Dr. Russell up in our opening case, the agreement that we had in the pretrial order was we were not going to have more than one expert, Dr. Ravetch as well as Dr. Russell doing the actual claim construction and mapping of isolated polypeptide to Adynovate. And Dr. Russell was never going to do that, he was just going to explain the PEGylation reactions on which Dr. Ravetch was going to rely. Ultimately Dr. Ploegh put in the PEGylation reaction.

At that time defendant's requested that Dr. Russell before I could put him on in the opening case

that he be moved to our rebuttal case, that he not go in the front case. And Your Honor, you allowed that request by defendants. So now Dr. Russell has been moved to this part of the case.

Yesterday we heard from Dr. Walensky, defendants' expert, a bunch of peak data based on a bunch of binders. And Dr. Russell had in his reply report addressed one point or a couple points in that piece data and we would like to give the jury an opportunity to hear him on his rebuttal just to the peak data, not the claim construction, not isolated polypeptide with respect to that, but simply what that peak data is and what the issue is with it so they have a complete picture. Now that they have pushed him to the tail end of the case, I want to give him an opportunity to get that out.

THE COURT: Okay. I understand generally the background. Thank you. So what is the objection?

MR. CHEN: Your Honor, good morning. Thank you.

The order of proof in the pretrial order is pretty clear. Neither party gets the final word on their burden of proof. That's what this is. They're asking for Dr. Russell to have final word on an infringement issue.

THE COURT: Well, so my memory of the procedure generally according to what Ms. De just said, and as I recall and tell me if I'm wrong, there was an objection to

Dr. Russell testifying in plaintiff's case in chief because all he submitted was a reply report. And I forget how much it was an agreement or how much it was that I sustained it, but I said he could testify in their rebuttal case to reflect whatever it is your experts say, I guess on non-infringement, that he's already addressed in his reply report, which if plaintiff had done things in perhaps the more usual thing of having their opening expert also file the reply report, that person could have addressed.

So whatever it is that we may have said in the pretrial order I think has been modified by subsequent events.

MR. CHEN: I guess, Your Honor, that what I had expected then, Dr. Walensky was a will call from day one. And if plaintiff is fully aware of his calculations, his positions, they could have put him on in their case in chief and said just like they did with Dr. Addanki, are you aware that defendants' expert has an opinion, X, Y, Z, do you have an opinion as to why you disagree? Yes, boom. They could have done that in their case in chief.

THE COURT: But didn't you object to that?

MR. CHEN: No. What I objected to was the duplicative testimony between Dr. Ploegh and Dr. Russell on the process conditions.

THE COURT: But Mr. Chen, I definitely remember

and plaintiff has been saying for a couple of days without any objection from you that Dr. Russell would be testifying in the rebuttal case. What did you think he was going to be testifying about?

MR. CHEN: On invalidity, Your Honor.

THE COURT: Is he a validity guy, too?

MR. CHEN: Yes, he has opinions --

THE COURT: Oh, right. Right. Right. Yes. Yes. Yes.

Now, I remember he did. Well --

MR. CHEN: And so, unfortunately, I'm left in the position now where had Dr. Russell put in his opinions responding to Dr. Walensky in their case in chief on infringement, I would have asked Dr. Walensky, What is your thought on that criticism, X, Y, Z?

I don't have Dr. Walensky here anymore. He had a family issue with his child, health issue. And so now he's not here. We would be prejudiced by not being able to address this.

THE COURT: Well, there's going to be prejudice one way or the other, and my distinct impression was that I was going to allow Dr. Russell to put in non or infringement testimony, I guess, in specific rebuttal to what your experts said, which was something that Dr. Ravetch hadn't addressed.

So Ms. De, are there things beyond with the brackets with the multiple peaks?

MS. DE: The peaks? No. He's just going to address the demonstrative with the peaks and show you the data of what the peaks actually look like.

THE COURT: Well, I'm going to allow that. Sorry, Mr. Chen.

MS. DE: Thank you, Your Honor.

MR. CHEN: Thank you, Your Honor.

THE COURT: Okay. What else?

MR. BADKE: Nothing from us, Your Honor.

MR. HAUG: I don't think we have anything either, Your Honor.

THE COURT: Okay. Well, then, so the jury has tended to be here on time. So why don't we take at least a 20-minute break. But if at 9:20, they're here, I'll come out.

Is that all right? Everybody ready to do that?

MR. BADKE: Yes, Your Honor.

MR. HAUG: Sure thing.

MR. BADKE: We're ready to go.

THE COURT: Okay. Thank you.

THE CLERK: All rise.

(Recess was taken.)

THE CLERK: All rise.

THE COURT: All right. So I believe the jury is here and ready to go.

Mr. Fleming.

MR. FLEMING: We're ready to go. The mic's not on.

THE COURT: I just sent an email to the Delaware counsel and one physical -- let's get the jury -- one physical copy. If we could just hand that up, one each side of the working draft of the verdict form.

You'll notice that there's some places where there's brackets or something, and in particular, I was hoping the parties could try to figure out today -- there's two places. One where I said at the bottom of Page 2 special interrogatory on DOE for the SEQ ID: 4. And the other on Page 5 at the bottom where it says special interrogatory on unexpected results.

I wanted to sort of be able to sort out whether, if we get there, they're using the Doctrine of Equivalents and if there's -- whatever secondary factors there are, the only one that seems like people are actually talking about are unexpected results. I'd like to see, under the appropriate burden of proof if the jury finds that that exists or not.

So you can try to work on that. And since I've emailed this version, work starting from the version that

I've sent you. I also tried to remove all reference -- well, in any event, let's get the jury in.

(Jury entering the courtroom.)

All right. Members of the jury, welcome back.

Mr. Fleming, you may proceed.

MR. FLEMING: Thank you, Your Honor. We call next Mary Bossard.

THE COURT: Okay.

MR. FLEMING: May I approach and hand up binders?

THE COURT: Yes.

THE CLERK: Please state and spell your full name for the record.

THE WITNESS: Mary Bossard. M-A-R-Y B-O-S-S-A-R-D.

THE CLERK: Do you affirm that the testimony you are about to give to the Court and the jury in the case now pending will be the truth, the whole truth, and nothing but the truth, you do so affirm?

THE WITNESS: Yes.

THE CLERK: Thank you. You may sit down.

DIRECT EXAMINATION

BY MR. FLEMING:

Q. Good morning, Dr. Bossard. I have a binder of exhibits that we're going to be referring to.

Dr. Bossard, are you currently employed?

A. Yes.

Q. By whom are you employed?

A. Nektar Therapeutics.

Q. Where do you physically work?

A. Huntsville, Alabama.

Q. How long have you worked at Nektar?

A. Since 2002.

Q. What did you do when you first joined Nektar?

A. I became the department head for the protein PEGylation group.

Q. What is your position today?

A. Principal fellow, which is the equivalent of a vice president.

Q. Would you please describe your educational background following high school?

A. Initially, I got a degree from Central College in chemistry in Iowa.

Q. And do you have any advanced degrees?

A. Yes, I have a Ph.D. in chemistry from the University of Nebraska in Lincoln.

Q. What was your Ph.D. in?

A. Chemistry with an emphasis on mechanistic enzymology.

Q. Did any of your work involve chemical modifications?

A. Yes.

Q. What is a chemical modification?
A. It's where you attach a small molecule or molecules, some kind to a preexisting molecule. In my case, I was attaching things to proteins.
Q. And what did you do following obtaining your Ph.D.?
A. Initially, I did about a year of post-doctoral work, also, at Nebraska, and I went to University of California in Berkeley in the chemistry department for a year. There I also got a grant from the National Institute of Health to do research for two more years.
Q. What was the area of your post-doc research at Berkeley?
A. It was mechanistic enzymology. In particular, I did chemical modifications of an enzyme called dopamine beta monooxygenase with mechanism-based inhibitors.
Q. Dr. Bossard, what did you do professionally after completing your work at Berkeley?
A. I went to Smithkline Beecham from 1999 to -- excuse me, from 1985 to 1999.
Q. And where was the Smithkline facility that you worked at?
A. Initially, I was at the Philadelphia location. Then I moved to King of Prussia, outside of Philly.
Q. What type of work did you perform at Smithkline?
A. I was in the mechanistic enzymology group. So there

the proteins were the drug targets. So I did a lot of the protein purification, characterization, assays development. I looked at the interaction of small molecules with the protein therapeutics, and we used that to guide the development of potential small molecule drugs. I also wrote research proposals.

Q. Okay. What did you do after you left Smithkline in 1999?

A. I went to a biotech company called BioNebraska, later renamed Restoragen and was there from 1999 to 2002.

Q. And can you describe briefly the scientific work you performed at Restoragen?

A. I was the manager of process research there for our flagship peptide that was in clinical trials. And so one of the things I was tasked with was developing a commercial process for recombinant enzymes that we used to chemically modify the peptide, did a lot of purification assay development, and I was responsible for ensuring that our processes could be transferred to a commercial process.

Q. And what do you mean by "a commercial process"?

A. A commercial process is large scale. So we did things at a small scale lab scale, and I needed to make sure that they could be transferred to a large GMP manufacturing facility.

Q. And what is GMP?

A. GMP stands for good manufacturing practices. And so, the FDA requires that anyone who's developing a therapeutic product has to have a robust manufacturing process that is very reproducible. So that when you make this product each time day after day, year after year, the product is the same, and is going to be safe and effective for the patient every time.

Q. I believe you mentioned that your work at Restoragen ended in 2002. If I have your career chronology correct, you performed four years post Ph.D. research, then you worked at SmithKline for fourteen years, then you worked at Restoragen for three years; is that correct?

A. Yes, twenty-one years.

Q. What did you do professionally following your departure from Restoragen?

A. I went to what was then Shearwater Polymers which is now Nektar.

Q. How long have you been working at Nektar?

A. Since 2002.

Q. When you arrived at Nektar in 2002, what was the focus of Nektar at that time?

A. Nektar was very well-known for its PEGylation reagent business. Shearwater Polymers had initially started out as a catalog company where customers could purchase the PEG reagents. It had developed a very robust manufacturing

facility to support its partner protein products and they were growing their internal research group to develop their own therapeutic process.

Q. I believe you mentioned the term PEGylation. What do you mean by PEGylation, Dr. Bossard?

A. PEGylation is specifically the attachment of a polymer PEG to an existing molecule.

Q. And what is the purpose of PEGylation?

A. PEGylation can improve the biological properties of a molecule. So it can improve stability, mobility, increase half-life. In simple terms, it takes a molecule, makes it last longer and makes it better, more effective.

Q. What type of molecules would a person be interested in PEGylating?

A. Typically proteins.

Q. When you joined Nektar in October of 2002, were there any ongoing projects that you became a part of?

A. Yes. There were many. At that time Nektar was very well-known for its PEG reagent business. We were the go to company for expertise in PEGylation.

Q. Did you get involved in any of those ongoing projects?

A. Yes. I was involved in all of them that had to do with the protein group. I was also responsible for potential new projects for the protein group.

Q. What were some of the new products that Nektar was considering in the 2002 time frame?
A. The main one at that point was potential PEGylation of Factor VIII.
Q. Why was Nektar interested in evaluating Factor VIII?
A. Factor VIII is an enzyme, and Nektar's PEG technology has been used for enzyme replacement therapy so we were interested in potentially using this technology to extend the half-life for other enzymes in blood disorders.
Q. Who was your supervisor at the time?
A. Dr. Mike Bentley. He was both my supervisor and he was also the vice-president of research in Huntsville, Alabama, at that time. He had a Ph.D. in chemistry. He had been a professor before.
Q. Did Mike Bentley and you work on anything when you joined Nektar?
A. Yes, immediately. The new project was to investigate feasibility of PEGylation of Factor VIII.
Q. How did you go about working on this assignment for Mike Bentley?
A. I talked extensively with Mike about PEGylation reagents, PEGylation conditions. I did literature searches. I talked with Mike Bentley some more. And then relying on my own decades of experience with enzymes and proteins, I put together the research strategy.

Q. I would like to direct in your binder exhibit, please, DTX-0939, please.
A. Okay.
Q. Do you recognize this exhibit?
A. Yes.
Q. Did you write this e-mail?
A. Yes.

MR. FLEMING: Move in exhibit DTX-0939.

MR. BADKE: No objection.

THE COURT: Admitted without objection.

(DTX-0939 was admitted into evidence.)

BY MR. FLEMING:
Q. Dr. Bossard, do you see the figure at the top of this e-mail?
A. Yes.
Q. First, what is the date of this e-mail?
A. It's the 24th of October, in 2002.
Q. And now I see a figure on this e-mail. Do you see that?
A. Yes.
Q. And I see various symbols across this figure?
A. Yes.
Q. Can you describe the figure, please?
A. The figure describes the domain structure of full-length Factor VIII. So each of those letters, the A's,

the B's and the C's are all specific structural domains.

The symbols at the bottom, the ones that look like a lollipop, those refer to the carbohydrate locations, that's the potential place for PEGylation. The ones that look like staples, those represent disulfide bonds. Those are important for maintaining the structure of Factor VIII. You do not want to disturb those. The straight up lines, those are representing where the location of free cysteines are. Those represent a potential PEGylation strategy. And the squiggles are cleavage sites. Full-length Factor VIII with that B-Domain has to have that B-Domain removed for activation and so where those squiggles are, those represent cleavage sites.

Q. I think we have gone through the definitions in kind of the table at the bottom. Can you generally describe, I think they are also listed on the Factor VIII figure as well; is that correct?

A. Yes.

Q. Can you explain what that is, please, where they are?

A. Okay. Up there on the left, those, the ones that look like lollipops, those are the carbohydrate sites. The ones that look like a staple are the disulfide bonds. The ones that are straight up, these are the free cysteines available for PEGylation, potentially. And the squiggles represent the cleavage site needed for PEGylation of Factor

VIII.

Q. Directing your attention to the third paragraph in the e-mail beginning with there are three free cysteine residues. Do you see that?

A. Yes.

Q. And there is reference to specific cysteines. Do you see CYS 310? Do you see that?

A. Yes.

Q. Can you explain what CYS 692 and CYS 2000 are?

A. Those are the three cysteines that are not in the sulfide bonds so they are potential sites for selected PEGylation and they are represented in the diagram by the straight up lines.

Q. What does it mean to be free?

A. It means it's not involved in the disulfide bond and it's potentially available for PEGylation.

Q. Why is that important?

A. Because there is not very many cysteine and so if you PEGylated by cysteines, then you would know ahead of time the limited number of places where your PEG could attach.

Q. I would like to turn to the final paragraph. It's on the second page of this e-mail. Do you see that?

A. Yes.

Q. And it starts with, "Random PEG modification of lysines was shown to show loss of activity."

Do you see that?

A. Yes.

Q. Can you explain what that is?

A. Random PEGylation of lysines refers to potential PEGylation strategy in which you would have a reagent that would react with any of the surface available lysines. You would not be able to direct it to a specific one, so therefore it's called random.

Q. What is a lysine, Dr. Bossard?

A. Lysine is a particular type of amino acid. It's found in full-length Factor VIII. There are a bunch of them. There are 158 of them in full-length Factor VIII.

Q. What is the difference between the cysteine PEGylation discussed in the earlier paragraph and the random lysine PEGylation described in the last paragraph?

A. The cysteine PEGylation refers to the free cysteines that are available. There is only a few of them. So when you do your PEGylation, you know ahead of time where the PEG is going to attach.

For random PEGylation of lysines, there are a bunch of lysines in Factor VIII, and so you do not know ahead of time which are the lysine the PEG will attach to and you can't make it go to a specific one or make it not go to a specific one, it's random, it will go to any of the ones that are available.

Q. Turning now to another exhibit in your binder, DTX-0891; please.
A. Yes.
Q. Can you describe this document, please?
A. Yes. This is an e-mail from Dr. Mike Bentley written on the 31st of October, 2002.
Q. Did you prepare this e-mail and attachment?
A. No. Mike sent this attachment. I have the correct one, 0891, that's an e-mail from Mike to me with the final version of our abbreviated business plan on PEGylation of Factor VIII.
Q. Thank you, Dr. Bossard.

MR. FLEMING: I offer exhibit DTX-0891.

MR. BADKE: No objection.

THE COURT: Admitted without objection.

(DTX-0891 was admitted into evidence.)

BY MR. FLEMING:
Q. The e-mail attaches something called an Abbreviated Business Plan on the second page?
A. Yes.
Q. What is an Abbreviated Business Plan?
A. That's an internal document used at Nektar that we would put together that we would evaluate the business potential for potential PEGylation of a new product.
Q. Can you turn to page 18 of the exhibit.

A. Yes.
Q. It has the heading Technology Evaluation. Do you see that?
A. Yes.
Q. Can you describe what this section is?
A. This is the first page of the technology evaluation that was written for this Abbreviated Business Plan.
Q. Did you prepare this?
A. I did in conjunction with Mike Bentley. I did the physical writing.
Q. What information is included in the technical portion of this Abbreviated Business Plan?
A. It includes some information, background information on Factor VIII and potential sources of Factor VIII. Most importantly, this plan outlines the four potential PEGylation strategies that were identified in preparing this document.
Q. Turning to the page 19, do you see that?
A. Yes.
Q. And there is a paragraph beginning, "The options for our PEGylation strategy include."

Do you see that?

A. Yes.
Q. And could you please describe the four options that follow?

A. Yes. The first one is -- number one is PEGylation on one or more cysteine thiols using a PEG maleimide. This PEGylation strategy is very selective for the few free cysteines that would be available.

Option number two is random PEGylation on lysines using PEG SBA or SPA technology. In this situation, you have a random PEGylation strategy where we would be addressing the lysines on Factor VIII, but you cannot pre-determine ahead of time which lysine will be PEGylated.

Option three is preferred PEGylation on N-termini with some PEGylation also occurring randomly on lysines. This would be selective for the N-termini.

And option four is PEGylation on cleaved glycosylation site via a PEG hydroxide reagent. This would be targeting the carbohydrates which were the lollipops in that previous diagram we saw.

Q. Dr. Bossard, directing your attention to the fourth line, there's a sentence towards the end that starts with, Strategy 2. Do you see that?

A. Yes.

Q. Can you read that out loud, please?

A. Strategy 2 may offer the most promise since some prior work exists which indicates at least some preservation of activity.

Q. And what was strategy two again?

A. Strategy two was random PEGylation of lysines.
Q. Thank you.
I'd like to go to another exhibit. Dr. Bossard, directing your attention to DTX 893, please.
A. Yes.
Q. Do you recognize this document?
A. I do.
Q. And what is it?
A. This is an email written by me on January 14th of 2003 to Mike Bentley, and it's -- the subject of this is a draft invention record. This is for PEGylation of Factor VIII.
MR. FLEMING: Defendants offer DTX 893.
MR. BADKE: No objection.
THE COURT: Admitted without objection.
(Exhibit DTX 893 was admitted into evidence.)
BY MR. FLEMING:
Q. What is the attachment to this email, Dr. Bossard?
A. This is a draft invention record of PEGylation of Factor VIII.
Q. And let's look -- that's what it says at the top, Invention Record. Do you see that?
A. Yes.
Q. And the paragraph 1 it says, CONTRIBUTORS TO INVENTION. Do you see that?

A. Yes.
Q. And who's identified?
A. Myself and Mike Bentley.
Q. And going down to paragraph number three, do you see Date Conceived?
A. Yes.
Q. And what is the date?
A. 15th of October 2002.
Q. And the next paragraph, four, says, Date invention was first disclosed and to whom. Do you see that?
A. Yes.
Q. And what does it state?
A. 28th of October 2002 to the McKinsey consultant.
Q. And who was the abbreviated business plan submitted to?
A. This was an -- abbreviated business plan was submitted internally to a number of departments within Nektar and the consultants as well.
Q. Thank you. Turning now to the fifth page, do you see that?
A. Yes.
Q. And there's a section novelty. Do you see that?
A. Yes.
Q. And it begins with, "This invention describes Factor VIII PEGylation strategy which include." Do you see that?

A. Yes. Yes.
Q. And then are those four strategies that follow?
A. Yes. Those are the same four strategies we -- in the abbreviated business plan.
Q. Dr. Bossard, do you know whether a patent was filed with respect to this invention disclosure?
A. Yes.
Q. Do you know whether that patent ever issued?
A. It did.
Q. And what patent is that?
A. That's the one where we're referring to as the Bossard '223 patent.
Q. Thank you. Turning to a little bit of a different subject.

Did Nektar work with any companies to attempt to perform these strategies that you had identified so far?
A. Yes.
Q. And who was the first company that Nektar worked with with respect to these strategies?
A. Green Cross.
Q. And who is Green Cross?
A. Green Cross was a Korean biopharmaceutical company.
Q. And when did you get involved with Green Cross?
A. Early in 2003.
Q. And can you describe the work Nektar did with Green

Cross regarding Factor VIII?

A. Yes. We PEGylated Green Cross' B-Domain deleted Factor VIII and gave them conjugates for testing.

Q. And what strategies did you use with Factor VIII from Green Cross?

A. We gave them conjugates on strategies one and two.

Q. Did any commercial products come out of the work with Green Cross?

A. No, the relationship ended before we got that far.

Q. What was the next company that Nektar worked with with respect to any of your strategies?

A. Bayer.

Q. And when was that?

A. That wasn't until 2004.

Q. Okay. Can you describe the circumstances in which you first met Bayer?

A. I first met Bayer people in conjunction with the drug delivery forum that their biopharmaceutical division was hosting in Berkeley.

Q. I'd like to direct your attention to DTX 912, please.

A. 912.

Q. Yeah, DTX 912. 0912.

A. Okay. I've got it.

Q. Okay. And what is this document, please?

A. This is an email that I wrote on April 17th of 2003

to Mike Bentley regarding a trip in March to California.

MR. FLEMING: I'll offer DTX 0912.

MR. BADKE: No objection.

THE COURT: Admitted without objection.

(Exhibit DTX 0912 was admitted into evidence.)

BY MR. FLEMING:

Q. Dr. Bossard, turning to the second page, do you see the top of the page?

A. Yes.

Q. And it says, "Trip Report, March 24th-31, 2003." Do you see that?

A. Yes.

Q. And is this the trip you were referring to?

A. Yes.

Q. In California?

A. Yes.

Q. And who did you meet with on this trip?

A. I met with people at Bayer. I also met with people from Cyclone.

Q. Okay. Going down about halfway through the document, do you see a heading, "Tuesday, March 25th: Bayer Drug Delivery Forum"?

A. Yes.

Q. Going down to the second paragraph, there's a sentence, "The talk was very well received by both the Bayer

participants as well as the competitors."

Do you see that?

A. Yes.

Q. Okay. What is that in reference to?

A. That's in reference to the presentation that I gave at the drug delivery forum covering Nektar PEG technology.

Q. What type of information did you present to Bayer at that forum?

A. It was an overview of all of our technology.

Q. Did this meeting result in any work with Bayer?

A. Yes.

Q. What type of work?

A. We received both their full-length Factor VIII and their B-Domain Deleted Factor VIII. We did the PEGylation and characterization for them and sent the conjugates.

Q. When did Nektar begin performing lab work on Bayer's Factor VIII?

A. In 2004.

Q. I'd like to turn to another exhibit, please. DTX 0892.

A. Yes.

Q. Do you recognize this document?

A. I do.

Q. And what is it, please?

A. It's a Nektar technical report.

Q. And I see your name on the first page and signature as reviewer. Do you see that?
A. Yes.
MR. FLEMING: I'll offer DTX 0892.
MR. BADKE: No objection.
THE COURT: Admitted without objection.
(Exhibit DTX 0892 was admitted into evidence.)
BY MR. FLEMING:
Q. What is this? What is this document?
A. This is a technical report that Nektar sent to Bayer upon completion of the PEGylation and characterization of the full-length Factor VIII work that we did for them.
Q. And what is the purpose of a technical report?
A. This summarizes the work that we did and the characterization, and it also includes that it's the last deliverable of the research plan.
Q. Okay. And was this report sent to Bayer?
A. It was, yes.
Q. Directing yourself to Page 37 of the report.
A. Yes.
Q. And do you see a Table 8 in the report?
A. Yes.
Q. And it says, "Total Yield Summary of Full-Length Factor VIII PEG Conjugates." Do you see that?
A. Yes.

Q. And what information is set forth in this table?
A. This summarizes Nektar's successful PEGylation of full-length Factor VIII for Bayer.
Q. I'd like to turn to -- were these samples sent to Bayer?
A. Yes.
Q. Turning to Page 46 of the report, please.
A. Yes.
Q. And what is set forth on Page 46?
A. This is an email dated the 22nd of March of 2004. It's a cover letter to Dr. Pan in regards to 22 samples of PEGylated full-length Factor VIII reaction mixtures.
Q. Do you know whether these 22 samples were sent in March of 2004 to Dr. Pan?
A. They were.
Q. Turning to another exhibit, please, Dr. Bossard. DTX 0927.
A. Yes.
Q. Do you recognize this document?
A. Yes.
Q. What is it, please?
A. This is another Nektar technical report.
Q. And you're identified as the reviewer; correct?
A. Yes.
Q. Were you involved in reviewing this report?

A. Yes.

MR. FLEMING: I offer DTX 0927.

MR. BADKE: No objection.

THE COURT: Admitted without objection.

(Exhibit DTX 0927 was admitted into evidence.)

BY MR. FLEMING:

Q. What is the difference between this technical report and the previous technical report we looked at, Dr. Bossard?

A. The previous technical report that we looked at was for Bayer's full-length Factor VIII. This particular technical report reflects the work that we did for Bayer's B-Domain Deleted Factor VIII.

Q. Turning to Page 31 of the report, please. Do you see a Table 2, Dr. Bossard?

A. Yes.

Q. And this was, "Yield Summary of PEG BDD Factor VIII Conjugate?

A. Right.

Q. And there's certain samples listed. Do you see that?

A. Yes.

Q. And were those samples sent to Bayer?

A. They were.

Q. What type of samples were these?

A. The linear or the lysine samples reflect our random lysine PEGylation of Factor VIII which we referred to as

strategy two. The N-terminal strategy was strategy number three, we mentioned before.

The cysteine also affects what we called strategy number one, which was the selective PEGylation of cysteine.

Q. Can we turn to Page 40 of the exhibit? What is reflected on Page 40?

A. This is a cover letter to Dr. Pan dated in March of 2004, March 9th. And it's in regards to eight PEGylated samples of B-Domain Deleted Factor VIII reaction mixtures that we will be sending from Nektar to Bayer.

Q. Dr. Bossard, I'd like now to direct your attention to DTX 6, please. Let me take a step back before we talk about Exhibit 6.

Did Nektar do anymore work with Bayer after it sent these samples that we just looked at?

A. No. There was no lab work done.

Q. After these reports were submitted; is that correct?

A. The reports were the final delivery. There was no more lab work.

Q. Okay. Now, looking at DTX 6, do you recognize this document?

A. Yes.

Q. All right. I'm not sure. Is this DTX 6?

MS. FARNAN: Yes, it is.

MR. FLEMING: Okay. Your Honor, I'm not sure if it's in, but we offer DTX 6.

THE COURT: I'm not sure, but it's admitted without objection.

MR. BADKE: Yes, Your Honor.

(Exhibit DTX 6 was admitted into evidence.)

BY MR. FLEMING:

Q. Do you recognize what we've marked as Exhibit 6, Dr. Bossard?

A. Yes.

Q. And what is it?

A. It's U.S. patent 7,199,223.

Q. And we'll just refer to it as the '223 patent. Okay?

A. Yes.

Q. Are you a named inventor on this patent?

A. Yes, I am.

Q. And does this patent relate in any way to the invention disclosure that we looked at earlier today?

A. Yes.

Q. And does this patent include the four strategies we discussed earlier today?

A. Yes.

Q. When was this patent filed, Dr. Bossard?

A. This patent was filed on February 26th of 2004.

Q. And was there a provisional application that was

filed before that?
A. Yes, the provisional was filed on February 26th, 2003.
Q. I'd like to direct your attention to JTX 1, please. Do you know what this document is?
A. Yes.
Q. What is it?
A. This is U.S. patent 9,364,520 which we refer to as the '520 patent.
Q. And have you reviewed this patent before?
A. I have.
Q. And what did you -- what did you see when you reviewed this patent?
A. This patent reads like a continuation of the Bossard '223 patent and an extension of the work plan that Nektar did for Bayer.
Q. And why --
A. PEGylated --
Q. Why do you believe that?
MR. BADKE: I'm going to move to strike. That's really opinion testimony.
THE COURT: I'm going to strike the question and answer as asked. It may be that you can ask a different question that I would not strike.
MR. FLEMING: Thank you, Your Honor.

BY MR. FLEMING:

Q. Dr. Bossard, you are the named inventor of the '223 patent; correct?

A. Yes.

Q. And you have reviewed, as part of your work, the '520 patent; correct?

A. Yes.

Q. Did you see similarities in the text of the '520 patent that relate to your patent, the '223 patent?

A. Yes.

Q. And what were some of the similarities that you saw in the '520 patent?

A. There are similarities in some of the language in different places. Particularly, it reflects similarity in that it's regarding mono-PEGylation of cysteine for mono-PEGylation of conjugates, large PEGs. We -- we show that in our '223 patent.

Q. Does any of the work that you've seen in the '520 patent relate in any way to the four strategies that we've talked about today?

A. Yes. In particular, Table 4, which is mono-PEGylation of the full-length Factor VIII was done for Bayer. This all relates to strategy number one which is selective cysteine PEGylation.

Q. Directing you to another exhibit, Dr. Bossard. DT --

or PTX 934. Do you recognize this article?

A. Yes.

MR. FLEMING: I'd offer PTX 934.

MR. BADKE: No objection.

THE COURT: All right. PTX-934 admitted without objection.

(PTX-934 was admitted into evidence.)

BY MR. FLEMING:

Q. And I notice certain of the authors. Can you see the authors at the top?

A. Yes.

Q. And the first author is Peter Turecek. Do you know who is he is?

A. Yes.

Q. Who is he?

A. He's a scientist at Baxalta.

Q. And the second author is you; correct?

A. Correct.

Q. And the third author is Freddy Schoetens. Do you know who that is?

A. He was from Jansen.

Q. Who was the fourth author?

A. Inge Ivens. She was at Bayer in San Francisco.

Q. So all of you wrote the article together?

A. Yes.

Q. Turning to the second page. There is a formula about halfway. Can you see that?

A. Yes.

Q. Can you describe what that formula is, please?

A. That formula is used to calculate the number of positional isomers that are possible when you PEGylate a protein if you know how many positions are available and how many PEGs you have attached.

MR. FLEMING: Thank you, Dr. Bossard.

Pass the witness.

THE COURT: All right. Mr. Badke.

CROSS-EXAMINATION

BY MR. BADKE:

Q. Good morning, Dr. Bossard.

I'm sorry, here I go, starting again without the binders.

So Dr. Bossard, when you joined Nektar in 2002, you had not -- you did not personally have hands-on experience with Factor VIII; correct?

A. I had reviewed the PEGylation, or excuse me, I had reviewed the blood factor coagulation pathway with regards to potential target when I was at SmithKline and we did select a potential target at that point.

Q. But you didn't personally work in the laboratory with Factor VIII?

A. That is correct.
Q. And you have also didn't personally PEGylate any proteins; correct?
A. I had done a lot of chemical modification. The chemistry that I have used is similar coupling chemistry to what was done for PEGylation.
Q. And then at the time you joined Nektar, Nektar didn't even have possession of any Factor VIII; correct?
A. Other blood factor work was going on, but you are correct, it was not Factor VIII.
Q. Now, I think that you spoke about work with Bayer; right? And so in -- do you know a Rinko Goesh?
A. Yes.
Q. And Mr. Goesh worked in business development at Nektar; correct?
A. Yes.
Q. And he also prior to entering into the agreement with Bayer, Mr. Goesh represented to Bayer in August of 2003 that Nektar had experience PEGylating full length Factor VIII, didn't he?
A. Yes.
Q. And that wasn't true, was it?
A. What we were doing at that time was presenting a slide show that highlighted our Factor VIII. The slide did show both the full length and the B-Domain deleted and I

immediately took corrective action the next day to correct that misstatement on his part.

Q. Could we go to PTX-477, please. So this is an e-mail pertaining to that PowerPoint that was presented; right. And this is an e-mail from you in 2003, correct?

A. Yes.

Q. So I would like to --

MR. BADKE: I don't think this has been moved into evidence. Can we do that?

MR. FLEMING: No objection, Your Honor.

THE COURT: All right. Admitted without objection.

(PTX-477 was admitted into evidence.)

BY MR. BADKE:

Q. Can we go down to the bottom of that e-mail. Do you see the paragraph -- let me read that. "Although he" -- meaning Mr. Goesh -- "removed the reference to the data, he still said we are working on full length Factor VIII which we are not. This is a deceptive business practice to tell potential clients we are working on molecules which we clearly are not yet doing. Rinko knows we are only working on B-Domain deleted material from Green Cross and to say otherwise is a flat out lie. I did not make a scene at the present time because it would not have looked good for the company."

Right. That's what your e-mail said?
A. In terms that the jury can understand, what happened here --
Q. Doctor --
A. -- I observed that an overstatement, an oversell was made. I immediately took corrective actions the next day to ensure that everything was completely technically accurate. Rinko was in business development. I was a technical person. I am very, very much of a stickler to make sure that everything is technically accurate. So this is the equivalent of telling the sheriff that this time I'm turning him over to the law and you handle it.
Q. But nobody reached out to Bayer, or you don't know that anybody at Nektar reached out to Bayer to correct that deception?
A. The deception was corrected, but I was not part of that.
Q. Do you recall giving deposition testimony in this case?
A. I did not see -- yes, I did deposition, yes.
Q. Could we put up -- could you look, I think you have your deposition transcript there. We'll put it up on the screen. This is on page 158.
THE COURT: I'm sorry. Mr. Fleming?
MR. FLEMING: This is an attempt at impeach, I

haven't heard the question that there is anything wrong. He's just publishing the deposition.

MR. BADKE: The answer was wrong.

A. No, the information, it was corrected. I was not part of the correction and in the immediate time frame, but eventually the information was corrected.

Q. So I would like to show up your deposition testimony.

A. Sure.

Q. Page 158:21 through page 159, line 3.

A. At that point in time, did anyone from Nektar reach out. I don't know.

Q. There is no question.

"Question: Did anyone from Nektar reach out to Bayer to correct that deception?

"Answer: I don't know. It would not have been my responsibility or it would not have been appropriate for me, at that point, to reach out directly to Bayer."

That was the question you were asked; right?

A. And in the context of that e-mail at that time, that is correct. Because I did what was appropriate. I turned it over to the law and it was up to other people to make that correction at that point in time.

I know that by the time we did the research work plan that had been corrected.

Q. So new topic, Dr. Bossard. Now, stage one of the

Bayer feasibility study ended in about September of 2004?
A. Yes.
Q. Now the activity of Nektar's CONJUGATES WAS not as high as Bayer wanted, was it?
A. That is correct.
Q. Could we go to PTX -- could you look in your binder at PTX-1228, please. Now, that's an e-mail that you sent to various members at Nektar, correct, in 2004?
A. That's what it looks like, yes.
MR. BADKE: I would like to move PTX-1228 into evidence.
MR. FLEMING: No objection, Your Honor.
THE COURT: All right. Admitted without objection.
(PTX-1228 was admitted into evidence.)
BY MR. BADKE:
Q. So I want to read you the first line of this e-mail.
THE COURT: Wait. I'm sorry, Mr. Fleming, did you say you objected?
MR. FLEMING: I said I didn't object. I thought you were about to say it was entered, but Mr. Badke started talking. I don't object to this.
THE COURT: I'm sorry. I thought I said admitted without objection. And I'm sorry, Mr. Badke, Mr. Fleming was I thought when you started talking, I

misinterpreted that he thought that I had ruled the other way and you were going ahead anyway. It's no big deal.

Continue, Mr. Badke.

MR. BADKE: Thank you.

BY MR. BADKE:

Q. So this e-mail says in the first line, "Bayer has data on the full length Factor VIII mixtures that we sent them. Surprisingly it was not completely 'dead'."

Do you see that?

A. I see what's stated.

Q. And the it -- you wrote this; right?

A. The e-mail is from me.

Q. The it refers to the full length Factor VIII molecule; correct?

A. I would have to see specifically which mixtures to which you refer because we sent them samples on more than one occasion, so I need to see the data.

Q. But the it is referring to some full length Factor VIII?

A. It is referring to something that we had sent to Bayer, but it doesn't specify exactly what it was. So at that time I would have known what it was, but I'm not sure right now exactly what you're referring to.

Q. Could we put up DTX-892; please. This is the report that Mr. Fleming questioned you about?

A. Yes.
Q. Can we go to page 39. The last paragraph. About the middle of the page, do you see the if, the third line. "If" -- this is what you told Bayer; right, Dr. Bossard?
"If PEGylation is occurring primarily on the B-Domain, it is possible that the beneficial effects of PEGylation could be lost upon cleavage of the B-Domain."
Right? That's what that says? Yes?
A. When Factor VIII is activated, it is required that you remove the B-Domain. So when the B-Domain is removed, if the PEG is there, then the PEG would be removed. But that doesn't specify what will happen. At that point you're going to have fully active Factor VIII which could be a benefit. And so it says it's possible. It doesn't say that it will, it says it's possible.
Q. And you reviewed this report?
A. I did.
Q. Thank you.
The last document and the last line of questions.
Could we put -- could you go in your binder to PTX-483, please.
A. 483?
Q. Yes.
Is that an e-mail from Jenny Filbey of Nektar to

you?

A. It is.

MR. BADKE: Move PTX-483 into evidence.

MR. HAUG: No objection, Your Honor.

THE COURT: Admitted without objection.

(PTX-483 was admitted into evidence.)

BY MR. BADKE:

Q. So after you finished work with Bayer you started working with Baxalta, right, Baxter?

A. Yes.

Q. And you were actually meeting with Baxalta while you were still talking to Bayer; correct?

A. We were talking to Bayer in the time frame. There was no exclusive arrangement with Bayer or Baxalta at this time, so we were free to communicate with whomever we wished. We at no point did actual lab work for any two companies on Factor VIII at the same time.

Q. So you met with Baxter, though, you had meetings with Baxter and you made a presentation to them?

A. This is regards to a presentation with Baxter, yes.

Q. And Baxter got back to Nektar and they gave you some feedback; right?

A. They gave the feedback to Jenny. I did not get the feedback directly from Baxter.

Q. So if you look at page two of that document, the next

page.
A. Yes.
Q. Now on this page is the feedback that you got, that Nektar got back from Baxter; right?
A. Yes.
Q. So let's go through that. And then just so we look at the same thing and then I'm going to ask you questions.
One thing they said, bullet one up there, No new information came from Nektar - they learned nothing. This is in about 2005?
A. This is the time frame of May 2005.
Q. So Baxter, Baxalta is saying no new information came from Nektar, they learned nothing, correct? That's what they said?
A. When I gave the presentation to Baxalta, Baxter at that point, the only information on B-Domain deleted that was beginning were things that were already in the '223 Bossard patent. There was no communication about anything that had been done with any partner, it was only what was already in the public domain, so that's what they mean by no new information.
Q. Right now I'm just going to ask you what they said if you don't mind just for the purposes of time because we're really short on time now, so I appreciate your cooperation. I'm going to go through the ones I want to highlight and

then I'm going to ask you questions.

The next one is number four, where's the magic? What did Nektar do that Baxter can't. The next one. Where's the value that Nektar brings? Baxter can just hire a couple of people and do this themselves. Nektar brings nothing.

If we go a little further down. Nektar doesn't have expertise in Factor VIII. Nektar has limited experience in PEGylation of large proteins. No clear roadmap and, therefore, no advantage in time working with Nektar. Trial and error approach is one that Baxter already uses.

Then a couple of down. Nektar is not capable of analytical for PEG derivatives. Nektar does not have appropriate methods for screening conjugates. Nektar not able to demonstrate advantage over PEGs from other companies.

Right?

So my question to you is, despite all of this that Nektar was saying to you --

A. That Baxter was saying.

Q. Despite all of this that Baxalta was telling you, they still entered into an arrangement with you, with Nektar; correct?

A. We still entered into an arrangement with Baxter.

THE COURT: I'm sorry, Mr. Badke.

Mr. Fleming.

MR. FLEMING: Your Honor, I think reading the document into the record is not asking a question. I request that it be stricken.

THE COURT: The document is in evidence, so I'm not going to strike it. But let's actually try to ask some questions other than just reading documents. Go ahead, Mr. Badke. And let's take it down.

BY MR. BADKE:

Q. And so you entered into a relationship with Baxalta; correct?

A. Yes.

Q. And then you engaged in a research program with Baxalta relating to releasable PEGs; right?

A. We did.

Q. And that program went on for two or three years?

A. I don't remember the length, but the releasable PEGs were new, they were things that were not in the public domain. So contrary to some of the statements that you read earlier, these releasable PEGs and the strategy with it was totally new, totally not in anyone -- you could not buy those releasable PEGs. Those were proprietary Nektar things, that was proprietary Nektar technology. It was totally new contrary to what you saw.

Q. And, in fact, they didn't work and Baxalta went on to develop after two or three years BAX 855 which is a subject in this case; right?

A. The releasable PEG conjugates that we made did not meet our criteria for what we decided to do for a commercial product.

MR. BADKE: No further questions, Your Honor.

THE COURT: All right. Mr. Fleming.

MR. FLEMING: Just very briefly Your Honor

REDIRECT EXAMINATION

BY MR. FLEMING:

Q. Dr. Bossard, despite these comments we just read in this e-mail, did Nektar finally reach an agreement with Baxter/Baxalta?

A. Absolutely. We signed an exclusive agreement for them with hemophilia A and later we signed one exclusively for hemophilia B.

MR. FLEMING: Thank you.

THE COURT: All right. Dr. Bossard, thank you very much. You may step down. Watch your step. Okay?

MS. FARNAN: Good morning, Your Honor. At this time the defendant would call Curt Dewan.

THE COURT: All right.

MS. FARNAN: We just have one exhibit, Your Honor. May I approach with the exhibit?

THE COURT: Sure.

THE CLERK: Please state and spell your full name for the record.

THE WITNESS: It is Curt Dewan. C-U-R-T. D-E-W-A-N.

DIRECT EXAMINATION

BY MS. FARNAN:

Q. Good morning, Mr. Dewan. Could you introduce yourself to the jury?

A. I'm Curt Dewan.

Q. What is your current job title?

A. I'm the head of financial planning at Shire.

Q. How long have you worked for Shire?

A. Seven years.

Q. What are your job responsibilities as the head of financial planning?

A. So that responsibility is quarterly forecasting process, the budget planning process, and longer term financial forecast and planning.

Q. How long have you been in your current role?

A. Since August of 2018.

Q. What was your job title at Shire in 2017?

A. I was a director of corporate finance.

Q. Does Shire use a financial management system?

A. We do Hyperion.

Q. Can you explain what Hyperion is?
A. Hyperion is a financial management system that collects our financials at a product level for sales and costs and it allows us to record actual results, our budget results and longer term financial planning.
Q. I think you mentioned costs. What kind of costs does Hyperion track?
A. So all of the costs that are product specific, for instance, for bringing products to market and selling and promoting products.
Q. And does it track those costs on a product basis?
A. It does.
Q. I just put up there on the stand for you DTX-471A. Could you take a look at that?
A. Yes.
Q. What is DTX-471A?
A. This is the October 2017 long-range plan, financial details for Advate and Adynovate.
Q. And you said October 2017. Is that when this long-range plan was prepared?
A. Yes.
Q. Is the information that's contained in DTX-471A from the time period of October 2017?
A. It is.
Q. Was the information that's in DTX-471A stored in

Shire's Hyperion system?
A. It is.
Q. Have you confirmed the accuracy of this data?
A. I have.
Q. Did Shire prepare long-range plans on an annual basis?
A. Shire does, yes.
Q. Was this DTX-471A prepared and maintained in the ordinary course of Shire's business?
A. Yes.
MS. FARNAN: Your Honor, I would move DTX-471A into evidence.
MR. O'BRIEN: No objection.
THE COURT: Admitted without objection.
(DTX-471A was admitted into evidence.)
BY MS. FARNAN:
Q. We put the document up on the screen. I wanted to take a look at a few of the line items here. I think you said what products does this document relate to?
A. Advate and Adynovate.
Q. Generally what does a long-range plan at Shire contain?
A. It's a seven-year financial plan that projects the overall Shire company profit and loss statement, and product specific for taxes and for sales.

Q. We're looking at cost of sales. Is that a standard cost of goods sold?
A. That's correct.
Q. Then I would to look at royalty expense. Is royalty expense including in the standard cost of goods sold?
A. It is not.
Q. Can you tell the jury what the Adynovate royalty expense for 2018 is projected to be?
A. $27,086,000.
Q. Okay. Can you tell -- I want to look at the sale and market, the line item that's contained in that line item.
A. So these are the advertising and promoting costs for the sales and marketing organization specific to the promotion of Advate and Adynovate.
Q. Okay. And for Adynovate, can you tell us what the sale and marketing expense for 2018 is?
A. $43,288,000.
Q. Okay. The next line is global medical affairs. Can you explain that is?
A. That's the global medical affairs organization. That's advertising and promoting on the basis of Advate and Adynovate.
Q. And then specifically for Adynovate, what is the global medical affairs expense for 2018?
A. $8,015,000.

Q. And then, finally, could you just tell us what research and development costs are?
A. So research and development costs are the costs, the clinical development costs to bring -- to complete the products, to be able to bring the products to market.
Q. Okay. And what are the expense for research and development for Adynovate in 2018?
A. $32,032,000.
MS. FARNAN: Thank you. No further questions.
THE COURT: All right. Thank you. Cross-examination. Mr. O'Brien.
MR. O'BRIEN: Very short cross, Your Honor. Permission to approach?
THE COURT: Yes.

CROSS-EXAMINATION

BY MR. O'BRIEN:
Q. Good morning, Mr. Dewan.
A. Good morning.
Q. So DTX 471, that's not the final LRP that's actually provided to Shire's management; is that correct?
A. So Shire's management produces its long-range plan and presents that to the Board of Directors. These are the final financials that compose that long-range plan.
Q. This is not the actual long-range plan, though, that is actually provided to management; isn't that correct?

A. This is not the complete long-range plan.
Q. And you didn't create DTX 471; isn't that correct?
A. That is correct.
Q. And you don't actually know who prepared DTX 471, do you?
A. That's correct.
Q. And you actually created a template that included additional financial details; isn't that correct?
A. That is correct.
Q. But that template is actually a different source of information than DTX 471; isn't that correct?
A. The source of information is the Hyperion system for the 2017 long-range plan. So in that respect, it's the same source of information.
Q. But the template that you created included additional information not included in DTX 471; isn't that correct?
A. That's correct.
Q. And that template, as far as you know, has not been produced in this litigation; isn't that correct?
A. That's correct.
Q. And on those line item costs, isn't it right that you have no personal knowledge of the details going into the line item costs, for example, the research and development costs that you mentioned earlier?
A. That is correct.

Q. And isn't it also the case that the royalty costs that you mentioned are actually included you in the gross profits line item; isn't that correct?

A. That's correct.

MR. O'BRIEN: No further questions.

THE COURT: All right. Any redirect?

MS. FARNAN: Just briefly, Your Honor.

REDIRECT EXAMINATION

BY MS. FARNAN:

Q. Mr. Dewan, the DTX 471A that I put in front of you, does Shire rely on that document in its ordinary course of business?

A. It does.

Q. And in fact, in the course of your work, have you had occasion to use or rely upon that document?

A. The information in this document is -- is -- I use the information in this document for a business case that Shire was working on and presented to the Board of Directors in October of 2017.

MS. FARNAN: I have no further questions.

THE COURT: All right. Mr. Dewan, thank you. You may step down. Watch your step.

MR. CHEN: Your Honor, defendants next call their chemist and PEGylation expert, Dr. Samuel Zalipsky.

May we approach, Your Honor?

THE COURT: Yes.

THE CLERK: Please state and spell your full name for the record.

THE WITNESS: Samuel Zalipsky.

THE CLERK: Can you speak up a little bit so the court reporter can hear you?

THE WITNESS: Samuel Zalipsky.

THE CLERK: And spell your name, please.

THE WITNESS: Yes. S-A-M-U-E-L Z-A-L-I-P-S-K-Y.

THE CLERK: Thank you. Do you affirm that the testimony you are about to give to the Court and the jury in the case now pending will be the truth, the whole truth, and nothing but the truth, you do so affirm?

THE WITNESS: I do.

THE CLERK: Thank you. You may be seated.

DIRECT EXAMINATION

BY MR. CHEN:

Q. Good morning, Dr. Zalipsky.

A. Good morning.

Q. Can you please turn to DTX 1366 in your binder? It's towards the very back.

A. DTX 13?

Q. Sixty-six. Second to last document in the binder.

A. You said 1336.

Q. 1366.

A. Sixty-six.
Q. It's the second-to-last document in your binder.
A. Yes.
Q. Do you recognize that document?
A. Yes.
Q. What is it?
A. That is my resume.
Q. Is it correct and accurate?
A. Yes.

MR. CHEN: Your Honor, we'd offer 1366.

MS. DE: No objection.

THE COURT: Admitted without objection.

(Exhibit DTX 1366 was admitted into evidence.)

BY MR. CHEN:
Q. Did you provide any demonstratives today to assist with your testimony, Dr. Zalipsky?
A. Yes.
Q. Dr. Zalipsky, could you please describe your educational background?
A. So I completed my Ph.D. studies in chemistry in University of Minnesota in 1986. I also hold a degree in polymer chemistry. My master's is in polymer chemistry, and undergraduate degree in chemistry and biochemistry, both from the Hebrew University of Jerusalem.
Q. Could you describe for us some of your professional

experience? Actually, hold on. Before that --

A. Yes.

Q. -- could you describe your thesis, your Ph.D. thesis?

A. So my Ph.D. thesis was the development of new functionalized polymers in the area of peptide chemistry. This was a work on use of -- use of polymers, solving problems of peptide chemistry.

Q. And Dr. Zalipsky, could you briefly summarize some of your professional experience?

A. Yes. So I spent my -- most of my professional tenure in the industry. I will mention just a few items that are listed here on this slide.

I started at Enzon. That was the first company that was developing polymers in therapeutics which the area of the chemistry depends on.

After a brief stay at Rutgers University as a visiting professor, I moved to the West Coast where I worked at ALZA Corporation as a senior research fellow, and director of protein and linker chemistry. There, too, I worked with peptide and protein formulations and conjugates as well.

And then Intradigm Corporation and PhaseRx, I worked as a vice president for research of technology development. And these companies were involved in developing in PEGylated nanoparticles.

Currently, I'm an independent consultant, and I assist biotechnology and pharmaceutical companies in various projects that they're dealing with nanotechnology of polymer conjugates of various types, including PEG protein conjugates.

Q. Dr. Zalipsky, has any of your work been published?

A. Yes.

Q. Could you describe some of that?

A. So I have over 90 publications. Some of them are authoritative reviews on the subject of PEGylation PEGylation chemistry, in particular. I also edited a book called Poly(ethylene glycol) Chemistry and Biological Applications. It is still widely used and cited.

Q. What about your experience on any advisory boards?

A. Yes. I served on several professional technical journals dealing with bioconjugation issues, bioconjugate chemistry, International Journal of Peptide Research and Therapeutic Journal of Bioactive and Compatible Polymers. Yeah.

Q. And are you an inventor on any patents relating to PEGylation?

A. Yes, I am. I am listed as an inventor on over 50 United States patents. I'm not counting the international ones here.

MR. CHEN: Your Honor, we'd offer Dr. Samuel

Zalipsky as an expert in chemistry and PEGylation.

MS. DE: No objection.

THE COURT: You may proceed, Mr. Chen.

MR. CHEN: Thank you, Your Honor.

BY MR. CHEN:

Q. Dr. Zalipsky, were you asked to consider any issues of infringement in this case?

A. Yes.

Q. And can you please briefly summarize what you were asked to consider and a very brief summary of what you concluded?

A. So in my opinion, this product, the accused product, does not infringe. What you see in front of you is the text of the first claim of the patent.

And there are two claim elements that the product does not meet. The first one is on the left top side, an isolated polypeptide conjugate.

The Court defined this term that it has to be obtained by conjugation that is not random. This claim element is not met because Adynovate is not an isolated polypeptide conjugate. According to this definition, it is made by random conjugation.

The other element of the claim is at the B-Domain. That was defined by the Court that it has to retain functional activity.

After PEGylation, the conjugate has to retain functional activity. Again, this claimed element is not met by the accused product Adynovate. So, no, there is no infringement in this claim element, either.

As you probably heard multiple times, all claim elements have to be present in the accused product, so there is no infringement.

Q. So we'll get into the specifics in a minute. First, could you explain, Dr. Zalipsky, what evidence you considered in arriving at your opinions?

A. Yes. So there is a summary on this slide of all the documents and things that I considered. Of course, number one is the Court's claim constructions, the Pan '520 patent and its history, biologic license application.

You've seen many documents. It's a very large body of documents. I relied on Dr. Salzberg's calculation of various molecules that are present in Adynovate and the number of these molecules. I relied on Dr. Walensky's calculation showing that only half of the B-Domain in Adynovate is PEGylated.

And characterizations of Adynovate as randomly PEGylated that were made by Bayer scientists and other independent scientists. I also relied on testimonies of various witnesses in this courtroom.

Q. Thank you, sir. Let me ask you now, first, about

your opinion on the isolated polypeptide conjugate term. You've been present in Court all week; right?

A. I was in the courtroom. Yes.

Q. And you heard the testimony of the various witnesses?

A. Yes.

Q. And you heard some testimony about whether the Adynovate process is a controlled process. Do you recall that?

A. Yes.

Q. Okay. Can you please explain how whether or not the Adynovate process is controlled relates to your opinions on whether the Adynovate process is random PEGylation or not?

A. Yes. So --

MS. DE: Objection, Your Honor. I don't think this is in his expert report.

THE COURT: Is there a paragraph, Mr. Chen, that you could point her to?

MR. CHEN: Counsel, paragraphs in his rebuttal report. Paragraph 117 to 125, as well as 66 to 75.

MS. DE: Can you show me where he talks about --

(Discussion held off the record.)

MR. CHEN: Counsel, the opinion is whether it's random or controlled. It's in those paragraphs.

MS. DE: I know. Can you tell me where it is?

MR. CHEN: It's in those paragraphs.

MS. DE: Your Honor, I don't see anything in here, about FDA PEG-approved therapeutics made by random PEGylation and what that means in the context of FDA approval.

THE COURT: Well, if you want, you can come over to side-bar, and I will resolve this.

(Beginning of conference held at side-bar.)

THE COURT: All right. Go ahead.

MS. DE: So his slide talks about most FDA PEG-approved therapeutics. And in his report, he does not discuss FDA approval of random PEGylation therapeutics or what that means.

THE COURT: All right. So Mr. Chen, is there something in particular you can show me?

MR. CHEN: Your Honor, Paragraph 124, in order to obtain FDA approval, that's one example.

MS. DE: It's not FDA.

THE COURT: So that's what this boils down to is --

MR. CHEN: It, honestly, may be one sentence where he says it can be controlled and random at the same time. We also --

THE COURT: All right. I'm sorry. Just to figure out what the dispute is, in order to obtain FDA approval, things must be reproducible, et cetera, et cetera.

And your objection is that his slide --

MS. DE: It talks about products generally and FDA approval generally.

THE COURT: Well --

MS. DE: I don't see him --

THE COURT: I think he is talking about FDA approval generally here.

MR. CHEN: I just heard from Ms. De this morning that they had no objection to our slides.

MS. DE: I didn't realize he was going to say it that way.

THE COURT: All right. Well, I think it's close enough.

MS. DE: Okay.

THE COURT: I'm going to overrule the objection.

MS. DE: Thank you, Your Honor.

MR. CHEN: Thank you, Your Honor.

(Conclusion of conference held at side-bar.)

BY MR. CHEN:

Q. I'll try the question again. Can you explain what you heard in the Court about whether or not Adynovate's process is controlled has any effect on your opinion about whether or not the PEGylation process in Adynovate is random or not?

A. Yes. So Adynovate is an FDA-approved pharmaceutical

product. It has to be made by a controlled process to make sure that every batch is the same. It has the same quality of materials.

So, yes, the process is controlled and consistent. It has to be. There are -- there is ten products probably that are PEG protein therapeutics that they're FDA approved. They already are on the market that are made by random PEGylation and on lysine residues just like Adynovate. They're only by controlled manufacturing processes. There is no equality between process being controlled and product being non-random. There is actually no relationship between these two -- these two words.

Q. Thank you, Dr. Zalipsky. Turning to your opinions on whether or not Adynovate is made by random conjugation.

Have you formed an opinion actually as to whether or not, in your opinion, Adynovate is made by random PEGylation?

A. Adynovate is made by random conjugation.

Q. Can you explain the bases for your opinion or summarize them?

A. Yes. So PEGylation process results in enormous heterogeneity. As I will show in a minute, peptide mapping of the product is consistent with the PEGylation. Adynovate is losing activity during the process which is also consistent with random PEGylation.

Q. Okay. Thank you, Dr. Zalipsky.

Let's turn to your first basis regarding the enormous heterogeneity in Adynovate. Can you please explain your opinion on that?

A. So I've taken the meaning of random modification directly from the patent, the '520 itself. So this is consistent with how the work -- the field is viewing this term, random PEGylation. So the patent is described in here, in these passages that are highlighted, that random PEGylation is PEGylation on lysine residues.

It is problematic, particularly for a protein as complex as Factor VIII. And one of the problems that this patent is offering as a solution is enormous heterogeneity of the product. Heterogeneity in this context means there is many different types of molecules that differ where PEG is attached in the molecule and how many PEG chains are attached to a single molecule. So enormous structural heterogeneity.

Q. Dr. Zalipsky, can I ask you for the record to reference which columns and line numbers of the patent that you're referring to?

A. So it's column three, line 50 to 52. Column 63, column 41 --

Q. Looks like that might be a typo. But you're referring to generally column three and four?

A. It is on the slide at the bottom, actually all the references to these.

Q. And can you explain why you believe there is enormous heterogeneity in Adynovate?

A. Yes. So first of all, Adynovate is characterized by average degree of PEGylation. It would have been known -- we wouldn't need to talk about averages. The range for this average of PEGylation as we already heard previously is between 2 to 3.2. In other words, on every molecule in the mixture on average there is between 2 PEGs to 3.2 PEGs.

There were 55 sites within the sequence that were identified after careful and extensive analysis, 55 sites. That's a lot. That's a large number of sites. And if you just consider that when two to three attachments per molecule spread over 55 different sites, that's a lot of different structures.

I relied also on Dr. Salzberg's calculation that showed that they're between 1,485 to 26,235 different molecules present in this mixture. In other words, there are tens of thousands of different structures.

Dr. Walensky's calculation showed that only half of the B-Domains in the mixture are PEGylated. So all these things are consistent with being random PEGylation product.

Q. Thank you Dr. Zalipsky. Let me ask you about your second basis for why Adynovate is made by random PEGylation.

You mentioned peptide mapping. Can you explain how that supports your opinion?

A. Right. So peptide mapping is essentially fingerprinting of a protein. What is done for peptide mapping, the long polypeptide chain of the protein itself is being chopped up into small fragments, so they're called peptides and those are separated by chromatography. What you see in each line on this slide, this is the separation. So this forest of peaks, there are many, many peaks because it's a complex big protein. So this is the fingerprint of this protein. Kind of like a bar code.

What you see with this marked in green, those are the peptide maps of several lots of the starting material, of unPEGylated protein. What you see in pink, what's labeled in pink those are several lots of the product. And what you can see is from one peptide map to the next one to the next one there is absolutely no difference. You cannot notice any difference between them, which is perfectly consistent with randomly PEGylated product with no material PEGylation, that's how Adynovate is described.

Q. Doctor, you show some data on this slide, the fingerprint that you refer to. Can you turn to DTX-50 in your binder, please.

A. 50?

Q. DTX-5 0.
A. Yes.
Q. Can you confirm that on 50.31, that's the data that you just referred to?
A. Yes. That's the same figure.
Q. And just to confirm, this is an excerpt from the Adynovate BLA; is that right?
A. Yes, it is.
Q. And so just in summary, I apologize if you actually referred to the statement in the document, I know you gave your opinion, but what does Baxalta say this data shows?
A. Right. So there is quoted one sentence saying from the report itself, it says, "No relevant decrease of peptide intensity was observed for a single peptide upon PEGylation likely due to the random PEGylation approach."

MR. CHEN: Your Honor, we offer DTX-50.

MS. DE: No objection.

THE COURT: Admitted without objection.

(DTX-50 was admitted into evidence.)

BY MR. CHEN:
Q. Dr. Zalipsky, let me ask you for your last basis for why Adynovate is made from random conjugation. You say Adynovate doesn't retain activity. Can you please explain what you mean?
A. Yes. This is table 4. What you see that explains to

us essentially what we need to understand from the patent about retention of activity. Table 4 comes directly from the patent itself. What is listed in table 4 are several different KG-2 conjugates and their specific activity. KG-2 was mentioned already, this is full length Factor VIII that Bayer has. This is Bayer's patent, obviously. So KG-2 itself is listed in the top line and several different conjugates are listed in this table with different size PEGs. These were characterized by three different assays that are highlighted in yellow. And you can see that percent activity retained by all three assays is essentially hundred percent. The activity is retained. It is not lost.

Q. Doctor, you referred to assay. Could you just maybe explain what an assay is in simple terms?

A. So those are tests. They're biological tests that performed in laboratory in a test tube that determine activity of the protein. And there are different types of this test. In this case there was coagulation assays, chromogenic assays, ELISA, three.

Q. What does the Pan '520 patent say about random PEGylation as it relates to retaining activity?

A. So the '520 patent says that one of the problems of random PEGylation is activity loss. And there is an example listed here from historical precedent where random PEGylation resulted in two-fold activity loss.

Q. So two-fold activity loss?
A. So 50 percent activity loss.
Q. So just for the record you're referring to column 3, line 50 to 57 of the Pan '520 patent.
A. Yes.
Q. Can you explain to us now how this concept applies to Adynovate?
A. So this exact quotation actually applies to Adynovate. You would expect that activity loss for a random PEGylation of protein such as Factor VIII. What you see in this table in front of you, again, table that comes directly from BLA, Biological License Application, they're experimental development lots here that are being created with different access of PEG. What is important in line one which is the starting material that was not treated with PEG at all. Activity is listed in the right column highlighted in yellow. 4,713 units per milligram.

And then a lot that is highlighted in yellow in the middle of the table, 39 PS, that was created using 25 PEG which is listed in the second column. If we go all the way to the right column, the activity value, the response to this lot, 2,281, which is approximately half, which means half of the activity is lost, only half of the activity is gained, there is also a pattern as you increase the amount of PEG reagent, the activity continues to go down. This is

completely consistent with random PEGylation.

Q. Dr. Zalipsky, can you turn in your binder to DTX-325, please.

A. Can you repeat the number? 325. Got it.

Q. Can you turn to page 23 in the bottom middle. Do you see a table 4 in that document?

A. This is page 23.

Q. On the bottom, DTX- 325?

A. This is the same table.

Q. That's the same table you're describing in your demonstrative?

A. Yes.

Q. This document is an excerpt from the BLA, also?

A. Yes.

MR. CHEN: Your Honor, we offer DTX-325 into evidence.

MS. DE: No objection.

THE COURT: Admitted without objection.

(DTX-325 was admitted into evidence.)

BY MR. CHEN:

Q. Dr. Zalipsky, do you know the conditions in which this reaction was conducted aside from the ratio of PEG to Factor VIII?

A. So those are pretty much the same conditions as in the process, it was done at neutral pH, it was done in

presence of calcium chloride, in the same buffer.
Q. How long is the reaction?
A. Two hours.
Q. And is it quenched?
A. It is quenched with lysine just like the current process.
Q. While that's happening, you said neutral pH. What number pH is that?
A. That is pH 7.
Q. Can you just blow up that first paragraph, please.
So is this what you're relying on for those conditions that you just recited?
A. Yes. So five millimolar calcium, yes.
Q. You heard Dr. Ploegh, his testimony on the process conditions?
A. Yes, I was here.
Q. And do Dr. Ploegh's opinions on those process conditions that we just discussed, calcium, pH, ratio of PEG, time and quenching, how does that relate in this data that we're looking at here?
A. So the conditions themselves have nothing to do with if the reaction is random or not random. As I said, there is just no relationship.
Q. And you're saying that because in part because of the above 50 percent reduction in activity?

A. Reduction of activity is typical for randomly PEGylated protein, so that's what we see in this case.

Q. Let me ask you a hypothetical question, Dr. Zalipsky. If it turns out that the jury determines that Adynovate meets this limitation and retains activity after PEGylation at the B-Domain despite this 50 percent loss in activity. Do you have an opinion as to whether the patent is valid or not?

A. Well, the patent tells us nothing to what extent, to what percentage of activity has to be retained. The only thing the patent says is that activity as retained by all the conjugates 100 percent. So if an accused product is retaining less than 100 percent, then what percentage does it have to retain. The patent doesn't specify. So it's kind of indefinite in this regard. It's ambiguous. It's not clear.

Q. Thank you, Dr. Zalipsky. Let me ask you about the next basis for your non-infringement opinion.

You referenced earlier that you also believe that Adynovate does not infringe at the B-Domain claim term because the conjugates don't retain functional activity. Do you recall that?

A. Yes, I did.

Q. Can you please explain the basis for your opinion?

A. Well, at the B-Domain is defined right underneath on

this slide, not on this one, but the one that you just -- can we go back? Yes. On this slide. At the B-Domain determines attachment at the B-Domain is such that the resulting conjugate retains functional Factor VIII activity. Adynovate does not retain full activity. So it does not satisfy this claim element.

Q. Thank you, Dr. Zalipsky.

So in summary, have you formed an opinion as to whether or not Adynovate infringes the other claims that are being asserted claims 2, 3 and 8?

A. So the remaining claims, they all depend on validity of the first one. Since Adynovate does not infringe claim 1, it also doesn't infringe the dependent claims.

Q. And if Adynovate is found to possibly literally infringe, again, another hypothetical, have you considered whether or not Adynovate could still avoid infringement under a theory called the reverse doctrine of equivalents?

A. So, reverse doctrine of equivalents.

Q. I'm sorry, Dr. Zalipsky, first did you form an opinion as to that?

A. Yes, I did.

Q. Can you explain that opinion?

A. Right. So I think I can. Sorry. Reverse doctrine of equivalents essentially requires us to compare the principle of the patent and the accused product. And in

this particular case, there is dramatic difference between the accused product and the principle of the patent.

Q. Can you briefly explain why?

A. Because the patent is really about cysteine conjugation at one site in the B-Domain, and results in uniformed conjugates that retain functional Factor VIII activity in full. And Adynovate is obtained by random PEGylation at lysines, it has enormous heterogeneity of the species that are present, and it does not retain activity as we just showed.

Q. Dr. Zalipsky, can you help us visually understand these differences that you're talking about?

A. I believe I can. So what you see here on the left side of this slide, the B-Domain is -- contains four cysteines. That's on the left. That's the principle of the '520 patent. Those are the only four sites that are possible for attachment. And only one of them is really reacting, or what was demonstrated in the patent.

On the right side, you see 55 different sites that were found actually in the product. They're distributed all over the molecule, some inside and some outside of the B-Domain. 55 different sites. They're not predetermined. There is a mixture of molecules in this product. It's very different. It's dramatically different principal.

Q. Thank you, Dr. Zalipsky.

I would like now to turn to a different subject matter, and whether or not you have formed opinions that the patent may or may not be invalid, the Pan '520 patent.

Have you considered that question?

A. Yes, I have.

Q. And can you explain a summary, a quick summary of the basis for your opinion?

A. Yes. So there is an enablement requirement, so the patent has to be enabled. The patent does not teach a person of ordinary skill in the art how to non-randomly PEGylate on lysines residues or any other amino acids residues with the possible exception of cysteine. The patent is also obvious in light of the Bossard patent combined with the Bossard work as well as several prior art references of Gruppo, Mosesson, that makes the claims asserted claims invalid.

Q. How did you go about assessing these invalidity opinions?

A. Well, first of all, it has to be done from the perspective of a person of ordinary skill in the art. And I define a person of ordinary skill as a person holding at least masters degree in chemistry, biology, pharmaceutics, pharmaceutical sciences with relevant several years of experience working with proteins, preparation, conjugation,

it has to be done from the perspective of the priority date of the patent which is November, 2005.

Q. Thank you, Dr. Zalipsky.

Let me ask you about your first invalidity opinion on non-enablement. What did you consider, or what factors did you consider in arriving at this opinion?

A. Yes. This is listed on this slide. There is a requirement that the patent has to describe how to practice the invention in the full scope of the invention. And what has to be considered is listed on the factors here. So the amount of experimentation that a person of skill would have to do to practice the invention, the amount of guidance that the patent itself provides. Are there descriptive examples in the patent how to do it, the breadth of the claims, nature of the invention, state of the prior art, relative skill of those who work in the art, and predictable as well, all this has to be taken into the consideration.

Q. And so, Dr. Zalipsky, can we jump ahead to slide 33, please. Is there any description or instructions in the Pan '520 patent on how to PEGylate at a cysteine amino acid?

A. So the only description that is in the '520 patent is about conjugating cysteines.

Q. Let me ask you about lysines that we have heard a lot about. Is there any description in the patent about how to non-randomly PEGylate with lysines on Factor VIII?

A. There is no such description in the patent. As you can see on the left side of this slide, there are 155 different lysines all over the molecule. And when you PEGylate on lysines, do you not know which one of them you're going to need? There is no teaching there how to do it in a non-random fashion. To my knowledge there is no such methodology, actually, how to PEGylate a protein with 155 -- 158 lysines non-randomly.

Q. Dr. Zalipsky, what about the eighteen remaining amino acids?

A. There is no teaching in the '520 patent how to PEGylate the remaining amino acids.

Q. Let me ask you about your last basis or the other basis of your invalidity opinions. Obviousness. Can you explain how you approached this question?

A. So for obviousness, we're required -- we're allowed to combine several different sources to demonstrate that the claims -- that the claims were obvious. And the requirement is also that there has to be motivation to combine this prior art reference, so in other words, prior art. And there was a reasonable expectation of success. Those are kind of the legal requirements.

Q. And you do understand that the patent owner, Bayer here may respond to obviousness with something called objective indicia of nonobviousness?

A. Yes. Objective indicia is used to rebut. In this case Bayer has not provided -- I haven't seen any evidence of unexpected results.

Q. Thank you.

And now, if you could give a very, very short summary, because I think we're running short on time, of what references you're relying on, what combination for obviousness?

A. I'm relying on the references that you already seen in this courtroom. I'm relying on the Bossard patent, the '223, as well as Bossard's work that was done on Factor VIII. The other references that help in this is the Gruppo reference that provides both therapeutic motivation to full length Factor VIII as well as some chemical motivation. And reasonable expectation of success I'm relying on Mosesson that is teaching that the B-Domain is large and would be exposed and contains half of all the lysines, and only four cysteines. So when you try to PEGylate this molecule it is very, very likely that you will hit a B-Domain.

Q. So Dr. Zalipsky, let's talk first about the Bossard work. Can you just very briefly since we have seen a lot of these documents already describe how that work informed your opinion on obviousness?

A. So, this timeline is suggesting that the work was actually derived from the Bossard's work. All these events

were probably mentioned in this courtroom. So the Nektar/Bayer agreement was signed at the end of 2003. Bossard patent was filed in February 2004. In March 2004, samples of full length PEGylated Factor VIII were sent from Bossard to Bayer for examination and analysis. Bayer examined those samples and reached conclusion that cysteine PEGylation was likely in this B-Domain. That's in their memos.

Later on, several months later, Dr. Pan conducted his own conjugation and reached the conclusion that the site is likely in the B-Domain. Conjugation is successful. The Bayer patent, '520 priority date was filed in November 2005. That's the timeline. That's the paper trail.

Q. Thank you.

So very quickly let's talk about the Bossard '223 patent. What is the title of that patent?

A. The title is Polymer Factor VIII Moiety Conjugates.

Q. Let's look at example 7 specifically in Bossard patent. What does example 7 of the Bossard patent teach?

A. Example 7 is dealing with PEGylation on cysteines using a reagent, the same type of reagent that is used in the '520 patent.

Q. And I'm sorry if you said this a moment ago, what type of amino acid does PEG maleimide target?

A. It is PEGylating on cysteine residues. Yes.
Q. Now, this example is something called a B-Domain Deleted Example. Do you see that in the title?
A. Yes.
Q. The Bossard patent, did it have any mention of full-length Factor VIII?
A. Yes, it does.
Q. Where is that?
A. Well, for example, when you look at Claim 15, it lists several different Factor VIII that can -- that can be used as Factor VIII moiety. One of them is Factor VIII itself, and it is designed also by a sequence of 2,332 amino acids which is also in the Bossard patent because it is essentially the same sequence as in the '520 patent that is asserted in this case.
Q. Dr. Zalipsky, you also mention a Gruppo reference. How did the Gruppo reference form your opinion on obviousness?
A. So the Gruppo reference teaches us that B-Domain may confer protection of Factor VIII. It is also teaching us that when -- in clinic, when people use full-length Factor VIII. There is lower incidence of breakthrough pleadings which is as compared to BDD Factor VIII. So it provides motivation to use full-length Factor VIII.
Q. And what about the Mosesson reference that you

mentioned --

A. Mosesson looks at the structure of Factor VIII, and he summarized his results by this type of illustration that he -- that you can see on this slide where Factor VIII is shown as a very large domain that's in purple. It is just as big as the rest of the protein, if not bigger. It is well exposed, extended into solution.

As we talked about, it contains four cysteines as well as other amino acids. So PEGylation on this domain is very likely. So Mosesson provides a reasonable expectation of success element.

Q. And what about Gruppo, does Gruppo do anything to inform your opinion on a reasonable expectation of success?

A. Well, one of the statements that Gruppo makes, it confirms that B-Domain is not necessary for activity. I will read that actually from the slide. "The B-Domain's role, if any, in circulating Factor VIII remains unclear. That domain is not necessary for direct coagulation activity.

If you know the portion of a molecule is not needed for activity, if you can PEGylate that portion of the molecule, that means that your chances to retain activity are very good.

Q. What about --

A. That's the part that you would want to modify.

Q. Sorry. What about the Bossard '223 patent, does that inform any or give any statements about activity?
A. So in Example 12 of the Bossard patent, it states that conjugates made in Examples 6, and 7, and 8 were tested for activity, and they were all found to be active -- bioactive.
Q. Okay. Now, Claim 8 of the Pan '520 patent discusses pharmaceutical compositions and excipients. Was there any discussion that you saw in the Bossard '223 patent about pharmaceutical compositions and excipients?
A. Yes. So the Bossard patent is talking here Factor VIII moiety conjugates. Clearly, it is -- it is contemplated as therapeutic. There are several passages starting from the abstracts that talk about compositions, pharmaceutical compositions. Pharmaceutical excipients.
So those are highlighted in the different passages that are used as an example.
Q. So just for the record, you're referring to the Bossard patent DTX 6, the abstract, Columns 39, Line 61 to Column 40, Line 58?
A. Yes.
Q. Okay. And also Column 28, Line 35 to 41, and Column 38, Lines 42 to Column 39, Line 60?
A. Yes.
Q. Okay. What about the objective indicia that Bayer

may raise? You said that you hadn't seen any evidence of any objective indicia.

Can you just please explain what you mean?

A. Well, so the objective indicia, so one of the characteristics of objective indicia is unexpected results. And as we just discussed a moment ago, it was known already. It was mentioned in this courtroom as well that B-Domain is not necessary for coagulation activity.

Q. What about half-life?

A. So the half-life is illustrated in this patent in patent '520 by Figure 20. And Figure 20 was otherwise -- you heard it yesterday by the expert on pharmacokinetics from our side, Dr. Thakker. And it was also analyzed -- the evidence was presented how it was referred to by Bayer's pharmacokinetic scientist.

And also, in my personal opinion from this figure, you cannot see that there it has improved the prolonged circulation of the conjugate from their starting material. And I've seen pharmacokinetic material results during my professional tenure. This is not how it looks.

Q. Thank you, Dr. Zalipsky. In summary, can you summarize your obviousness opinion?

A. So I just indicated, the claims are obvious in light of Bossard, Bossard's work, and these several prior art references that we just discussed, which makes the claims

invalid.

Q. So Dr. Zalipsky, I apologize for jumping out of order here. I just want to ask you one last question on infringement, which I should have addressed earlier.

Ms. Debonis, can we turn to Slide 7? I neglected to ask you earlier about Sequence ID No: 4.

Do you see that in the middle?

A. Yes.

Q. All right. Have you reviewed documents from the Adynovate BLA?

A. Yes.

Q. And have you seen any documents that inform you as to what quantity of Factor VIII with Sequence ID Number: 4, the 2,332 amino acids is present or not present in Adynovate?

A. Right. So the only place where I saw related information in characterization with the starting material which is full-length Factor VIII from Baxter, that is called Advate. So when Advate is analyzed by chromatography, there are a couple of peaks in this chromatography that it says that they contain full sequence. They're small peaks. They're less than ten percent of the -- of the total.

To my understanding, these peaks contain not only this. So ten percent is very -- actually, very liberal estimated. It's below ten percent of the starting material.

There is no information of how these particular species are PEGylated or even if they are PEGylated.

The main components of Advate, more than 90 percent of the poly peptide is in Advate which is, again, starting material. They do not contain the full 2,332 amino acid sequence.

Q. Thank you, Dr. Zalipsky.

THE COURT: All right. So members of the jury, we'll take our morning break here. 15 minutes. Start up again about 20 of 12:00.

THE CLERK: All rise.

(Jury leaving the courtroom.)

THE COURT: All right. Everyone, be seated. Am I correct in thinking, Mr. Chen, that you've dropped anticipation as a defense?

MR. CHEN: Your Honor, we didn't present it through Dr. Zalipsky. I think we'd like to review the trial transcript.

We likely will, but we'd like the opportunity, if it's okay, to review the trial transcript after this morning's testimony.

THE COURT: I think your answer speaks for itself.

MR. BADKE: Your Honor, if I could just say one thing. We'd like to know this before we have to put up

Dr. Ravetch on --

THE COURT: Unless something happens between now and you put it on, it's dropped. Unless Mr. Chen comes back and tells me some other way or says something, but I think it's been dropped.

And then the other thing is the defenses in this case, are they affirmative defenses, or are they also counterclaims?

MR. CHEN: My recollection, Your Honor, is that they are affirmative defenses.

THE COURT: Okay. All right.

Thank you. So we'll be in recess.

THE CLERK: All rise.

(Recess was taken.)

THE CLERK: All rise.

THE COURT: All right. Are we ready to proceed?

MR. HAUG: Your Honor, before we do, if I may raise two things. One, I do want to confirm, in the interest of time, we have not put in anything on anticipation at this point. So that is out.

THE COURT: Thank you.

MR. HAUG: Okay. And the second thing is because of time, again, while we're doing our best, by our calculation, we have about 45 minutes left in this case. We have our damage expert who will still come up.

So I would like to request 15 minutes for cross in their case if they put in a rebuttal case.

THE COURT: Wait. No. We've got a time limit. Do the best you can.

All right. Let's get the jury.

(Jury entering the courtroom.)

THE COURT: All right. Members of the jury, welcome back. Everyone, you may be seated.

Members of the jury, I did notice that it seems to be a little cool in here, but I think as long as nobody is freezing, we'll just keep it at this temperature.

Go ahead, Ms. De.

MS. DE: Thank you, Your Honor.

BY MS. DE:

Q. Good morning, Dr. Zalipsky.

A. Good morning.

Q. You testified on direct that Adynovate PEGylation chemistry gives a random distribution of PEGs across Factor VIII. Do you recall that?

A. I testified that the Adynovate is made by random PEGylation.

Q. And full-length Factor VIII contains approximately 158 lysine residues?

A. Yes, that's what's in the sequence. It's not approximate. It is exact.

Q. Exactly 158 lysine residues. And they're distributed across the Factor VIII molecule; right?
A. Yes.
Q. And half of those lysines are located in the B-Domain? About half?
A. Approximately, yes.
Q. And the other half are located outside the B-Domain?
A. Yes.
Q. Now, you've said that the reactivity of lysines in various parts of Factor VIII is similar; right?
A. So ahead of time when you don't know the protein, you have to assume that lysines will have similar reactivity.
Q. I'd like to put JTX 1, which is the Bayer '520 patent up on the screen. And specifically, let's take a look at claim 1 of that patent. If we could bring that up.

Now, claim 1 is directed to PEGylation at the B-Domain. It's the very last phrase; right?
A. Yes. The polymer has to be covalently attached to the functional Factor VIII polypeptide at the B-Domain.
Q. And doesn't require PEGylation at any particular site within that B-Domain, does it?
A. The claim says it has to be at the B-Domain.
Q. And it doesn't exclude PEGylation at lysines, does it?
A. The claim is silent on the issue of lysines. I'm

not --

Q. And you understand that the Court's Claim Construction Order in this case said that lysines are not excluded from the scope of this claim?

MR. CHEN: Objection, Your Honor.

THE COURT: So I'm going to sustain the objection. The jury will have my claim constructions. You've already seen them. That Order is the extent of my claim constructions.

MS. DE: Thank you, Your Honor.

BY MS. DE:

Q. Some PEGs can attach outside the B-Domain in this claim; correct?

A. So if I understand you correctly, that this claim allows -- you're alleging that it is okay for you to PEGylate inside the domain and outside the domain. It still falls under this claim; is that what you're telling me?

Q. If the B-Domain limitation is met when there are more PEGs inside the B-Domain then would have resulted from random PEGylation; is that right?

MR. CHEN: Objection, Your Honor.

THE COURT: I'm going to overrule that objection.

THE WITNESS: So the claim doesn't say anything, neither does the patent, to what extent any domain has to be

PEGylated. This patent talks about PEG site-specifically at B-Domain to form site-specific conjugate. We already know that the site in this patent is an amino acid site within the sequence of particular position within the sequence which is a cysteine. We know it from reading the patent.

Q. Hang on. I just want to talk about the lysines for a second. Just hang on a second.

We were just discussing the amount of lysines, half of them being in the B-Domain and half of them being outside of the B-Domain in full length Factor VIII. Do you remember that?

A. That's correct.

Q. Can we pull up PTX 607. And this is the site analysis report that Baxalta submitted to the FDA. Do you recognize that?

A. Yes.

Q. And Baxalta in this report analyzed where PEG actually attached in Adynovate; right?

A. So this document determines all the possible sites in Adynovate.

Q. And in the first page of this document, you see that Baxalta checked across several batches to figure this site analysis out. So there is pre-clinical batch, clinical phase one batches, clinical phase two batches, clinical phase three batches, conformance batches and extended hold

time batch. So several batches were analyzed; right?
A. Right.
Q. And Baxalta reported in the paragraph right below that that there is excellent batch-to-batch consistency of PEGylation sites, occupancy and distribution. And that happened even after process changes, scale up and transfer to a new manufacturing facility. Do you understand that?
A. Right. I think the big misunderstanding. The consistency between batches is done based on fingerprinting of the PEGylated peptide. That's another assay. This site analysis is not done on every single batch that is produced. That took two years to obtain this data.
Q. Based on this data, on the next page of the same exhibit Baxalta reported that 73 percent of the PEGylation site were in the B-Domain; right?
A. So that is frequency of PEGylation sites. It's simple, 40 out of 55 detected.
Q. You had seen this site analysis report when you had formed your opinions in this case; correct?
A. Yes.
Q. Thank you. You can put that down.
You also talked about Adynovate in terms of its specific activity. Do you recall that testimony?
A. Yes.
Q. Can we get DTX 325 up, please. And if you go to the

second page. And you relied on this document to talk about Adynovate's specific activity. Do you remember that?

A. Yes.

Q. If I could go to DTX 325, page 23. And if you blow up table 4, please. And you relied on this table 4 to talk about the loss in activity; right?

A. Yes.

Q. And the loss in activity here is loss in specific activity; right?

A. Yes.

Q. And if you look at the top of that table, it is referring to specific activity measurements of protein that was obtained by AEC? That stands for ion exchange chromatography; right?

A. AEC.

Q. I'm sorry, anionic exchange chromatography. I apologize.

A. That's what it says.

Q. If I could turn your attention now to the very -- not the very last page, second to last page, which is DTX 325, page 45. And if you look at the section at the top of this, it refers to optimization of a chromatographic purification procedure. Do you see that?

A. Yes.

Q. It says in the first sentence it explains that to

improve the purification procedure, two different batches were processed using something called a CEC step instead of anion exchange. And CEC, that stands for cationic exchange chromatography; right?

A. Yes, that is correct.

Q. And the following paragraph talks about that same CEC MacroCap step, you see it's referring to that as an efficient purification procedure?

A. Yes.

Q. As a result of that -- keep that highlighted -- Baxalta here explains that a specific activity of 93 percent of the starting material was obtained when measured with this CEC step. Do you see that?

A. Right.

Q. And you understand that the final ID product was actually made using a CEC step?

A. Right.

Q. You can put that down.

Let's go back up to the '520 patent, JTX 1. And let's look at claim 1 one more time.

Now the term "specific activity" is not in the '520 patent claim, is it?

A. The activity enters the claim through the definition of at the B-Domain. So the at the B-Domain was defined as the attachment of polymer to the B-Domain does not cause

loss of activity, that's what it says.
Q. But the term "specific activity" isn't actually recited in the claim, is it?
A. I don't see it in the claim.
Q. Okay. The term functional Factor VIII polypeptide is, however, recited in the claim. Do you see that?
A. Right. It is.
Q. Okay. And if we could go to column 9, line 39 of the '520 patent. The term functional Factor VIII polypeptide, there is a definition there; right?
MR. CHEN: Objection, Your Honor.
THE COURT: Overruled.
A. Yes.
Q. And you had testified that a person of skill wouldn't be able to figure out how much functional Factor VIII activity would be required. Do you remember that?
A. Yes.
MR. CHEN: Objection.
A. Yes. I said that a person of ordinary skill in the art would not know how much activity needs to be retained because the only activity that is discussed in the '520 patent is retained activity.
Q. And here in the definition of functional Factor VIII polypeptide, it says that such a polypeptide is able to correct human Factor VIII deficiencies. Do you see that?

A. Yes.
Q. And if you look a few lines below that down at line 55, actually 55 through 58, it says that the Factor VIII derivatives have the requisite functional activity and can be identified by straightforward in vitro tests described herein. That refers to functional activity; right?
A. Okay. But we're talking about conjugates, the patent is about making conjugates. When you make conjugates, you also compare activity of the parent protein to the conjugate that you made and you compare how much activity is retained.
Q. It doesn't recite the term specific activity in this passage, does it?
A. That's what is important, specific activity. When you compare conjugate to the starting protein, you always compare specific activity. Table 4 is the only place where activity is specified, and it is specific activity. That's activity for a protein, that is what's important.
Q. You don't see the term specific activity in the definition of functional Factor VIII polypeptide, do you?
A. Let me read this paragraph.
Q. Do you know what, Dr. Zalipsky -- I'll blow it up a little more clearly. But if it's in there, perhaps your counsel can redirect you to the specific activity term in that passage.
A. I believe there is a statement in this paragraph that

says the activity should be retained in kind.
Q. Yes.
A. That tells me that activity has to be completely preserved.
Q. Okay. And if I could direct your attention now to column 23 starting at line 55, you see a heading there that says activity measurement?
A. Yes.
Q. And underneath that, there is a coagulation assay that's identified that one could use; right?
A. I see that.
Q. And at the top of column 24, the very next paragraph it describes a chromogenic assay that one could use, do you see that?
A. Yes.
Q. And those are assays that a person of skill would learn from this patent and go to; isn't that right?
A. And those are the assay results that are shown in table 4.
Q. Those particular assay descriptions that you're seeing here, they actually report activity in micro -- sorry, international units per milliliter, that's not the specific activity unit, is it?
A. That's not how you calculate conjugates. The conjugates are characterized and summarized in table 4.

Q. Thank you.
A. It's just a description of assays.
Q. Yep. Thank you.
If I could direct your attention to PTX 905. And this is the Adynovate label. Do you recognize that?
A. Yes.
Q. Now, hemophilia A -- in the indications which is on page two at the very top, that Adynovate actually is used to treat hemophilia, it works to treat hemophilia; right?
A. No doubt.
Q. Thank you.
You can leave the label up.
Now, you had testified on direct that some ten percent of Adynovate is full length sequence ID 4 2,332 amino acids. Do you recall that?
A. That's not what I said.
Q. What did you say?
A. I said that the only hint about full length we can find in the starting material which is Advate, so there are a couple of peaks in chromatography that were described as a complete protein, and they respond to less than ten percent by integration of the chromatography. So we know that this peak contains not only this full length protein, that it's not the only component. This is the starting material. When starting material is subjected to conjugation,

purification, whatever processing steps, I have no information how this component of the starting mixture, we know that there is a mixture of polypeptides and Advate. So the starting mixture is processed in conjugated, how it comes out, how it is conjugated, this particular full length sequence, we have no idea. There is no information on that.

Q. Let me direct you to page 3 of PTX 905, right-hand column, the very bottom, last paragraph. It says Adynovate is a recombinant full length human coagulation Factor VIII, 2,332 amino acids. Do you see that?

A. Yes.

Q. The label doesn't say that only ten percent of Adynovate is a recombinant full length human coagulation Factor VIII, does it?

A. I didn't say that ten percent of it is, either. I will repeat. There is less than ten percent by chromatography in the starting material. There is no evidence that was shown, I haven't seen anything that tells me how these ten percent material might have been conjugated, processed, purified, and what is the content in Adynovate. I don't know. There is a trace in Advate itself. And we already know that when we say full length Factor VIII, that's not really a single chain polypeptide.

Q. All right. Dr. Zalipsky, we are going to move on to another topic. We have your opinions from your direct

testimony.

Now, you also talked about something called the reverse Doctrine of Equivalents on direct. Do you remember that?

A. Yes.

Q. And you understand that the reverse Doctrine of Equivalents arises when an accused product is found to literally infringe a claim element; right?

A. Right.

Q. And you testified that Adynovate doesn't infringe under the reverse Doctrine of Equivalents because it is prepared using random PEGylation. Did I understand your reverse theory?

A. So, my --

Q. That basically boils down to --

A. My understanding of what you need to compare is the principle of the invention to the product. And what I said that they're fundamentally different is because the invention is about uniform site specific conjugated cysteine in the B-Domain. The product is randomly PEGylated full length Factor VIII. They're fundamentally different.

Q. And if the product literally infringes, it means that it has to meet the claim requirement that the conjugation was not random, right, you understand that?

A. Yes.

Q. Now, you also mentioned on direct that the '520 patent does not enable a person of ordinary skill in the art to non-randomly conjugate the B-Domain at lysines. Do you recall that testimony?

A. Yes.

Q. And you said that the Bayer patent has a priority date of November 14th, 2005; right?

A. Yes, that -- I think that is correct.

Q. Now, by 2005, persons of skill would have known that Factor VIII can be PEGylated by a number of methods, that was known at that time; right?

A. We're talking about PEGylation that is non-random that is required to be site specific. So site-specific PEGylating on a lysine, on a protein that has 158 lysines, I'm not aware of such a method. I don't think it is available for Factor VIII or for any protein that would have this number of lysines unless you make protein that has one single lysine, maybe, but that's not the reality. Most proteins have ten percent or even higher of their sequence with full lysines.

Q. Let me try it this way: Both lysine and cysteine directed PEGylation of Factor VIII had been achieved in the art by 2005; right?

A. So lysines were PEGylated only in a random PEGylation approach. That's the only thing that was done.

Q. Okay.
A. And that's what the Adynovate is, it's randomly PEGylated.
Q. I'm not asking about Adynovate. We're talking about the enablement issue now. Now, the '520 patent, I'm not quite at.
The '520 patent published in April of 2010; right?
A. I think that is correct.
Q. And you mentioned Adynovate. Adynovate was not submitted for FDA approval until November 2014; right?
A. Well, I don't remember the exact date when it was submitted for approval.
Q. Adynovate is PEGylated at lysines, that much we agree on; right?
A. Yes. Adynovate is PEGylated on the lysines predominantly, yes.
Q. Okay. And let's get PTX 446. This is Baxter's letter to the FDA on Adynovate.
Do you recognize this?
A. Yes.
Q. Okay. I would like to direct your attention to appendix one of that PTX, which is on Page 22. And according to the title of that appendix, Baxalta told the FDA that it targeted PEG to the B-Domain.

Do you see that?

A. Well, I can read the statement. Yes.

Q. Yes. And you didn't discuss this FDA letter in your expert reports, did you?

A. I don't think that I was aware of this letter when my report was prepared.

Q. I apologize. You can take that down.

All right. Now, you also testified about the Bossard patent on your direct; do you recall that?

A. Yes.

Q. Okay. And Bossard doesn't expressly disclose conjugates PEGylated at the B-Domain, does it?

A. It is inherently disclosed, but not expressly.

MS. DE: Your Honor, I'm going to strike that. They were not doing an anticipation argument.

THE COURT: I'm not going to strike it. You asked a question, and he answered it.

MS. DE: Okay. That's fine.

BY MS. DE:

Q. Let's try it this way: You said that the Bayer patent claims are obvious based on Bossard?

A. Yes.

Q. Okay. And you testified that it would be obvious to use a full-length Factor VIII based on Bossard's Claim 15; right?

A. Well, obviousness arguments combine several different sources, not only Bossard.

Q. Sure. But one of the things that you -- I'll get to the other ones, I promise you. But one of the things that you talked about in the context of the Bossard patent was Claim 15.

Do you remember that?

A. Yes.

Q. Okay. If you could take a look at DTX 6. And if you could go to column -- the page that has Column 73 and 74. And just keep all the claims up there, if you will, Mr. Lee, when you get to that.

There you go. Could I get the next page as well, please?

Now, Claim 15 is one of 31 claims in the Bossard patent; right?

A. Yes.

Q. And the Bayer '520 patent, claim 1 recites the sequence for full-length Factor VIII; right?

A. Are you referring to SEQ ID No: 4?

Q. Yes, sir.

A. Yeah, it sites SEQ ID No: 4.

MS. DE: Don't blow up the claim yet. Okay.

BY MS. DE:

Q. Now, you picked claim 15 over all the other claims in

Bossard because it recites Factor VIII that you say is full-length Factor VIII?

A. Well, this is what was relevant to our discussion to the argument --

Q. Now --

A. -- because it says Factor VIII.

Q. Sure.

A. It says Factor VIII. That means full length. Unless it specifies that it's a sub-degree of Factor VIII.

Q. Claim 15 is not limited to full-length Factor VIII; though; right?

A. There are a few types of Factor VIII that are listed in claim 15, and one of them is Factor VIII itself.

Q. And one of them has no B-Domain; right?

A. Well, let me see.

Q. Yes. So if you look at claim 15 --

A. This is not large enough for me to read.

Q. No, it's okay. I'll put claim 15 up on the screen. Take a look at claim 15.

There's a recitation of Factor VIII. That's activated Factor VIII; right?

A. Yes.

Q. And that means it has no B-Domain, does it?

A. Yes, that's correct.

Q. Let's blow up claim 16 instead. The very next claim

only recites a B-Domain Deleted Factor VIII; right?

A. Yes.

Q. Okay. And unlike the Bayer '520 patent, none of the Bossard claims specify any location of attachment at the B-Domain; right?

A. As I mentioned, they take full-length Factor VIII and subject it to conditions that are described in the Bossard patent. You will -- you will inevitably get -- get PEGylation on the domain.

Q. Dr. Zalipsky, you were deposed in this case; do you recall that?

A. Yes.

Q. Okay. I'd like to direct your attention to Page 103 of your deposition, Line 21.

And you were asked: "And the claims" -- and we were talking about the Bossard patent, "though, do not specify attachment at the B-Domain?

"Answer: Place of attachment. They don't specify place of attachment."

Were you asked that question, and did you give that answer?

A. Right. It's not spelled out.

Q. Thank you. Now, you said that there would be a -- can you take down the claim?

You testified that there would be a reasonable

expectation of success in PEGylating full-length Factor VIII. Do you recall that?

A. Right. An expectation of success also refers to PEGylating the B-Domain.

Q. But Factor VIII is a highly complex protein right?

A. It is, indeed.

Q. And isn't it true that PEGylation of complex molecules such as Factor VIII is actually highly unpredictable?

A. Generally, yeah. There's -- there's always things in protein chemistry that are complex, and those are very complex molecules. They're highly functional. There are different confirmations and post-translational modifications.

Q. And on --

A. There are certain things that we can be sure of that if you take lysines --

Q. I think you've answered the question.

A. -- Lysines react --

Q. I think you've answered my question. Dr. Zalipsky, I think I've got it.

MR. CHEN: Your Honor, objection.

THE COURT: All right. I'm going to overrule the objection, but go ahead, Ms. De.

MS. DE: Okay.

BY MS. DE:

Q. In forming your opinions in this case, you did not run any tests using the exact steps of any Bossard examples such as Example 7 on full-length Factor VIII to see what would happen, did you?

A. I have not conducted any experiments for this case.

Q. Okay. Now, you also said that there were reasons to pick full-length Factor VIII to PEGylate. But wouldn't you agree that there are also reasons to go with a B-Domain Deleted Factor VIII?

A. You can always justify your peak.

Q. And --

A. And it depends on what you put your emphasis on, what is important to you. So I -- what I focused here in the -- on my slides that were shown on the reasonable rationale for peak in full length.

Q. And in terms of reasons to go with B-Domain Deleted, for example, as of November 2005, the B-Domain was more well defined; isn't that right?

A. Okay. So if your -- if your priority --

Q. Sorry. I'm sorry.

A. It depends --

Q. Let me withdraw my question. I misspoke.

As of 2005, the B-Domain Deleted Factor VIII was more well defined. There was crystal structures of it.

We've seen them in Court; right?
A. It depends what you mean by more well defined really.
Q. Okay. Now, you had talked a bit about the Mosesson reference on direct?
A. Yes.
Q. And Mosesson is directed to Factor VIII from a pig. It's a porcine Factor VIII; right?
A. So porcine Factor VIII is still used in clinical humans. It's very, very similar to human Factor VIII.
Q. And Mosesson didn't discuss any PEGylation of Factor VIII; correct?
A. There is no PEGylation in Mosesson, to my recollection. There are no mention of it.
Q. You also discussed a Gruppo reference on direct; right?
A. Well, yes.
Q. And the Gruppo reference has no mention of PEGylation, does it?
A. No, it does not.
Q. Now, you opined against the validity of the Bayer patent claims on a number of grounds. You mentioned obviousness. You mentioned enablement. And I think you also said something about definiteness.

Do you remember that? Is that right?

A. Yes, in connection to obviousness.

Q. Okay.

MR. CHEN: Your Honor, objection, relevance. That wasn't presented in direct --

THE REPORTER: I'm sorry?

THE COURT: I'm sorry. I don't understand your objection.

MR. CHEN: Relevance objection, Your Honor. I think she's going where testimony wasn't even presented. It's outside the scope.

THE COURT: Well, so far I haven't heard anything. I don't know where she's going, so I'll let her ask another question.

MR. CHEN: Sure, Your Honor.

MS. DE: Okay.

BY MS. DE:

Q. Now, the Bayer patent, the Bayer '520 patent was reviewed and issued by the Patent And Trademark Office; right?

A. Yes.

Q. Okay. And that patent issued on June 14th, 2016; right?

A. I think that is correct.

Q. Okay. And so it was pending before the Patent Office for over the course of nearly 11 years, 2005 priority date, 2016 issuance date?

A. If you say so.
Q. Okay. Now, you had testified on direct that you yourself have a number of patents; right?
A. Yes.
Q. Right. And you understand that, as part of the process of getting a patent from the Patent And Trademark Office, the patent is reviewed, not just for obviousness against the prior art, but also for things like enablement and definiteness?
You understand that; right?
MR. CHEN: Objection; foundation.
THE COURT: Overruled.
THE WITNESS: Well, in an ideal world, everything would be hundred-percent proof, but we know that that occasionally the Patent Office makes errors. And what I'm expressing is not an opinion of the Patent Office. I'm expressing my opinion.
BY MS. DE:
Q. Sure. Why don't we go to PTX 3-A.
A. You said DTX?
Q. PTX 3-A. And I have it up on the screen for you. If you could go to the second page of that exhibit, Mr. Lee, please. In this particular case, the Bayer patent was reviewed, not just by the first examiner, but before the Patent Trial And Appeal Board.

Do you recall seeing that?

MR. CHEN: Objection.

THE COURT: So take the exhibit down.

MS. DE: Mm-hmm.

THE COURT: You can ask the question.

MS. DE: Okay.

BY MS. DE:

Q. And let's see. You relied on the Bossard patent as part of your obviousness case; right?

A. Yes.

Q. And the lysine PEGylation in Bossard is not within the scope of the '520 patent claims because it yields random conjugation; right?

A. So is the Bossard?

Q. Actually, Dr. Zalipsky, I could help you out, if you'd like to go to your reply report, Paragraph 79.

(Discussion held off the record:)

BY MS. DE:

Q. And you say there that you further explained in your supplemental opening report that the lysine PEGylation disclosed in Bossard is not within the scope of the claims of the '520 patent because it yields a random conjugation. Did I read that correctly?

A. You read this correctly.

Q. Okay. And in terms of cysteine -- can you take that

down? In terms of cysteine PEGylation, the Patent Trademark And Appeals Board, the administrative judges there, they considered as part of their analysis the Bossard patent; right?

MR. CHEN: Objection, Your Honor.

MS. DE: I'm still going to show it to him.

THE WITNESS: I don't recall exactly what was the question and the point of contention with this Board. And if I'm not mistaken, it was anticipation only, but I don't recall exactly.

BY MS. DE:

Q. Do you recall --

A. If I understand correctly, you're saying that it is okay to PEGylate on the B-Domain and outside of the B-Domain. And as long as some of it is in the B-Domain, the patent infringement, but that is in the prior art, that is described by Bossard.

Q. All I'm asking you, Dr. Zalipsky, is in reviewing the prosecution history of this patent, you reviewed the fact that the patent trial -- the patent trial and appeal board considered the Bossard patent including cysteine PEGylation and issued in Bayer patent over it, isn't that true?

MR. CHEN: Objection, Your Honor.

THE COURT: Overruled. But this is the last topic on this question.

Q. You understand that an issued patent is presumed valid; right?

THE COURT: Strike the last question. Go on.

Q. As part of the legal standards --

THE COURT: No. Go on to something else.

MS. DE: You know what, Your Honor, I'll pass the witness.

THE COURT: Okay.

MR. CHEN: No redirect, Your Honor.

THE COURT: All right. Dr. Zalipsky, thank you. Watch your step going down.

All right. Mr. Fleming.

MR. FLEMING: Let me go get the witness.

THE CLERK: Please state and spell your full name for the record.

THE WITNESS: Gordon Rausser. Last name is spelled R-A-U-S-S-E-R.

Gordon Rausser, Ph.D., was examined and testified as follows:

DIRECT EXAMINATION

BY MR. FLEMING:

Q. Good morning, Dr. Rausser.

A. Good morning.

Q. I guess it's good afternoon. Sorry.

Good afternoon, Dr. Rausser. Could you please

state your profession?
A. I'm an economist and a statistician as well as a financial analyst.
Q. Can you briefly state your background?
A. Yes. I have a masters degree, a bachelors of course, and a Ph.D.
Q. I direct your attention to DTX 1357, please.
A. Yes.
Q. In your binder. I gave you have a binder.
A. Thank you.
Q. There is an exhibit, DTX 1357.
A. I got it.
Q. And can you identify that for the record, please?
A. Yes. This is my CV.
MR. FLEMING: Your Honor, we offer DTX 1357.
MS. FUKUDA: No objection.
THE COURT: Admitted without objection.
(DTX 1357 was admitted into evidence.)
BY MR. FLEMING:
Q. Dr. Rausser, did you prepare some slides to help with today's presentation?
A. Yes, I have.
Q. Where do you work?
A. I am on the faculty at the University of California Berkley. My formal title is the Robert Gordon Sproul

Distinguished Professor.

Q. What is your job at the University of California?

A. My job is to conduct research, working with Ph.D. students, I teach undergraduate courses in statistics and microeconomics.

Q. How long have you been teaching at the University of California?

A. Since 1978.

Q. Have you taught at any other universities or colleges?

A. Yes. I was on the faculty of Harvard University, University of Chicago, one here in the Department of Statistics and Economics at Iowa State University. I have also been a visiting processor at Oxford University.

Q. Have you written anything that has been published?

A. Yes. I have published more than 250 referee journal articles. Books, I think the books are up to fourteen or fifteen books and a numbered of commissioned reports.

Q. And what does the term peer reviewed mean?

A. Peer reviewed means that a process is conducted by referee journals where a paper is submitted and it's sent out to reviewers to evaluate the quality of the research, whether, in fact, there is causal relationships. In economics we care about causality, not correlation. And the external reviewers end up assessing and determining whether

or not the publication should be accepted for being published in that journal.

It turns out for the very best journals only five to ten percent of the manuscripts that are submitted are actually published. They don't pass the peer review process.

Q. In addition to these publications, are there other ways that your work has been recognized by economics on the top of your profession?

A. Yes. Over the course of my career I have won 24 research awards for publications of enduring quality, research discovery, teaching awards while I was teaching at Harvard in the graduate school of business administration; also awards from international agencies including the World Bank for work that I have done while I was chief economist at the Agency For International Development.

Q. What does it mean to be an elected fellow of these organizations?

A. Each organization is like a tribe. And they have high standards for naming members of the tribe to be fellows. Anybody can become a member of an association, all you have to do is pay the subscription fees for the journals that are being published. But only a select few of the members are actually elected to become fellows. And on three separate occasions I have been elected a fellow of the

American Association for the Advancement of Science. Given all my work in statistics, a fellow, elected fellow of the American Statistical Association. And finally an elected fellow in the Agriculture and Applied Economics Association.

Q. Aside from the articles and books you have personally written, have you played any other roles in peer reviewed publications?

A. Yes. I have served as editor and continue to serve as editor of the Annual Reviews of Resource Economics. I have been serving in that role for more than fourteen years at this juncture. And the Annual Reviews is an overall disciplinary organization that covers all the major science, including social science, and moreover, it sets the peer reviewed standards for the entire profession.

I have also served as editor of the American Journal of Agricultural Economics, associate editor of the American Statistical Association, and then finally associated editor of the Journal of Economics Dynamics and Control.

Q. Have you ever been employed outside of the academic community?

A. Certainly. On two separate occasions, I took leave from U.C. Berkley. I served on the President's Council of Economic Advisor for two years in 1986 and 1987. And then again subsequent to that, I accepted the role as chief

economist at the Agency For International Development. And in that role, there were 500 economists that were reporting to me that were located in missions throughout the developing world, lower incomed countries where we, the U.S. government, provided humanitarian aid to these specific countries, but there is an issue about doing economic analysis to help the countries grow economically.

MR. FLEMING: Your Honor, we offer Dr. Rausser as an expert in economics, statistics and expert analysis.

MS. FUKUDA: No objection.

THE COURT: You may proceed.

BY MR. FLEMING:

Q. Dr. Rausser, what were you asked to do in this case?

A. I was asked to objectively assess what was the result of a hypothetical negotiation between Bayer and Baxalta in setting a reasonable royalty rate.

Q. Are you expressing any opinion about whether the Pan patent asserted in this case is valid and infringed?

A. No. I'm required to assume in my analysis that it's valid and that it's infringed.

Q. What kind of information did you evaluate to assist you in arriving at a reasonable royalty rate?

A. I prepared a slide which list all the material that we have evaluated in the discovery record. And my staff and I have looked at all the patent filings. We've looked at

the deposition testimony, the trial testimony that's unfolded over the course of the last four days. And we also evaluated academic and industry journals to see what evidence was available about the issue for which I have been assigned to conduct an objective analysis.

Q. In general, how do you go about arriving at a reasonable royalty rate in a patent case?

A. You're asked, if you've already heard, that there must be conducted a hypothetical negotiation. We have to put ourselves in the shoes of both parties. And moreover, we're asked to assume that they will reach a cooperative solution. They will willingly proceed in the negotiations, elected all the relevant facts, the causal relationships, and come to a cooperative solution which both can accept, willingly.

Q. Are you the one that came up with this approach for determining a reasonable royalty rate in a patent case?

A. Yes. May I have the next slide?

Here, hypothetically in this negotiation, I have a chair for Bayer, I have another chair for Baxalta, and they are going to proceed through this willing negotiation and come to a cooperative solution.

Q. Have you used this approach before?

A. Many times.

Q. In your opinion, what is the key to getting the

analysis right in the terms of setting a correct reasonable royalty?

A. Well, we're given guidance from a very old case from 1970. It's called the Georgia-Pacific case, which specified a number of factors, 15 factors. You already heard a bit about those in earlier testimony a few days ago. And those Georgia-Pacific factors, you as the expert are assigned evaluating those factors with regard to how the two parties would be positioned and how they would go about reaching a resolution to arrive at a cooperative solution.

Q. What's the first issue you believe the parties would have been focusing on in this hypothetical negotiation?

A. The first and most issue is Bayer would be concerned about how much the product's value, Adynovate, how much of that comes from extended half-life.

In contrast, Baxalta would also be concerned about that, but they would be focusing on the Pan patent, or the '520 patent with regard to what its contribution would be.

Q. How do you figure out what contribution to Adynovate's value?

A. By going through the process of evaluating first what are the attributes and characteristics of the product in question, the smallest saleable unit, namely Adynovate. And here, let me give you a simple analogy. If you're

evaluating the purchase of a house, it's a saleable unit, it has value. Now the question, what's the decomposition of that value? How many bathrooms does it have? How many bedrooms? What's the quality of the architecture? Is the house in good shape? Is it in a safe neighborhood? Are there good schools near by? All of those have a contribution to the value. The house may be, for example, offered for sale and someone offers a hundred thousand, they reach an agreement. But now the question is how is that hundred thousand decomposed or apportioned among all of the various qualities and attributes.

We're doing the same thing here with regard to Adynovate. What I have done is looked at all the literature that was available that went out and surveyed patients and parents of patients evaluating what was their value. What value, what willingness to pay did they have for the different components of Adynovate, just like the analogy to a house.

Here what I have done by evaluating all this literature is discovered that first, dosing frequency which is the extended half-life that is provided by the '520 patent, that represents 20 percent of the value.

But there are other attributes and characteristics that must be assessed as well. These others are listed here. Is it slightly more effective? That gets

a weight of 18 percent. A very important weight in the minds of these patients and their parents is how safe -- how much safety exist with regard to the administration of the therapy. Does it have a low risk of inhibitors? That's given a value, a relative value of 40 percent. The manufacturer's identity is also important. That's 14 percent. The number of vials that one has to use each time you would administer the therapy is six percent. The volume of the fluid that is injected is estimated to be in the neighborhood of two percent.

What this all means as I have noted at the bottom of this particular slide is that the extended half-life has no more than 20 percent of the value of Adynovate.

Q. Dr. Rausser, do these facts tell us the value of the Pan patent or just the value of achieving extended half-life?

A. These tell us with regard to the Pan patent what is its potential upper bound with regard to its relative contribution, which as I indicated is 20 percent.

Q. Did you try to identify differences between the Pan patent and Baxalta's Bossard patent that was issued years earlier?

A. Yes. This is critically important, because we are directed in making this assessment of the hypothetical

negotiation and recognizing all the Georgia-Pacific factors, we have to look at the patented features, which in this instance is the Pan patent or the '520, plus all other contributions to value. And I have listed here even though we made the actually administering this particular therapy twice a week, and I noted that on the calendar on the left of the chart, but on the right, we have to recognize that there are a number of non-patented features that must be recognized and valued as well. And that includes what you heard about this morning, the Bossard patent, the Nektar special PEGylation R & D that was conducted. The actual commercialization that took place by Baxalta. The Nektar know-how. And then, of course, finally the patent, the Pan patent at issue.

Q. Thank you, Dr. Rausser.

Do you recall Dr. Addanki testified Wednesday about an analysis where he said the following: "But even if Baxalta's damages expert is right that only ten percent is infringing, every single vial has infringing product in it so every single vial that Baxalta makes and sells is practicing the '520 patent. It would be wrong to say that you could take out 90 percent of the value that Baxalta is getting because there is no way for Baxalta to be able to separate out the 90 percent that isn't infringing and sell it separately. It's all in the same vial."

Do you recall that?

A. I do.

Q. What opinion do you have with respect to that?

A. It's false. Quite simply, you're required to make a separation between the patented features and the non-patented features with regard to the value that's created.

And what I know here on this next slide is I have looked at claim 1 of the underlying '520 patent, and you've heard a lot about claim 1. And the other claims, it's my understanding that claim 9 has been deleted from this.

MS. FUKUDA: Objection, Your Honor.

THE COURT: So claim 9 is not an issue, so don't talk about it.

THE WITNESS: Fine. Thank you.

And what I have highlighted here is the key point about the sequence ID number four which basically you've heard this morning from the scientific expert that that particular sequence is critical in terms of the volume of material that is used to manufacture Adynovate. And that only ten percent of that vial is, in fact, sequence ID number four.

Q. Dr. Rausser, what else would objectively have influenced the parties' view about the value of the Pan

patent?

A. Yes. The other facts are critically important. And here there is a very sharp distinction from what you heard from Adynovate versus what you're going to hear from me.

Both parties when they sit down to negotiation, they're going to be concerned not only about the net sales that are being generated and the costs that are incurred, the manufacturing costs which is the only cost if you remember, the cost of goods sold. That's the only cost that Dr. Addanki examined. The only cost.

But there are other costs that are incurred, and those costs generate market value. They're critically important to try to increase what would otherwise be the royalty base.

And both parties being negotiators would be aware of all those costs and how important they are in causing increased sales, net sales.

For example, I have got here Bayer would be concerned about the royalties that were being paid by Baxalta, and it turns out Baxalta because of some of this prior non-patented issues with regard to our evaluation of the hypothetical negotiation, that some of that information, for example, the '223 patent that you heard about this morning, there is four percent that has to be paid from Baxalta to Nektar for that intellectual property.

In addition, medical affairs, promotions, we heard Dr. Addanki said, Gee, when I see it's a one-shot promotion, it shouldn't count. But if that one-shot promotion conferences actually having formal presentations to patients and prescribing doctors, all of those costs have the potential to increase the net sales.

Q. Dr. Rausser, turn now to, please --

A. May I -- may I come back to this slide for one second --

Q. Sure.

A. -- please? Now, why is this so important? In this hypothetical negotiation, you have to have incentive compatibility. That is to say, both parties benefit from the net sales increasing. You have to incur other costs aside from the manufacturing costs to increase those sales.

Bayer wants to see those sales much larger, and so does, of course, Baxalta. That's a common interest the two have.

And to achieve incentive compatibility, you have to recognize all these other costs, in addition to manufacturing costs. As a result, Dr. Addanki's analysis doesn't satisfy the fundamental principle of incentive compatibility.

Q. Turning now, Dr. Rausser, to what do you believe could have endangered Adynovate's future.

A. Yes. Here's another analysis that we have to worry about, how might the cost change in the future? If I set a very high reasonable royalty, it may turn out that there are costs that will take place in the future that's going to change dramatically whether or not that reasonable royalty is going to keep both of the two parties satisfied with their agreement.

With regard to the future -- may I back up, please?

Q. Sorry. I'm getting ahead of you.

A. Yes. With regard to the future, this is already on the market, a very dramatic therapy that's referred to as Hemlibra. And this is a therapy that's not administered twice a week or the standard three times a week, but instead, once a week. And moreover, you don't have to inject through a blood vein. You can do it beneath the skin.

That is a dominant new therapy that's going to change the cost structure of Baxalta in their attempt to capture value in the marketplace with regard to Adynovate. Why? Because their cost is going to go up with regard to marketing sales, offering rebates to third-party insurance companies to be able to more effectively compete with this new drug.

In addition, there are other developments coming

down the road which both parties would be well aware of in their negotiation.

Q. Dr. Rausser, turning to the maximum portion of Adynovate value for the Pan patent. What is your conclusion?

A. My conclusion, as this chart suggests, is two percent. How do I get there? We've already established that the dosing frequency has a relative value of 20 percent. In addition, because of the materials that are directly sourced with the Pan patent or the '52 patent is only ten percent. As a result, a maximum portion of the Adynovate value is the multiplication of the two which is nothing more than two percent.

Now, the next step is to look at the Georgia-Pacific factors and ask ourselves: What role do they play in setting what would be a reasonable royalty rate? Start at the top of this chart, and you'll see the two percent which I just explained in the prior chart. That two percent is a result of apportionment.

How do I go about dividing up what is the relative value of the '52 patent versus all of the non-patented developments that have taken place prior to the issuance of the '52 patent. And those Georgia-Pacific factors that I've listed up there, nine, ten, 11 and 13 all go to apportionment.

Now, we heard Dr. Addanki say that he looked at the Georgia-Pacific factors. He did not, however, look at those four factors with regard to their critical role in setting an apportionment analysis.

Q. Dr. Rausser, having reviewed the factors that are set forth on the slide, factors six and eight, five and six, six and eight, five, are you counting them double here? Can you explain that?

A. No, because they're different issues that come under the umbrella of each one of those factors. For example, reduce costs, Baxalta costs, reduced profit. That is factor six and eight.

But the fact that Bayer itself doesn't have any other options for capturing value with regard to the '52 patent, they're not pursuing the commercialization of that. They've turned to Jivi and are not pursuing a commercialization of the '52 patent.

So what are the other opportunities for them to license the '52 patent? As I understand it, there are no other opportunities. So that's just a different causal reason -- explanation that comes under that factor.

Q. Okay. And what is your conclusion with respect to a reasonable royalty in this case?

A. Okay. I start with the two percent based on apportionment, and then I look at those factors with regard

to what their qualitative effect would be on my two percent running royalty. Each of them has the effect of reducing the amount of the royalty step by step.

And that leads me to the conclusion and the opinion that the reasonable royalty rate should be one percent.

Q. What royalties would be payable, Dr. Rausser? This is only if the patent is found valid and if the patent is found infringed; correct?

A. Correct.

Q. Okay. Have you come to a conclusion on this?

A. Yes, I did. And here it's a simple multiplication. You take the one percent. It's a running royalty. And if we look at the data on Adynovate, net sales by Baxalta from the point of the negotiation, and you've already -- it's already been explained a number of times during this trial, that that negotiation date is June 14th, 2016.

Taking that out to the last date of the data that's available to me, which is through the end of November 2018, I apply the one percent royalty rate. And I come to the conclusion that the amount of the royalty payments should amount to $8,748,361.

Q. Thank you, Dr. Rausser. Let's now turn to a different subject.

What did Dr. Addanki do wrong?

A. Yes. What I've done is provided an analysis of a sharp distinction between his analysis and mine. First, I start with all the Georgia-Pacific factors.

You're asked to analyze in the Georgia-Pacific factors what drives the demand for Adynovate. I gave you the decomposition, the relative values of all the characteristics and attributes of Adynovate. He didn't.

I identified the value of the patents to the extended half-life feature. I did. He didn't. He simply said Adynovate versus Advate is, in fact, all the '520 patent.

And looking at Bayer's lack of other options that I just briefly explained, I took that into account. He didn't even mention it.

With regard to the future market dynamics, particularly with Hemlibra coming out being -- already being launched on the marketplace, I took that into account. He didn't.

Evaluating Baxalta, surprisingly his testimony, he said Baxalta actually is already on the market. And as a result, they're more willing to pay a higher royalty. In contrast, if I'm Bayer, I want to license it to the leader in this field which is Baxalta. And that runs in the opposite direction. He, of course, didn't evaluate that.

Q. Dr. Rausser, you said Dr. Addanki incorrectly --

well, strike that. Do you have other criticisms of Dr. Addanki's method?

A. Yes, I do. First, he gives two opinions. One is what he refers to as his high point which is 42.4 percent. And in arriving at that point, he makes three major mistakes.

The first mistake is he uses gross profits, ignoring net profits. And as I've already explained, at the hypothetical negotiation, the two parties would be aware that it's in their collective interest to try to expand net sales. And that requires more in the way of sales and marketing effort.

Now, if he was sitting here, he'd say sales and marketing is a fixed cost. That is simply false because if I take my sales staff, even though I don't change the total number of salespeople, but I ask them to spend more time with Adynovate, instead of Advate, there's an opportunity cost of doing so. And that is the relevant economic cost.

And you have to take that into account. Think simply about when you go to a movie: What's the cost of going to the movie? Ticket price? Is that all it is?

Economists, in contrast to accountants, say, No, it's more than that. It's the opportunity foregone. You could have, instead of going to the movie, worked and then been compensated for that work. That's your real cost of

going to the movie or economic cost.

And as a result, he has eliminated that as a cost and misrepresented what the hypothetical negotiators would take into account given their desire to maintain incentive compatibility.

Secondly, on the switching analysis, he actually does what some economists do, they make assumptions which give them the conclusion they want. And that is not the scientific method within economics. You should, instead, simplify, quite obviously, make some assumption, but don't make the assumptions in such a way that they dictate the conclusion.

And then, finally, there is flawed statistical analysis in his assessment of market shares.

Q. Dr. Rausser, would you explain briefly the differences between gross profit and net profits and why Dr. Addanki was wrong to use gross profits?

A. Well, he's wrong because the two parties negotiating would have taken into account other costs that would result in increased net sales or increased royalty basis. What I've done here is looked at the Baxalta 2017 long-range plan, which you've heard about today, and I would have looked at it for the year 2008.

Now, he -- if you look at -- he looks at net product sales, and he looks at cost of goods sold. He stops

there. He goes no further than that.

However, the negotiators are going to be well aware of these other expenses. Royalty expense, four percent is being paid from Baxalta to Nektar. He neglects that, acts as if it doesn't exist or assumes that it's been included somehow in the cost of sales.

There's no evidence that anybody, to my knowledge, looking at this basic data would assume that it's embedded in the cost of sales. It's not. The sales and marketing, as I've already explained, are costs that generate a higher potential royalty base. And that, too, has to be taken into account.

Global medical affairs, research and development costs, he said, oh, it just -- if it just happens once and it's not reoccurring, you can't count it. That's false because if it has a direct causal relationship with sales that are generated, it has to be taken into account.

As a result, when we look at including these other costs, his gross profit margin for this data, he would represent the gross profit margin at 84 percent. That's blatantly wrong, okay, particularly in the context of the hypothetical negotiation. Instead, it would be -- may I see that?

I'm sorry. I don't have it memorized.

It's 62 percent. Thank you.

Q. Dr. Rausser, now, turning to his upper endpoint, and we can -- you can bring this into your discussion. Can you conclude how you've recalculated his 42.4 number to a different number, please?

A. Yes. What I've done is made adjustments for each of these mistakes. First with regard to gross profits and recognizing once you look at net profits, Adynovate is actually no more profitable. In fact, less profitable over the course of the history through November of '18 than Advate.

So 6.8 profit premium drops to zero. Moreover, with regard to the assumed switching where he made the assumption that it was constant, and it turns out not to be constant, that drops his 48.7 percent to 10.7 percent. And then his flawed statistical analysis of market shares also ends up being rejected.

And when we recompute his 42.4 percent and go through the simple arithmetic, we end up with 5.6 percent.

Q. All right. Dr. Rausser, turning to the other endpoint that Dr. Addanki proposed, it was 5.1 percent; correct?

A. Correct.

Q. And you have opinions with respect to mistakes associated with gross profits, inaccurate projections with respect to Kovaltry share and patient switching; correct?

A. Correct.

Q. And when you take that into account, can you explain how you arrived at a new calculation with respect to a final number as to the low end of Dr. Addanki's opinion?

A. Yes. First -- now, I would go to Bayer's data with regard to their costs because Kovaltry is their product. And he used a gross profit of 60.2 percent. When you take into account these other costs to get net profits, it turns out that that's only 28 percent.

Secondly, with regard to Kovaltry's share, he took two projections that were made first by Bayer and secondly by Baxalta, and they're widely different. But he averaged the two, and he gets 17.5 percent.

However, the negotiations, remember, were in June. Kovaltry came onto the market three months before that. There was already evidence about what kind of share Kovaltry was getting. When I say share, I should make it clear, it's the share of extended half-life products that are on the marketplace of which Kovaltry, he says, is one of those.

However, you heard from Dr. Young in testimony that he doesn't view Kovaltry as an extended half-life. And it turns out, if you look at the actual data, it's not. Its dosing frequency is 2.7 times per week, not two as Adynovate, or not three, obviously, as Advate.

Q. Dr. Rausser, am I correct that your conclusion with respect to the lower end of the range is 0.15 percent; correct?

A. Correct.

Q. And then looking at the last slide, does this summarize your opinions with respect to Dr. Addanki's estimated range and then your corrected estimate of his range?

A. It does.

Q. And could you just read the numbers into the record?

A. His numbers for his range is 5.1 percent to 42.4 percent. And once they're corrected, the range instead is from 0.15 percent up to 5.6 percent.

Q. Thank you, Dr. Rausser.

MR. FLEMING: Pass the witness.

THE COURT: All right. So members of the jury, I think we should take our lunch break now. I believe that, in fact, we will just have one session after lunch. It may last close to two hours, but then I'll let you go.

So let's take 45 minutes for lunch and be back here at quarter of 2:00. And then we'll get through the end of the testimony.

Can we take the jury out?

THE CLERK: All rise.

(Jury leaving the courtroom.)

THE COURT: All right. So see you at 1:45.

MR. FLEMING: Thank you, Your Honor.

(Luncheon recess was taken.)

THE COURT: All right. Are we ready to go?

MS. FUKUDA: Yes, Your Honor.

THE COURT: Dr. Rausser, wherever you are, come on up. Let's get the jurors.

Have you talked to each other about how long you want for closing arguments?

MR. HAUG: No, we haven't.

THE COURT: When you have an opportunity, why don't you see what each other thinks. I probably have my own ideas, but I will hear first what you all think. Okay?

MR. HAUG: We will definitely finish on Monday.

THE COURT: Good one. So the aim here is to go straight through without a break until we're finished. Right?

MS. FUKUDA: Absolutely.

MR. FLEMING: Yes, Your Honor.

(Jury entering the courtroom at 1:50 p.m.)

THE COURT: And you all know how much time you have left? Okay.

All right, members of the jury. Welcome back. Everyone, you may be seated. Ms. Fukuda, you may continue, or start.

MS. FUKUDA: Thank you, Your Honor.

CROSS- EXAMINATION

BY MS. FUKUDA:

Q. Dr. Rausser, I'm Ching-Lee Fukuda, counsel for Bayer, meeting you in person.

Now, you would agree that for purposes of your analysis, the only material difference between Adynovate and Advate is the extended half-life?

A. Yes.

Q. And at the hypothetical negotiation, both parties would view Bayer's '520 patent to be valid?

A. That's the assumption that's required.

Q. And with regard to the validity of the '520 patent, it is also presumed that PEGylation at the B-Domain does, in fact, extend the half-life of Adynovate; right?

A. That's the assumption.

Q. Now, you would also agree that at the hypothetical negotiation, Bayer would be motivated to maximize the royalties that it would earn from the result of that negotiation?

A. Not entirely. It's in their self interest to have the largest net sales possible. But moreover, it's in their interest to make sure that all opportunities in terms of costs that are incurred to expand that base. So it's not just maximizing the royalty, reasonable royalty rate, but

the royalty base.

Q. Could we take a look at your deposition. It should be in your binder, page 77.

A. 77.

Q. Thank you. And lines one to five, please. And we'll pull that up for you on the screen as well. And you agree this is your sworn testimony in the deposition? And the a question is:

"Question: And Bayer would be motivated to maximize royalties earned from the hypothetical negotiation?

"Answer: From the cooperative solution, yes."

You were asked that question and you gave that answer?

A. I did give the answer. But let's clarify. There is a pathway to the cooperative solution and you have to take into account not only the ultimate outcome, namely the cooperative solution, but the path that you cover in your negotiation before you get there.

Q. Well, thank you. You can pull that down.

Now, you would also agree that Bayer can make the threat that they can assert the '520 patent and keep Adynovate off the market at the hypothetical negotiation; correct?

A. Under the assumption, yes.

Q. And that also is consistent with your opinion that it

would not have been economically feasible for Baxalta to redesign Adynovate in any significant way to avoid infringement on the date of the hypothetical negotiation; correct?

A. To redesign within a day, is that your question?

Q. On the date of the hypothetical negotiation.

A. Yes.

Q. Your answer is yes?

A. Yes.

Q. And because all Adynovate vials have infringing conjugates, Bayer would have a threat point to prevent Baxalta to continue to market all vials; correct?

A. That would be one threat point.

Q. And if Baxalta were to say I don't want to do this deal, I'm going to engage in a holdup and walkaway, that would force Adynovate off the market?

A. Would it? Under the assumption that the patent is valid and infringed, yes.

Q. And that would have harmed Baxalta's reputation in the marketplace to do that?

A. It certainly wouldn't have helped. But the question of harm is -- turns on whether they were effective given their reputation with regard to Advate and Recombinate. What additional investment they would have to make to protect their reputation.

Q. Dr. Rausser, could we pull up your deposition, page 266, lines 18 through -- page 266, starting line 18 going through 267, line 1. And this is your testimony.

"Question: If Baxalta were to engage in a holdup and a walkaway, that would force Adynovate off the market in the context of the hypothetical negotiation; isn't that correct?

"Answer: As -- as presumed by the hypothetical negotiation, yes.

"Question: Couldn't that harm its reputation in the marketplace?

"Answer: Yes."

Were you asked those questions and did up give those answers?

A. I did.

Q. You can pull that down.

Now, you would also agree that in Baxalta's view, Adynovate is a business critical product, wouldn't you?

A. In whose view?

Q. In Baxalta's view.

A. That it's a critical --

Q. I'll repeat the question for you. You would agree that in Baxalta's view, Adynovate is a business critical product?

A. It is certainly an important business product. How are you defining critical?

Q. Let's take a look at your deposition. Can we pull up page 134, starting with line 24. And let's go to 135, line 4. At your deposition:

"Question: So do you agree Adynovate is a business critical product for Baxalta?

"Answer: Certainly that was their view, yes."

Were you asked that question and did you give that answer?

A. I was asked the question, I did give that answer.

Q. Thank you.

Now, if -- well, let me put it this way. And you have also seen Baxalta documents from 2016 that say that it has committed to the rise of the EHL as a commercial strategy to move patients to Adynovate, didn't you?

A. A strategic document, yes.

Q. And this commitment that Baxalta had to providing EHL or extended half-life product was done to ensure that it protects its brand against market share erosion; isn't that right?

A. There is language that they use their strategic documents, and that's all part of their messaging to themselves and the rest of the world, yes.

Q. Thank you.

And you have also seen Baxalta documents from 2016 that say that there is an unprecedented level of competition that threatens Shire's hemophilia leadership position, didn't you?

A. Now you're moving to Shire instead of Baxalta, but they're one in the same. Yes, they are concerned about the launch of Hemlibra and other technologies that are likely to become available in the near future.

Q. Let's take a look at that document. Could we pull up PTX 617. Do you remember seeing this document?

A. Yes.

Q. And that's dated September 15, 2016?

A. Yes.

Q. And that's about three months after the hypothetical negotiation?

A. Yes.

Q. And this is a Baxalta -- let me address one point you made. You understand that Shire owns Baxalta?

A. Yes.

Q. So this is a Shire/Baxalta business plan for 2017; is that right?

A. Yes.

Q. Let's turn to page two. This document, if we look at that first sub bullet, and here, Shire/Baxalta is saying maintain our 65 percent market share for recombinant Factor

VIII and defend against new competitors in the market with the launch of our EHL Adynovate and continued strength and resilience of base rFactor VIII business. That's one thing that you saw in the document; right?

A. Yes.

Q. Let's move to that second sub-bullet. In the same document, Shire/Baxalta says take leadership position in EHL category with Adynovate. That's what that says, too; right?

A. That's what it says.

Q. Let's go to the last section. And the heading says defending against competitive pressures. And there it says, "Unprecedented level of competition threatens Shire hemophilia leadership position. Continued competitive pressure in rFactor VIII with Eloctate's presence and Kovaltry expected to gain patients in 2017, the competitive landscape remains challenge." You agree that that was Shire/Baxalta's view at the time of this document?

A. At the time of the document, but certainly as factual evidence emerged, they wouldn't have that view of Kovaltry a year later.

Q. Let's focus on September of 2016 here right now. And the Kovaltry product right there, that's the Bayer product that we have been talking about; correct?

A. Yes, which isn't actually extended half-life.

Q. But in this document, Baxalta and Shire point to the

fact that Kovaltry is expected to gain patients in 2017; correct?

A. That's what it says.

Q. And the conclusion by Baxalta and Shire is that defending our share will be imperative. Those are the words they used; isn't that right?

A. Yes.

Q. Now, if we could pull up your demonstrative, DDX 12.22.

Thank you. Okay.

This was how you conducted a portion of your apportionment analysis; right?

A. No. That's not quite right, but go ahead.

Q. Okay. Well, let's take a step at a time.

First, on the left, you assigned 20 percent of Adynovate's value to the extended half-life feature; right?

A. Correct.

Q. And you did that by assessing the value that it would have to patients?

A. Yes.

Q. Based on a number of articles --

A. Yes.

Q. -- that talk about surveys and things; right?

A. Yes.

Q. These articles are not talking about the value of EHL

to Shire and Baxalta, are they?
A. No. They're talking about the value to patients --
Q. Okay.
A. -- and what the patients' views are about value relative to other values embedded in the therapy.
Q. Okay. I understand.
But those surveys and articles don't talk about the profit that Baxalta is making from selling Adynovate, do they?
A. No. In fact, under the Georgia-Pacific factors, you're asked to evaluate what the consumers source of demand, or willingness to pay, or their preferences for therapy, not the profits of Baxalta or Bayer.
Q. Well --
A. You're asked to look at the demand side of the market.
Q. Well, in fact, as one of the Georgia-Pacific factors to consider, the realizable profit from practice of a patented feature; correct?
A. Yes. That's one of the 15 factors.
Q. Okay. Thank you.
Now, from that 20 percent in that middle column, you say of that 20 percent, right, now, you take it -- you remember the vial that you relied on?
A. Yes.

Q. And that's a vial of Adynovate that you're depicting there?
A. Yes.
Q. And you see how you have a ten percent at the bottom?
A. Yes.
Q. And you say that you rely on Dr. Zalipsky to give your opinion; right? You're not qualified to formulate any opinions?
A. That's correct. I'm relying on his opinion with respect to the volume, only representing ten percent that is attributable to the '520 patent. Yes.
Q. So is it your testimony today that Dr. Zalipsky has given an opinion that ten percent of an Adynovate vial infringes the '520 patent?
A. That's my understanding, yes.
Q. Now, were you in the courtroom when Dr. Ravetch testified about this?
A. I may have been, but I wasn't there for the full testimony. No.
Q. Okay. Are you aware of Dr. Ravetch's testimony on this point?
A. I am not completely. No.
Q. You're not. So would you be surprised if I tell you that Dr. Ravetch testified that the SEQ ID No: 4 limitation, which is what you're talking about here, is met

by Adynovate?
A. Would that surprise me? Since I haven't heard his testimony or read his deposition or his report, it wouldn't surprise me or not surprise me.
Q. If Dr. Zalipsky's noninfringement opinion about SEQ ID No: 4 for 90 percent of it, right, is wrong, then your apportionment down to two percent, also, is wrong?
A. Certainly if the ten percent turns out to be 20 percent, it would change my arithmetic. That's all. If it turned out to be 30 percent instead of ten percent, it would change the arithmetic, but the fundamental logic remains the same.
Q. Okay. Now, do you remember when Adynovate launched in the U.S.?
A. Yes, November 30th, 2015.
Q. That's when it was approved; right? So the launch was maybe late November, early --
A. You said when Adynovate was launched in the U.S.?
Q. Okay. Close enough. Let's go with that.
A. Close enough? I don't think it's close enough. I think that's precisely correct.
Q. I'm just saying that the approved first and then the launched probably happened within a short time of each other?
A. It did.

Q. Now, the hypothetical negotiation here is in June of 2016; correct?
A. Correct.
Q. And so that's about, say, seven months later?
A. A little less than seven months, yes.
Q. Okay. Thank you.
Now, as of the hypothetical negotiation, wouldn't you agree that almost all of the R & D costs associated with making Adynovate has already been paid for?
A. What do you mean "almost all"?
Q. Well, in order to do research and development and invest, you would have put money to lead to the launch of the project; right?
A. That's right.
Q. All that money has been paid for as of the hypothetical negotiation date; correct?
A. Yes. In fact, you can be more precise than that. It would be some cost at that point.
Q. Right.
A. But look at the financials, R and D expenditures continue going forward. Why? Because Baxalta is attempting to expand the market for Adynovate by improving its indications for particular segments of the patient population that's ongoing R and D.
Q. Okay.

A. So.
Q. But as -- my apologies. As of the date of the June 2016 hypothetical negotiation, whatever money Baxalta had already paid for for Adynovate, that's in the past. So even if Baxalta says, I'm not doing this deal, I'm walking away, they'll never get that money back; isn't that right?
A. The money that's gone before, but not the ongoing expenditures --
Q. Okay.
A. -- even though they may be lumped in after the hypothetical negotiations going forward in time.
MR. DE: Thank you, Dr. Rausser. I have no further questions.
THE COURT: All right. Any redirect, Mr. Fleming?
MR. FLEMING: Just one question, Your Honor.
BY MR. FLEMING:
Q. Dr. Rausser on direct or cross, you were asked some questions if Baxalta's reputation would be harmed if Adynovate was pulled off the market. Do you recall that?
A. I do.
Q. Can you tell me, do you have an opinion as to what Bayer's reputation would be if the Adynovate was forced off the market and how hemophilia patients would feel about that?

A. Well, they would certainly -- patients that are on Adynovate would be very upset about it, but Bayer's already moved away from the '520 patent with regard to their Jivi patent.

MR. FLEMING: Thank you, Your Honor.

THE COURT: All right. Dr. Rausser, you may step down. Watch your step.

THE WITNESS: Leave this here?

THE COURT: Leave it here. Somebody else will get it.

THE COURT: Mr. Haug.

MR. HAUG: Defendants have no further witnesses, so we rest our case, subject only to looking for exhibits that we may want to be admitted.

THE COURT: All right. Thank you.

Mr. Badke.

MR. BADKE: Yeah. We have that legal issue. Should we defer it?

THE COURT: Consider it to be taken up later.

MR. BADKE: Okay. Your Honor, there's one document that I'm told I forgot to move into evidence. It's the BLA application, the PTX 6. I thought I moved it in, but it's not on the list.

MR. HAUG: I don't think we object to that document, but that's what I was saying. I've spoken to

counsel, and we agreed we would go through all the exhibits to make sure we have them all on both sides.

THE COURT: Well, you all can do that later.

MR. BADKE: Sorry.

THE COURT: That's all right.

MS. DE: Good afternoon, Your Honor. Good afternoon, everyone.

Plaintiff calls Dr. Alan Russell.

THE CLERK: Please state and spell your full name for the record.

THE WITNESS: Alan James Russell. A-L-A-N J-A-M-E-S R-U-S-S-E-L-L.

THE CLERK: Do you affirm that the testimony you are about to give to the Court and the jury in the case now pending will be the truth, the whole truth, and nothing but the truth, you do so affirm?

THE WITNESS: I do.

THE CLERK: Thank you. You may be seated.

THE COURT: Can you get the left over volumes, the ones that are not relevant? Thank you.

DIRECT EXAMINATION

BY MS. DE:

Q. Can you please introduce yourself to the Court and the jury?

A. My name is Alan Russell.

Q. What do you do for a living?
A. I'm a professor at Carnegie Mellon University in the department of chemical engineering.
Q. What's your title?
A. I'm the high mark distinguished career professor.
Q. What do you do in that role?
A. In that role, I run a research group. I perform research and lead and coordinate the research of others.
Q. What's your area of research?
A. I work in the area of protein engineering. We're interested in how to make proteins better than what they do, and particularly using polymers.
Q. What degrees do you hold?
A. I hold a bachelor of science degree from the University of Manchester Institute of Science and Technology, and a Ph.D. from the Imperial College of Science and Technology in London.
Q. When did you earn your Ph.D.?
A. 1987.
Q. Did you do a fellowship after that?
A. I did. NATO offered me a fellowship. I came to the United States and spent two years at MIT.
Q. What did you do between your fellowship and joining Carnegie Mellon in 2012?
A. I spent about 20 years at the University of

Pittsburgh where I joined the department of chemical engineering as an assistant professor. Rose eventually to the chairmanship of that department, and then was the director of a research institute for ten years or so at that university.

Q. Have you done work doing PEGylation?

A. I have.

Q. Since when?

A. Probably since the late 1980s.

Q. And what kind of work have you done with PEG?

A. Again, we're just interested in how to make proteins better or what they do. So we pick problems that are important to society and try and solve them by using PEG and other polymers together with proteins.

Q. Do you have any stake in the outcome of this case?

A. I do not.

Q. Have you published on your research in peer-reviewed journals?

A. I've published about 200 papers.

Q. Do any of your publications touch on PEGylation work?

A. They do. Many of them.

Q. Can you give us one or two examples of honors or awards that you received for your work?

A. I was awarded the Greatest Invention Award from the United States Army. I was awarded a Lifetime Achievements

Award from the Tissue Engineering and Regenerative Medicine International Society. I could go on.

Q. What was the invention that was recognized by the U.S. Army?

A. We used polymers, PEG, and proteins in order to develop sensors and decontamination systems that would protect soldiers from were chemical weapons and nerve agents.

Q. Can you please turn in your binder to PTX 1132?

A. I would be delighted to, if I had a binder.

MS. DE: May I approach, Your Honor?

THE COURT: Sure.

BY MS. DE:

Q. Once you get there, it's 1132.

A. Yes.

Q. Can you tell us what this is?

A. This is my resume.

MS. DE: Plaintiffs move PTX 1132 into evidence?

MR. CHEN: No objection, Your Honor.

THE COURT: Admitted without objection.

(Exhibit PTX 1132 was admitted into evidence.)

MS. DE: Bayer offers Dr. Russell as an expert in protein modification, including PEGylation.

MR. CHEN: No objection.

THE COURT: All right. You may proceed.

MS. DE: Thank you, Your Honor.

BY MS. DE:

Q. Can I get PDX 8.3? Next one.

Dr. Russell, what documents did you review for this case?

A. I was able to review the patent, the Bossard patent, the documents on Nektar's work that was done for Bayer, and the FDA documents that were submitted by Baxter for Adynovate.

MR. CHEN: Your Honor, should we side-bar or not? It relates to our earlier discussion.

THE COURT: So hold your fire.

MR. CHEN: Sure.

MS. DE: We can take that down.

BY MS. DE:

Q. Did you understand that the claimed conjugates in the Bayer '520 patent, are those where conjugation is not random? Have you heard that in the courtroom?

A. I did.

Q. Okay. What do you understand not random to mean in this context?

A. The context that I used in thinking about it was that not random meant the PEG was accumulating in the B-Domain.

Q. I'd like to direct your attention to DTX 6 which is the Bossard patent.

A. Yes.

MR. CHEN: Your Honor.

THE COURT: So, Ms. De, are we getting to the thing that has been called for?

MS. DE: No. We're getting to Example 7 and what the reaction condition is that Dr. Zalipsky talked about on validity.

THE COURT: Okay. Wait. I'm sorry.

Can you come over to side-bar?

MS. DE: Sure.

THE COURT: I'm sorry. Did you say we're going to Dr. Zalipsky's validity opinion relating to --

MS. DE: So I'm sorry. So Dr. Zalipsky with respect to his validity opinions, he talked about the Bossard patent and how Example 7 has cysteine PEGylation and somehow that is, you know, antic -- makes the Bayer patent claims obvious. He relied on that. That was the example he showed in his slides.

THE COURT: But I thought he was -- oh, wait. I'm sorry. So we've got both non-infringement and invalidity?

MS. DE: Yes, sir. Yes, sir.

THE COURT: Sorry.

MS. DE: That's correct. He's going to do a little -- he's just going to talk through those PEGylation

reactions.

THE COURT: What is your reaction, Mr. Chen?

MR. CHEN: I don't think this is in the scope of his report because his invalidity rebuttal was responding to that '01 Commumique that we've been talking about where we were relying on Adynovate.

THE COURT: That seems to be out of the case.

MS. DE: He did the analysis of the Bossard example in both of his reports. He has an invalidity report as well as noninfringement.

He analyzed the Bossard example. This is the guy to be able to explain the PEGylation reaction, and he's going to do the same thing for the Nektar work. And then we'll move on to the one thing that we talked about this morning.

THE COURT: I'm not worried. I thought that's what Mr. Chen was objecting to.

MS. DE: Sorry, Your Honor.

THE COURT: You don't need to be sorry.

So if he's analyzed the Bossard, whatever he analyzed in the obviousness section or the anticipation section, if it's kind of relevant to whether or not the patent is obvious, I'm going to let it in.

MS. DE: Thank you, Your Honor.

MR. CHEN: But my objection, though, would be if

he's comparing it to Adynovate --

MS. DE: He's not. He's not. He's just going to the work itself that's in the prior art, Your Honor.

(Conclusion of conference held at side-bar.)

BY MS. DE:

Q. Okay. We were on DTX-6, the Bossard patent, example 7. And do you recall Dr. Zalipsky talking about this example, Dr. Russell?

A. I do.

Q. This was a cysteine conjugation; is that right?

A. That's right, yes.

Q. I direct your attention to the -- before we get into this, at high level how would you characterize this PEGylation reaction?

A. I would characterize this as a random PEGylation.

Q. I direct your attention to the reference to four millimolar cysteine -- I'm sorry, four millimolar calcium at line 40. How does that factor in to this reaction?

A. So, the calcium could be there for a number of different reasons, but I just remind everybody that in all of the examples in the Bossard patent, the protein that's being used is the B-Domain deleted version of Factor VIII. So you'll remember when Dr. Ploegh talked about the basketball and putting out the arm of the B-Domain, that isn't happening here. So I can't tell you exactly what the

calcium is doing here, but it's not doing anything to the B-Domain because there is no B-Domain.

Q. I would like to direct your attention to line 51 in that column. And there is a reference to 100 to 1. Do you see that ratio?

A. I do.

Q. What's that telling us?

A. What that's telling us is there is a hundred times more PEG than there is protein. So for each molecule of protein there is a hundred molecules of PEG at the end of the process.

Q. What's the reaction time here?

A. That's a little hard to define precisely from the way it's written. The first part of the reaction is to add the PEG once, they then wait for 30 minutes, then they cool that down. Then over a period of hours, we don't know how long in between each they add PEG, another four times, and then they leave it overnight, so overnight can be a number of different things. It could be six hours. It could be maybe 15 hours. So the exact reaction time I can't tell you, but it's at least let's say 10 to 15 hours.

Q. How did these factors work into the overall reaction in your opinion?

A. So in my opinion, when up look at a set of reaction conditions like this, if you got a very long time to react

and if you have a large excess of PEG, PEG has the opportunity to get all sorts of different places and react to all sort of different places. This is sort of the epitome of setting up a reaction where you don't really mind where it's going, what you care about is whether it goes there and how much goes there.

Q. Did you look at the other examples in the Bossard patent?

A. I did.

Q. At a high level, how would you characterize them?

A. At a high level I characterize them as random as well.

Q. Did any of the Bossard examples analyze where PEG attached?

A. They did not.

Q. I would like to direct your attention to column 37 of the Bossard patent.

A. Yes.

Q. And specifically at the passage that starts at line 45.

A. Yes.

Q. What does this passage describe?

A. So this is a passage that at a very high level is explaining the strategy by which these conjugates would be analyzed. And in this those cases and those examples where

the conjugates were analyzed, which wasn't all of them, but it was in example 7, they did look at how much PEG attached.

Q. Is there anything in the Bossard patent that reflects the analysis that you did of the PEGylation reaction?

A. No, there is nothing in the Bossard patent that talks about what we're talking about is whether or not it accumulates on the B-Domain. So there is nothing in the Bossard patent about that. And there wouldn't be because there was no B-Domain in these proteins.

Q. Is there anything else in this passage that speaks to the PEGylation reaction?

A. So there is. A little bit further down it starts, for example, it says in an exemplary reaction where a 100,000 Dalton protein is randomly conjugated. When I read that, what that tells me when I look at the reaction conditions and the sense that they are random reaction conditions and then when I look here and see in this generic description reference to randomly conjugated proteins, that tells me that indeed these reactions are random.

Q. In the context of the work that you did on this case, were you also able to access PEGylation reaction details during the Nektar/Bayer work that Bayer did not have access to at that time?

A. I was.

Q. Can you please turn in your binder to PTX 1102. Let

me know if you recognize that?
A. I do.
Q. What is this?
A. This is an internal report. It says prepared for Bayer, but it's an internal report that was produced at Nektar describing the reactions that they did.
MS. DE: Plaintiffs move PTX 1102 into evidence.
MR. CHEN: I'm sorry. I missed that number.
MS. DE: PTX 1102. It's the internal Nektar report for Bayer.
MR. CHEN: No objection.
THE COURT: Admitted without objection.
(PTX-1102 was admitted into evidence.)
BY MS. DE:
Q. I would like to direct your attention to the PEGylation reaction that starts on page 42 of the exhibit. Can you tell us what amino acids that PEGylation reaction is working with?
A. So this is essentially the same PEG. It's a similar sort of nonselective PEG that's designed to react with cysteines. It's the same one that we were talking about before when we talked about example 7.
Q. There is a reference a few lines down to 2.5 millimolar calcium. Do you see that?
A. I do.

Q. What does that mean?
A. So in this case, the reaction is being performed with a full length Factor VIII that does have a B-Domain, but interestingly to me anyway the calcium concentration that was selected here was less than the calcium concentration that we talked about in example 7. So what that told me is it wasn't really in the mind of the people doing these reactions at that time to alter the structure, the very native structure of the protein in order to extend that arm like Dr. Ploegh described, and the concentration of calcium was just there probably for similar reasons as it was in the prior reaction.
Q. There is a reference in the line below that that says TCEP was added. Can you explain what that means?
A. That's a new reagent we haven't talked about yet that's a reductant. And you will have learned through the week that cysteines are coupled together, sometimes, and they're sort of hidden and not able to react. So in this case there has been an attempt to open up as many sites as possible by adding this reactant.
Q. A few lines below that there is a reference to 200-fold molar excess. Can you explain what that is?
A. You'll remember in example 7 it was a hundred times more PEG than protein. This time there is 200 times more PEG than protein.

Q. If you could expand that text so we can see both pages and the text that continues on to the following page. Can you let us know what the reaction time was in this example?

A. I can. So again, I can't tell you exactly, it has a references to overnights again. But essentially the PEG is added once, we see the same sort of structure of the way this reaction is performed here at Nektar. And in this case it's left for 30 minutes, then more and more additions over a period of time. And then it's left if I remember right for an entire day.

Q. Was there a quenching step?

A. There is no quenching step.

Q. Was the TCEP ever removed?

A. No.

Q. What happens then?

A. I think that's important. If one were to remove the TCEP, then those cysteines that are free might have an opportunity to become hidden again. So by leaving the TCEP in this reaction, it again tells me that when performing that reaction the main interest was simply in getting PEG to react wherever it could react without regard to where.

Q. And how would you characterize this reaction?

A. I would characterize this as built on the same foundation as example 7 and call it a random reaction.

Q. Did you review the other cysteine and lysine PEGylation reactions that Nektar did that were produced in this case?
A. I did.
Q. How would you characterize that?
A. I would also characterize them as random.
Q. Were you in court yesterday when Dr. Walensky testified?
A. I was.
Q. Can we get Walensky slide 30. And do you recall that Dr. Walensky showed us four separate peaks on that demonstrative?
A. I do.
Q. Is that an accurate depiction of the actual peak data?
A. It's not.
Q. I would like to have you turn in your binder to DTX 142.
A. Yes.
Q. Do you recognize this?
A. I do.
Q. What is this?
A. This is one of the documents that Baxalta submitted to the FDA in the process of getting Adynovate approved.
MS. DE: Plaintiffs offer DTX 142 into evidence.

MR. CHEN: No objection.

THE COURT: Admitted without objection.

(DTX 142 was admitted into evidence.)

BY MS. DE:

Q. I would like to direct your attention to page 35 of DTX 142. And figure 12 in particular. What does this show?

A. So I suppose this is some of the sort of dirty laundry of PEGylation. This shows the real data. It's not at all like the cartoon.

Q. Why is this important?

A. So what you see on the left of this figure are four peaks and the one that's labeled A, you see the four peaks. Peak 1 is the B domain and those are the four peaks from the native protein. What you see on the right is other peaks as well. And you see very importantly that the peaks all sort of mush into each other. And there are extra peaks and all sorts of other things in there and they need to be explained. And when you see a cartoon that looks very simple, perhaps one could get confused as to what the real data looks like.

Q. I would like to direct your attention -- before we go, are the peaks separate?

A. So here the peaks if you look at the top and just focus on the top, they look like separate peaks. If you look in the valleys between the peaks, you can see that it

isn't a flat line. So on the cartoon, you just saw four separate mountains and nothing connecting them. This looks like, much more like a mountain range where you got valleys in between that connect.

Q. What's in the valleys in between?

A. So in the valleys in between here are other peaks. And what we'll find I think in a moment as we look forward into the document is what might be hiding under there.

Q. I would like to direct your attention to page 31 of this exhibit. And in that paragraph you'll see a sentence that says, "Consequently, this leads to a reduced intensity for the B-Domain peak as the PEGylated B-Domain elutes in the range of nonPEGylated 73 kilodalton fragment, 50 kilodalton fragment and 43 kilodalton fragment. What does that mean?

A. It's not as complicated as it sounds. It does sound a little complicated. It's actually quite simple. What it means is the PEGylated B-Domain is missing. What it's actually saying is that fragment, the PEGylated B-Domain can't be seen when you try to do this particular analysis. It's basically hiding under the other peaks.

Q. I would like to direct your attention to page 32 of the exhibit, and direct your attention to the last sentence in that paragraph that says, "A quantitative comparison of relative areas for peaks one through four of nonPEGylated

and PEGylated Factor VIII shows especially a decrease in peak one for PEGylated batches as for both nonPEGylated and PEGylated peak one is the nonPEGylated B-Domain, these data suggest that B-Domain is a hot spot for PEGylation."

How is Baxalta interpreting this data in the context of Adynovate?

A. Yesterday Dr. Walensky showed you the very big binders full of all of this data and there are hundreds if not thousands of these. I think today Dr. Zalipsky shared with you that they spent two years and a great deal of money looking in great detail, and they were super up front with the FDA. They shared these data, they shared I wouldn't call them concerns, just facts about the real data with the FDA and they thought a lot about what -- how to interpret the data in the context of the real stuff. And what they say is very clear. What they say is that the non-Pegylated B-Domain these data suggest that B-Domain is a hot spot for PEGylation. So they looked at the exact same set of data and told the FDA that actually the PEG is in the B-Domain.

Q. I would like to direct your attention to page 33 of this exhibit. And there is a discussion there that talks about peak two separating into a peak for PEGylated B-Domain. Peak three and peak four. What's this describing?

A. So, what this describes is when they realize that the

important peak, because the FDA has said to them, you got to show us that you PEGylated the B-Domain, we heard that in testimony in the week, so they had to show that. So when the peak was missing, they did a clever trick, they said okay, we'll take each of the peaks that we see and we'll separate them out and we'll see what's hiding in each peak. This is very important because it goes back to Dr. Walensky's decisions that he made. They just looked at the peaks. So they took the peaks and they did more analysis. What they showed is that in that extra analysis, the B-Domain PEGylated material again hid, and it hid under each of the peaks.

Q. How does this impact Dr. Walensky's estimation of B-Domain PEGylation?

A. So what Baxalta did is when they looked at those peaks, because they collected the data, it was the right thing to do. They didn't collect the valleys, but they pointed out right here in these documents that the PEGylated B-Domain was hiding not just under the peaks, but under the valleys. So in other words, what that meant is that in Dr. Walensky's calculations, he's underestimating throughout how much PEGylated B-Domain there was.

Q. Can PEGylation at lysines be either random or non-random?

A. It can. And I know there has been a lot of

conflicting back and forth on this issue, but it absolutely can.

Q. And what determines whether you have random PEGylation as opposed to non-random PEGylation?

A. So the reaction conditions, the process steps, the decisions you make and what PEG you select, what protein you select, how you put them together, how long you leave them, how carefully you manipulate those conditions defines not just how much PEG goes into place, but as you have seen from this data that Baxalta presented to the FDA, where it goes.

Q. What is your conclusion as to the PEGylation reactions that were in the Bossard patent and in the Nektar work that was done for Bayer?

A. They are random.

MS. DE: Thank you, Dr. Russell. Pass the witness.

CROSS-EXAMINATION

BY MR. CHEN:

Q. Hi, Dr. Russell.

A. Hello.

Q. Nice to see you again.

A. It's a pleasure.

Q. You started off this direct examination by discussing how in your opinion the examples of the Bossard patent are random. Did I hear you correctly?

A. Yes.
Q. The Bossard is PEGylation with proteins; is that right?
A. Yes.
Q. Isn't it true that you believe that PEGylation reactions with proteins are not random in any way and have never been thought to be random by anyone?
A. That's not my definition.
Q. Did you not say that in your deposition?
A. I think I prefaced when I said it by saying it's not my definition.
Q. Did you say that in your deposition?
A. Like I just told you, I think I said given the definition you just gave me, which is not my definition, this would be what I would say. So no, it's not my definition.
Q. Did you say that statement in your deposition or would you like me to put it on the screen?
A. You're more than welcome to put it on the screen. I mean, I assume you will put the whole thing on the screen.
Q. Mr. Haug, can we put up the excerpt from Dr. Russell's deposition on page 99 starting on line 2.
MS. DE: Your Honor, this is incomplete. The question and the answer actually starts on page 98 at line 18 which is what the witness was testifying about. It makes

an improper impeachment.

THE COURT: Well, so put up, give it some context.

MR. CHEN: I'm trying to be efficient with my time. I apologize, Your Honor.

THE COURT: Yes.

BY MR. CHEN:

Q. Let's go back to page 96.

A. Might I actually see the deposition?

MR. CHEN: May I approach, Your Honor?

THE COURT: Sure.

BY MR. CHEN:

Q. Your deposition is the last tab in the binder, tab B. Mr. Haug, can you go back to page 96, line 24. I asked you the question:

"Question: With that knowledge in mind, how may PEGylation at lysines in a protein be random?"

You answered.

"Answer: So it would be better for me when you ask questions using the word random PEGylation or non-random PEGylation if you don't want to refer to reaction rates that you define whether you're using the term in the way the literature uses it or in the literal meaning of the word."

I then asked you:

"Question: I would ask you to answer the

question with whatever understanding you have of random, and you can explain that in your answer if you would like.

"Answer: I have explained my answer many times already in terms of what random reactions are between PEG and lysines. It means that the reaction rate is the same for every different lysine. So -- and it's not really my definition, it's just the meaning of the word random. The literature has confused the meaning of the term random, but always intended to refine what it meant. So the literature said that the word random if I was going to define it, I would say that it's not using a process in order to alter the consequences or capture a PEGylation reaction at a moment in time in order to drive PEG to a reasonable or another region. So random PEGylation would just throw PEG, throw the protein together and you get what you get.

"In answering the first part of the question -- I have already forgotten the last half of the question, but I have at least set it up.

"Question: I was actually using your definition of random.

"Answer: Okay.

"Question: Which I think means the reaction rate is the same for every lysine.

"Answer: Well, I -- so I am comfortable using either definition. I wouldn't call it my definition. It is

not -- the word random has a definition. We can look it up in the Oxford English dictionary or get the meaning of the word random. Here we are.

"PEGylation reactions with proteins are not random in any way and have never been thought to be random by anyone. It is probably the least controversial element of this entire case."

Did I read that correctly?

A. No. You changed the intonation pretty importantly at the key point.

Q. Did I read the words correctly without intonation?

A. The words, yes.

Q. Thank you.

Now, can we look at the Bossard '223 patent, example 7, please. This is the example 7 you were talking about; right?

A. Yes.

Q. At the bottom, they characterize the conjugate and you see it says mono pegylated product. Do you see that, mono PEGylated product, it's right there on the screen?

A. I do see that. Yes.

Q. Mono-PEG means one PEG?

A. Yes.

Q. You're telling the jury that means random PEGylation?

A. Well, if you look a little later, sometimes you click

these off, but if you look a little later on, Column 47 where it refers to Figure 4, which is what this section is also talking about, they're referring to the six percent Factor VIII PEG heimers (phonetic), I think, which means multiple PEGs.

Q. So multiple PEGs is random PEGylation?

A. It certainly can be. Yes.

Q. Okay. Multiple like two to three PEGs is random PEGylation?

A. Well, if I have two to three sites to PEGylate and I PEGylate all of them, yes, would I call that random.

Q. Now, you talked about the reason why you think Example 7 is random PEGylation. You referred to, I believe, the hundred to one PEG to Factor VIII ratio and overnight reaction conditions; is that right?

A. Well, I personally believe you have to look at everything. I don't think you can pick out one thing or another. So I think what I said was that it's actually the set of reaction conditions that are most important, not any individual one.

Q. The two parameters you highlighted were the PEG ratio a hundred to one and overnight; right?

A. Well, I didn't do the highlighting, but I responded to the questions that I was asked about those particular ones.

Q. Right. Those were the two particular ones you referenced; right?
A. Those were two particular ones that I was asked to talk about.
Q. Can I see Dr. Zalipsky's reply report? Did you ever look at Dr. Pan's notebook, the lead inventor on the '520 patent?
A. I've seen it. Yes.
Q. Do you know what ratio he used and what length of time for his reactions for the '520 Pan conjugates that are supposedly non-random?
MS. DE: Objection. This is beyond the scope of my direct, and now it sounds like it's beyond the scope of his opinions.
THE COURT: I'm going to allow it.
THE WITNESS: I would be more than happy to look and --
BY MR. CHEN:
Q. You've seen Dr. Zalipsky's report; right?
A. I've looked at Dr. Zalipsky's report. Right.
Q. So Dr. Zalipsky looked at Dr. Pan's notebook relating to the very figure that Dr. Pan talked about earlier in this case, and you were here for that; right?
A. Yes.
Q. Yeah. And so Dr. Pan, it turns out, used overnight

reaction time.

It also turns out that Dr. Pan used two different ratios of PEG, one of which was 368 to one. Do you see that?

A. I did.

Q. That doesn't change your opinions?

A. Well, first of all, I would actually like to see the notebook. I think these are calculations that were done using the notebook. But if we could have a quick look at the notebook, that would certainly help.

Q. You haven't done the calculation yourself?

A. I did not do the calculation.

Q. But you knew Dr. Zalipsky had this opinion?

A. I do know. Yes.

Q. So you didn't check yourself?

A. No, I didn't check.

Q. And so sitting here right now, you can't decide whether or not these reaction conditions are inconsistent with your opinion on the Bossard Example 7?

A. I think I've said consistently that it's the entirety of the set of reaction conditions that are important.

Q. Okay. Switching gears. You criticized Dr. Walensky's calculation on the peaks; right?

A. I'm not sure I'd use the term criticized. Scientists disagree. I wouldn't call it criticize, but I merely

provided a little more clarity perhaps on what the real data looks like.

Q. So I have to confess, I can't keep up with you and Dr. Walensky on the peaks.

A. I apologize.

Q. But I would like to ask you: You did not provide your own calculation; isn't that right?

A. No. I trusted Baxalta, so I -- you know, yes, I could have gone --

Q. But you did not?

A. -- and recalculated everything that Baxalta did in order to come up with an answer that would suit the context of this case. I just trusted what Baxalta did, what they presented to the FDA.

Q. Dr. Russell, yes or no, please: You did not provide your own calculation?

A. I think I said no and explained why.

Q. Thank you. Now, actually in your report, when you criticize -- sorry. When you disagree with Dr. Walensky's calculations, you actually said he should have considered a different type of analysis. Do you remember that?

A. Yeah.

Q. Right?

A. Actually, I don't remember specifically saying it, but if he was going to do calculations, the word accurately

predict and assess the concentrations that he saw, then yes, he would need to do a different kind of analysis.

Q. In fact, you said he should have considered an analysis called the Western Blot Analysis; isn't that right?

A. I think the discussion that we had is that I had seen Western Blot data or that contradicted maybe his conclusion.

Q. I didn't have a discussion with you. I'm just reading your report.

Didn't your report, when you disagree with Dr. Walensky's calculation, say that he should have considered a Western Blot Analysis?

A. I'd be happy to look at it. I don't know whether I'd use the word considered, but I'd be more than happy to consider.

Q. Let's look at Dr. Russell's Reply Report, please, Paragraph 39 on Page 21. Do you see that here, I'm sorry, disagreeing with Dr. Walensky's calculation --

A. Yes.

Q. And do you see highlighted in two places the Western Blot Analysis, and you say that -- let me see right before the first highlight. That data to analyze Adynovate should have been considered, the sentence starting "Given the problems. Do you see that?

A. I won't parse your words. I don't see where -- that I said he should have considered the Western Blot Analysis,

but I do see what you mean.

Q. Right. So you agree, right, that the Western Blot Analysis is a better approach for the answer to the question?

A. No. Actually, in the entirety of my report, what I talked about was that I felt like Dr. Walensky presented one set of facts. And what I tried to do is say, Look, there are lots of different facts. Most of them were presented to the FDA. All of them were interpreted by Baxalta to mean that there was a hot start in the B-Domain.

So it's searching to try and understand how you could take one little piece of the puzzle, and analyze it, and come up with a different answer. I was simply saying that there are other ways that you could do it.

Q. Okay. Let's look at those other ways, but let's just confirm: You said the Western Blot Analysis in the last sentence. You say, In my opinion, these data also support whatever your opinion is; right?

A. Yes.

Q. Okay. Let's look at the Western Blot Analysis.

Can I see DTX 48, please? This is an excerpt from the BLA.

Do you recognize this?

A. I don't recognize it specifically, but I'll take your word for it.

Q. I'm sorry. This is entitled the Western Blot Analysis; right?

A. Yes. Is there a place in the binder that I can find it?

Q. DTX 48, sir. Have you considered this document?

A. I'm happy to review it with you.

Q. Okay. Let's turn to the very last page where it says Discussion and Conclusion.

Did you consider the last sentence that says, "Using antibodies with different epitope specificities showed the apparent PEGylation of all domains, reflecting the random PEGylation of Factor VIII"? Did you consider that?

A. I don't recollect reading the specific sentence. No.

Q. Okay. Mr. Haug, can I see Dr. Walensky's reverse doctrine of equivalents slide?

Last question, Dr. Russell. Isn't it true that if someone were to ask you to non-randomly PEGylate Factor VIII that PEG NHS -- let me stop.

Back up a second. PEG NHS is a PEG type that targets lysines; right?

A. Correct.

Q. Okay. Isn't it true that if someone were to ask you to non-randomly PEGylate Factor VIII, that would be your first choice?

A. In my laboratory, with the kinds of proteins that I work with, that is the PEG of choice that we use and we -- we use both random and non-random PEGylation.

Q. That wasn't my question, sir. My question is: If someone were to ask you to non-randomly PEGylate Factor VIII, would PEG NHS be your first choice?

A. I think -- I think -- I'm sorry if I didn't answer it clearly, but I'll just say it again. In my laboratory, so me, if I was telling one of my students to non-randomly PEGylate something, we have spent the last two or three years learning how to do that with PEG NHS, and publishing papers to do so.

So, yes, I would probably tell them, Use what we've learned and go ahead and control the process.

Q. Right.

A. PEGylate the protein.

Q. So --

A. I -- so I think the answer is yes.

Q. So PEG NHS with targeted lysines with Adynovate on the right, right, those 55 sites?

A. The other amino acids as well as we've heard it targets.

Q. Right. Okay. And cysteines, as we know from the patent, the Pan patent, there are only four accessible cysteines in Factor VIII; right?

A. Maybe you mean three, or are you talking about just the B-Domain?

Q. In the B-Domain.

A. Okay.

Q. The Pan patent says there's only four accessible cysteines; right?

A. Sure.

Q. Okay. So you want the jury to believe that your first choice to non-randomly PEGylate Factor VIII would be the reagent on the right and not the left; is that what you're saying?

A. Well, you didn't ask me about Factor VIII. You said if I -- I believe you asked me what my preference would be, which PEG I would use. And in terms of Factor VIII, obviously, there are many, many lysines. But there's good news for me, I don't need to guess, and we don't need to guess.

This protein was non-randomly PEGylated by Baxalta. They managed to figure out how to do it. They reported throughout their documents that they sent to the FDA that they PEGylated the B-Domain. I don't have to guess.

So actually PEGylated NHS turns out is a very good choice to non-randomly PEGylate the protein.

MR. CHEN: No further questions, Your Honor.

THE COURT: All right. Redirect?

MS. DE: Shortly. Thank you, Your Honor.

REDIRECT EXAMINATION

BY MS. DE:

Q. Dr. Russell, you were asked about some different definitions of random that came up in the course of your deposition. Do you remember that?

A. I remember it well.

Q. Okay. Do different people use the word random to mean different things?

A. They do.

Q. Okay. And I'd like to direct your attention -- if you have your deposition testimony in front of you, you can go ahead and look at Page 98 and 99 to get the context of the answer that counsel was going to.

And you mentioned that there is something off with the intonation. Did you understand what random means in the context of this case from the Court's claim construction?

A. I did.

Q. And what did that mean?

MR. CHEN: Objection, Your Honor.

THE COURT: So I'm going to sustain the objection, but if you want to ask him what he meant by intonation, go ahead.

MS. DE: Sure.

BY MS. DE:

Q. Okay. Can you take a look at your answer from Page 98 to 99 and explain what the distinction is between the definition you're using here versus the definition that you were given to use in the context of this answer?

THE COURT: Overruled.

MR. CHEN: Okay. Thank you.

THE WITNESS: So we did go through a lot of back and forth, as you can imagine, about different definitions of the word random. And this is, of course, a very important part of the case.

At this point, I was simply asked, you know, to comment -- and we've been talking about two different definitions. I felt like Mr. Chen asked me about the one that wasn't mine. And actually earlier on in the document, I gave a very precise definition of my understanding of the meaning of random as it was in this case.

So I responded by saying, I'm comfortable using either definition, meaning I'm happy to talk about Mr. Chen's definition, or I'm happy to talk about mine. He had just given me his definition. He had said which I think means the random -- the reaction rate is the same for every lysine.

And what I was saying ineloquently -- it was my

first deposition -- was that everybody knows that every single lysine doesn't react at the same rate. And I said it is not my definition. And I don't know if there's an opportunity to share what my definition was, or if it doesn't matter.

Q. If you could just go to the top of Page 98 in that same passage, perhaps that can refresh your recollection.

THE COURT: Wait. Wait. What are you trying to refresh his recollection about? He seemed to answer the question just fine.

MS. DE: Okay. Then we're done with that.

Thank you very much, Dr. Russell.

THE COURT: All right. Dr. Russell, thank you very much. You may step down. Watch your step.

MR. BADKE: Bayer calls Dr. Jeffrey Ravetch.

BY MR. BADKE:

Q. Good afternoon, Dr. Ravetch.

A. Good afternoon, Mr. Badke.

MR. BADKE: Oh, Your Honor, can Ms. Bercier approach?

THE COURT: Of course.

MR. CHEN: While we're doing that, can I just do a housekeeping matter?

THE COURT: Sure.

MR. CHEN: I forgot to offer DTX 48 into

evidence. That's the Western Blot Analysis.

MR. BADKE: No objection.

THE COURT: All right. Admitted without objection.

(Exhibit DTX 48 was admitted into evidence.)

MR. CHEN: Thank you.

BY MR. BADKE:

Q. Dr. Ravetch, have you prepared a demonstrative that summarizes what you were asked to do with respect to validity in this case?

A. Yes, I was.

Q. Can we have DTX 9.2, please? Okay. So which issues did you analyze?

A. So I analyzed all the issues on this slide, but I believe we're now focusing on only some of them. So is this the current slide?

MR. CHEN: Your Honor.

MR. BADKE: Okay. Why don't you take that down.

BY MR. BADKE:

Q. Why don't you just tell the jury which issues you looked at?

A. Right. So I -- I was asked to offer opinions on whether the '520 patent was obvious in light of certain prior art references and certain work that was done at Nektar. I was asked to offer opinions on aspects of the

Nektar work that may be related to the question of whether the invention of the '520 is some way derived from that, and whether the '520 patent was enabled.

And you heard testimony from Dr. Zalipsky about what enablement means, whether one of skill in the art could practice the full scope of the invention without unduly experimentation.

Q. Could we have PDX 9.3 up there? Okay.

Dr. Ravetch, in forming your opinions on validity, what materials did you consider?

A. Well, of course, the '520 patent again. The expert opinions from the defendants' experts, the various prior art references that have been asserted by those experts, and various testimonies from fact witnesses.

Q. Okay. And what is your opinion?

A. Well, on obviousness, my opinion is that the '520 patent is not rendered obvious by the prior art references that have been presented, and the testimony of their experts, I think, does not meet the burden of providing clear and convincing evidence that the patent would have been obvious in light of the prior art.

I also reached the conclusion that enablement -- that the patent is enabled and that one of skill in the art with the knowledge of what skill in the art means, which we'll probably get to in a moment, would be able to practice

the invention over the complete scope.

Q. Did the Patent Office determination issuing the patent play a role in your opinion?

MR. CHEN: Objection, Your Honor.

THE COURT: Overruled.

THE WITNESS: So I think, as you've heard, when you apply for a patent, you submit to the Patent Office your application as well as supporting documentation of what you consider to be all relevant prior art. And the Patent Office does their own independent examination to find if there are other parts of prior art that might be relevant, and it's an ongoing process, and you often supplement with additional prior art that you then discover in the process of this sometimes drawn-out discussion with the Patent Office.

And the examiner will respond with various comments and questions, and you respond back. This give and take goes on until a point is reached where the examiner has been satisfied that all of the concerns about the patent's validity, for example, are met. And then the patent will be in a position to be issued, and they issue a Certificate of Allowance.

So, yes, some of the references that were presented were, in fact, before the examiner. And the examiner and multiple examiners, it turns out, were involved

in this discussion and came to the conclusion that the prior art references that were brought forward were not such that the patent was not valid, and they did not render it non-obvious. Obvious, excuse me.

Similarly, the patent was examined for enablement and it was found that the claims were enabled given the facts of the case.

Q. Dr. Ravetch, were you present when Dr. Zalipsky testified that the '520 patent would have been obvious over the Bossard patent, the Nektar, or for Bayer, a prior art reference by the name of Mosesson, and a prior art reference by the name of Gruppo?

A. Yes. I had heard all that testimony.

Q. Now, do you understand that a claim may be obvious only if there was a motivation to combine the prior art references to arrive at the claimed invention?

A. Yes. That's a very important component of the -- of the exercise.

Q. Okay. Could we have PDX 9.5 on the screen, please? Okay. From who's perspective is obviousness determined?

A. So it's from the perspective of POSA which stands for person of ordinary skill in the art, and it's a strange term. And it's an even stranger definition because a POSA is really a hypothetical individual. It's not one person. It's not me sitting here.

It is this hypothetical individual who has this collective knowledge of a field that is under consideration. In this case, a POSA would have the knowledge of clinical medicine related to Factor VIII, to blood coagulation, would have knowledge of protein structure and function to understand something about molecular biology because we have issues of making, you know, various kinds of constructs and expressing recombinant protein, would of course, have knowledge and expert familiarity with polymer chemistry and conjugation chemistry.

So all of these, you know, fields are combined within one of skill in the art, and that's a prospective you take. You say what would somebody with this global knowledge of this field have understood that could be done? Right.

And would that individual, collectively individual reading the prior art, for example, have said, Oh, this would have been obvious. We knew about all of this before, and we can combine these pieces and derive that particular invention.

Q. So you have up there hindsight with an "X". Can you explain what you mean by that?

A. Right. So you can use prior art, you can combine prior art if you were motivated to combine prior art, you use your common sense and your knowledge of the field, but

what you cannot do is use hindsight. You cannot use the patent as a roadmap to tell you what to select from the prior art to combine it. That's not permissible in the obviousness consideration.

Q. You heard again, you heard Dr. Zalipsky's analysis; correct?

A. Yes, I did.

Q. Did he apply hindsight in his analysis?

A. Yes, he did. I think he took the '520 patent and applied that as a roadmap to select those prior art references that could be combined to read on the patented invention, the patented claims.

Q. Now, looking at all the references that -- or why don't we put up PDX 9.6. Now, reading -- looking at all the references that Dr. Zalipsky testified about in his obviousness analysis, how would you characterize them?

A. Well, they fall into two categories. There is one category of references that relate to random PEGylation, like the Bossard patent that you just heard Dr. Russell testify about, like some of the Nektar work that was done under contract for Bayer. That's random PEGylation. The other collection of references are references that have nothing to do with PEGylation. They talk about the Factor VIII protein itself and various kinds of analyses that would go into the Factor VIII protein.

So what is being done then is to combine these two into an obviousness analysis that taking the random PEGylation and knowledge of Factor VIII protein, you would somehow get the claimed invention. And what's lacking, of course, besides the individual references not being appropriate, is that why would you combine these. Why would you think that this is a relevant combination to derive an invention that when I reviewed it struck me as being quite unexpected, given everything one of skill in the art knew about that field up until that time.

Q. I think I heard you say that the Bossard and Nektar would fall into the random category?

A. That's correct.

Q. Did you say that?

A. That's correct.

Q. Where would the Mosesson and Gruppo references fall?

A. Into the unPEGylated Factor VIII, full length Factor VIII category.

Q. Let's talk about the Bossard patent first, if we can, Dr. Ravetch. You heard Dr. Zalipsky rely on Bossard for his obviousness combination?

A. Yes.

Q. Was the Bossard patent before the U.S. Patent and Trademark Office during prosecution?

A. Yes, it was.

Q. Could we put JTX-1 up on the screen, please.

So there is the patent. Can we go to the next page. And U.S. patent documents. Do you see the '223 patent up there, Dr. Ravetch?

A. Yes, I do.

Q. I'm having trouble finding it myself. There it is. Do you see the '223 patent?

A. Yes.

Q. So could we put now -- so that means it was considered by the Patent Office, right, Bossard?

A. Absolutely.

Q. Could we put -- could we put DTX 6 up on the screen. That's the Bossard patent, '223 patent that we have been hearing about. Right?

A. Yes.

Q. Could we go to example 12 of that patent. So my question is, you heard Dr. Zalipsky say that the conjugates in Bossard were bioactive?

A. Yes.

Q. Do you agree that this example 12 shows functional Factor VIII polypeptides?

A. I do not.

Q. Why is that, Dr. Ravetch?

A. Well, one, bioactive is not a term that's used in the '520 patent. The term that's used is functional. And it

defined very clearly in the '520 patent to mean that it's capable of replacing the activity of Factor VIII and hemophilia both in vitro or in vivo, outside the body or inside the body. Bioactive doesn't really tell me if that would meet that requirement, would it replace the activity.

And if you look at the '223 patent, you see that they provide a range of activity that they consider to be bioactive. It goes all the way down to .1 percent. .1 percent activity is bioactive, and that in fact wouldn't be something that would replace Factor VIII activity. I don't think that that example is showing functional Factor VIII activity.

Q. Let's move on to the Nektar work. Were you present this week for the testimony by Bayer's witnesses, Mr. Fournel and Dr. Murphy?

A. Yes, I was.

Q. What type of tests could you use to determine B-Domain PEGylation?

A. Well, the tests that were developed to look at that particular domain in this very large complicated protein including thrombin digestion which is an enzymatic digestion that liberates just the B-Domain from the Factor VIII molecules allowing it to be separated out and then using other techniques you can detect the B-Domain from all the other fragments of Factor VIII.

You can also use peptide mapping and we have heard about that, that's how Baxalta was able to determine where the distribution of PEGs were in the Adynovate.

Peptide mapping was a technique that Bayer used, of course, and thrombin digestion were two of the methods that would give you the analysis of the B-Domain PEGylation.

Q. Did Nektar do any testing that showed B-Domain PEGylation?

A. They did not.

Q. Did you hear Dr. Russell testify that the Nektar work is random on PEGylation?

A. Yes, I did.

Q. Do you agree with his assessment?

A. I do.

Q. I now would like to move on to the Gruppo reference.

A. Okay.

Q. That falls into the category that you identified as unPEGylated references; correct?

A. Yes, that reference has nothing to do with PEGylation. They're not interested in PEGylation. They're not talking about PEGylation. It's certainly not one of the goals of that study. It's a study that's looking at the comparison between B-Domain deleted Factor VIII and full length Factor VIII in clinical populations that are being treated with these two preparations. They do something

called a meta analysis which means that they collect all the data which is available and combine it in a statistical fashion to derive conclusions about what the two products do in terms of preventing bleed and controlling bleed episodes, demonstrated half-life and all this rest.

Q. Was Gruppo considered by the U.S. Patent and Trademark Office when it was considering issuing the '520 patent?

A. Yes, it was.

Q. Can we put JTX-1 up on the screen, please. Can we go to page two. I think it's on page three, actually. Go to page three. Down a little bit on the left. There it is. Right in the middle of the page. Gruppo. Is that the Gruppo reference that Dr. Zalipsky had testimony about?

A. Yes, it is.

Q. So this was considered by the U.S. Patent and Trademark Office?

A. Yes, it was.

Q. So could we put DTX 80, please, on the screen. You can look in your binder if you like.

Now, you were here when Dr. Zalipsky talked about Gruppo; correct?

A. Yes, I was.

Q. What is Gruppo about at a high level?

A. As I said, so Gruppo is comparing the effectiveness

of full length and B-Domain deleted Factor VIII for prophylaxis, which means the prevention of bleeding episodes. So they're looking at clinical data from all these patients who are being treated with these various Factor VIII products.

Q. I think you said studies, you referred to some studies?

A. Clinical studies.

Q. Clinical studies?

A. These are all clinical studies. They are actual clinical population that are being studied.

Q. You heard Dr. Zalipsky that these studies show that B-Domain deleted more bleeding instances and a shorter half-life than Factor VIII?

A. Yes, that's what he was interpreting this paper to demonstrate.

Q. What did the authors say about those conclusions?

A. The authors are far more cautious. For example, just in the abstract if we scroll down a little bit, they say that although -- going back to the abstract on the right-hand side, "Although the results of the meta analysis need to be interpreted with caution, that's just a summary."

When you go into the body of the text, they say explicitly that there are serious problems with their conclusions based on other confounding factors. So they

repeat in their discussion in several locations, for example, on page DTX 80.6, they say there are several limitations to our study that justify caution in interpreting our observation. And they list some of these. One limitation was inability to assess the diligence of monitoring for breakthrough bleeds in various studies.

And they list several others. They also talk about their pooled half-life studies. So do these two products show the same half-life in patients. And that's a very actually important issue. That's on page 80.7. And they say our pooled half-life results are also subject to uncertainty due to differentiation in assay methodology, high patient-to-patient variability.

And then they go on to say that no study has directly compared the therapeutic efficacy of full length Factor VIII with BDD Factor VIII. And that's kind of the important issue. If you really want to know if these two types of Factor VIII behave the same way or differently, you do a patient controlled study where you compare patients directly with these two products as opposed to just taking samples of populations that are treated with one or the other. So you have a controlled experimental environment to do a clinical study. And that's how clinical studies are ideally done.

So based on all of that, you know, Gruppo, you

know, correctly says be careful with interpreting these data, yeah, there may be some discussions but I would say that really needs to be done now and their conclusion, this meta analysis should be confirmed by further results.

So that's not the kind of reference that I'd rely upon to say one of skill in the art reading this would say ah-hah, I would certainly want to choose full length Factor VIII to PEGylate as opposed to BDD to PEGylate.

Q. When was this article published?

A. This was published in 2003, March 2003.

Q. Can we turn to page eight of this exhibit. Do you see up there in the left, in the left-hand corner, can you highlight that under acknowledgment where it says this investigation was supported by an unrestricted grant from Baxter Bioscience? Do you see that?

A. Yes.

Q. What does that tell you?

A. What that says is that the funding for this study, to carry out this meta analysis came from the Baxter Company. They paid for this study.

Q. And what kind of Factor VIII did Baxter or Baxalta have on the market in 2003?

A. Well, they had Advate which you heard is the full length Factor VIII.

Q. So this article was advocating the use of full length

or BDD?

A. Full length.

Q. And Advate on the market was also full length?

A. Correct.

Q. Now, does this article motivate a person of skill in the art to use full length instead of B-Domain deleted?

A. No, it doesn't provide that kind of inclusive reference that I would chose one over the other, nor does it mention anything about PEGylation as a way to extend half-life. So there would be no reason to read this article if you're skilled in the art and say this would drive me towards a full length PEGylated product.

Q. Could we put DTX -- can you take a look at DTX 107, please, and put that on the screen. I would like to now turn to the Mosesson reference.

Dr. Ravetch, you heard Dr. Zalipsky's opinion, or did you hear Dr. Zalipsky's opinions that a person of skill in the art would reasonably expect to succeed in PEGylating the B-Domain based on Mosesson?

A. Yes, I heard that opinion.

Q. Do you agree?

A. No, I don't.

Q. Why?

A. So I think I discussed this a few days ago in my cross-examination. This is a study that is attempting to

look at the three-dimensional configuration of Factor VIII with the B-Domain. And as I said, the most sensitive techniques, x-ray crystallography were impossible on full length Factor VIII. So they did a technique called scanning transmission electron microscopy or STEM which is a very different way of looking at it. You look at it under a special kind of microscope, a scanning transmission electron microscope and they used porcine Factor VIII as a material that they're going to study and using those techniques, they present a model for how they think the Factor VIII molecule looks with the B-Domain.

And I believe that was shown by Dr. Zalipsky as extending out into space like a noodle coming off of Factor VIII.

So what's my problem with this? Well, it says nothing about PEGylation, of course. Does it provide any motivation that you would want to do that? But even expectation of success is absence because one, we're using porcine. It's not human Factor VIII. And the B-Domain of porcine Factor VIII does not have any homogeneity or relationship to human Factor VIII. They're very different sequences. You can't really extrapolate from one to the other because they're not showing the kind of relationship that you would like to see.

And finally the condition under which you do

PEGylation are vastly different from the conditions under which you do scanning transmission electron microscopy. You can't just assume that because I seen a structure under one condition that's the same structure I'm going to find when I do that experiment in the test tube with the buffers and reagents that are necessary for PEGylation.

Q. What does porcine mean?

A. It comes from a pig. Sorry.

Q. So I would like to move on to motivation to combine.

Would a person of ordinary skill in the art be motivated to use a full length Factor VIII instead of B-Domain deleted, based on these unPEGylated Factor VIII references?

A. No. In fact, we spoke about this before. In this time frame, 2004-2005 time frame, B-Domain deleted Factor VIII was clearly viewed as a more convenient better behaved molecule than full length Factor VIII. And therapeutics had been developed based on B-Domain deleted Factor VIII that were successful in the clinic at correcting bleeding disorders in hemophilia patients.

And I said some of the reasons are because it's smaller. It can be expressed more efficiently in production. You get higher yields. It has a more reliable presentation when you work with it. And if anything, one of skill in the art knowing all this would say I prefer using

B-Domain deleted. It's a easier, more reliable way to start.

Q. Just so that we're clear, the Mosesson reference did not involve PEGylation?

A. No, it didn't.

Q. So my next question is, would a person of skill in the art be motivated to select a B-Domain for PEGylation based on the Bossard patent in combination with these unPEGylated Factor VIII references?

A. Once again, I think you have heard from several of the witnesses that Bossard only addressed B-Domain deleted which confirms what I said before that that was the preferred starting material. And all the examples in Bossard are to B-Domain deleted. So there is nothing there saying take full length and combine it with PEGylation step.

Q. Would a person of skill in the art have expected to make non-random, non-random B-Domain PEGylation by combining the Bossard patent with these unPEGylated Factor VIII articles?

A. There is absolutely no teaching at all of that combination. In fact, I think that was, I said in my prior testimony, that was a breakthrough of the '520, that you could get PEGylation on the B-Domain, and that would have preferable desirable pharmacokinetic properties retaining functional properties as well for a domain that by

everyone's account was discarded, unnecessary, didn't have a role to play in these reactions.

Q. Thank you, Dr. Ravetch. I would like to move on to enablement.

Do you recall Dr. Zalipsky's opinion that the patent does not enable conjugates non-random by PEGylated at lysines in the B-Domain?

A. I do recall that.

Q. Does enablement require describing every method that can make the claimed conjugates?

A. Not at all. In fact, one of the principles of enablement is that if something is well-known in the art, you don't have to repeat it. People who do this know these things. This is their skill set. And this POSA would know certain skills, certain reactions. You don't have to list every possible component if those are well-known and those reactions are well established and are practiced routinely. So no, you don't have to go through that type of level of minute detail.

Q. How long has lysine PEGylation been known in the art?

A. Well, we heard from defendant's experts, 20, 30 years prior to these patents. So a long time.

Q. And does the '520 patent mention lysine PEGylation?

A. Yes, it does.

Q. Do you recall Dr. Zalipsky's opinion that the claims

do not enable one of skill in the art to make non-randomly PEGylated conjugates with any other amino acids?

A. I do recall that testimony, yes.

Q. Would a person of skill in the art expect to be able to PEGylate at every kind of amino acid?

A. No. Once again, protein chemistry is a well-defined field. It goes back 150 years at least when proteins were being characterized and the sophistication and knowledge has accumulated over time and we understand that amino acids are different. Not all amino acids behave the same way and different amino acids have different reactivities under different conditions so some amino acids are more amenable than other amino acids for modification. And that's known in the art.

Q. Would a person of skill in the art -- all of this is at the time the application was filed, correct, all these considerations?

A. Yes.

Q. Would a person of skill in the art have expected the scope of the claim to cover those nonreactive amino acids?

A. Absolutely not. That was not something that had ever been demonstrated, and it would be purely speculative that that could happen. Maybe in the future it might, but at the time the patent was written, we knew the chemistries behind amino acids and proteins and which reacted, which kind of

reacted groups.

Q. Could we put PDX 9.8 on the screen, please.

Now, Dr. Ravetch, you have been here all week; right?

A. Yes, I have.

Q. You have been in court every day?

A. I have, indeed.

Q. Have you heard the testimony of Dr. Zalipsky?

A. Yes, I did.

Q. And have you heard actually the testimony of all the witnesses this week?

A. I believe I did.

Q. And have you factored in all of their testimony?

A. Yes, I have.

Q. So have you seen anything or heard anything here this week at trial to change your opinion that the '520 patent is valid?

A. No, I haven't.

MR. BADKE: Dr. Ravetch, thank you. That concludes my questioning.

MR. HAUG: No questions, Your Honor.

THE COURT: All right. Dr. Ravetch, you may step down. Watch your step.

MR. BADKE: Sorry, Your Honor. That concludes our rebuttal case.

THE COURT: All right.

Mr. Haug.

MR. HAUG: Nothing further, Your Honor, other than to work out our exhibit issue.

THE COURT: Okay. So members of the jury, we're finished with the testimony. We're going to -- there are some things that I have to do with the lawyers including work on the jury instructions. And so we'll reconvene Monday morning and hopefully be ready to go at 9:30.

And sort of order of business will be that I'm going to read you some jury instructions about the law relating to patents and the claims in this case and the various issues, infringement, obviousness, et cetera, that you have been hearing about.

And then the lawyers will have a chance to argue again with the plaintiff going first and the defendant going second. And I haven't talked to them about exactly how long the arguments will be yet, but they will have some time limit.

And then when they're done, I'll have a few more instructions. And roughly speaking, you'll be getting the case what I would like to call before lunch, if you think that might be as late as 1:15, it's hard to tell. But essentially that will be the plan. And then once you get the case, it's yours to deliberate about.

And one of the things is once you're deliberating, you're in charge of your own schedule so that if, in fact, all of you want to stay later than 5 o'clock, you can do that, or if you decide no, you really -- it's a long day, you're only going to stay to 4:00, you can do that, too. You're in charge. The main thing, just bear in mind, you know, sometimes people have obligations, so don't stay beyond the regular hours unless it's agreeable with everyone.

So while there is plenty of things to do this weekend, some people watch the Super Bowl, the lawyers aren't going to be doing that because they're going to be getting ready for Monday morning. So you can be smiling if you like watching the Super Bowl thinking about how hard they're going to be working.

But in any event, whatever you do, I would like you to follow the two instructions I have been giving you at the end of every day, which is one, even now, don't talk to each other about the case. You can't talk to each other about the case until you're back in the jury room and you're deliberating, which means we have to finish my instructions and the arguments. Don't talk to anyone else about the case. Don't let anyone talk to you. Don't talk online to anyone about the case. Make sure that you keep an open mind, at least until you get back to the jury room. Even

then I'm going to tell you to listen to each other. But don't let anything impact you about this case between now and Monday.

And the other thing is, don't do any research. Don't Google anything. Don't look something up. Everything that you learn about the case that goes into your decision ought to be something that you learned while you're sitting here in the courtroom. And even though you have heard all the evidence now, if closing arguments are good, these are good lawyers, they should help take all this information that you have been hearing over the last five days and help put it in some framework that should give you a way to figure out the various things that you're going to have to figure out.

All right. So have a nice week even. Let's take the jury out.

THE CLERK: All rise.

(Jury leaving the courtroom at 3:30 p.m.)

THE COURT: All right. Everyone, you can be seated.

So what I was thinking is we need to take a short break so I can make a couple of copies of the proposed jury instructions and give them to you. I also need to give you some time to actually look at them before we have the charge conference, and then there may be various motions

that you want to bring to my attention.

So what I was thinking was we take a short break. I'll get these jury instructions together. Come back, hand out the jury instructions. I've already handed out the proposed verdict form.

And then we can hear whatever motions need to be heard, and then turn to the jury instructions and the verdict form.

Does that work?

MR. BADKE: Yes, Your Honor.

THE COURT: Okay. So I don't think it will take more than ten minutes to come back with a couple copies of jury instructions. But in the mean time, we'll be in recess.

THE CLERK: All rise.

(Recess was taken.)

THE CLERK: All rise.

THE COURT: All right. Everyone be seated.

So I've handed out the jury instructions that we have right now. I was advised that the defendants handed up some document that's about ten pages long, 11 pages long called Proposed Final Jury Instructions on invalidity. I gather that this is not something that, whatever the changes between this and what I have already, are something that plaintiff has seen, and so I really don't know what to do

with that.

In any event, before we get to the jury instructions and the verdict form, why don't we deal with any other motions.

Mr. Badke, I believe it's your turn.

MR. BADKE: Yes, Your Honor. I don't know if you just want me to say the words, but we do have a Rule 50 motion. We are just finalizing a brief now to file. If you would prefer that we just file the brief --

THE COURT: Why don't you tell me about it. Give me the highlights, starting in the order of those which you believe you're most likely to persuade me you're right because then I'll know when to stop listening.

MR. BADKE: Well, that's a tough order, Your Honor. We -- it's our view that we have established infringement, literal infringement, and also infringement, of course, under the doctrine of equivalents, and necessarily follows. But the evidence is really --

THE COURT: Yeah. Yeah. So that's not your best argument, I hope.

MR. BADKE: Okay.

THE COURT: All right.

MR. BADKE: So another one is on reverse doctrine of equivalents, they haven't actually followed the correct legal standard. So that one should come out. The

expert actually followed random PEGylation. He actually compared the -- he actually used this as a basis, random PEGylation, you're supposed to assume infringement. He was distinguishing applying this reverse doctrine of equivalents.

I'm not sure I exactly understand, but it was based on his view, his conclusion that Adynovate practiced random PEGylation. And so he used actually the wrong legal standard.

THE COURT: Okay. That may be your best argument, but right. So you'd like to get a JMOL on reverse doctrine of equivalents. Okay. Well, certainly, that I will consider.

What else?

MR. BADKE: Derivation by Dr. Bossard, the record does not establish that Bayer derived any invention from Dr. Bossard. I think there was a complete lack of proof that she conceived the invention of B-Domain PEGylation, along with an active molecule, much less communicated to Bayer. In fact, we have a document where in that report to Bayer where she's saying she thinks B-Domain is -- it's actually teaching against as communicated to Bayer. She says B-Domain PEGylation will not work.

And so there was really no proof that she conceived the invention, much less communicated it to Bayer.

The evidence is that Dr. Pan, to the extent, you know, when he had the invention, he said he thought of it himself. There's no corroboration, and I think it really fails for the corroboration standard which is required in a -- in a derivation invention.

THE COURT: Okay. All right. What else?

MR. BADKE: That the Bossard patent, the '223 patent, the evidence has shown that it is related only to B-Domain Deleted, and it is completely random PEGylation. And there's nothing in there about B-Domain PEGylation.

THE COURT: Yeah. I'm not likely to grant that one for you, so why don't you go on to the next one.

MR. BADKE: Okay. I think that's --

MS. DE: 01 Commumique.

MR. BADKE: Could you address that one?

MS. DE: Sure. It's an oldie, but a goodie. The 01 Commumique alliance argument that defendants had, I think at the last minute, they didn't do the aligning with argument of Adynovate aligns with the Bossard patent.

THE COURT: I don't think they did, either.

MS. DE: So no evidence on that and --

THE COURT: But --

MS. DE: -- it should be out.

THE COURT: There's no defense based on that, is there? I mean, what is it you want me to grant a JMOL on?

MS. DE: Okay. So it's withdrawn?

MR. HAUG: With particular events, yeah.

MS. DE: Then that one is done. Thank you, Your Honor.

THE COURT: Glad to be of service. Anything else?

MS. FUKUDA: Your Honor, on the damages side, we heard Dr. Rausser testify that he relied on Dr. Zalipsky's conclusion that ten percent of the Adynovate vial infringes. And he wasn't here listening to either what Dr. Ravetch said about it or any of that, so his reliance on technical opinion based on infringement or non-infringement is completely unreliable. And we're asking that Dr. Rausser's testimony on damages be excluded -- be disregarded.

THE COURT: Well, there may or may not be some merit to what you say, but I'm not going to exclude the testimony or prevent it from going to the jury. If there's a verdict, then we'll see what the damages figure is. If there's a verdict in your favor, try to sort it out afterwards if there has been a problem. But I would not be confident at this time to knock out aspects of either side's damages case.

MS. FUKUDA: Okay. So if I don't bring up the next point, can I still brief it?

THE COURT: Well, why don't you just tell me

what it is because maybe I'll go Eureka.

MS. FUKUDA: The second issue is that it's regarding these late-produced so-called net profits. We think that that's completely inappropriate. They haven't established that this was something used in the regular course of business. The one witness who testified about these new production of financials of lower profitability, he himself didn't create it, didn't know who did, didn't understand the details that --

THE COURT: This is when he said it came from the Hyperion system?

MS. FUKUDA: Yes, that's correct.

THE COURT: I don't think it's a requirement that he knows who input the information.

MS. FUKUDA: They haven't established that this is actually a document that the company itself, you know, either they have that document as of fact discovery and didn't produce it to us or they didn't have it, and they created it for the purposes of litigation.

THE COURT: Okay. All right. Well, yeah, so that's not going to the Eureka moment, either.

So you may be about to file whatever you're going to file, but based on what I've heard I would say, reverse doctrine of equivalents and derivation from Dr. Bossard, those are the two things that I might

conceivably rule in your favor.

Mr. Badke, what, do you have more?

MR. BADKE: I'm trying real hard to get to that Eureka moment. The one that I forgot, I should have said when I was up here, functional Factor VIII. As Your Honor has heard over and over again, they do have a functional Factor VIII molecule. We see it in the request for admission. We also see it in their package insert which says they replace Factor VIII in the blood for them -- it really -- the evidence is overwhelming and especially their own admissions.

So I don't see that that's an issue that should go to the jury because I don't think there's any other reasonable outcome then or maybe I'm not using the right legal standard with the jury, but really that shouldn't be in the jury's hands because the evidence is just overwhelming, and they should be held to their admission.

THE COURT: Yes. Okay. All right. Thank you.

MR. BADKE: Okay.

THE COURT: Does anybody care to respond to the reverse doctrine of equivalents, the Dr. Bossard derivation and the functional polypeptide that Mr. Badke was just speaking about.

MR. HAUG: Yes, Your Honor. With respect to the reverse doctrine of equivalents, there was testimony from

Dr. Zalipsky, I believe, that follows the correct legal standard. He said that he assumes there's literal infringement, and then he went on to say how the Adynovate product and process is completely different from the goal of the invention, the scope of the invention.

THE COURT: I heard him use the word principle.

MR. HAUG: Whatever, correct principle of the invention. So there was testimony rebutting that allegation in terms of -- not the testimony, rebutting it. It was our defense of reverse doctrine of equivalents. So I think there's -- there is evidence in the case on that.

Of course, that goes with the actual evidence of the product, and the testing, and everything else that the experts have said. And if they file a motion on it, we'll be more than happy to respond to it. We will --

THE COURT: Okay. Well, so that brings up a good point. Before you go on, I think Ms. De or somebody said that you were about -- maybe Mr. Badke, somebody said you were about ready to file your motion, or you used some words. I forgot what they were. I'm just curious when do you expect to file it?

MR. BADKE: We expect to file it today. I've actually got a draft of it right here that I was reading before Your Honor came in. So, yeah, we need to put cites in and --

THE COURT: Okay.

MR. BADKE: -- make a couple of changes.

THE COURT: I'm just trying to -- so here's the thing: They're not the only ones who are going to be watching the Super Bowl. So I can't be deciding this Sunday night.

So if you're going to get something in today, Mr. Haug, when are you going to get in your response?

MR. HAUG: If I can get it at a reasonable hour tonight, I can get it in by noon tomorrow or sometime earlier. Noon, for sure.

THE COURT: Well, noon would be fine. Well, reasonable hour tonight, I guess, patent lawyers here, what specifically do you mean by that? What's the outer bounds?

MR. HAUG: Eight o'clock?

THE COURT: Eight o'clock seems ambitious. What about ten o'clock?

MR. HAUG: Well, it's his motion.

THE COURT: What time did you have in mind?

MR. BADKE: We need the trial transcript, so --

THE COURT: Well, I'll tell you what, why don't you go for whatever time tonight, and Mr. Haug, I'll give you until three o'clock tomorrow.

MR. HAUG: Very good, thank you.

THE COURT: Okay. Is that good on both? Good

with you?

MR. BADKE: Yes. Yes, Your Honor.

THE COURT: Okay. Let me just write that down.

All right. So Mr. Haug, you were responding to reverse Doctrine of Equivalents. What do you have to say about Dr. Bossard and derivation?

MR. HAUG: So the derivation defense as a 102 anticipation defense is out of the case. We dropped it. The only thing we're relying on for derivation at this point is the derivation, the work at Nektar, Mary Bossard, that was communicated to Bayer, we believe that satisfies 102(f) as a piece of prior art.

This would be -- I would cite the case Odd Zone, O-D-D, Z-O --

THE COURT: Before you start citing the cases, I thought I saw Odd Zone cited somewhere recently.

MR. HAUG: Probably what we handed up just now.

THE COURT: When you say a 102(f) piece of prior art, does that mean that this is basically just part of the obvious combination.

MR. HAUG: Yes.

THE COURT: Not a separate.

MR. HAUG: Not a separate defense, consider it like a piece of prior art.

THE COURT: Okay.

MR. HAUG: Under 103.

THE COURT: That's helpful. And so then in terms of the extent that they're saying JMOL on the derivation defense as opposed to just a piece of prior art, you dropped derivation defense?

MR. HAUG: Correct.

THE COURT: Okay. I guess you don't have to tell them the cite on that one.

And so is there anything you want to say about it being -- so what you're saying is, because maybe this may make life easy, but I'm guessing probably not, the technical reports that have been entered as exhibits, and I seem to think maybe there were about three of them altogether, what you're saying is those things are pieces of 102(f) prior art?

MR. HAUG: Correct. Take those in combination with, for example, the Bossard patent which is published, obviously, the '223 patent together with the articles that were testified about, that's the obviousness, the basis for obviousness.

THE COURT: So in that -- and that relies on the fact -- so in order to be 102(f) prior art for the purpose of this obviousness defense, other than Dr. Bossard wrote it or somebody wrote it, it was possessed by the inventors and it predated the invention. Are there anymore requirements?

MR. HAUG: It has to be communicated. It has to be communicated, which we believe it was.

THE COURT: Okay.

MR. HAUG: And that's basically it. It's like nonpublic prior art.

THE COURT: But, in other words, in the derivation defense, as a defense there were issues about conception, things like that. Are they no longer relevant?

MR. HAUG: I think we still have to show that they match up to the extent we're relying on it as a piece of prior art, it at least goes to the elements that we're relying on it for.

THE COURT: In other words, you could have a publication, a piece of published prior art, once you establish it was prior art, it was in the relevant field, you don't have to -- you know, it says in it, there is a sentence saying it's always good to PEGylate the B-Domain because you get much better results, even if it doesn't say much else in there, you can use it. Right?

MR. HAUG: Right, if it wasn't for Factor VIII.

THE COURT: So hold that thought. I don't know who -- I'm guessing it's on either side of you, Ms. Fukuda, but in terms of -- using it for that purpose, is there anything -- is there any actual, any dispute that it can be used for that purpose?

Ms. Bercier?

MS. BERCIER: Your Honor, I disagree with Mr. Haug. I'm not sure exactly what defendants are now saying Dr. Bossard conceived of and communicated to Bayer --

THE COURT: Sorry to interrupt. So I'm not sure conceived of is the right word. And maybe -- well, but you go ahead, actually.

MS. BERCIER: So they've just said they're relying on the technical reports which show that they potentially PEGylated Factor VIII. That's something Bayer had already done. I don't understand exactly how that can be considered derivation for purposes of combining it with 103, other prior art when that's something Bayer already had in its possession. So if they're saying it's something different, if they're saying that they conceived of and communicated all the elements of the invention, then we need to know that.

THE COURT: I don't think they're saying that. It sounds like they're saying something different than they are.

MS. BERCIER: Your Honor, in Mr. Haug's opening statement, he did have a slide that said Dr. Bossard conceived of and communicated the invention.

THE COURT: Right. But I don't think he's going to be saying that in his closing argument; right?

MS. BERCIER: We can talk about it during the jury instruction portion, but I think --

THE COURT: That's kind of what I was going to. But okay. So just in -- so why don't we bring it back up at that point.

In terms of functional Factor VIII, Mr. Haug, do you have anything to say about that? Functional, I can't even remember the words.

MR. HAUG: Retained, retained activity.

There is evidence obviously. There is evidence in the record from their side that says it has to be a hundred percent. I think it's Dr. Murphy, for example. And then I think there is other evidence in the record saying that when the -- when Adynovate was PEGylated, the activity went down as much as fifty percent.

And so the question really is how much is retained activity within that, the scope of that claim. We believe their position is it's a hundred percent. At least that's how we understand the testimony to be.

So that's a non-infringement defense. So I think there is ample evidence in the record for non-infringement of that claimed element, understanding that in the claim construction there was no construction as to the percentage, so I think that's not an issue of claim construction, I think it's an issue of infringement.

THE COURT: Okay. Speaking of which, because I thought the various defenses were indefiniteness, no one has mentioned that.

MR. HAUG: Dr. Zalipsky did.

THE COURT: I know he mentioned it, you all didn't mention it. I take it that's because that's not part of your JMOL.

MS. DE: It's in there. It will be.

THE COURT: Sorry, I'm not trying --

MR. HAUG: I haven't gotten to our Rule 50 because it's going to be in ours, too, because I don't think they rebutted it.

THE COURT: Save your breath on that one. All right? Well, in any event, they didn't mention it.

So why don't we move on from that. I mean, for sure I'm not going to grant infringement or the damages parts of their motion. If you have similar cross motions, I'm not going to grant them either, but if you want to make a record now as to what they are, go ahead.

MR. HAUG: We would. We renew the earlier motion we made under Rule 50 to the extent it was not granted based on the further evidence that we've heard here in the case. We also again, object to the claim construction that came out of the Markman based on what we had proposed. Obviously that isn't going to change now, but

we do preserve that objection.

THE COURT: Sure.

MR. HAUG: That's all I'm doing. And on indefiniteness, I already mentioned I don't think I heard anything coming back to the allegation of indefiniteness, so the defense of indefiniteness.

THE COURT: Just tell me in a sentence what you think your indefiniteness argument is.

MR. HAUG: Did they didn't say.

THE COURT: No, your argument, not their's.

MR. HAUG: Well, claim 1 is indefinite because they don't tell you how to measure the retained activity.

THE COURT: Okay. All right. Well, you did it in a sentence. That's good. Okay?

MR. HAUG: And then one other one, Your Honor, on unexpected results, we didn't hear anything, I don't think, on objective indicia.

THE COURT: Well, I thought I recall that Dr. Ravetch or somebody, maybe it wasn't him, but somebody in their opening case I'm pretty sure had the words something with the unexpected result; right?

MR. HAUG: He did make a conclusionary statement to that effect, yes, he did. And so we, too, we'll file -- if we do file one, I think we will file a written motion JMOL on invalidity to preserve all our defenses. If we do

that, it will be this evening.

THE COURT: All right.

MR. HAUG: I think that's it. So we reserve all rights on all our burdens of prove.

THE COURT: Thank you, Mr. Haug.

MR. HAUG: Thank you.

THE COURT: So the jury instructions. Wait a second. So I just handed these out a little while ago. Do I need to give some more time for people to look at these, because I don't want -- I want to do it when you're ready to do it.

MR. HAUG: Can we take ten minutes?

THE COURT: Sure. Do you want more time?

MS. BERCIER: Ten minutes will be fine, Your Honor.

THE COURT: Thank you.

(A brief recess was taken.)

THE CLERK: All rise.

THE COURT: All right. Be seated. Have you had enough time to look over the jury instructions?

MR. BADKE: I think so from our side, Your Honor.

THE COURT: Mr. Haug.

MR. HAUG: Well, we've been looking at them. Yes, we can start.

THE COURT: Okay.

MR. HAUG: Have we really had enough time? No?

THE COURT: Well, I mean, I'm perfectly willing to give you more time. There's no reason to, you know, do this when you're not ready to do it. So do you want some more time?

MR. HAUG: No. I think we can raise the issues that we see right now.

THE COURT: Well, except I really want to get them all out on the table. If you don't raise them now, when are you going to raise them, Monday morning?

MR. HAUG: Okay. We're all right. We're fine.

THE COURT: I'm sorry?

MR. HAUG: We're all right. We're fine.

THE COURT: All right. So just as a preliminary thing, we've got this 20 pages of stuff that is in the jury instructions before we even get to the heart of what the jury is going to be wanting to hear about. So my plan is to basically start on Page 21 of these instructions. What I want to know is what you would like to do about the other 20 pages that proceed it. My preference would be to basically tell the jury that a number of the -- many of the instructions that occur before are ones that I either gave at the opening or which the parties may refer to as they're necessary or as they want in closing argument, but not to

read them to the jury.

What do you think about that?

MS. BERCIER: Your Honor, we have one clarification in Section 1.16.

THE COURT: Sure.

MS. BERCIER: So there was an issue with the litigation stamp highly confidential on one of the BLA documents.

THE COURT: Right.

MS. BERCIER: We don't want the jury to be confused as to original confidentiality designations that appeared on the document, you know, as added by the author. And so we would ask just to add another line saying something like, This is not to be confused with an original confidentiality designation that was placed there by the author, custodian of the document.

THE COURT: Okay. Well, so we can talk about that. Hold on just a minute. Okay.

But in terms of the point that I was actually asking about, what's your view?

MS. BERCIER: I think we're okay with that.

THE COURT: All right. Thank you.

Defendants?

MR. HAUG: We're fine with that.

THE COURT: Oh, okay. So but now let's go to

what Ms. Bercier has raised which is we have an instruction, so Ms. Bercier, what exactly do you propose to add?

MS. BERCIER: Maybe just one sentence distinguishing litigation-added confidentiality designations from designations that appeared on the original document.

THE COURT: Well, so let me just ask: What difference does it make whether it has a confidentiality designation on the original document?

MS. BERCIER: Defendants have raised a defense to non-infringement saying that everyone thought Adynovate was random looking at all these scientific references, public documents that say it's random. And our position is that those individuals didn't actually have the confidential information that Bayer and its experts had.

THE COURT: Okay. I get your point.

All right. So in concept, what do you think about adding a sentence here, defendants?

MR. HAUG: I don't think we would object to it. Do we?

THE COURT: Okay. So Ms. Bercier, propose the sentence, please.

MS. BERCIER: Original confidentiality designations appearing on these documents -- I'm sorry, Your Honor. Let me start over. These --

THE COURT: I'll tell you what: Are you doing

all the arguments here?

MS. BERCIER: I am.

THE COURT: Oh, I was going to say why don't you sit down and write the sentence, and we'll go on.

MS. BERCIER: I can read you the draft sentence I have.

THE COURT: Well, do that.

MS. BERCIER: This is not to be confused with an original confidentiality designation that was placed by the author or custodian of the document.

THE COURT: So here's the thing is the jury is not going to be all that able to tell which are added during litigation confidentiality things and which are, you know, added in normal course of business. I mean, it's going to be difficult; right?

MS. BERCIER: It could be difficult. The litigation-added stamps also have the Bates stamping with it, so --

THE COURT: Well, no, you know --

MS. BERCIER: Right.

THE COURT: -- so the people who have seen a lot of this stuff, you can figure out a lot of this, but the jury probably hasn't seen that much, other than what they've seen this week.

All right. Well, so here's the thing: I'm

happy to add a sentence rather than spending time now. Why don't you see if you all can't agree on a sentence.

And Mr. Smith --

MR. SMITH: Yes, sir.

THE COURT: -- you're going to be responsible for any changes that we make to this, okay? So why don't you --

MR. SMITH: Yes, Your Honor.

THE COURT: -- see if you can't agree on a sentence. You know, and what I'd suggest is maybe before you start, if you have a sentence that proceeds it that says something like in the normal course of business, pharmaceutical companies often label documents as being confidential, period. In the course of this case and then kind of go into this.

That's just a suggestion, but why don't you see if you can't think of something. And I will give you some deadline. So why don't you see if you can't agree on something and put it in somewhere in here, and it's fine by me.

Okay? If you can't agree on it, mark it as a disagreement, and we'll come up with a procedure that probably involves Mr. Smith sending me a revised version sometime tomorrow, and I will resolve the dispute. But rather than -- okay?

MS. BERCIER: Okay.

THE COURT: Anything else in this first 20-odd pages? So, actually Page 20, you know, I added in here -- is there actually a stipulation? The heading says Request for Admission. I'm guessing that, in fact -- well, I'm not sure what you -- the parties intended by this, because as it is, it doesn't make much sense. And at least as far as stipulations go, I don't think there's been any actual stipulations presented to the jury.

MS. BERCIER: There have been, I think, four, Your Honor. And PTX 1200, you'll remember Dr. Ravetch brought up to support his functional Factor VIII activity opinions. It had RFA is directed to Adynovate --

THE COURT: They're not stipulations, they're requests for admissions; right?

MS. BERCIER: Yes. So we've actually prepared a document. You had requested we take out the extra pages and redact, the, you know, RFA we're not relying on. And so we have that prepared, and maybe that will take care of this issue.

THE COURT: Okay. Well, so but if you want to have something under Request for Admission that say -- I think the language of the rule is conclusively presumed, but if you want to say a request for admission or an exhibit that is a request for admission, you know, under the rules

-- probably not under the rules, but is a statement that is conclusively presumed to be true, something that tracks what the rule is.

I mean, I think you should make that, and I'd be happy to do that. And again, I would ask that you try to come up with some language among yourselves.

Okay?

MS. BERCIER: Okay.

THE COURT: So does that take care of the first 21?

MR. HAUG: Well, no. I have a couple points, too.

THE COURT: Okay.

MR. HAUG: 1.3, which is The Parties. Our version here still has --

THE COURT: Yeah, sorry. We noticed that there were a few where we had Nektar. So, yeah. Thank you.

Any references to Nektar as a party should be removed. So is there anyplace else that you want to bring that up, Mr. Haug, because I think there may be more than just that?

MR. HAUG: Yeah, 1.4, the next one. We actually proposed to add something here on summary of contentions and patent issues about invalidity, and I think Your Honor didn't put it in here.

THE COURT: Well, let's see. Oh, yeah, so I think I may have misled -- I meant to have that in. When it came in, it was single spaced, and I wrote 2X, but I think that was interpreted as double delete. It actually meant double space. So, yeah, we'll add that back in.

MR. HAUG: Okay. Thank you.

THE COURT: All right. Anything else in the first 20 pages?

MS. BERCIER: I don't believe so.

THE COURT: Okay. Page 21, Issues Presented, it seems to me that's non-controversial.

Page 22, the role of claims in a patent, any objections?

Page 3 or Instruction 3.2 on Page 23 about Independent and Dependent Claims, any objections?

MR. HAUG: Not from defendants.

MS. BERCIER: None from us, Your Honor.

THE COURT: All right. Okay.

Page 25, construction of claim terms. So first off, do we have the exhibit number of the Claim Construction Order?

MS. BERCIER: I believe it's -- I believe it's DX 200.

THE COURT: Oh, the --

MS. BERCIER: Oh, the exhibit number? We'd have

to check the exhibit number. I don't know if it was admitted.

It wasn't admitted, Your Honor. It's DI-195 is the opinion, and I think --

THE COURT: Well, okay. Well, so why don't we do this, why don't we change it to say, I did a Claim Construction Order that is attached to these written instructions at the end of these written instructions. We can just staple it to them, and then we don't need to give it a claim construction number. I mean, an exhibit number.

Okay. So what about this Page 25?

MS. BERCIER: Your Honor, I brought this up at side-bar. It might have been yesterday, but there was quite a bit of testimony presented concerning what random means as meaning lysine conjugation or amine conjugation. I think Dr. Walensky yesterday gave quite a bit of testimony that the PEG itself is random, and you don't have to look at the process to determine whether something is random.

We also heard testimony that the '520 patent is, or the only way to PEGylate in a non-random way is to use cysteines and to use the one method in the '520 patent. And this all goes back to our issues that we raised in the motion in limine concerning improper claim construction arguments that we believe Your Honor already resolved.

THE COURT: All right. So what is it you want

me to do here.

MS. BERCIER: I think we would like some limiting instructions on those particular issues.

THE COURT: Okay. Can you be more specific?

MS. BERCIER: Random conjugation does not exclude PEGylation at lysine.

MR. HAUG: Your Honor, if I may --

THE COURT: So.

MS. BERCIER: Non-random does not exclude. Let me correct that. Sorry about that.

THE COURT: Okay. So that's what you want, you want -- so really what you want in a claim construction kind of way, I think, is that the claim scope is not limited to cysteine.

MS. BERCIER: I think that would work, Your Honor.

MR. HAUG: Your Honor, we object.

THE COURT: Mr. Haug, do you disagree with that?

MR. HAUG: Yes, I think we would object. We do object to anything going to the jury about claim construction other than your claim construction order. And I think that's what I heard earlier today that Your Honor intended to do, if I heard that correctly. In other words --

THE COURT: So there is a difference between

what I ruled -- or there could be a difference between what I said at side-bar with the clock ticking and no time for reflection and what I think we ought to do in terms of the jury instructions. What I'm concerned about is taking into consideration the Federal Circuit multiple times saying that claim scope is something that ought to be decided by the judge. And I remember some case not that long ago where they reversed Judge Sleet for not resolving something even though it hadn't been brought up until trial.

So that's my concern from my point of view. And so -- and it seems to me that the way that I have construed the terms and the way the patent reads, that claim scope is not limited to cysteine being something or another.

MR. HAUG: Well, I'm not necessarily disagreeing with that because the claim doesn't use the word cysteine. And I'm not -- what I'm objecting to is any further claim construction now proposed by the plaintiff, which one, we didn't try the case based on that; and two, I think it would be confusing for the jury now after hearing repeatedly all week long about what the claim construction is and then all of a sudden an instruction is given to them that is further clarification or however they would a take it, I don't know. I think there has been testimony here elicited from our witnesses that they agree that the claim doesn't say cysteine.

THE COURT: I think they have said that, grudgingly, but they did say that. But they certainly -- you know, so they -- so it seemed to me that your main non-infringement defense was we use random PEGylation. It's not we use random PEGylation on lysines and the lysine is not a cysteine, it was we use random PEGylation.

MR. HAUG: Correct. And the reason random is because it's a lysine in the process that they use.

THE COURT: And so that's the thing that worries me in terms of scope which is for whatever reason, at least until trial we haven't gotten to the point -- I haven't found it necessary to do claim construction and say the key thing here is random PEGylation or non-random PEGylation, but whether it's a cysteine or a lysine sort of intrinsically makes no difference. Right? I think you just said you agree, I decide whatever I might need intrinsically, it doesn't make any difference, you agree there is no difference between cysteine and lysine, it's a distinction between how the process relates.

MR. HAUG: I think there is a world of difference between cysteine and lysine. That goes to some of the other defenses in the case like lack of enablement, non-enablement. Our position very clearly is that if plaintiffs take the view that claim 1 covers lysine PEGylation.

THE COURT: Which is pretty obvious they do, yes.

MR. HAUG: Which they do, that claim is clearly not enabled because they believe the evidence in this case is no one has yet ever done that. I realize that they take the opposite view that somehow through these FDA ancillary documents that shows that they did it, but there is no direct evidence that they ever did it, and there is plenty of evidence in this record that no one in the world has ever done it.

When Dr. Zalipsky was up here he was talking about PEGylation from a scientific standpoint, he wasn't construing the claims in any way other than what the Court has construed the claim as to being a requirement that you had to be non-random. He's now giving his scientific expertise as to what is known to be random and non-random and so on and so forth.

I think if we start trying to add to the claim construction, I'm very concerned. I could propose additions, too, which I'm sure won't be acceptable to the other side. And so -- and we did as Your Honor will recall, we did file a motion in limine, and at one point did ask whether the Court would want to entertain a construction on random and non-random and you declined to do that as not being necessary. That's fine. That's how we have now tried

the case. It comes down to both sides coming forward and giving evidence as to whether they think it's random or non-random.

We're not arguing non-infringement because we use lysine, that's not the argument. The argument is the process used to make Adynovate, Adynovate is made by a lysine PEGylation process of Factor VIII which results in a random, it is random. That's the argument of non-infringement. It's not non-random. And it's their burden of proof to prove that it is.

THE COURT: Here is how I think I'm going to resolve that. I'm going to operate under the assumption that the closing argument of the defendant is going to be along the lines of what Mr. Haug just said, so I'm not going to further explain cysteines and lysines. But what I would like you to do, Ms. Bercier, is sometime before Monday morning submit me just so I have it at the ready as to what the curative instruction would be if -- because of lack of sleep or something else, an argument is made that goes too far. Okay?

MS. BERCIER: Thank you, Your Honor.

THE COURT: So on this page, I think in the instructions, I think somebody -- hold on a minute.

MS. BERCIER: Your Honor, we had also added a curative instruction that at the B-Domain does not require

complete homogeneity and that was based on your recent Daubert opinion.

THE COURT: I think that's like a side issue which is the reason why I wasn't going to give that. I think the key issue is the issue that the parties have litigated heavily over the last week which is randomness or non-randomness and that the arguments that are made --

MS. BERCIER: Your Honor, I think what Mr. Haug said is that Dr. Murphy said something that's not random has to be completely homogeneous and I think he's going to say that to the jury during closing arguments. He's go to say that lysine PEGylation is random, which is what I just heard from him.

THE COURT: You may have heard better than me, but I didn't hear that. He's now shaking his head. If he did say that, he didn't mean to say that. He didn't say that is actually what he's saying.

So I'm going to not do that because what I understand the parties to have been arguing through their experts is whether there is homogeneity and how much of it there is, and I remember the last, maybe not Dr. Ravetch, maybe Dr. Zalipsky, you know, talking about complete homogeneity, I think it was something he was saying. So I think the argument about homogeneity, homogeneity goes to whether something is random or not. So I'm not going to

give that instruction either.

Anything else on this page?

MS. BERCIER: Not from us, Your Honor.

THE COURT: So basically I'm going to cross off my comments here and just stick with -- other than the thing about the claim construction order, stick with this the way that I have given it to you and go on to the next page.

MR. HAUG: So the last part, in addition to the construction I just read, we include that, keep that, is that what you're saying?

THE COURT: Yes. I'm going to keep that. So I'm just going to cross it off my comment, but otherwise, I'm keeping that.

So on to infringement generally. Any objection there, that's page 26. Any objection from defendant?

MR. HAUG: None.

THE COURT: Okay. Page 27, literal infringement. Any objection from plaintiff?

MS. BERCIER: None from us.

THE COURT: From defendant?

MR. HAUG: No, Your Honor.

THE COURT: All right. Infringement of comprising claim, which I think was undisputed earlier. Is it still undisputed, Ms. Bercier?

MS. BERCIER: I believe so.

THE COURT: And you're good?

MR. HAUG: It is fine.

THE COURT: All right. Infringement by the Doctrine of Equivalents. Hold on a minute.

Well, so somebody is going to object to this, probably. Ms. Bercier, what about the instruction on page 29, are you good with that?

MS. BERCIER: We have one addition, Your Honor, and that's in the second paragraph, the third line, sentence starting with here.

THE COURT: Yes.

MS. BERCIER: We would want to add here in addition to asserting that Adynovate falls within the literal scope of this element, Bayer asserts that Adynovate includes equivalence of SEQ I.D. 4, so we asserted literal for SEQ I.D. 4.

THE COURT: But we have just done literal --

MS. BERCIER: I think that the --

THE COURT: The whole thing starts off with if you decide that Adynovate does not literally infringe, then you must decide. So I think you're just adding unnecessary words which is against my general principles.

MS. BERCIER: Okay.

THE COURT: Okay.

MS. BERCIER: Okay.

THE COURT: How about the defendant here, Mr. Chen.

MR. CHEN: Your Honor, would you happen to have the claim in front of you, because it's quite lengthy.

THE COURT: The claim?

MR. CHEN: I can give you my copy.

THE COURT: I have got a volume here. And it has JTX-1 so yes, I do. Does somebody have an extra copy of the claims?

MR. CHEN: I can hand up my marked up version.

THE COURT: That's all right. What is it, Mr. Chen?

MR. CHEN: So your issue here is that Sequence I.D. 4 is not really an element by itself. So if you look at the claim, four lines down.

THE COURT: Right, I see it. The amino acids sequence of SEQ ID No. 4.

MR. CHEN: Actually, it starts the amino acids sequence, then it goes on to say of SEQ I.D. 4, I'll skim that, and it says has a B-Domain. Right? And then unfortunately it's quite wordy, but it goes on to say -- okay. And so our issue is that if there's a doctrine of equivalents issue in the case that that's the question that needs to be evaluated as to whether or not, if there is -- whatever the Factor VIII is in Adynovate that's PEGylated,

should be assessed as to equivalents, that whole phrase of the claim. In other words, the sequence --

THE COURT: Wait. What you're saying is the -- I can't remember, when the experts had the non-infringement charts or infringement charts, depending on whose expert it was, it was broken down into -- wasn't it broken down into like five different things?

MR. CHEN: Not for infringement. Maybe the plaintiff's side.

MS. BERCIER: For in Dr. Zalipsky's slides today, Your Honor, he actually didn't even identify SEQ ID 4.

THE COURT: Well, so what about your slides, Ms. Bercier?

MS. BERCIER: We went through all the elements of the claim to make sure that we met our burden.

THE COURT: Okay. But so what do you think the element of the claim is here?

MS. BERCIER: I think it's the SEQ ID 4 element.

THE COURT: Right. But when you say the SEQ ID No: 4 element, I'm absolutely positive Mr. Chen is right that when you did the infringement chart, it didn't stand out as element number three is SEQ ID No: 4. It has some longer phrase.

MS. BERCIER: I believe it was. It's the amino

acid sequence of SEQ ID 4. So we broke out functional Factor VIII polypeptide SEQ ID 4 and then went through the remaining elements.

THE COURT: Okay. So --

MS. BERCIER: As a practical matter, Dr. Zalipsky did not include any analysis of SEQ ID 4 today in his infringement presentation.

MR. CHEN: Your Honor, it's not our burden. If I could just -- sorry.

THE COURT: So I take it, Mr. Chen, what you're saying is whatever the element is, the limitation is, the doctrine of equivalents, the Court says limitation by limitation, that the limitation ought to be identified or at least -- that's your basic point; right?

MR. CHEN: It should be contextualized because it's taken out of context. So the issue here is the patent is not about Factor VIII. The patent is about PEGylated Factor VIII.

And so if they're going to assert whatever Factor VIII is equivalent in Adynovate, it's not just the Factor VIII. It's the PEGylated Factor VIII that should be assessed as part of the equivalents.

THE COURT: Well, and so I guess what I'm wondering is I don't understand why the key phrase for what you're saying here isn't, "the amino acid sequence of SEQ ID

No: 4 or an allele variant thereof.

MR. CHEN: So that's just talking about the Factor VIII portion irrespective of any PEG"

THE COURT: Right, but it's an element. The PEG comes later.

MR. CHEN: Right. But then if the jury says okay, maybe let's say there's no literal infringement hypothetically, and they say, A, is equivalent to the claims, and that's just the Factor VIII, then they don't -- then they're not asked the question: Well, is whatever we have that that's the PEGylated equivalent to what the claim requires?

MS. BERCIER: Your Honor, it sounds like a doctrine of equivalents analysis for the entire conjugate which is claim 1.

THE COURT: Well, so --

MR. CHEN: In other words, it's only addressing half of the issue on Factor VIII in the claim.

THE COURT: Yeah. So, and you say the other half is somewhere down here where it says is covalently attached to the functional Factor VIII polypeptide at the B-Domain.

MR. CHEN: Right.

THE COURT: So the question is whether --

MR. CHEN: The dispute has been whether or not

the claims require a full B-Domain -- entire B-Domain of Sequence ID No: 4 in the Factor VIII. And our view is the next question is: Whatever is PEGylated, is it PEGylated at the full sequence of the B-Domain? The way they've framed it, it's only asking half of the question.

THE COURT: But where is it that you see or where you're getting that it says --

MS. BERCIER: Your Honor, defendants can contest infringement here because of the whole process in variants argument that I think Dr. Ravetch explained. One of the issues that was up at the PTAB and in front of the patent examiner was whether this claim was directed to BBD or full-length Factor VIII. And I believe Bayer added the SEQ ID No: 4 language to clarify that it was not BDD. It was, in fact, SEQ ID No: 4 performing Factor VIII polypeptide.

THE COURT: All right. So hold on a minute. Joyce.

(Discussion held off the record.)

THE COURT: All right. So I think I at least partly agree with Mr. Chen, but I don't think I agree completely with him. It seems to me the way the claim breaks down, the doctrine of equivalents if the amino acid sequence of SEQ ID No: 4 is met by the doctrine of equivalents, then the -- when you're talking about the functional Factor VIII polypeptide later on, that's going to

include that.

But I think perhaps that just having the SEQ ID No: 4 is not the best way to put it in here. And so what I'm thinking, Ms. Bercier, is in the second paragraph in line 3, where it says, Here, Bayer asserts that Adynovate includes equivalents of SEQ ID No: 4, I think maybe what I'd like to do is to change it to say Bayer asserts that Adynovate includes equivalents of "the amino acid sequence of SEQ ID No: 4."

MS. BERCIER: I think that's fine, Your Honor.

MR. CHEN: Your Honor, if I may say one last word? I'm sorry.

THE COURT: No. No, that's all right. You need to make sure you protect the record and whatever else.

MR. CHEN: So respectfully the way you just analyzed it is exactly the fear of the prejudice that we have. So the way you just articulated -- I apologize if I'm not expressing it accurately, is that if that Sequence ID No: 4 is met from an equivalents perspective, I believe you said, well, then it's met at the end of the claim term with the functional Factor VIII. That's exactly what I'm saying is the problem because --

THE COURT: Okay.

MR. CHEN: There's two steps here to the claim. The first question on this issue is: Do you have Sequence

ID 4 on the full B-Domain, yes or no? That's Factor VIII.

The next question is: Is that sequence -- does that actually have PEG attached to it, and is it functional?

THE COURT: So isn't that covered by the rest of the claim as is?

MR. CHEN: But if the question is just set up does the Factor VIII have an equivalent sequence, yes or no, then the danger is that the jury is going to just automatically assume that the last element is satisfied. But as you heard Dr. Zalipsky say, there's at most ten percent of the full sequence in, and he said, and it doesn't even include whether or not it's PEGylated.

THE COURT: Right. I did hear him say that.

MR. CHEN: Right. So that's what I'm fearful of is if they check the first box, then they assume that the last part is satisfied.

THE COURT: But I think that's a factual argument. You're going to say exactly what you just said.

MR. CHEN: Right.

THE COURT: They're going to say something else.

MR. CHEN: Well, then, I'm sorry to interrupt. Are we allowed to argue then that they had failure of proof on that last element?

THE COURT: I think, as I understand what you plan to rely on, I think so.

MR. CHEN: Okay. If that's -- Ed?

THE COURT: Right. Am I wrong, Ms. Bercier?

MS. BERCIER: I'm not exactly sure. What Mr. Chen is arguing, to me, this claim has two elements with comprising claims. It has a functional Factor VIII polypeptide and a biocompatible polymer. For functional Factor VIII polypeptides, you have to check the amino acid of SEQ ID 4. And then for biocompatible polymer, it has to be covalently attached to the B-Domain.

So to me, I'm perfectly happy --

THE COURT: But it does have to be attached to the amino acid sequence of SEQ ID No: 4 or the equivalent thereof; right? It can't be attached to some other thing.

MS. BERCIER: I agree, Your Honor, but I think there's a dispute as to whether, for example, Dr. Ravetch has given extensive testimony on what I think Mr. Chen is pointing to is when Factor VIII is expressed and secreted from a cell, it automatically undergoes natural processing. That doesn't mean it's no longer full-length Factor VIII and that it didn't have the SEQ ID 4 element.

THE COURT: Okay. But that sounds like you've got a factual dispute. You can argue -- both sides can argue their positions.

All right. So let's make that change, Paragraph 2, Line 3. And there may be some other changes

because we keep seeing -- you know, there will need to be some corresponding changes, and I think it's actually better to just write it out each time.

Okay?

MS. BERCIER: Okay.

THE COURT: So onto 4.2, the reverse doctrine of equivalents. Hold on just a second. Is there any objection to this? I know there was some objection about the placement. But beyond that, was there some other objection?

MS. BERCIER: I mean, beyond our JMOL motion that I don't think defendants have met their burden on this.

THE COURT: But you're okay with the substance of if I don't grant your JMOL?

MS. BERCIER: That's right.

THE COURT: And defendant?

MR. HAUG: Yes. I think we're okay with this.

THE COURT: Okay. Thank you. Invalidity, Page 31. Is there any objection to that?

MR. HAUG: No.

MS. BERCIER: None from us.

THE COURT: Okay. Person of ordinary skill in the art, Page 32, any objection there? I don't think there was.

MR. HAUG: No.

THE COURT: Okay. Prior art. So I think we

wrote this before -- well, so as you can see, I did have a question here on Page 33, and I think I'm getting it now. Now that the defendant has said they're just using this as prior art, I'm kind of thinking that the Baxalta Nektar language is probably the better language.

MS. BERCIER: We disagree, Your Honor. I'm not sure exactly what defendants are saying that they conceived of and communicated to Bayer. I'm looking at Dr. Zalipsky's Slide 39, and it says Dr. Bossard conceived of and provided Bayer with PEGylated full-length Factor VIII at the B-Domain with activity.

Earlier Mr. Haug said they were relying on technical reports. This sounds like they're relying on the actual conjugates that were provided. Dr. Bossard didn't give any testimony that she conceived of a B-Domain PEGylated full-length Factor VIII polypeptide conjugate with activity.

THE COURT: Okay. But this sounds more like you're arguing the JMOL then the jury instruction.

MS. BERCIER: I think my question is: What does subject matter mean? Is that just a PEGylated conjugate?

THE COURT: Well, I think that's going to be -- but I guess the main point is I don't think the invention is right. It doesn't have to be an invention to be essentially prior art; right?

MS. BERCIER: I think it's our position that they still have to prove derivation to get derived prior art as part of an obviousness combination.

THE COURT: Okay.

MS. BERCIER: If it's under 102(f), it's automatically part of derivation, and Mr. Haug said earlier they're not asserting 102 anymore. So you know, I'm not sure why there's this entire section of derivation broken out afterwards which is coming up next.

THE COURT: All right. Anybody from defendant want to say something?

MS. BERCIER: I would just add, Your Honor, subject matter here can't be just general knowledge. There's got to be some inventive concept that's included.

THE COURT: Well, it says --

MR. CHEN: Your Honor, may I give you a citation with a subject matter quote?

THE COURT: The Odd Zone.

MR. CHEN: Yes.

THE COURT: I told you I seen it before somewhere.

MR. CHEN: I believe it's 122 F.3d 1396.

THE COURT: Maybe you're doing it for the record, but I'm sitting here looking at the citation.

MR. CHEN: It's Lexis page 1404. It says we

therefore hold that subject matter derived from another not only is itself unpatentable for the party who derived it under 102(f) and then goes to combine it with obviousness.

THE COURT: So do you think it would be -- so part of what maybe goes to Ms. Bercier's view and which may be fair is the context here is this is subject matter that is not otherwise prior art; right, it's private subject matter so to speak.

MS. BERCIER: Yes, not publicly known otherwise.

THE COURT: So I don't know, that probably wouldn't completely take care of your objection, Ms. Bercier, but would you like to add in something along those lines?

MS. BERCIER: Well, the jury instruction sample that we pulled our language from actually uses an invention and that's the W.L. Gore ECR Bard instructions.

THE COURT: Yeah. And you know, it's very hard to tell, part of the thing is that may have been perfectly appropriate for that case, that doesn't mean it's appropriate for this case, you just can't tell, or I can't tell.

So what I'm going to do is provisionally I'm going to go with Baxalta's language of subject matter, and if there is some phrase that you want to add in to indicate that what we're -- subject matter that is not otherwise

prior art, if you want to add in a phrase there, or Mr. Chen, what I'm trying to do here, what's your view?

MR. CHEN: I think that would be okay. Our biggest issue was the invention as you noted.

THE COURT: So why don't you see if you can't think of a phrase to add in here to indicate what we're talking about when we talk about subject matter in the sense of it's something that wasn't known and so it won't otherwise be prior art, see if you can resolve that between yourselves.

MR. CHEN: Thank you.

THE COURT: All right. So the derivation, I take it 5.3 is now unnecessary?

MR. HAUG: It's unnecessary maybe as a stand-alone, but I think it has to be put in as the prior art, maybe obviousness section.

MS. BERCIER: Your Honor, our concern it sounds like they're just trying to shoehorn in a derivation claim here.

THE COURT: So Mr. Haug just said yes, he agrees it doesn't belong here. So let's remove it from here. And let me just think about this. So I think what we may have to do here is -- how much of this, Mr. Haug, do you think is actually even relevant to obviousness?

MR. HAUG: How much of it? I think we --

personally I think we should take the derivation out and put it under prior art.

THE COURT: But there is a lot of stuff here -- but, you know, I have just given you the subject matter, so all this stuff about invention.

MR. HAUG: I agree, so I think we should just delete 5.2.

THE COURT: That's what I was trying to get to.

Ms. Bercier.

MS. BERCIER: Your Honor, this all goes back to my original objection with the 102(f) prior art. This makes it sound like anything that Dr. Bossard sent to Bayer is ultimately subject to 102(f) prior art even if it was something that was already known in the public or something that they already had in its possession. I think defendants need to identify exactly what they're asserting Dr. Bossard conceived and communicated because right now it's very unclear.

THE COURT: That may be a helpful observation. So somebody, Mr. Haug or Mr. Chen earlier, I think you said the technical reports were what you were talking about here. And I think there is two or three of them. Is it something where we could put in the subject matter that we could identify it as being exhibits one, two and three?

MR. CHEN: So is your proposal then to say

subject matter included in X, Y, Z exhibits?

THE COURT: Yes. Something like that.

MS. BERCIER: We absolutely object to that, Your Honor.

THE COURT: No, they're claiming -- it sounds like you're trying to have it both ways. Because you're claiming, you know, it could be anything they're talking about. And you've said they have been all over the lot which may not be exactly unfair, but they seem to have identified three things that were confidential in the sense that they weren't public, and they're saying what they're talking about. So --

MS. BERCIER: Your Honor, if I may. We would like to know for purposes of our own closing argument exactly what defendants are relying on for this 102(f) prior art. We're not saying we want to include it here in the jury instructions. If the jury instructions are going to say subject matter, we need to be able to rebut what that subject matter is and whether it was derived or not.

THE COURT: Why should you all know what it is but the jury not.

MS. BERCIER: Well, I think Mr. Chen is going to go up and say something, or Mr. Haug on Monday, and we at this point don't know. We have got a slide from Dr. Zalipsky saying that it's the conjugates Dr. Bossard

sent.

THE COURT: I'm sorry to interrupt. Is it the case that the defendant is willing to narrow it down which is what you just said you want them to do, the fact that somebody else said something at some different times at least in terms of giving the instruction, that seems to be irrelevant.

MS. BERCIER: Our objection is the subject matter here needs to be the subject matter for Bayer claim, not some generalized knowledge, or just a general concept.

THE COURT: So do you happen, Mr. Chen, to be able to say right now what exactly it is that you think is derived subject matter?

MR. CHEN: PEGylation at the B-Domain of full length Factor VIII.

MS. BERCIER: That's not the claim.

THE COURT: So I guess -- I guess what I meant differently was the pieces of prior art, what are they?

MR. CHEN: The 102(f) prior art you're talking about?

THE COURT: Yes.

MR. CHEN: Don't hold me to this, because I'm just doing it off memory and timeline. There was the research agreement between Nektar and Bayer.

THE COURT: But the research agreement doesn't

have anything in it.

MR. CHEN: It did have a work plan, actually, Your Honor, with proposed ideas.

MS. BERCIER: Again, Your Honor, generalize concept, a business plan that's not part of 102(f).

THE COURT: I thought you said earlier technical reports.

MR. CHEN: I was getting there. I didn't want on the record leaving out that agreement. Nektar did the initial reaction I believe in February on BDD.

THE COURT: I appreciate what you're doing trying to answer my question. But there are two or three different documents that you could identify because they're entered into evidence as exhibits. I don't expect you to remember which of the 1,500 it was.

MR. CHEN: I'm a little tired. We can do that. We can identify the exhibits.

MS. BERCIER: Your Honor, if that's going to go in, I think we're going to ask for another limiting instruction here going back to the proposal we made, communication of a general goal suggestion or research plan does not constitute communication of a definite affirmative idea required for conception. That comes right out of Cumberland Farms v. Mylan. That's 846 F.3d --

THE COURT: I got that cited in here somewhere.

MS. BERCIER: -- 1213, Your Honor.

THE COURT: Hold on a minute.

MS. BERCIER: Your Honor, if they start including documents to support their derivation claim, then that just leads down the road to what documents does Bayer want to include.

THE COURT: No, I don't think it actually leads that way. I mean, in other words, if -- I don't think it leads that way. Hold on just one second.

MS. BERCIER: Your Honor, in Cumberland the Federal District said, "Derivation is not proved by showing conception and communication of an idea different from the claimed invention even where that idea would make the claimed invention obvious."

I think that's directly relevant here. So if they're not asserting 102(f), communication and conception of all elements of the claim, I don't see how we can move forward with including exhibits that are going to point the jury directly to --

THE COURT: Okay. A couple of things. One of which is earlier when I asked Mr. Smith to add in something about the nonpublic, I notice that's actually already in, it's just a few lines below, so you can forget that idea.

In terms of this, I have certainly seen people identify pieces of prior art so that the jury knows what

they're talking about. I am going to -- I'm not going to direct that that happen here.

I do think the sentence about the communication of general goal suggestion, et cetera, which is already on page 49 of plaintiff's instructions, should be included here somewhere. And so we've got -- we've got 5.2, we're going to take 5.3 out when we get to obviousness, which I guess is the next thing.

MR. CHEN: Just to clarify, Your Honor, does that mean 5.2 has the subject matter language?

THE COURT: Yes.

MS. BERCIER: So, Your Honor, would we add the line from your proposed jury instructions on page 49 within the section on prior art, 5.2?

THE COURT: Hold on. Yes, maybe you would add it with two sentences in the paragraph, maybe you would add it after the first sentence before the second sentence.

MS. BERCIER: So just to clarify, Your Honor, the communication from Dr. Mary Bossard, so that the whole paragraph which is two sentences to page 49 of our proposed.

THE COURT: Communication of general goals suggested a research plan does not constitute communication of the -- it's not going to read just like that in there. All right? So you know what, let's -- I don't think I'm going to resolve this right now. I'm going to have to go

back and look at this some more. But in any event, work on the idea that I want to add in something to the effect of what Bayer has on page 49 that comes from I guess its Odd Zone note.

MS. BERCIER: Cumberland.

THE COURT: Cumberland. Thank you. We're going to move to page 53. We're going to do something with it.

Let's go on to obviousness.

So this instruction starts on page 35. And it continues on for three pages to 37. Are there any objections by plaintiff on this?

MS. BERCIER: I don't believe so, Your Honor.

THE COURT: How about from the defendant?

MR. REITBOECK: Georg Reitboeck for Baxalta.

Your Honor, by taking out the section on anticipation, you also took out language on inherency and inherency is something that is valid for a prior art generally and not just anticipation. When you put the pieces in, it's usually addressed in anticipation, but we would ask that we include language on what inherency means in the section on prior art.

THE COURT: Why? Because I don't think there was any actual testimony that some piece of art inherently disclosed something else, was there?

MR. REITBOECK: My understanding was there was

some evidence on the Bossard patent it inherently discloses, I wasn't here all the time, I can't confirm it.

MS. BERCIER: We object to that, Your Honor.

THE COURT: I don't think there is any basis for that, Mr. Reitboeck. Is that right?

MR. REITBOECK: That's right.

THE COURT: So I'm not inclined to do that. Is there any other objection?

MR. REITBOECK: To the obviousness section?

THE COURT: Yes.

MR. REITBOECK: No, Your Honor.

THE COURT: Let's move on. Lack of enablement, I believe you jointly submitted this and there was no objection by either side. Is that right?

MS. BERCIER: There was one objection.

Never mind, Your Honor.

MR. HAUG: There is one, Your Honor, dropped what we had proposed about teaching away.

THE COURT: Yes. So I think that's just argument.

MR. HAUG: Okay. I hear you.

THE COURT: Well, I'm going to stick with not putting in that sentence because I really think that's just a factual argument. So the next thing after that is indefiniteness. And I believe nobody objected to this

instruction; is that right?

MR. HAUG: We're fine with that.

5.6.

THE COURT: 5.6.

Ms. Bercier, you're okay?

MS. BERCIER: No objection.

THE COURT: All right. Let's keep going here. Damages, generally, 6.1.

MS. BERCIER: I'm going to let my colleague, Mr. O'Brien, take over for me.

THE COURT: That's fine.

Mr. O'Brien.

MR. O'BRIEN: Hello, Your Honor. We do have at least one issue or maybe just one issue from your side on damages generally. We really do think that some of the language in here is just a little bit, maybe not the best way of facing what the standard is, where it says that your damages award you should reach this issue should put Bayer in approximately the same financial position that it would have been had the parties reached agreement, you know, my concern is that -- my concern is that that could cause the jury to go back and thinking that wow, Baxalta would never really agree to that in the real world, but in the real world Baxalta hasn't been judged to infringe a valid patent.

And typically the assumption of infringement and

validity has the affect of pushing the royalty rate up from where it would be in the real world where there is some uncertainty discounting what that rate might be, so our preference would be some language along the lines of your damages award, if you reach this issue, should put Bayer in the financial position that it would have been in if the parties had reached a hypothetical negotiation.

THE COURT: Okay. You know, I looked at this. I couldn't quite figure out what the point of the dispute was, but I think that -- let me just check one thing, Mr. O'Brien.

MR. O'BRIEN: Sure.

THE COURT: So Mr. O'Brien, I think the reason we picked the Baxalta suggestion was that we looked at the very recent model instructions from the Northern District of California, and that's about the language that they have there. So I think --

MR. O'BRIEN: Okay.

THE COURT: I understand your point, but I think I'm going to go with the language from the model instructions that we were looking at. Okay.

MR. O'BRIEN: Okay.

THE COURT: Anything else, Mr. O'Brien?

MR. O'BRIEN: I think from our side, everything looks good on the damages section.

THE COURT: All right. And I noticed we've got and Nektar on the third paragraph there, Mr. Smith. I would suggest somebody with a search thing search the document essentially to make sure we got rid of all the Nektar.

MR. SMITH: I don't believe we have a electronic version.

THE COURT: I'll take care of that later.

MR. SMITH: Thank you.

THE COURT: Remind me before we walk out of here because, otherwise, I'll forget.

All right. So we're on to 6.2, reasonable royalty is a measure of damages. Did I understand, Mr. O'Brien -- I was optimistic when you said you have no objections to the rest of damages, period?

MR. O'BRIEN: Yeah. I think from our perspective, everything else looks fine. I don't know about the other side, though.

MR. HAUG: 6.2 is fine.

THE COURT: Okay. So we'll cross out the footnote. And the factors for determining a reasonable royalty citing three pages worth of stuff.

MR. HAUG: No objection.

THE COURT: Okay. No objection.

Availability of non-infringing substitutes on Page 46, Number 6.4.

MR. HAUG: No, for the defendant.

THE COURT: No objection for the defendant.

THE COURT: Okay. 6.5, Reasonable Royalty: Apportionment.

MR. HAUG: We are fine with that one, too, 6.5.

THE COURT: Okay. We'll cross off the reference.

6.6, Date of Commencement of Claimed Damages. So we're good on that? All right.

MR. HAUG: We're fine.

THE COURT: Okay. So is there anymore objections to anything here?

MR. HAUG: I think we're okay.

THE COURT: Okay. So we owe Mr. Smith an electronic version of this, and we have to decide something about the derivation instruction. But otherwise, I've ruled on everything here, I think. And I would ask once you have the electronic version, Mr. Smith, that you do check it for Nektar.

MR. SMITH: Happy to do it. Will you be implementing some of the rulings?

THE COURT: I'd like you to implement all of them once we're done here. You'll get an email copy, and I will copy the other side, too.

MR. SMITH: Thank you. And so there was some

little things you were supposed to be meeting and conferring and hopefully agreeing on, and I think we're going to have to get you something that's our view on derivation. But, otherwise, if you could send me something by like four o'clock tomorrow.

MR. SMITH: Seems reasonable, Your Honor, yes.

THE COURT: And then I'll read it once to make sure I'm happy, and then you'll be in charge of production for Monday morning.

MR. SMITH: Yes, sir.

THE COURT: Thank you, Mr. Smith.

All right. The verdict form.

So I worked off, I believe, the defendants' version which seemed to me to have one or two -- actually the two versions of verdict form were pretty close to each other. But there were a couple things that I thought about that I would kind of like to do. One of which is on this doctrine of equivalents issue, assuming that it's going to go to the jury, which is what I think is going to happen. I wanted to have a question so we could tell whether the jury decides there's literal infringement or doctrine of equivalents infringement.

And so in the last trial I had, which I thought I brought out the verdict form -- wait a second. Oh, not this one.

Oh, so in the last trial I had, which was called BioRad versus 10X, we had the same issue. And somewhere in the verdict form -- wait. Hold on just a minute. I'll be right back. Don't go anywhere.

(Recess was taken.)

THE COURT: So in this case, BioRad versus 10X, which is docket item 15-152 or the docket item is 477, in the verdict form, after having boxes to check whether or not the jury found infringement, then there were two questions. And the first was if you found infringement of the claims, with some explanation.

Did the plaintiff prove it's more likely than not that that element was literally satisfied by such and such? Yes, no.

Then the next question was: If you answered yes to question four or the previous question, please skip this question. But if not, then it was asked whether or not they had proved it by the doctrine of equivalents.

So what I'm wondering is it strikes me that it's just a good thing to find out what the answer to this is. Is there any objection to the principle?

MS. BERCIER: No objection to the principle.

THE COURT: Mr. Haug.

MR. HAUG: No. I don't have any objection to the principle. I think it should be as clear as we can make

it, so they're not confused by the verdict form, obviously. And what I would propose now is maybe we should propose to you, see if we can't agree on a form on this one.

THE COURT: Okay. That's what I was hoping you would say.

MR. HAUG: Yeah. We can do that hopefully.

THE COURT: Okay. So that's good.

So actually so I should probably just start with I guess we don't need question two, anticipation. Actually on the proposed verdict I submitted, are there any objections?

There's some more blanks to be filled in or things, but are there any actual objections?

MR. HAUG: We would object to question seven, reasonable royalty damages.

THE COURT: Hold on a minute. Question seven is the damages.

MR. HAUG: Correct. I think sub B, I think, is confusing.

THE COURT: Well, you mean where it says, oh --

MR. HAUG: Royalty base.

THE COURT: -- please answer this question only if at least one -- yeah, actually you proposed this language, Mr. Haug, but I agree with you. You know, actually at least one, same claim, that's not a good

question.

I'll tell you what, the concept here, though, do you agree with the concept which after all is your concept?

MR. HAUG: Yeah. We would agree with A and C down at the bottom. I think B is confusing.

THE COURT: Oh, you're talking about the royalty base?

MR. HAUG: Right.

MR. O'BRIEN: Your Honor, I don't think that makes sense. I think we need --

THE COURT: No. So let me just actually say what I was doing here, the royalty -- so your expert, Mr. O'Brien said some, and I don't remember whether there was zeros or actual dollars. Don't you guys agree on what the royalty base is here?

MR. O'BRIEN: I believe so. I'm pulling up Dr. Rausser's, the net sales number he has here times a one percent royalty rate. That's the exact for one. That's the same net sales or royalty base number we want to use. And then he times it by the royalty base, and then equals -- it equals the damages amount. It's pretty much the same as this proposal is here.

MR. HAUG: This slide doesn't say royalty base, it says net sales. We agree on the net sales number that both sides were using in their various different

assessments. And so I think saying royalty base and putting in a number in there, I don't think is appropriate, and I think it's confusing.

THE COURT: Okay.

MR. HAUG: If you have the royalty base percent, and you have a total damages, you can figure out what they use as a royalty base.

MR. O'BRIEN: I think this would confuse the jury because it's suggesting he wants the jury to pick a lump sum or something. I think he's --

THE COURT: So hold on just a minute. So is one of the slides -- because I think I seem to recall somebody's expert report was put in or a page of it. Does the jury actually just have whatever is the royalty base or net profits is written out, all nine digits?

MR. HAUG: I think that was theirs.

THE COURT: Okay.

MR. O'BRIEN: Yes, we would like that.

THE COURT: As long as they already have it, I'm perfectly happy, if there's disagreement, to just let them fill in the blanks, but I think we ought to have -- so, wait.

What you're telling me, Mr. Haug, because it's getting late here is you think the royalty, there should only be fill in the royalty rate, fill in total damages.

MR. HAUG: Yes.

MR. O'BRIEN: Your Honor, just to --

THE COURT: And just I am correct, you did submit this form with all three; right?

MR. HAUG: We did. We did submit this form, and Bayer came back and wanted to put a number in there.

THE COURT: Yeah. Yeah. Well, so I'm --

MR. HAUG: I mean, I'm okay leaving our form blank, but I know they didn't want that.

THE COURT: Yeah. Yeah. So I'm going to take out -- I'm not going to put the number in.

MR. BADKE: But the number is undisputed, though.

THE COURT: Yeah. Well, Mr. Haug says the one side calls it a royalty base, the other side called it the net profits. I think the number is there. It is undisputed.

It apparently is called different things or maybe it's referred to as different things. So if there's no agreement, I'm not going to put it in.

MR. O'BRIEN: We can call it net sales as long as we get the number that's already in the damages --

THE COURT: No. I just --

MR. O'BRIEN: -- on the verdict form. Or even no name at all, just the number is fine.

THE COURT: No. I think I'm going to pass on that.

MR. O'BRIEN: Okay. Just --

THE COURT: So that was your only objection, Mr. Haug, was to this, basically to having something filled in in the B there?

MR. HAUG: Correct. It's either blank or out.

THE COURT: Okay. We'll just leave it blank. So that's your only objection to the verdict form?

MR. HAUG: Well, but for what I think we're still trying to work on --

THE COURT: Sorry. Which?

MR. HAUG: Number one.

THE COURT: Yeah. Well, that's not an objection so much as you're going to work on it and figure it out.

MR. HAUG: It's not an objection except that --

MS. BERCIER: Your Honor, we don't think it's necessary in question four to include a special interrogatory on unexpected results.

THE COURT: Well, so here's what I'm thinking about that. Well, first off --

MR. O'BRIEN: Can I just preserve something for the record on that last damages dispute? We just wanted to say that, you know, we think because it's undisputed, the net sales or royalty base should be included in the verdict

form just to avoid the chance that the jury makes an error. That's our concern just for the record.

THE COURT: Well, you know, I think the jury may make a math error. Probably not if they go with your side, but they might make a math error if they go with something else. But so the record is preserved.

Mr. Haug, do you have any actual other objections?

MR. HAUG: We don't have any other objection except I note on the question four for obviousness, I think Your Honor put in note, special interrogatory on unexpected results.

THE COURT: Right. So I was going to get that, but right now I was -- okay. So in any event, we're getting rid of question two. We'll have to do some renumbering because of that not being there.

I guess I actually, at the risk of causing more work -- no. Actually, no, I think I'll keep that thought to myself.

So, wait. And in fact, I don't need question three, derivation, either.

MR. HAUG: No. No. We're getting down to five pages.

THE COURT: Well, we're doing a good job here.

So here's what I was thinking on this special

interrogatory, and so there's only one secondary consideration that's been advanced here; right?

MS. BERCIER: Yes, Your Honor.

THE COURT: And so I thought because that is a factual finding, and I'm guessing that there's a reasonable chance someone is going to be asking me on JMOL to decide obviousness. It would be helpful to know what the jury thinks is a factual matter on the unexpected results because I don't have to spend a lot of time deciding that myself when the jury presumably is going to decide it.

MS. BERCIER: Your Honor, our concern is there is four factors for obviousness and including one of those which is objective indicia, calling it out might just confuse the jury in terms of what else they're supposed to be finding.

THE COURT: That's the reason, partly, Ms. Bercier, that I didn't try to write the question because I figured it would require some effort, but I think it would could be done. I think most of the books encourage us to do things like this. I don't actually read the books, but that's what I've heard.

Mr. Haug, what's your view on this?

MR. HAUG: I think we should have a special interrogatory that's directed to unexpected results like the one we actually proposed.

THE COURT: You had one?

MR. HAUG: We did. I guess they proposed it to me. I'm sorry, we didn't give that to you.

THE COURT: So you already ruled against this. But you changed your mind.

So here is the thing. My belief is that on -- well, so let's do this. I think it would be good to have the question. Why don't I add that to your list of things to try to work out between you. You know, and so why don't you do that. And that will take care of the verdict form. Right?

MS. BERCIER: Yes.

THE COURT: Right?

MR. HAUG: Yes, Your Honor.

THE COURT: Okay. So I wrote this down somewhere. So I think, Mr. Smith, I said you're going to get me the revised jury instructions before on tomorrow.

MR. SMITH: That's what you said, Your Honor. Would you like the verdict form at the same time?

THE COURT: Thank you very much.

MR. SMITH: We have that already.

THE COURT: You have that?

MR. SMITH: Yes.

THE COURT: Revised jury instructions. Verdict form. And so we have got -- and I've got to send you the

electronic version of the jury instructions. And I have got to send you something about derivation. And then we have got our marching orders both ways. Right?

MR. SMITH: I believe so, Your Honor. Thank you.

THE COURT: Is there anything else you all want to -- I doubt that this will help, but Mr. Smith, you want the Bio Rad verdict form just to see what I did the last time?

MR. FLEMING: I'll give it to him, Your Honor.

THE COURT: Because it's got how I did the Doctrine of Equivalents before. You don't have to do it exactly like that, but I thought it might help. As I recall it took us more time than I care to. If there is anything else.

MR. FLEMING: Your Honor, I got one thing, a quick housekeeping. Mr. Badke and I have been discussing there are a couple of exhibits that we got confused on whether they are in the record or not. We're going to work it out tomorrow, and hopefully we'll agree that they should all go in. Perhaps we can do it early on Monday when the court is back in session, just so we can work with them over the weekend.

THE COURT: Sure. If you agree on something you want to send me a letter or file it with the clerk or

something else, but obviously if you agree on something, it's not going to be a problem.

MR. HAUG: Right. I do have a question about closing.

THE COURT: Thank you, Mr. Haug. How long do you all think you want?

MR. BADKE: We actually agree on this.

THE COURT: Okay.

MR. BADKE: I think we both would like an hour-and-a-half each.

THE COURT: Yeah. All right. You're both very experienced lawyers and you know what you're doing, so you can have an hour-and-a-half each. I think I forget whether it was with you or with someone else, so basically that means you get ninety minutes, so Mr. Badke, that means basically you can reserve nine minutes for rebuttal, so you get eighty-one minutes, but if you go past eighty-one, then how much rebuttal you get goes down. Okay?

MR. BADKE: I can only reserve up to nine minutes?

THE COURT: Yep.

MR. HAUG: Maybe we should only make it an hour.

MR. BADKE: Okay.

MR. HAUG: Does Your Honor object -- we haven't made any kind of decision, would Your Honor object if the

closing was split between two lawyers?

THE COURT: Well, what does the other side say?

MR. HAUG: I didn't discuss that with them.

MR. BADKE: Fine with me.

THE COURT: It's fine by my if there is no objection by Mr. Badke.

MR. HAUG: I was just asking. We haven't thought about that.

THE COURT: Okay. If there were -- if you're both agreeable to the concept, then I'm fine. And, in fact, it might give the jury, they might respond better to having two people just in terms of the change of pace and style. So all right.

So I'll be here at 9:00. Hopefully there won't be any disputes. And after I get these things from Mr. Smith, I will read them Saturday night and hopefully resolve them, if there is anything to resolve, get back to you then so that you're not working on this Sunday night, Mr. Smith, you can be working on something else.

MR. SMITH: Thank you, Your Honor.

THE COURT: All right. Anything else? Okay. We'll be in recess.

(Court recessed at 6:11 p.m.)