IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

ALLERGAN, INC.	*	Civil Docket No.
	*	2:09-CV-97
VS.	*	Marshall, Texas
	*	
	*	August 3, 2011
SANDOZ, INC.	*	1:15 P.M.

TRANSCRIPT OF BENCH TRIAL
BEFORE THE HONORABLE JUDGE T. JOHN WARD
UNITED STATES DISTRICT JUDGE

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P R O C E E D I N G S

COURT SECURITY OFFICER: All rise.

THE COURT: Please be seated.

Ms. Brooks.

MS. BROOKS: Thank you, Your Honor.

ANGELO P. TANNA, M.D., DEFENDANTS' WITNESS,

PREVIOUSLY SWORN

DIRECT EXAMINATION

BY MS. BROOKS:

Q. Good afternoon, Dr. Tanna.

A. Good after, Ms. Brooks.

Q. Right before the lunch break, I was frantically looking for a copy of Walters. We now have

one before you in your binder. And it's DTX138. Oh, I'm sorry. That's the abstract actually, which you did look at. Now, let's look at DTX137. And that is the Walters paper.

So you say, Dr. Tanna, you had not had a chance to look at this before rendering your opinion; is that right?

A. No, that's not true. Now that I see it, I do recognize it. I have looked at this reference.

Q. So you did consider it in rendering your opinion?

A. I did consider it, yes.

Q. All right. Then let's look, if we could, please, at Bates No. 346, the page ending in that Bates number.

MS. BROOKS: And highlight, if we could, in the right-hand column where it begins similar means -- mean decreases in IOP.

A. 346?

Q. (By Ms. Brooks) Yeah, 346. It should be the bottom right-hand corner, the Bates No. 000346.

Do you have that?

A. Yes, I do.

Q. Okay. And it's also up on the screen.

So let's see what Walters also disclosed about

this study. It says: Similar mean decreases in IOP were noted for both dosing regimens at hours 2, 4, and 7 in the diurnal measurements.

In the three-times-daily group, an additional mean decrease in IOP of 3.5 millimeters of mercury was observed at hour 9, after the morning dosing, or two hours following the afternoon dosing.

Do you see that, Dr. Tanna?

A. Yes, I do.

Q. So isn't it true that one of skill in the art would look at Walters and see that there was a statistically significant decrease in IOP at 9.0 hours after morning dosing on the three-times-a-day Brimonidine?

A. Yes. And it is overall, in my opinion, that three-times-a-day Brimonidine is more effective than twice-a-day Brimonidine. And, in fact, that is in my expert opinion, and I used a different reference as the main reference for that, specifically Konstas.

THE COURT: Doctor, she hadn't asked you any of that.

THE WITNESS: I'm sorry, Your Honor.

THE COURT: If they want you to repeat that testimony or what's in your expert report, they'll ask you. But unless everybody's not listening to me,

the Court's going to start tightening up. I'm not here to listen to lectures. I'm here for you to answer the questions asked, and stop talking.

Are we clear?

THE WITNESS: Yes, Your Honor.

THE COURT: Thank you.

Q. (By Ms. Brooks) And let's just see if we can find the graph that correlates to this data in PTX134, which you don't have before you, Dr. Tanna, because it's too large, but has previously been discussed with Ms. Batoosingh.

MS. BROOKS: If we can go to PTX134 and specifically at Bates No. 676465, Mr. Exline.

Q. (By Ms. Brooks) And do you see this graph, Dr. Tanna?

A. Yes, I do.

Q. Could you show the Court where that 3.5-millimeters of mercury difference occurs between the twice-a-day dosing of Alphagan and the three-times-a-day dosing of Alphagan?

A. It's not doing --

Q. Here, I'll try to help you.

A. I have a pointer. May I use a laser pointer?

Q. Sure. Or did I get it close right there?

A. Well, that's it, yes.

Q. Okay. And so, again, you agree that -- one of skill in the art would know, based on this data, that there was an actual statistically significant decrease in the reduction of intraocular pressure at approximately hour 9 between the three-times-a-day dosing of Alphagan and the twice-a-day dosing?

A. Yes, in this study.

Q. Now, let's move to your discussion of how the amount of BAK that was claimed would have been obvious. You said the BAK was the most common preservative; is that correct?

A. Most commonly used in ophthalmic formulations, yes.

Q. And, in fact, we saw --

MS. BROOKS: Mr. Exline, could you pull up Defendants' Slide 10 that they used in opening statement? And if not, I can always put it on the ELMO.

There we are.

Q. (By Ms. Brooks) So this was shown to the Court by the Defendants in opening statement showing all the different drug products that contain BAK.

Do you agree with that, Dr. Tanna?

A. I do.

Q. But let's look at the amount of BAK in these various products. Isn't it true that there are no less

than six different amounts of BAK in these various ophthalmic products?

A. That looks right.

Q. Thank you.

Let's move on now to your discussion of other combination drugs. You told us about a drug called Timpilo; is that right?

A. I did, yes.

Q. And you told us about a drug called Cosopt. Of course, we know about that, right?

A. Yes.

Q. And also a drug called Xalacom; is that right?

A. That's correct.

Q. In fact, on Slide 36 that you used, you showed both the Timpilo, the Cosopt, and the Xalacom.

Now, in looking more closely at the Timpilo picture that you used, that's not actually a picture of Timpilo, is it?

A. I don't know that -- I can't tell from that picture. I don't know.

Q. Isn't it, in fact, just a picture of the bottle of Pilocarpine?

A. I don't think so, because it typically would have a green cap. So I can't tell from this picture. I am not sure what that's a picture of.

Q. Okay. Now, Timpilo has never been approved for use in the United States, correct?

A. I was under the impression that it was in use in the United States. That's my impression. I could be mistaken about it, but my understanding is that it was in use in the United States.

Q. Okay. What about Xalacom; has Xalacom ever been approved for use in the United States?

A. No, it has not.

Q. Now, while we're talking about Xalacom --

MS. BROOKS: Let's just leave that up there, if we could, Mr. Exline.

Q. (By Ms. Brooks) We're going to revisit some organic chemistry.

Xalacom is the active ingredient in Latanoprost; is that right?

A. That's correct.

Q. And Latanoprost is what's known as a prostaglandin analog; is that correct?

A. That is correct.

Q. Are the prostaglandin analogs normally your first choice of medication for a new glaucoma patient?

A. For me today, yes.

Q. And, in fact, the Latanoprost is sold here in the United States as Xalatan; is that right?

A. That's correct.

Q. But the combination of Xalatan and Timolol, also known as Xalacom, has never been approved for use in the United States; is that correct?

A. That is correct.

Q. And you yourself have never prescribed the use for Xalacom, correct?

A. I have never prescribed Xalacom. That's correct.

Q. Now, in that same category of prostaglandin analogs, would you put Travoprost?

A. It is in the same category.

Q. And that's also known as Travatan; is that correct?

A. That's correct.

Q. There is no combination drug of Travatan and Timolol approved for us in the United States; is that correct?

A. That is correct.

Q. And also within what you would call a prostaglandin analog, or we would call a prostamide, is a compound called Bimatoprost.

Are you familiar with that?

A. Yes, I am.

Q. And Bimatoprost is sold here in the United

States by Allergan under the name Lumigan.

Are you familiar with that?

A. Yes, I am.

Q. There are no -- I think you mentioned that Ganfort, which was a combination of Bimatoprost/Timolol drug; is that right?

A. Correct.

Q. But Ganfort is not approved for use here in the United States; is that correct?

A. No, it's not.

Q. And just to show how subtle differences make a very big difference, Bimatoprost and Latanoprost, would you put them in the same category as far as mechanism of action?

A. There may be small differences in terms of the mechanism of action. I think it's a matter of controversy.

Q. Well, in fact, Latanoprost is what's known as 17-phenyl-PGF2-alpha, correct?

A. I know there's a PGF2-alpha-agonist.

Q. Okay. And at the C1 position on the alpha chain is an ester; is that right?

A. That I don't know offhand.

Q. So I may know a little more organic chemistry. What about Bimatoprost? Are you aware that if the C1

position on the alpha chain of Bimatoprost is an amide?

A. I believe that I can picture that and agree with you on that, but I would have to look at the structure to be sure. It's a complex -- it's a big molecule, and I don't know offhand for sure.

Q. Would you agree with me that an ester is different than an amide?

A. It certainly is.

Q. And can, in fact, behave differently in situ?

A. Yes, it can.

Q. Now, let's go to -- back to the Timpilo. You should have in your binder, Dr. Tanna, the label for Timpilo, I hope. And I don't know if we numbered it since it wasn't actually previously in use, but if you go through your binder, you should see a label for Timpilo.

A. Can you tell me approximately where?

Q. Oh, it's not in your binder. Sorry.

MS. BROOKS: May I approach, Your Honor?

THE COURT: Yes.

Q. (By Ms. Brooks) Now, Dr. Tanna, you've referred to Timpilo as a combination drug; is that right?

A. It is a combination drug, yes.

Q. Well, if we actually --

MS. BROOKS: If we can go to the ELMO, Mr. Exline.

Q. (By Ms. Brooks) And here's the label for Timpilo.

THE COURT: Not quite. Here we go.

COURTROOM DEPUTY: Can you push the doc cam up there?

MS. BROOKS: I sure can. Let's see here. Doc cam?

COURTROOM DEPUTY: Uh-huh.

MS. BROOKS: Perhaps -- Mr. Exline, do you know -- do we have the Timpilo label in the system? We don't? Okay. It would help if I turn it on. I apologize. There we go. It's my fault. I'm sorry. I didn't even turn it on.

Q. (By Ms. Brooks) Dr. Tanna, isn't it a fact that Timpilo is dispensed in what is described as a unique, two-chambered vial system?

A. Yes.

Q. And one of the chambers contains a concentrated solution of Timolol and Pilocarpine at a pH of approximately 3.5; is that right?

A. Correct. Correct.

Q. Now, in relation to the pH of the eye, 3.5 is extremely acidic, is it not?

A. It is more acidic than the ocular surface and the pH of the eye in general, yes.

Q. And the need for this low pH is to prevent the hydrolysis of Pilocarpine prior to dispensing; is that correct?

A. Yes.

Q. So you would agree with me, Dr. Tanna, that a pH can have a significant effect on an active ingredient?

A. Yes, it can.

Q. And it says the other chamber contains -- can you pronounce that word for me, so I make sure I say it right?

A. It's diluent.

Q. Diluent solution with a pH of 7.8 to 8.2 for Timpilo 2; and 8.5 to 9.5 for Timpilo 4.

Did I read that correctly?

A. Yes, you did.

Q. And the two solutions are separated by an internal plug?

A. Yes.

Q. So this isn't the convenience of having two active ingredients in one bottle, correct?

A. It is a little more complicated than that. You have to mix them together effectively by using the

system.

Q. And for whatever formulation reason, the formulators were not able to simply put the Timolol and the Pilocarpine into one bottle for shelf life?

A. Correct.

Q. And had to go to this two-chambered system with two different pHs and a plug in the middle; is that right?

A. That's right.

Q. Now, another -- so that's the Pilocarpine/Timolol one.

You also mentioned a combination product called Probeta, which is Levobunolol and Dipivefrin?

A. It's pronounced Dipivefrin (pronounces).

Q. Dipivefrin (pronounces). Thank you.

MS. BROOKS: Should I push something to go?

MR. LOVE: It's there.

MS. BROOKS: There we go. I think we're back.

Q. (By Ms. Brooks) And that's called Probeta; is that right?

A. That's correct. That's available in Canada.

Q. So that's never been approved for use here in the United States, correct?

A. That's correct.

Q. And you yourself have never prescribed it?

A. Correct.

Q. Then we have the Xalacom, which we've already talked about, the Ganfort which we've already talked about, and then something where it's Travoprost/Timolol combination; is that right?

A. DuoTrav, yes.

Q. DuoTrav. That also has never been approved for use in the United States, correct?

A. That's correct.

Q. And you yourself have never prescribed it?

A. That's correct.

Q. Now, I take it you weren't part of -- well, have you ever been part of an FDA approval process for a combination drug?

A. Well, we were one of the clinical trial centers for DuoTrav for one of the Phase 3 studies in the U.S.

Q. So there were Phase 3 clinical trials conducted on DuoTrav here in the United States, correct?

A. That's correct.

Q. And I assume that you, as one of the centers, attempted to perform those studies accurately, correct?

A. Yes, we did.

Q. And attempted to gather the best data that you could?

A. Correct.

Q. And despite your efforts and all the other centers' efforts, to this day, the FDA has refused to approve DuoTrav for use in the United States?

A. That's correct. They're stuck in the approvable letter stage.

Q. And that's been going on for years, has it not?

A. Correct.

Q. Just a couple more areas to cover, Dr. Tanna. You showed us DTX167 on direct examination. That was the Larsson reference, and you said that this showed that the patients -- well, actually, why don't you tell us your recollection of what this study showed.

A. Well, this looked at normal subjects, not normal volunteers, and they were dosed with Timolol concomitantly with Brimonidine, each on a sort of BID schedule, but only a total of three doses were given. And then the investigators evaluated the rate of production of aqueous humor in the eyes as well as the intraocular pressure. And what they observed was that the intraocular pressure was lowest in the group of people getting both Timolol and Brimonidine, and the

aqueous production flow rate was also lowest in that group. And the pressures were higher in the other two groups, people getting just Timolol or just Brimonidine.

Q. So this would lead one to believe that there may be some benefit to concomitant therapy with Timolol and Brimonidine, correct?

A. It sort of validates and explains that when you use the two together, you get a lower pressure and you get an additive reduction in the production of aqueous humor.

Q. But this doesn't tell anyone of skill in the art whether one would be able to successfully combine these two drugs in the same bottle, correct?

A. That is correct.

Q. And the individuals who were tested in this reference were actually healthy volunteers and not actually individuals suffering from glaucoma; is that right?

A. That is correct.

Q. And there were only a total of three doses given?

A. That is correct.

Q. And Larsson itself, this reference, is actually disclosed on the face of all of the patents in this case; is that right?

A. That is correct.
Q. Now, let's move on. You showed and discussed with the Court the 19T study and the 0 -- 507T study.
Do you remember that?
A. I do.
Q. Now, neither the 19T study nor the 507T study are prior art to the patents-at-issue; is that correct?
A. That is correct.
Q. Now, let's go, if we could, to your written description opinion.
You stated in your opinion that Claims 1, 2, and 3 of the '149 patent were invalid based on lack of written description; is that right?
A. That's correct.
Q. You did not render that opinion in relation to Claim 4, correct?
A. That is correct.
Q. Now, Claims 1, 2, and 3 deal with a method of treating glaucoma or ocular hypertension by topical administration of about .2% Brimonidine by weight to an eye of a person in need thereof, said improvement comprising topically administering to said eye in a single composition about .2% Brimonidine by weight and about .5% Timolol by weight twice a day as the sole active agents, wherein said method is as effective as

administration of .5% Timolol twice a day and .2% Brimonidine three times a day to said eye, wherein the two compounds are administered in separate compositions.

Did I get the claim correct, I hope?

A. Yes.

Q. All right. Now, let's look at where the effectiveness of administration is discussed in the patent itself.

If you would go, please, sir, to Column 4 and begin with Example 2. Do you see that?

A. I do. I can go to it in my own exhibit, because I can't see -- okay. There we go.

Q. There we go.

So this is saying here, this is a study that it's describing, correct?

A. In Example 2, yes.

Q. Yes.

A. Uh-huh.

Q. And did you have an opportunity, Dr. Tanna, to compare the description of this study to the 13T study that was submitted by Allergan to the FDA?

A. I did.

Q. Now, were you here when Dr. Whitcup testified?

A. I was.

Q. Did you hear Dr. Whitcup say that what the FDA

requires for initial clinical trials of a combination product is that the combination product be compared to each of the monotherapies?

A. Yes, I heard him say that.

Q. And you have no reason to disagree with that; is that right?

A. I don't disagree.

Q. So what the FDA wanted to see was the efficacy of Combigan as compared to Brimonidine three-times-a-day monotherapy, correct?

A. Yes.

Q. And the FDA wanted to see the efficacy of Combigan as compared to twice-a-day Timolol monotherapy, correct?

A. That was part of what the FDA wanted to see, yes.

Q. And if we go on Example 2, which begins at Column 4, Line 49, it goes all the way through to the bottom of Column 4, all the way through to the Column 5, and all the through to Column 6, 7, 8, and essentially ends at Column 9 where it ends with Example 2; is that right, Dr. Tanna?

A. That's correct.

Q. And what the conclusion as reported of the 13T study in the patent says: Conclusions -- and I'll stick

with the right specification so we have the numbers right.

Conclusion starts at the bottom of Column 8 and runs over into Column 9. Here we go.

Conclusions: The combination treatment, Brimonidine Tartrate .2% with Timolol .5% administered twice a day for three months was superior to Timolol twice a day and Brimonidine three times a day in lowering the elevated IOP with patients with glaucoma or ocular hypertension; is that right?

A. That's what it says.

Q. And it says the combination administered twice a day demonstrated a favorable safety profile that was comparable to Timolol twice a day and better than Brimonidine three times a day with regard to the incidence of adverse events and discontinuations due to adverse events; is that right?

A. Yes.

Q. So all of this is in the specification of the '149 patent, correct?

A. That's correct.

Q. Both the methodology of how the test was run, correct?

A. That's correct.

Q. The fact that there were three groups in the

test, correct?
A. Correct.
Q. The dosing regimen for each of the groups, correct?
A. Correct.
Q. And, in fact, Dr. Whitcup told us that in order for the Timolol-only group not to know that they weren't getting Brimonidine, they were given a third drop as a placebo?
A. And the same is true for the fixed combination group.
Q. Exactly. So in order to keep this a double-masked study, there was even a placebo drop administered to the combination group, and a placebo drop administered to the Timolol monotherapy group; is that right?
A. Right. That's very standard.
Q. And this is all detailed in the patent, correct?
A. Correct.
Q. Then if we look specifically at Table -- the table that is at the bottom of Column 3, Mr. Beck told us that this is the actual formulation that was the final formulation for Combigan.
Are you aware of that, Dr. Tanna?

A. That he testified to that effect, I was not aware of that, but I accept that to be true.

Q. Okay. So in the patent, one of skill in the art would know how to make Combigan, correct?

A. Correct.

Q. And one of skill in the art would know how to conduct a study to determine whether or not Combigan was as effective as Brimonidine three-times-a-day monotherapy and as effective as Timolol twice-a-day monotherapy, correct?

A. That one wouldn't know how to conduct such a study?

Q. Yes. It's all laid out in the patent itself.

A. I'm not sure it really tells you how to conduct a study in the future. I don't -- I don't see that in the patent.

Q. Is the methodology of the study laid out in the patent?

A. The methodology of the study that was done in the example is laid out in the patent, but you're describing a different study, aren't you?

Maybe I misunderstood.

Q. Oh, I'm sorry, Dr. Tanna.

The study as described in the patent is a study where Combigan or the combination product was

compared to Brimonidine three-times-a-day monotherapy and was compared to Timolol twice-a-day monotherapy, correct?

A. That's correct.

Q. And that study is laid out in the patent, correct?

A. Yes, it is. Yes.

Q. And the results of that study are laid out in the patent, correct?

A. Yes.

Q. And the formulation for the combination product is out -- also spelled out in the patent, correct?

A. That's correct.

Q. Thank you.

Now, I have just one more area of questioning, and it sort of goes to your overall obviousness opinion.

My understanding, if I heard you correctly, Dr. Tanna, is that -- well, I don't want to overstate it. You seem to show us references that would encourage one to want to combine Brimonidine with Timolol in the same bottle.

A. Correct.

Q. And you didn't show us any references that might discourage one from doing that; is that right?

A. That's correct.
Q. Now, let's look at the Brimonidine label itself. It's DTX129 that you showed the Court.
MS. BROOKS: And if we go to the second page of that reference and blow up, Mr. Exline. It's very hard to see, but if we can blow up the top part here.
Oops, I don't know what happened. If you can -- the second column, if we can blow up about -- a little lower than that, please, about -- blow up the top part but all the way to where there's a break.
There we go.
Q. (By Ms. Brooks) If we look right down here, Dr. Tanna, right before it says at the very bottom tricyclic antidepressants.
Do you see that?
A. I do it. It specifically says to use it with caution and take with beta-blockers.
Q. Timolol is a beta-blocker?
A. That's correct.
Q. And the actual label for Brimonidine tells one of skill in the art to combine Brimonidine with caution with a beta-blocker, correct?
A. That's correct.
Q. And certainly one of skill in the art would

have read the label?

A. That's correct.

Q. Thank you.

MS. BROOKS: No further questions.

THE COURT: Redirect?

REDIRECT EXAMINATION

BY MR. BENSON:

Q. Good afternoon, Dr. Tanna.

A. Good afternoon.

MR. BENSON: If I could have the Timpilo reference that Counsel was showing you on the screen, if that's possible.

Was there a DTX number with that or anything?

MS. BROOKS: No, I'm afraid not, but we gave you a copy.

MR. BENSON: Well, that's okay.

Q. (By Mr. Benson) Do you have a copy of that in front of you?

A. You're referring to the Timpilo product label?

Q. That's right.

A. I have it.

Q. Now, you agreed with Counsel that the Pilocarpine and Timolol Maleate of Timpilo could not be formulated in the same bottle, correct?

A. Well, I would say that they weren't formulated in the same bottle. I don't know for sure that they cannot be formulated in the same bottle, but they were not.

Q. Well, let's look at the front of this -- of this label, and Counsel showed you the first -- the first paragraph right under presentation.

Do you see that?

A. I do.

Q. And that was the paragraph you testified about?

A. That's correct.

THE COURT: I've got a copy of it here, so I can follow you.

MR. BENSON: That's okay.

Q. (By Mr. Benson) Well, now Counsel didn't show you the next paragraph, correct?

A. Correct.

Q. Okay. Could you please read that into the record?

A. Prior to use of Timpilo, the two solutions are mixed together, the resulting solution for administration has a pH of 6.4 to 6.8.

Q. Does that indicate the Timpilo formulation is formulated into the same bottle?

A. I'm not sure what you mean by formulated into the same bottle.

Q. Okay.

A. Well, it is one bottle that has two separate chambers in it, so I guess you would call that one bottle.

Q. Let's go to -- do you see where it says -- well, it says here prior to the use of Timpilo, the two solutions are mixed together.

Do you see that?

A. Yes, I do.

Q. So you'll agree with me that the two separate solutions are being mixed together, correct?

A. Correct.

Q. If you could go to Page 8 of 10, and do you see where it says pharmaceutical precautions?

A. Yes, I do.

Q. And it says here -- and I'll read this into the record -- store at room temperature; do not freeze; protect from light; Timpilo is stable for four weeks after mixing.

Did I read that correctly?

A. Yes, you did.

Q. What, if anything, does that suggest to you as to whether or not these two drugs are being formulated

into the same bottle?

A. I think they are formulated into a special bottle that has two separate chambers and then you kind of bring them together right before you're about to start using it. And then they're stable for four weeks. That's how I read it and hear it.

Q. So for four weeks the two drugs are mixed together, correct?

A. Correct.

Q. Now, in any -- in Claim 1 through 4 -- Claims 1 through 4 of the '149 patent and Claim 1 of the '976 patent, did you see any limitation relating to the shelf life stability of the formulation?

A. No, I did not.

MR. BENSON: I have no further questions, Your Honor.

MS. BROOKS: No questions. Thank you, Your Honor.

THE COURT: Okay. You may step down.

Who will be your next witness?

MR. BENSON: Your Honor, we may re-call Dr. Tanna in a rebuttal case, if time allows.

THE COURT: Okay.

THE WITNESS: Shall I remove these items?

THE COURT: No. Somebody else will take

care of that.

Next witness.

MR. RUZICH: Defendants call Dr. Laskar.

THE COURT: Okay.

(Witness sworn.)

MR. RUZICH: Good afternoon, I'm Rich Ruzich, and I'll be handling for all Defendants, including Apotex.

THE COURT: Okay. Thank you, Mr. Ruzich.

MR. RUZICH: May I proceed, Your Honor?

THE COURT: Please do.

MR. RUZICH: Thank you.

PAUL LASKAR, Ph.D., DEFENDANTS' WITNESS, SWORN

DIRECT EXAMINATION

BY MR. RUZICH:

Q. Good afternoon, Dr. Laskar. Would you please introduce yourself to the Court.

A. My name is Paul Andrew Laskar.

Q. And are you currently employed?

A. Yes, I am.

Q. By whom?

A. I am self-employed. I have a consulting organization called Paul Laskar Associates.

Q. And what does your company do?

A. My company provides consulting services to my

clients in the area of chemistry manufacturing and controls with a focus on ophthalmic formulation as well as respiratory, dermatological, and nasal formulation. There's analytical chemistry issues around that, stability assessment, and preparation of regulatory documents and regulatory reports in -- in support of my clients.

Q. Okay. Now, Dr. Laskar, you have a binder in front of you that we're going to refer to throughout your testimony here today. And I'd ask you to please turn to DTX107 in your binder, which I believe is a copy of your CV.

And let me know when you have that document in front of you.

A. It seems to be missing a few pages. Oh, the pages are in an order in which I'm not familiar.

That's okay.

Q. Well, I want to keep you on your toes, right?

A. After lunch, I think that's a good idea.

Q. Okay. We'll take a few moments to review that document. Is that document up-to-date?

A. Yes, it is substantially up-to-date.

Q. Okay. So what I want to first do is talk about your education, and then we'll get into your experience.

So why don't we first start with your first degree you earned from the University of Rochester.

A. Yes. I attended the University of Rochester and earned a BA degree in 1965 in general science with a focus in chemistry and biology. Subsequent to that, I attended and earned a BS in pharmacy and a master of science in pharmacy from the College of Pharmacy, University of Illinois, in 1968 and 1971, respectively.

After which, I attended the Oregon State University and earned a Ph.D. degree in pharmaceutical science in 1974.

Some years prior to that, after obtaining my bachelor of science degree in pharmacy, I took the licensure exam and became registered as a pharmacist and practiced pharmacy on a part-time basis between 1968 and approximately 1977. Somewhat later, I earned an MBA from the University of California-Irvine in 1988.

Q. Okay. So let's now talk about your actual experience as an expert drug formulator. After your Ph.D., what did you do?

And I want to break it down to your academic experience as well as your private sector. So let's first take the academic experience.

A. Very well.

I joined the faculty of the College of

Pharmacy at the University of Illinois in 1973 and remained there until 1980, during which time I developed educational materials for pharmacy education as well as teaching in basic pharmaceutics, various aspects of pharmaceutical -- pharmaceutical technology, and pharmacokinetics.

In 1988 -- excuse me -- 1980, I joined the faculty of the School of Pharmacy at Creighton University and taught substantially the same course materials until 1982.

Q. And then after that?

A. Subsequent -- in late 1982, I joined Allergan as a scientist in their R&D area, focusing on ophthalmic therapeutics and was a scientist and section manager in the ophthalmic area until, I believe it was, 1986. During which time, I participated in the development of Allergan's Levobunolol project, their beta-blocker, which they market as Betagan, as well as the combination product that has subsequently been marketed as Pred-G, as well as a leukotriene antagonist compound that was a formulation I participated intimately in, as well as a combination of two antimicrobial agents, a cephalosporin that was combined with a Polymixin B Sulphate, which had some significant formulation challenges inasmuch as the two active ingredients were incompatible.

We managed to formulate that into a successful product that required lyophilization and reconstitution prior to use.

In 1986, I transferred into the product development area of Allergan's Dermatological Division and spent the rest of my career at Allergan in the Dermatology Division.

Q. Just so I'm clear, when you say Allergan, are you referring to the Plaintiffs in this case?

A. That is correct.

Q. Thank you.

Please continue.

A. In 1988, in the fall of 1988, I joined a startup company called Procyte in the Seattle metropolitan area who had a new chemical entity with a dermatology focus.

In the middle of 1989, I actually rejoined Allergan in the dermatology area with the same position, manager of product development, that I left some 10 months earlier, and continued and was promoted to Director of Product Development at Herbert Laboratories. And during that time, worked on several dermatological projects for Allergan at that time.

In 1993, I joined another startup company called CoCensys, whose area was neurology as Director of

Pharmaceutical Sciences, and they had two new chemical entities. One an oral product and the other intended for injection as a sterile product, and developed formulations for both of those to the point of an IND.

In 1994, I joined Santen, a -- in their U.S. subsidiary. Santen is an ophthalmic specialty company headquartered in Osaka, Japan, and I joined them as Director of Pharmaceutical Development, and was with Santen for about nine years beginning as Director and then promoted to Vice President of Pharmaceutical Development, and was involved in their ophthalmic portfolio that included three successful NDAs during that period of time, as well as a number of INDs.

One of the projects I worked on was a beta-blocker that Santen was interested in that was ultimately not pursued for the U.S. market, but is, I believe, currently marketed in Japan and some other markets.

In addition, I served as a technical advisor to Santen's finished subsidiary, who was trying to develop a ready-to-use or was in the process of developing a ready-to-use combination of Pilocarpine and Timolol. They preferred not to use the reconstitutable version that was discussed just a short time ago, and advised them relative to formulation as well as market

stability and obtaining a reasonable shelf life.

In addition, I worked on a combination product that is a combination of a corticosteroid and an antimicrobial, which entered clinical investigation by way of IND in the United States and, I believe, also in -- outside the United States. It is -- I don't know what its current development status is. It was still in development at the point I left Santen.

Q. Okay.

A. Also was involved in Santen's Prostonoid and its formulation and early development. That formulation was not pursued for clinical development in the United States due to the crowded marketplace that's been alluded to previously, but is approved and marketed in Europe, Japan, and other markets outside the United States.

During the course of that time, I wrote two expert reports in support of regulatory filings for those -- the -- two of the compounds that Santen was registering. Those are in support of the European filings.

In 2003, I joined Dey, LP. That is a -- as Senior Director of Pharmaceutical Development. They are a specialty company in sterile nebulized products as well as nasal products.

And directed the formulation, development, analytical chemistry, clinical supplies, technology transfer functions with Dey, and was intimately involved in preparing for an NDA submission that has subsequently been successful, as well as an ANDA for a nebulized product.

And formulated a combination product for respiratory use for nebulization. And for a time, was involved in two ophthalmic projects when Dey had an interest in developing a generic ophthalmic. One of those was developing a generic for Latanoprost and the other was a combination of Dorzolamide and Timolol, a generic version of Cosopt.

In the fall of 2006, I left Dey, and very shortly thereafter, formed Paul Laskar Associates and have been associated with this organization since that time.

As I alluded to or mentioned earlier, I provide consulting services to my clients, primarily startup companies, in the course of which I've been intimately involved and directed the formulation of several ophthalmic formulations, including two ophthalmic combinations.

One is a combination of -- of an antimicrobial and a corticosteroid. Another is a combination that's

used in the amelioration of dry eye, and revisited the combination of Dorzolamide and Timolol again on behalf of a client as -- which is, as I mentioned, the generic version of Cosopt.

Q. So if my math is correct, you've been formulating drugs for just over 30 years or thereabouts?

A. I don't like to think about the age, but it's probably pretty close to that.

Q. Okay. Let's just focus on the products that you've been involved with as a drug formulator.

You mentioned sterile products --

A. Yes.

Q. -- a moment ago. How many sterile products have you developed?

A. In excess of 30.

Q. Okay. And is your experience in sterile products relevant to the development of ophthalmic products?

A. Yes. I would say more generally that formulation of almost any liquid is generalizable, and with sterile products being a subset of that and with -- within the somewhat larger arena of sterile products, ophthalmic formulations are a subset with special requirements and special considerations.

Q. With regards to ophthalmic drugs, how many of

those have you developed?

A. Approximately 20.

Q. And how many combination products have you developed?

A. I've -- I've been involved in the development of -- excuse me -- seven sterile combinations and a few non-sterile combination.

Q. And I believe you touched on a few of those while you were explaining your practical experience as a formulator.

A. I was -- I did. Excuse me.

Q. Dr. Laskar, I noticed that you published about eight times; is that right?

A. Yes.

Q. And do people who work in the industry tend to publish as much as academics?

A. Not in literature that's publicly available.

Q. Does that diminish at all your ability to formulate a drug?

A. I do not believe so.

MR. RUZICH: Defendants offer Dr. Paul Laskar as an expert in the fields of pharmacy, pharmaceutical drug formulation, and ophthalmic drug formulation, Your Honor.

THE COURT: Permit him to testify within

the confines of his opinions as revealed in his expert report.

MR. RUZICH: Yes, sir. May I proceed?

THE COURT: Please do.

MR. RUZICH: Thank you.

Q. (By Mr. Ruzich) Dr. Laskar, did you offer any reports in this matter?

A. Yes, I did.

Q. And how many?

A. The initial report and reply report.

Q. And did you have your deposition taken in this matter?

A. I did indeed.

Q. Okay. Now, let's take a look at your binder, and let's turn to JTX003.

Do you recognize this document?

A. I do.

Q. And what is it?

A. It is U.S. Patent 7,323,463 issued on the 29th of January, 2008, titled Combination Brimonidine and Timolol for Topical Ophthalmic Use.

Q. So for ease of reference, I'm going to refer to this patent as the '463 patent.

Does that sound fair?

A. Sounds fair.

Q. And have you reviewed the '463 patent in it's entirety?

A. I have.

Q. And have you reviewed all the claims of the '463 in its entirety?

A. I have.

Q. Can you please explain to the Court just generally what the claims of the '463 cover?

A. In a general overview sense, the claims of the '463 patent encompass a composition containing -- or comprising .5% Timolol, .2% Brimonidine in a single composition with using Benzalkonium Chloride as a preservative in an article of manufacture for topical treatment of glaucoma or ocular hypertension.

Q. Okay. Were you here during the testimony of Dr. Tanna?

A. Yes, I was.

Q. And do you recall him relating his understanding of the legal standard for anticipation?

A. Yes.

Q. And do you adopt that standard here for your testimony today?

A. Yes, I do.

Q. And you also heard Dr. Tanna's understanding of the legal standard for obviousness, correct?

A. I do.
Q. And do you adopt that standard for your testimony here today?
A. I do.
Q. Dr. Laskar, in connection with your testimony here today, have you reached any opinions about the claims of the '463 patent?
A. I believe that the claims of the '463 patent are invalid on the basis of anticipation and/or obviousness.
Q. Can you please turn to JTX004?
A. I have it.
Q. Okay. Do you recognize this document?
A. I do.
Q. And what is this document?
A. This document is U.S. Patent 7,642,258, issued the 5th of January of 2010, whose title is Combination Brimonidine and Timolol for Topical Ophthalmic Use.
Q. And just for ease of reference again, I'm going to refer to this patent as the '258 patent.
A. Understood.
Q. Great. And have you reviewed this document in its entirety?
A. Yes, I have.
Q. And have you reviewed all of the claims of the

'258 patent?

A. Yes, I have.

Q. And, again, if you could explain to the Court just generally what the claims cover of the '258 patent.

A. In a general sense, they cover the same ground as the '463 patent with some additional specificity of Brimonidine being referred -- being referred to as Brimonidine Tartrate and Timolol as being referred to as Timolol Tartrate (sic).

Q. And do the claims cover a fixed composition of those two ingredients?

A. In the same fashion as it does for the '463.

Q. And does the '258 patent also cover an article of manufacture?

A. Yes, it does. And together with the use of Benzalkonium Chloride as a preservative.

Q. Let's back up for a moment here, just so I'm clear. With regards to Timolol that's claimed in the '258 patent, is that Timolol Maleate or Timolol Tartrate?

A. In the -- in -- I'm sorry. In the --

Q. In the '258 patent, yes, sir.

A. If I misstated, I apologize. It's Timolol Maleate and Brimonidine Tartrate.

Q. Thank you.

And does -- do the claims of the '258 patent also cover a method of treatment both of glaucoma and IOP?

A. Yes. And as I mentioned early on, it is -- is -- is substantially the same as the claims for the '463 with the additional specific -- specificity concerning the -- the salts of Brimonidine and Timolol.

Q. Dr. Laskar, in connection with your testimony here today, have you reached an opinion about the claims of the '258 patent?

A. Yes, I have.

Q. And what is your opinion?

A. My opinion is that the claims of the '258 patent are invalid by virtue of anticipation and/or obviousness.

MR. RUZICH: Your Honor, there's some overlap between the '258 and the '463 patents, and so I'm going to make every attempt to streamline things here for Your Honor, okay?

Q. (By Mr. Ruzich) Have you reviewed the specifications of both the '463 and the '258 patents?

A. I have.

Q. And how do they compare?

A. They appear to be substantially the same. The '4 -- the specifications of the '463 and the '25 -- '258

patent appear to be substantially the same. The '258 patent adds two additional examples, Example 2 and Example 3, that are not present in the '463 patent.

Q. Okay. And, Dr. Laskar, you're here today to provide testimony only as to the '463 patent and the '258 patent, correct?

A. That is correct.

Q. Okay. But have you reviewed the '149 and the '976 patents?

A. Yes, I have.

Q. And why have you done that?

A. I've reviewed those inasmuch as it's my understanding that the '463 patent and the '258 patent derive in some fashion from the '149 patent.

Q. Isn't it a fair characterization that the '258 and '463 claims are similar to the '149 and '967 (sic) patent claims?

A. The '976. I think you --

Q. I'm sorry. The '976.

A. They are. The principal difference is that the '149 patent and the '976 patent referred to a method of treatment, whereas the '463 and the '258 patents refer to compositions.

Q. Okay. And just quickly, we've -- you've heard of the DeSantis patent?

A. I certainly have.
Q. Okay. And with regards to the DeSantis patent, was that disclosed -- is your understanding whether it was disclosed during the prosecution of the '149 patent?
A. I do not believe it was.
Q. And as to the '976 patent, was DeSantis disclosed during its prosecution?
A. I do not believe so.
Q. Okay. And finally, as to the '463 patent, was DeSantis disclosed to the Patent Office during this prosecution?
A. No.
Q. Okay. And we all know it was disclosed during the '258 prosecution; is that correct?
A. Yes, we do.
Q. Okay. We're been bandying about this phrase critical date. And just for the -- just to clarify, what is your understanding of a critical date?
A. My understanding of the critical date is that it is the date of filing of the patent application for the '149 patent, which is the 19th of April, 2002.
Q. Okay. And you just testified a moment ago that you were here when Dr. Tanna testified, correct?
A. That is correct.

Q. And in his testimony -- or is his testimony consistent with your understanding of what was known to a person of ordinary skill in the art with regard to Brimonidine, Timolol, and the treatment of glaucoma in April of 2000?

A. Yes.

Q. And you also heard --

A. 2002.

Q. 2002. Okay. I was just go about to get to that.

All right. And did you hear Dr. Tanna's opinion as to what a person of ordinary skill in the art is?

A. Yes.

Q. And is this consistent with your understanding?

A. Yes.

Q. Okay. All right. I just want to talk a little bit about the knowledge of a person having skill in the art with regards to the Alphagan and Timoptic products.

I believe earlier Counsel and Dr. Tanna's testimony referred to them as the Alphagan labels and the Timoptic labels. Are you familiar with both of those --

A. Yes.
Q. -- labels?
A. Yes, I am.
Q. Okay. And do you recall Dr. Tanna's testimony regarding what was known by one of ordinary skill in the art regarding the Alphagan product prior to 2002?
A. Yes.
Q. And just in general terms, what was known?
A. Well, the information that was known on or before April 2002 was that Alphagan is a -- is a brand name by Allergan of Brimonidine Tartrate at a concentration of .2% in an ophthalmic solution that has Benzalkonium Chloride at .005% and that is used in the treatment of glaucoma or ocular hypertension with a dosage regimen in the U.S. label of three times a day.
Q. And is there any publication that exemplifies the understanding of one of ordinary skill in the art as it relates to the Alphagan label in 2002?
A. Yes. In April of 2002, a person of skill in the art might readily consult a Physician's Desk Reference.
MR. RUZICH: Can we pull up DTX129, please.
A. And this is the reproduction of the cover of the Physician's Desk Reference, very often referred to

by its acronym that appears at the top of that page, PDR. And this one happens to be the edition from 1998. And as Dr. Tanna mentioned, it is published on an annual basis.

Q. (By Mr. Ruzich) Okay. And was this a document that was available to a person of ordinary skill in the art at that time?

A. Absolutely.

Q. And do you recall Dr. Tanna's testimony regarding what was known by one of ordinary skill in the art regarding Timoptic prior to 2002?

A. Yes.

Q. And what was known to one of ordinary skill in the art about that product?

A. To one of ordinary skill on or before April of 2002 concerning Timoptic, one would know that it is Merck's brand of Timolol Maleate solution and that that solution was available to the market in two concentrations, 0.25 and 0.5% solution, intended for multiple use, and that multiple-use product was preserved with 0.01% Benzalkonium Chloride.

I would also just note that Timoptic was also available in a format called Ocudose, in which it was available without any Benzalkonium Chloride.

Q. And is there a publication that exemplifies

the understanding of one skilled in the art as to the Timoptic label in 2002?

A. Yes.

MR. RUZICH: And can we pull up DTX134, please.

A. And this is, again, the -- a reproduction of the cover page of the Physicians Desk Reference. This one is from 2001. And there's a monograph for Timoptic present within this volume.

Q. (By Mr. Ruzich) Okay. That's fine.

Now, let's jump to discussing some background in formulating a combination product. And, again, let's take a broader view for the Court.

We're heard from Dr. Tanna, and now we're going to hear from an expert formulator. What would a person of ordinary skill in the art do to develop a fixed combination product?

A. To develop a fixed combination product -- and I think, at this point, I would make the assumption that both the monotherapy products are available, and that would -- and that certainly within the glaucoma field, I'm not aware of any de novo combinations used in glaucoma, wherein neither of the monotherapies are not already available.

So taking that as a base, I would consider the

information about those monotherapies that were intended to be formulated as a fixed combination and use that information as a tool from which to build my fixed combination.

Q. Okay. Is it fair to say that you try to keep it as simple as possible?

A. Absolutely.

Q. Okay. To a person of ordinary skill in the art, is there an ideal number, in terms of the -- you know, the general number of excipients to be used in an ophthalmic product?

A. As few as would be required to accomplish the goal that you have.

Q. Dr. Laskar, if you could flip to DTX98 in your binder, and I want to draw your attention to Page 10 that's numbered in the report.

MR. RUZICH: And, Your Honor, do you have a copy of that?

THE COURT: Yes.

A. I have that page.

Q. (By Mr. Ruzich) Fantastic. Dr. Laskar, do you recognize this document?

A. Yes, I do.

Q. And what is it?

A. It is my initial expert report that's dated

the 27th of May of this year.

Q. And I asked you to direct your attention to Page 10 that's numbered in your report.

MR. RUZICH: And, Ms. Sarwan, if you can, can you highlight the first two columns.

Q. (By Mr. Ruzich) And, Dr. Laskar, once that's highlighted, can you please describe what is shown.

A. Yes. Those two columns are -- the left-hand column is a general descriptor of the components of an ophthalmic formulation, that is to say the active ingredient, which is, in row one, buffer, preservative, tonicity agent, viscosity agent, pH -- and I should -- might have modified that by saying pH fine tuning or adjusting agent.

And then although not included there would be the diluent. And in both -- in essentially all cases, that's water.

Q. Okay. And --

A. And in the column -- excuse me.

Q. No. That's fine. Go ahead.

A. The column on the right-hand side provides the purpose of each of those components, buffer meaning being designed to obtain the desired pH for the particular ophthalmic formulation.

Preservative, that is required to be used in

multidose ophthalmic products.

The purpose of what a tonicity agent accomplishes, that is to obtain, as close as possible, a composition that's isosmotic with tear fluid.

And if a viscosity agent is added, it's generally designed to increase the viscosity to thicken the eyedrop, to extend the residence time on the ocular surface.

And then the pH fine tuning, adjusting agent, is to fine tune the pH after putting these -- the above components together to attain more sharply the desired pH for the particular formulation.

Q. Let's talk about that for a moment. As to pH adjusting agents, is that a specific concern with regard to ophthalmic products or drugs?

A. Absolutely.

Q. And what does that concern?

A. There are -- the pH can impact an ophthalmic product in a number of ways, some in a more general sense than others. In the case -- in the case of an ophthalmic product, the pH can impact the -- the stability of the product as it would any -- essentially any liquid product.

It can -- in the case of an ophthalmic, more specifically can impact the comfort of the ophthalmic,

inasmuch as the eye has a surface pH of approximately 7.4. And although it's quite tolerant of -- of variations around that, if one moves to extremes, then discomfort sets in.

And in addition, pH can have a significant impact on the ocular bioavailability of the drugs in -- residing in the ocular formulation.

Q. Okay. Is there a single pH value that you must formulate with in connection with an ophthalmic product?

A. That you must formulate with, no. It is -- you -- you -- the pH that you formulate in is designed to optimize those attributes that I just discussed.

Q. Okay. And you also mentioned preservatives, and it's also up here on your chart. So let's talk about those generally.

For ophthalmic formulations, are preservatives required?

A. In all -- it is required that all multidose ophthalmic products maintain stability during patient use. And this is accomplished most frequently by addition of an exogenous preservative.

Q. And are there different categories of preservatives?

A. Yes, there are.

Q. And what's the most common?

A. The most common is the category of quaternary ammonium compounds of which Benzalkonium Chloride is the predominant example.

Q. Okay. We're going to refer to that as BAK for the rest of your testimony. Is that fair?

A. I tend to use the word BAK.

Q. Fantastic.

A. It comes from my history.

Q. So let's go back to DTX98. You have that open, and that's your opening report. Could you go to Page 13 as numbered in the report itself?

A. I have it.

Q. And can you describe for me what this is.

A. Yes. This is a table that I prepared to -- as an illustration, and it depicts the glaucoma products that were available on the U.S. market on or before 2001.

And as I mentioned, it is restricted to those that are available or used in the treatment of glaucoma. And I think you can see in the second column that Benzalkonium Chloride, BAK, is the preservative exclusively used in all of these glaucoma therapeutic agents.

Q. And a moment ago, we were talking about the

Alphagan label, as well as the Timoptic label. Do they appear on this table?

A. Yes, they do. And you can see on the top line and then the fourth from the bottom line, those two products are identified.

Q. Okay. Is it fair to say that half of these concentrations are less than 0.01% of BAK?

A. I believe you're correct in that. I think there are only two examples that are greater than .01%.

Q. Okay. So let's go back to Page 10, to that chart in your expert report.

So let's look at two specific examples that you've provided in this chart, again, Timoptic and Alphagan.

MR. RUZICH: And if you could highlight those. Okay.

Q. (By Mr. Ruzich) All right. In formulating a fixed combination product, which formulation would a person of ordinary skill in the art choose to start with in formulating a fixed combination of two active ingredients?

A. In -- in -- of those two, ocudose would be the Timoptic vehicle inasmuch as it has the fewest excipients present and would be the most straightforward point from which to begin my formulation of a fixed

combination.

Q. Okay. And as to the number of excipients, any opinion as to how a person of ordinary skill in the art would take those into account in formulating a fixed combination?

A. As I mentioned, the fewest in number. And as you can see, in this particular instance, there are the two components of the buffer, mono and dibasic sodium phosphates, the preservative, BAK, and some sodium hydroxide used to fine tune the pH, and water used as the diluent for the entire product, together with the two actives.

Q. Let's go back to the ingredients of Timoptic. What's the active ingredient in Timoptic?

A. Timolol Maleate.

Q. And do you have an understanding of what that drug was initially used before it was used in the eye?

A. Yes, I do.

Q. And what is your understanding?

A. It was used in the treatment of -- as a cardiovascular in the management of blood pressure.

Q. And when did Timolol come out?

A. For ophthalmic use, it was in 1978. It was available or used in -- in cardiovascular treatment as a systemic drug prior to this.

Q. So just so I'm clear, before 1978, it was used as a cardiovascular drug?

A. By a systemic administration as a tablet, if I recall correctly.

Q. Okay. And as to the Alphagan agent active ingredient, Brimonidine --

A. Yes.

Q. -- was that also used as a cardiovascular drug?

A. That I'm not aware of.

Q. Okay. And you're not a physician, correct?

A. I certainly am not.

Q. Okay. As to the pH of these two products, would there be any particular importance as to the pH level of these two products?

A. Yes. As I mentioned before, the three elements that contribute to the desirable pH are stability, comfort, and bioavailability.

In -- in -- in the case of stability, it is to -- and in the formulation of a fixed formulation would be to identify a pH at which both the Timolol Maleate component and the Brimonidine component of that fixed combination would have a suitable stability, such -- such that the expiry date would be commercially viable and desirable by the marketing group of the

pharmaceutical company.

Q. So if a person of ordinary skill in the art chose the Timoptic vehicle as its base, what would the next steps be in formulating a fixed combination?

A. As I mentioned some time ago, I would, first of all, look at the information that I could garner concerning both Timoptic and Alphagan concerning the pHs of the individual products, information that I would have access to relative to the stability of both of these agents at various pHs, information that I might have available to my -- to -- to -- access to concerning the impact of pH, for example, on the bioavailability of those agents and whether any other excipient components could impact the bioavailability, in fact, of either or both of the agents used in the fixed combination and would identify a pH to attain the -- the desirable expiry date and so as not to compromise the bioavailability of the agents when they might -- when they were used as monotherapy.

Q. Okay. As to pH, would a person of ordinary skill in the art know the pH of Brimonidine?

A. Yes.

Q. And I believe you referenced a moment ago the PDR, the Physicians Desk Reference, correct?

A. Yes.

Q. For the Alphagan label?
A. Yes.
Q. Would a person of ordinary skill in the art understand the pH of Timolol?
A. Yes.
Q. And the Timoptic product?
A. From a -- from a similar reference.
Q. And that similar reference was the PDR?
A. That is correct.
Q. Okay. With those steps in mind in formulating a fixed combination product, would a person of ordinary skill in the art have a reasonable expectation of success if they followed those steps?
A. I would believe so --
Q. And --
A. -- from the standpoint achieving a stable formulation.
Q. And is it your understanding that the -- this process was followed by the inventors in designing the product that was disclosed in the patents-in-suit?
A. It appears from the verbiage in the specifications of the '463 and the '258 patents.
Q. And is it your opinion whether there was any part of the development of the formula mentioned in the patents that was not routine development by one of

ordinary skill in the art?

A. For a person of ordinary skill in the art, I believe that the processes that were necessary and that were pursued appear to be those that are routine to a person of skill in formulation in April of 2002.

Q. Okay.

MR. RUZICH: If we could pull up JTX004, please.

Okay. Now I want to focus on Example No. 1, which is -- which appears in Column 4. And if we could highlight that, please.

Q. (By Mr. Ruzich) And, Dr. Laskar, let me know when you have that example in front of you.

A. I have it.

Q. Okay. What formulation has been used as a starting point to create the patented combination here?

A. From reading the text of the patent beginning in -- I believe that's Line 19: The formulation vehicle is based upon a Timolol ophthalmic solution, which contains an isotonic phosphate buffer system at pH 9. The formulation preservative Benzalkonium Chloride (BAK) at concentration of .005% (weight volume) 50 part per million.

Q. And is that in keeping with how a person of ordinary skill in the art would have formulated the

patented combination?

A. To obtain a stable product, yes, and then some additional work to validate, verify, and qualify the concentration of BAK.

Q. So just to clarify, as described in the patent itself, both the '463 and the '258, in your opinion, was that process -- the formulation process routine?

A. Absolutely, yes.

Q. And were you here for the testimony of Mr. Beck?

A. I was.

Q. And do you recall him testifying about any of the problems that he set forth in formulating the patented drugs in -- the patented product in the '258 or the '463?

A. I do not recall Mr. Beck referring to any problems concerning the formulation of the composition in this table.

Q. Okay. You mentioned earlier and there's been a lot of testimony on the fact that a preservative has to be used, but how would one of ordinary skill in the art, from a formulator's perspective, determine that amount of preservative to be used?

A. A person of ordinary skill in the art understands that a preservative -- and has been

testified to, I believe, by multiple individuals -- a preservative, such as Benzalkonium Chloride, has some downsides relative to cytotoxicity and ocular irritation, and as such -- and, in fact, it would be true for other excipients as well, is that the desired goal is to minimize the amount of any excipient required.

So as a part of routine testing, one would use what's called a PET test that -- or preservative effectiveness test that has also been mentioned by others as a methodology to identify an appropriate level of the preservative Benzalkonium Chloride to be used. It's a routine test that is -- that's currently employed and was employed in -- in late '90s and -- and before 2002.

Q. So let's focus on before 2002. What were the respective amounts of BAK in Brimonidine and Timolol products prior to 2002?

A. Prior to 2002, for the Brimonidine products, which would be exclusively Allergan's brand of -- brand known as Alphagan, it was .005%.

In the case of the Timoptic products, it was either 0 in their Ocudose product or .01% in their multidose product.

Q. And there's been a lot of testimony that BAK

has some toxic issues, correct?
A. That is correct.
Q. Dr. Laskar, do the patents disclose the toxicity issue --
A. Yes, they do.
Q. -- or any toxicity issue?
And how do they disclose it or discuss it?
A. They discuss it in -- in -- as others have mentioned, that Benzalkonium Chloride has a -- has, as I noted as well, some issues with respect to toxicity, and therefore, it would be a desirable goal to minimize the amount present and thereby minimize the exposure of the ocular surface to Benzalkonium Chloride.
Q. Is it fair to say that the possibility of a toxic event or the toxicity of BAK was known -- well known before 2002?
A. Oh, yes. It's well recorded in textbooks and literature back -- back several decades.
Q. So with that in mind, would a person of ordinary skill in the art still use BAK as of April 2002 despite these known side effects?
A. Yes.
Q. And why is that?
A. Yes, they would. And I think, as has been testified to by many person -- many of the witnesses,

that Benzalkonium Chloride, in 2001, was the prevalent preservative, it was before that, and to this day, it is the prevalent preservative.

Q. From the perspective of a formulator, is it the go-to preservative in ophthalmic products?

A. At the present time, yes, it is. It's the go-to. It's the preferred preservative. Because to -- to a formulator, a formulator understands its attributes, both positive and negative.

To a physician, it is well known concerning the positive attributes that it has, as well as the adverse possibilities that it has.

And I might note that there's a significant burden of entry to any new preservative inasmuch it is treated by physicians as being something new, untested, and therefore perhaps with skepticism, and the safety and effectiveness and efficiency and compatibility must be established of that candidate, new preservative, with what other formulation is being worked on.

Q. Okay. So do the patents discuss any problems whatsoever with the development of the claimed formulations?

A. Not that I've been able to find in the text of the '463 or the '258 patents.

Q. Do the patents discuss any concerns regarding

degradation products?
A. No. They mention -- there's no mention of degradation products.
Q. And do the patents mention anything about FDA compliance?
A. I was unable to find any text having to do with any regulatory review or FDA-approval issues.
Q. Do the claims of the patents discuss anything or mention anything about FDA approval?
A. None whatsoever.
Q. I'm going to switch gears now, and we're going to talk about DeSantis, and I think that we can move quite quickly on DeSantis, given the length of treatment that it's already been given so far in this trial.
We know that DeSantis was available to one of skill in the art before April 2002.
MR. RUZICH: If we could pull up DTX123, please.
Q. (By Mr. Ruzich) And do you recognize this document?
A. I do.
Q. And did you hear Dr. Tanna discuss DeSantis?
A. I did.
Q. And do you agree with his discussion of DTX123?

A. Yes.
Q. And in your opinion, was a fixed combination of Brimonidine and Timolol formulated with BAK disclosed prior to 2001?
A. Yes. I believe it's disclosed in this DeSantis patent '052.
Q. Are there more than one kind of Alpha-2 agonists?
A. Yes.
Q. And in your opinion, does the DeSantis reference -- reference disclose Brimonidine as an Alpha-2 agonist?
A. It does by incorporation.
Q. Okay. And where and how is it disclosed in DeSantis?
A. Brimonidine is disclosed by -- in DeSantis by incorporation of the article by Timmermans.
Q. And what's your understanding of incorporating a document into a patent?
A. My understanding of incorporation of a document -- or incorporation by reference to a document is that it is tantamount to reproducing the entire text of whatever is being referred to within the body -- within the specifications of the patent.
Q. Okay. We'll get to Brimonidine and Timmermans

in a moment, but in general, what information was provided to a person of ordinary skill in the art by the Timmermans reference.

MR. RUZICH: And if we could pull up DTX124, please, Page 217. Let's go to DTX124.

Q. (By Mr. Ruzich) Doctor, do you recognize this document?

A. Yes, I do.

MR. RUZICH: And let's turn to Page 217.

Q. (By Mr. Ruzich) You mentioned a moment ago that Brimonidine is disclosed in the DeSantis patent by way of incorporation by reference, right?

A. Yes.

Q. And that incorporation by reference was the Timmermans document?

A. Yes, it is.

Q. And where in the Timmermans document does -- is Brimonidine disclosed?

A. I have it in front of me, but not on the screen, it's got Page 230.

Q. Okay.

A. Do you want me to wait until it's shown on the screen?

Q. Sure.

A. Okay. There we go.

Q. Great. Thank you.

A. Brimonidine is disclosed in -- on this page in Figure 31 where there appear substructures of Clonidine analogs, and one of those substructures has -- has the UK-14,304-18. And when you join that substructure to the substructure identified with an R, then one has the Brimonidine molecule.

Q. Is it fair to say that this is chemistry shorthand?

A. Yes.

Q. Okay. You mentioned the designator UK-14,304-18.

A. Yes.

Q. Why not just say Brimonidine?

A. At the -- at the time that Timmermans wrote this chapter, this compound did not have a trivial name such as Brimonidine. It was known only by its compound name that Pfizer assigned to it as UK -- as this UK-14,304-18.

And, in fact, I might just mention that when Allergan brought this molecule to Irvine, they, I believe, relabeled it as AGN 190342, and then at some point, it became the adopted USAN name, and I think the BAN name of Brimonidine.

Q. Okay.

MR. RUZICH: And if we could turn to the next page, please, of the Timmermans reference. And I just want to highlight the second column here, let's just go down to the second full paragraph. I'm sorry. The first column. And let's go down a little bit further. Okay.

Q. (By Mr. Ruzich) Dr. Laskar, is Brimonidine discussed in this column?

A. Yes, it is.

Q. Where?

A. Beginning with -- and at the top of this called-out section: The quinoxaline system found in the experimental compound UK-14,304-18 (Pfizer) refers to Brimonidine.

Q. Okay.

A. And then it discusses that this substance is somewhat less active than Clonidine, and it seems likely that the mechanism which underlies the hypotensive effect is identical to that of Clonidine, and then it refers to how that -- how Timmermans came to know that.

Q. And I think right below it, there's also another mention of Brimonidine, too?

A. Yes. There's mentioned elsewhere in the text that, in fact, the tartrate salt of that particular compound was used in this particular experimental

protocol.

Q. Would it surprise you as an expert formulator, over your 30 years' experience, that a formulator looking for a formulation for the eye would turn to an antihypotensive drug?

A. From my understanding as a person of art and as -- as a trained pharmacist, no.

Q. And let's be clear. Before the critical date of April 19th of 2002.

A. Yes. I'm sorry. I did not qualify.

Q. And I believe you mentioned before that Timolol was an antihypotensive drug as well?

A. That's correct.

Q. Okay. Is there any doubt, from a chemistry standpoint, that this Brimonidine that's disclosed in DeSantis by way of Timmermans is not the same Brimonidine that's claimed in the '463 and '258 patents?

A. None whatsoever.

Q. You're certain?

A. I would just mention that the last organic chemistry class I took, Ms. Brooks was probably in diapers.

MS. BROOKS: Thank you.

THE COURT: You didn't mention me, Doctor.

[Laughter]

THE WITNESS: Well, you might have been in high school.

THE COURT: I was in organic chemistry before you were, but go ahead. But I had the good sense to get out.

Q. (By Mr. Ruzich) Let's get back to your testimony here.

Would a person of ordinary skill in the art understand which Alpha-2 agonists were considered pharmaceutically acceptable for the treatment of glaucoma to one skilled in the art as of 2002?

A. Yes. To a person of skill in the art on or before April of 2002, they would have understood that there were an extremely small number of possible Alpha-2 agonist compounds with which one might formulate a fixed combination.

Q. Okay. And in your opinion as an expert drug formulator, how many Alpha-2 agonists were available to a person of ordinary skill in the art to create a fixed combination drug before April 2002?

A. To a person skilled in the art on or before April of 2002, I believe that there is one Alpha-2 agonist that one would functionally use to make a fixed combination for the treatment of glaucoma.

Q. Is it fair to say there are a lot of Alpha-2 agonists that are disclosed in Timmermans?

A. Absolutely.

Q. But from the perspective of a drug formulator, from the perspective of a person having ordinary skill in the art as a drug formulator, which Alpha-2 agonist would a person of skill in the art choose from Timmermans as of 2002?

A. In 2002, a person of skill in the art would have chosen Brimonidine.

Q. Okay. And what would -- let's just bring this full circle now.

What would DeSantis have taught a person of ordinary skill in the art with respect to formulating that fixed combination product with that Alpha-2 agonist?

A. DeSantis would have taught that one would take that particular -- that Alpha-2 agonist, Brimonidine, and formulate it with the beta-blocker, Timolol, which is the beta-blocker identified in the title of the -- of the DeSantis patent.

Q. Does DeSantis disclose any beta-blockers?

A. In the specifications of the '052, there are a significant number of beta-blockers identified.

MR. RUZICH: And if you can pull up

DeSantis for a minute. I think that was -- you got it.

THE WITNESS: That's Timmermans.

MR. RUZICH: Right. Get to the DeSantis in a moment.

THE WITNESS: There we go.

Q. (By Mr. Ruzich) And just out of clarity, you mentioned that it's disclosed here in DeSantis, correct?

A. Yes.

Q. Okay. And to a person of ordinary skill in the art, does Timmermans and DeSantis disclose thousands of potential combinations for a fixed product, for a fixed combination glaucoma drug?

A. I suppose if one does the hypothetical mathematics of taking the number of beta-blockers that are listed in the specification to DeSantis and takes, again, the list of Alpha-2 agonists that are listed both in Timmermans and in DeSantis and do the math and overload the calculator, yes, one would have a humongous number.

Q. And we're not talking about math here today.

A. No.

Q. And you're not a -- you're not testifying as an expert on odds, in other words, mathematical odds, correct? Or mathematics combinations, are you?

A. No, I'm not.

Q. So you're here to testify about the perspective of a person of ordinary skill in the art in formulating a drug.

A. That is correct.

Q. As to the number of combinations that are potentially disclosed in DeSantis and Timmermans, what can you say about that?

A. I can say that DeSantis would identify one potential combination; that is, a combination of Timolol and together with Brimonidine to a person skilled in the art on or before April of 2002.

Q. And you were here during the testimony of Mr. Beck, correct?

A. I was.

Q. And were you here when he testified that there was only one Alpha-2 agonist of choice in 2002?

A. I heard that.

Q. And do you agree with Mr. Beck?

A. Yes, I agree with Mr. Beck.

Q. And are you familiar with the testimony of Ms. Batoosingh?

A. I -- although I did not hear her testimony, I'm familiar with it.

Q. Okay. And would you agree that -- with her assessment that Timolol was the beta-blocker of choice

as of 2002?

A. Yes, I would agree with her assessment of that.

Q. Okay. We've been talking about your background. We've been talking about your experience as a formulator. We've been talking about the -- what a formulator would do in formulating a fixed combination glaucoma product.

So let's now discuss in-depth both of the patents for which you're here to testify about.

The first one, the '463 patent. And, Dr. Laskar, did you prepare a set of demonstratives to use in conjunction with your testimony here today?

A. Yes, I did.

Q. And would those demonstratives assist you in explaining your testimony to the Court?

A. I hope so.

Q. Okay. Fantastic.

MR. RUZICH: Well, you beat me to the punch here. You must have read my mind. So let's go to the next slide, the '463 here.

Q. (By Mr. Ruzich) Can you explain to the Court real quickly what this is?

A. Yes. This is just to illustrate a way of summarizing some information. In the left-hand column

is the '463 patent, and on this screen, Claims 1 through 3 of that patent.

The next column over is -- indicates a box which -- with an indicator of whether it is -- whether that claim is anticipated by DeSantis.

And the right-hand column, in an analogous fashion, indicates whether that claim is obvious when DeSantis is viewed by one of skill and their knowledge.

MR. RUZICH: Your Honor, Dr. Tanna testified earlier, as you know, about the '149 patent, as well as the '976. Dr. Laskar is here to testify, as you know, about the '463 and the '258.

So we're going to have to cover some ground, and I'm going to do this in an efficient manner, I promise.

Q. (By Mr. Ruzich) What does DeSantis disclose about Claim 1 of the '463 patent?

A. Claim 1 of the '463 patent has -- teaches -- states: A composition comprising about .2% Brimonidine by weight and about 0.5% Timolol by weight as the sole active agents in a single composition.

Q. Okay. And let's focus on this phrase, quote, about 0.2% Brimonidine. I think we've established that Brimonidine is disclosed in DeSantis, correct?

A. Yes.

Q. And I think we've already went over that, how it is disclosed in DeSantis, correct?

A. Yes.

Q. Okay.

MR. RUZICH: So let's go to the next slide, Slide 6.

Q. (By Mr. Ruzich) So let's go back to the claim again and look at the phrase 0.2% Brimonidine. Do you have that in front of you?

A. I do.

Q. And is there a disclosure in DeSantis as to the range of the Alpha-2 agonists?

A. Yes.

Q. And can you also provide the column number and line number?

A. I apologize.

Q. That's fine.

A. I didn't have my --

Q. I overlooked that, and we can recapture that in a moment. Go ahead.

A. I neglected my own cue card about that. In Column 6, Line 3 to 6 of the '052 patent, there is text which reads: Alpha-2 agonist in the amount of about 0.2 (sic) to 2% by weight.

Q. Okay. And let's just jump back to Claim 1

with regards to the 0.2% Brimonidine. Can you explain to the Court just the line -- the column and line number as to where that appears in DeSantis?

A. If I can have that slide again, please.

MR. RUZICH: Sure. If you could punch back to that. Thank you.

A. For Brimonidine, it is noted in Column 4, Line -- beginning Line 42 of the patent and then on Page 20 -- 28, which is part -- which is Table 31 of the Timmermans article.

Q. (By Mr. Ruzich) Okay. So let's focus in on the actual percentage of Brimonidine, 0.2&. What would a person of ordinary skill in the art have known about that specific percentage?

THE WITNESS: And if we can skip forward to that. There we go.

MR. RUZICH: Great.

A. The particular percentage, 0.2% Brimonidine, would be known to one skilled in the art in April 2002 that that is the concentration of Brimonidine used in Allergan's brand, Alphagan, used clinically in the treatment of glaucoma and ocular hypertension --

Q. (By Mr. Ruzich) Is it fair to --

A. -- and had been for a number of years.

Q. Is it fair to say that a person having skilled

in the art would have envisioned that 0.2%?

A. Absolutely.

Q. Okay.

MR. RUZICH: Let's go to the next slide, please.

Q. (By Mr. Ruzich) And for the sake of our discussion here today, is there any publication that exemplifies your understanding?

A. Yes. As we noted just a little while ago, the PDR and the Alphagan monograph within the PDR would have identified the fact that Alphagan is composed of .2% Brimonidine Tartrate.

Q. So let's go back to the claim and look at the phrase, quote/unquote, about 0.5% Timolol.

Do you see that?

A. I do.

Q. Does DeSantis disclose Timolol?

A. Yes, it does, in two places: Column 1, beginning on Line 33, and secondly, in Column 6, beginning Line 42, which is the single claim of the patent.

In Column 1, it states: Other preferred beta-blockers include -- and I might mention firstly that Timolol is explicitly identified in the title of the patent.

Then secondarily, it's listed as first among a list of beta-blockers, and finally, it is listed as the beta-blocker in the claim of -- excuse me -- the '052 patent.

Q. And does DeSantis disclose that the beta-blocker can be used in any amount or any specific amount?

A. Yes, it does. It -- DeSantis identifies that the Timolol can be used at 0.01 to 3%. And one skilled in the art would immediately envision, based on their knowledge, that the concentration to be used would be .5%.

Q. So let's focus in on the actual percentage of Timolol at 0.5%.

Okay. What would a person of ordinary skill in the art have known about that specific percentage?

A. A person of skill in the art, April 2002, would have known that .5% was the -- was one of the two concentrations of Timolol that was marketed as Timoptic and that the .5%, as we've heard from multiple individuals, was the most predominant concentration of Timolol used in the clinical treatment of glaucoma and ocular hypertension.

Q. Okay. And for the sake of our discussion here today, is there a publication that exemplifies that

understanding?

A. Yes, there is. And as we mentioned previously, it is the PDR and the Timoptic monograph that appears within that volume.

Q. And so based on this disclosure, is it fair to say that this is how a person of ordinary skill in the art would be expected to practice the claims and the disclosures of the '052 patent, the DeSantis patent?

A. I believe so.

Q. All right. So let's take --

MR. RUZICH: We're moving along, Your Honor.

Q. (By Mr. Ruzich) Let's take a look at the term sole active ingredients in a single composition.

Do you see that?

A. I do.

Q. And what does sole active agents refer to?

A. Sole active agents refer to the two items above, that is to say, Brimonidine and Timolol.

Q. And are Brimonidine and Timolol in a single composition disclosed by DeSantis?

A. Yes, it is. It's disclosed in two places. One in Column 1, beginning Line 19, and second -- second -- secondly, Column 3, beginning at Line 3. And in Column 1, it states: A pharmaceutical

composition which includes as principal active ingredients combinations of one or more Alpha-2 agonists and one or more beta-blockers.

And then later: A combination of a therapeutically effective amount of one or more -- one or more Alpha-2 agonists and a therapeutically effective amount of one or more beta-blockers.

Q. As to Timolol, does Column 5 and Line 33 of the '463 patent shed any light as to that disclosure?

A. I'm sorry. Column 3?

Q. Column 5, Line 33, the Lines 33.

A. I don't have that immediately in front of me. Hang on.

Q. Sure. You have the full --

A. Yeah. Column 5, Line --

Q. And I believe that's JTX4 -- that's JTX3.

We'll just take it from Lines 31 through 35 on Column 5.

MR. RUZICH: Not of DeSantis, of the -- I'm sorry. Of DeSantis, correct.

A. Would you repeat the question, please?

Q. (By Mr. Ruzich) Sure. Does Column 5, Line 33 -- or Lines 30 to 35, shed any light as to the disclosure of Timolol in DeSantis?

A. Yes. It discloses Timolol in Line -- it

appears to be 33 explicitly, and then further, in the following paragraph, it discloses the amount of the beta-blocker.

Q. Okay.

MR. RUZICH: Let's go to Slide 11, please.

Q. (By Mr. Ruzich) And just to wrap this up, Dr. Laskar, is it your opinion that DeSantis discloses all the elements of Claim 1, either explicitly or inherently, of the '463 patent?

A. Yes.

Q. And is it your opinion that DeSantis anticipates Claim 1 of the '463 patent?

A. Yes.

Q. Now, let's turn now to obviousness.

You see on this chart here, we have an Anticipation column, as well as an Obvious Over column.

A. Yes, I do.

Q. Okay. Do you have an opinion as to whether Claim 1 is rendered obvious?

A. Yes, I do.

Q. And what is your opinion as to whether Claim 1 is rendered obvious?

A. My opinion is that Claim -- that DeSantis and the information available to one skilled in the art

would immediately envision that the Claim 1 of the '463 patent is obvious.

Q. And why is that?

A. Because the information in DeSantis describes the Brimonidine. It leads one to the -- by virtue of information to the .2% of Brimonidine. It identifies Timolol explicitly. And one with knowledge would immediately identify 0.5% and that those would be in a single composition.

Q. Okay.

MR. RUZICH: Let's go to Slide 12, please.

Q. (By Mr. Ruzich) Let's focus now on Claim 2 of the '463 patent. What does Claim 2 recite?

A. Claim 2 of the '463 patent says: The composition of Claim 1 further comprising from 0.001 to 0.01% Benzalkonium Chloride.

Q. Do you understand that Claim 2 depends from Claim 1?

A. Yes, I do.

Q. And what's your understanding of dependent claims?

A. My understanding of dependent claims is that the text of the claim referred to in the dependent claim is essentially copied into that dependent claim.

Q. So do you understand that all the limitations of Claim 1 are now in Claim 2, correct?
A. Yes, I do understand that.
Q. And does your analysis of Claim 1 still apply to those same limitations that are now incorporated into Claim 2?
A. Yes.
Q. Okay. And we've talked a lot about preservatives. Specifically what is disclosed in DeSantis with regards to preservatives?
A. DeSantis discloses in Column 5, Line 41 to 46 -- it discloses a list of antimicrobial preservatives of which Benzalkonium Chloride is the first listed and then further identifies a concentration in which it might be used that ranges from .001 to 1%.
Q. Let's go back to Claim 2 and the range of BAK, which is from 0.001% to 0.01%.
Do you see that?
A. I do.
Q. Is there a range of BAK disclosed in DeSantis?
A. Yes. It is .001 to 1%.
Q. As to the upper range, you noticed that that's different.
A. Yes.
Q. So what would a person of ordinary skill in

the art do to limit that range in DeSantis any further?

A. A person of skill in the art would immediately envision that the concentration -- the upper concentration that -- that might reasonably be used would be .01%.

Q. And so just so we're -- just so we're clear, based on this disclosure, is it your opinion that this is how a person of ordinary skill in the art would be expected to practice the claims of the DeSantis patents?

A. Yes, I believe so.

MR. RUZICH: Okay. Let's go to Slide 13.

Q. (By Mr. Ruzich) Does the Timoptic PDR we looked at earlier support your opinion that a person of ordinary skill in the art would have known Timolol was formulated at 0.01%?

A. Yes, they would. It is explicitly explained in the Timoptic monograph in the PDR wherein the concentration of Benzalkonium Chloride is identified as .01%.

MR. RUZICH: Next slide, please.

Q. (By Mr. Ruzich) And just to wrap this up, Dr. Laskar, is it your opinion that DeSantis discloses all the elements of Claim 2 either explicitly or inherently of the '463 patent?

A. Yes.

Q. Does DeSantis, in your opinion, anticipate Claim 2 of the '463 patent?
A. Yes.
Q. Turning now to Obvious in the second half of this chart here, do you have an opinion as to obviousness with regards to Claim 2 of the '463 patent?
A. Yes.
Q. What is your opinion?
A. I believe that DeSantis, together with the information available to one skilled in the art, would render Claim 2 of the '463 patent obvious.
Q. Let's move on now to Claim 3.
MR. RUZICH: It's Slide 15.
Q. (By Mr. Ruzich) What does Claim 3 recite?
A. Claim 3 states: The composition of Claim 2 comprising about 0.005% Benzalkonium Chloride.
Q. And you'll notice that Claim 3 depends on Claim 2, and Claim 2 depends on Claim 1.
Do you see that?
A. I do.
Q. Okay. And you now understand -- you understand that all the limitations of Claim 1 and Claim 2 can now be found in Claim 3, correct?
A. That is correct.
Q. And does your analysis of Claim 1 and Claim 2

that we just went over still apply to those same limitations that are now incorporated into Claim 3?

A. Yes.

MR. RUZICH: So let's go to the next slide. Le's turn now to Claim 3.

Q. (By Mr. Ruzich) Does DeSantis disclose the contents of this claim?

A. Yes, it does.

Q. Okay. And what about the specific concentration of BAK? Would a person of ordinary skill in the art have knowledge of that percentage, precisely 0.005%?

A. Yes, they would.

Q. And how's that?

A. A person of skill in the art, in April of 2002, would have understood the .005% Benzalkonium Chloride explicitly and immediately envisioned that by their knowledge of the information contained in the Alphagan monograph of the PDR.

Q. And the Alphagan monograph is the one we had -- that's been found in the PDR, correct?

A. Yes.

Q. Okay.

A. And that we've shown and discussed on several occasions.

Q. Great.

MR. RUZICH: Let's go to Slide 16. Okay. I see that one there.

Q. (By Mr. Ruzich) Okay. Just to wrap this up, Dr. Laskar, is it your opinion that DeSantis discloses all the claims -- or all the elements of Claim 3 either explicitly or inherently of the '463 patent?

A. Yes.

Q. In your opinion, does DeSantis anticipate Claim 3 of the '463 patent?

A. Yes.

Q. Okay. Let's turn now to the obviousness analysis. Do you have an opinion as to whether Claim 3 is rendered obvious?

A. Yes.

Q. And what is your opinion?

A. My opinion is that a person -- that DeSantis, together with information available to one skilled in the art, would render obvious the -- Claim 3 of the '463 patent.

Q. Let's move on to Claim 4 of the '463 patent.

MR. RUZICH: The next slide, Slide 17.

Q. (By Mr. Ruzich) And we have, I think, three remaining claims to go here.

Generally, what is Claim 4 directed to?

A. In general, it -- it talks to an article of manufacture that contains the combination -- a fixed combination and also describes the uses of that fixed combination.

Q. Okay. And let's look at that term article of manufacture.

What would a person of ordinary skill in the art, as of April of 2002, have known regarding this phrase?

A. A person of ordinary skill, in April of 2002, would have known that an article of manufacture refers to the plastic ophthalmic dropper bottle and the solution that it contains.

Q. And is this understanding supported by the PDRs that we just went over?

A. Absolutely.

Q. And where?

A. In both of the Alphagan monograph and the Timoptic monograph, there is an -- information which describes how Alphagan is packaged; that is to say, as you can see in the highlighted section, white opaque plastic dropper bottles, and in the Timoptic monograph described as a white translucent dispenser.

MR. RUZICH: Let's go to Slide 19.

Q. (By Mr. Ruzich) Now, let's carefully look at

this next limitation of Claim 4, which recites, quote: Wherein said composition comprises about 0.2% Brimonidine by weight and about 0.5% Timolol by weight in a single composition.

Do you see this?

A. I do.

Q. And is this similar to Claim 1 of the '463 patent?

A. Yes.

Q. And would you apply the same analysis as you applied to Claim 1 to this claim?

A. Yes, I would.

Q. Does DeSantis disclose this limitation?

A. Yes. Just as I mentioned in my analysis of Claim 1.

MR. RUZICH: Let's go to Slide 20, please.

Q. (By Mr. Ruzich) And let's tackle the last limitation of this claim. Can you please read to the Court this last limitation?

A. The last limitation is: And wherein said packaging indicates that the composition is useful for treating glaucoma or ocular hypertension by twice-a-day topical administration of the composition to a person's eye.

Q. Okay. So let's break that down.

Is treating glaucoma or ocular hypertension disclosed in DeSantis?

A. Yes, it is.

Q. Where?

A. In the DeSantis patent, Column 1, beginning in Line 13, it refers to -- that the invention relates to the treatment of glaucoma and associated elevations of intraocular pressure and to the treatment of ocular hypertension.

MR. RUZICH: Let's go to the next slide, Slide 21.

Q. (By Mr. Ruzich) Is, quote, twice-a-day topical administration, end quote, disclosed by DeSantis?

A. Yes, it is. It is disclosed in Column 6, beginning at Line 37 in which it says: The methods will typically comprise topical application of one to two drops to the affected eye one to two times per day.

MR. RUZICH: Let's go to the next slide, Slide 22, please.

Q. (By Mr. Ruzich) Is, quote/unquote, topical administration of the composition to a person's eye disclosed by DeSantis?

A. Yes, it is.

Q. And where?

A. It's disclosed at Column 11, beginning Line 42, which is the claim of the DeSantis patent where the text reads in part: Comprises applying topically to the affected eye a therapeutically effective amount of a compensation, et cetera.

Q. So with your Claim 1 analysis in mind and now your analysis you just went through a moment ago, is it your opinion that DeSantis discloses all the elements of Claim 4, either explicitly or inherently, of the '463 patent?

A. Yes.

Q. Is it your opinion that DeSantis anticipates Claim 4 of the '463 patent?

A. Yes.

Q. Okay. Now let's turn to obviousness here.

Do you have an opinion as to whether Claim 4 is rendered obvious?

A. Yes.

Q. And what is that opinion?

A. My opinion is that, considering DeSantis and the information available to a person skilled in the art, would render Claim 4 of the '463 patent obvious.

Q. And the information that was available to a person of ordinary skill in the art as of April 2002 --

A. Oh, yes.

Q. -- would be --

A. Yes.

Q. If you can elaborate a little more, Dr. Laskar.

A. I'm sorry. I didn't qualify that. I apologize.

Q. And, again, if you could elaborate a little bit more.

A. And that would be for the -- the first element of Claim 4. A similar analysis for the second and third elements of Claim 4 relative to anticipation and to obviousness, that the -- those two are anticipated by DeSantis and that to a person of skill in the art in April of 2002, together with the information that -- to which they would have access would render the other elements of Claim 4 obvious.

Q. Okay. And before we move on to Claim 5 --

MR. RUZICH: I'm sorry. Okay. All set? Okay.

Q. (By Mr. Ruzich) Let's now move on to Claim 5 of the '463 patent. It specifically cites --

MR. RUZICH: 24.

Q. (By Mr. Ruzich) What does Claim 5 recite of the '463 patent?

A. Claim 5 of the '463 patent says: The article

of manufacture of Claim 4 wherein the composition is further -- further comprises from 0.001 to 0.01 Benzalkonium Chloride.

Q. And, again, you'll see that Claim 5 depends from Claim 4?

A. I do.

Q. And you understand that all limitations of Claim 4 can now be found in Claim 5?

A. Yes, I understand.

Q. So does your analysis of Claim 4 still apply to those same limitations that are incorporated into the Claim 5?

A. Yes.

Q. Okay. Is this the same amount of BAK that was recited in Claim 2 of the '463 patent?

A. Yes, it is.

Q. And so your analysis of Claim 2 of the '463 patent would be applicable to Claim 5?

A. It would be the same.

Q. And does DeSantis disclose this range?

A. Yes, it does.

Q. Where?

A. Column 5, beginning at Line 40, and in which -- there are the -- a number of antimicrobial preservatives are identified of which Benzalkonium

Chloride is the first noted, and then secondarily, with respect to concentration, DeSantis notes the concentration to range from .001 to 1%.

Q. Does the Timoptic PDR that we looked at earlier support your opinion that a person of ordinary skill in the art would have known that the Timolol was formulated at 0.01%?

A. Absolutely. As soon as -- as soon as one reads DeSantis, they would immediately envision that the concentration that would be employed would be .01%.

MR. RUZICH: Let's go to Slide 26, and let's wrap this up.

Q. (By Mr. Ruzich) Dr. Laskar, is it your opinion that DeSantis discloses all the elements of Claim 5, either explicitly or inherently, of the '463 patent?

A. Yes.

Q. In your opinion, does DeSantis anticipate Claim 5 of the '463 patent?

A. Yes, I do.

Q. Turning now to the obviousness review, do you have an opinion as to whether Claim 5 of the '463 patent is obvious?

A. Yes.

Q. And what is that opinion?

A. My opinion is that DeSantis, together with the

person of ordinary skill in April of 2002 and the information available at that time, would have rendered Claim 5 obvious.

Q. Now let's turn to Claim 6, and we can go to Slide 27. Can you please read Claim 6 to the Court?

A. Claim 6 of the '463 patent states: The article of manufacture of Claim 5 wherein the composition further comprises about 0.005% Benzalkonium Chloride.

Q. And as you know, Claim 6 depends from Claim 5, which in turn depends from Claim 4.

Do you see that?

A. I do understand that.

Q. Okay. And so all the limitations of Claim 4 and 5 can now be found in Claim 6, correct?

A. Yes.

Q. And does your analysis of Claims 4 and 5 still apply to those same limitations that are incorporated now into Claim 6?

A. Yes.

Q. Okay. Is this the same amount of BAK that was recited in Claim 3 of the '463 patent?

A. Yes.

Q. And does DeSantis disclose this amount of BAK?

A. Yes, it does.

Q. Does the same analysis that we went through from Claim 3 apply to your analysis of Claim 6?
A. My analysis would be identical.
Q. Okay. So let's just focus in for a moment here, because I think it's important that we do, that with regards to the Alphagan PDR that we looked at earlier, is it your opinion that a person of ordinary skill in the art would have known that Brimonidine was formulated at 0.005% BAK?
A. Absolutely, yes.
MR. RUZICH: Let's go to the next slide.
Q. (By Mr. Ruzich) Dr. Laskar, is it your opinion that DeSantis discloses all the elements of Claim 6, either explicitly or inherently, of the '463 patent?
A. Yes.
Q. And does DeSantis anticipate Claim 6 of the '463 patent?
A. Yes.
Q. Turning now to obviousness, do you have an opinion as to whether Claim 6 is obvious?
A. Yes, I do.
Q. And what is that opinion?
A. My opinion is that DeSantis and a person of ordinary skill in the art in April of 2002 and the information that they would have access to would have

rendered Claim 6 of the '463 patent obvious.

Q. Okay. Just to nail down one fine point here, I wanted to turn your attention to the PDR label, the Alphagan label found in the PDR.

And as we know, it discloses 0.05 percentage of BAK, correct?

A. 0.005.

Q. Correct.

How does that disclosure compare to the 0.05% weight by volume limitations of the claims?

A. The -- in Alphagan, the expression is .05 milligrams, which is equivalent to .00 -- and that's milligrams per ml, which is equivalent to .0005%.

Q. Okay. I just want to nail down. We're dealing with different percentages and --

A. Units.

Q. -- and milligrams, correct. And the units, exactly. So great.

Now we're going to --

MR. RUZICH: We're on the last patent, Your Honor, the '258 patent.

Q. (By Mr. Ruzich) So let's focus our attention on that, Dr. Laskar.

MR. RUZICH: And if we can go to Slide 30, please.

Q. (By Mr. Ruzich) As I mentioned before, there was some --

MR. RUZICH: If we can go -- hit it again.

A. And I would just mention that this -- this is formatted in the exact analogous fashion as the summary chart of the '463 patent.

Q. (By Mr. Ruzich) Okay.

MR. RUZICH: And can we go to the next slide?

Q. (By Mr. Ruzich) Would you please read Claim 1 of the '258 patent.

THE COURT: Well, I'll tell you, I'm really not trying to prove how long I can sit up here. I'm going to take a break until 2:30 -- I mean 3:30.

COURT SECURITY OFFICER: All rise.

(Recess.)

COURT SECURITY OFFICER: All rise.

THE COURT: Please be seated.

Counsel?

MR. RUZICH: May I proceed?

THE COURT: Please do.

MR. RUZICH: Before we jump to the '258 patent, I want to clarify a couple of points.

If we can go to Slide 17, please.

Let's go to Slide 18.

Q. (By Mr. Ruzich) All right. Dr. Laskar, you earlier testified as to the meaning of article manufacture in Claim 4, correct?

A. Yes.

Q. And you'll notice in the claim, it also requires packaging material.

A. Yes.

Q. Do you see that?

Okay. And I believe -- well, why don't you tell us in terms of what a person of ordinary skill in the art would understand an article of manufacture to mean in 2002?

A. An article of manufacture, when comprising a packaging material, which is the ophthalmic dropper bottle, in the vast majority of cases, together with the required label to identify its contents, as well as secondary packaging, which would include, in most cases, an outer carton and a package insert or prescribing information insert that is included within each pack -- unit of the product.

Q. An example of that packaging insert or packaging material would be the two PDRs that we discussed, one for the Alphagan label as well as the Timoptic label, correct?

A. The information contained in those monographs is the information that is contained within that prescribing information.

Q. Okay.

A. That text.

Q. Okay.

MR. RUZICH: Let's go to Slide 23, please.

Your Honor, we had a technical glitch. I just want to make certain that these boxes were checked.

THE COURT: Okay.

MR. RUZICH: Okay. Just to make certain, Your Honor.

THE COURT: Mr. Davis, I want you to give me a case, if I fail to check the box.

Go ahead.

MR. RUZICH: Okay. I just wanted to -- I wanted to clarify that.

One more point of clarification, Your Honor, just so if you're reading the '463 patent, you should know that there's a certificate of correction that's attached, and the certificate of correction is important, because certain lines in the claims that are related to the claims where they transposed Timolol for Brimonidine.

So you might be reading it say, oh, goodness, the ranges are different from Timolol and Brimonidine than what we told you here today. So I just wanted to draw that to the Court's attention.

Q. (By Mr. Ruzich) All right. So let's now jump to the '258 patent.

MR. RUZICH: And if I could have Slide 30, please.

And, Your Honor, again, there's overlap with these claims, and I think we can save this Court some time by addressing that overlap in an efficient manner.

And I believe right before break -- oh, right. Thank you. Thanks, Bo.

Q. (By Mr. Ruzich) Dr. Laskar, right before the break, we were about to discuss the '258 patent, correct?

A. That's correct.

Q. So let's take a look at Claim 1 of the '258 patent. And would you please read that claim to the Court.

A. Claim 1 of the '258 patent says: A composition comprising 0.2% Brimonidine, paren, weight/volume, and 0.5% Timolol, paren, weight/volume, in a single compensation.

Q. And I'm going to be make a reference to the claims of the '258 and the '463 patents, so I ask that you be patient with me and make sure you listen to my question.

And for the Court's reference, you'll notice that we have the '258 patent on the left-hand side of this demonstrative, and the '463 to the right, and we're addressing the claims to the right here.

So with regards to Claim 1 of the '258 patent, do they differ from Claim 1 of the '463 patent?

A. They are essentially the same, although there are some slight differences, and those are highlighted in the right-hand column in which Claim 1 of the '463 patent is identified and the differences are the word about prefacing .2% Brimonidine as well as .5% Timolol as well as the phrase, sole active agents, which appears in Claim 1 of the '463 but does not appear in Claim 1 of '258.

Q. Okay. And those are the bolded words that appear in the top right?

A. That's correct.

Q. Great.

Would one skilled in the art interpret these claims differently?

A. No.

Q. So does DeSantis in your opinion disclose all the limitations of Claim 1 either expressly -- or explicitly or inherently of the '258 patent?

A. Yes, it does, for the same reasons that I indicated for Claim 1 of the '463 patent.

MR. RUZICH: Let's go to Slide 32.

Q. (By Mr. Ruzich) Dr. Laskar, is it your opinion that the DeSantis discloses all elements of Claim 1 either inherently or explicitly of the '258 patent?

A. Yes.

Q. Is it your opinion that DeSantis anticipates Claim 1 of the '258 patent?

A. Yes.

Q. Okay. Let's turn now to the obviousness portion of your opinion.

Do you have an opinion as to whether Claim 1 of the '258 patent is rendered obvious?

A. Yes, I do.

Q. And what is that opinion?

A. It is that using DeSantis as well as information available to a person skilled in the art in April of 2002, the information that they would have available would render Claim 1 of the '258 patent obvious.

Q. Okay. And just so I'm clear, your analysis of

Claim 1 of the '463 patent is readily applicable to your analysis for anticipation and obviousness of Claim 1 of the '258 patent?

A. That is correct.

Q. Okay. Let's move on now to Claim 2 of the '258 patent.

MR. RUZICH: Next slide, 33, please.

Q. (By Mr. Ruzich) Can you please read that claim to the Court, Claim 2?

A. Claim 2 of the '258 patent reads: The composition of Claim 1 further comprising from 0.001 to 0.01 of Benzalkonium Chloride.

Q. And you understand that Claim 2 depends from Claim 1?

A. Yes, I do.

Q. And from your earlier understanding, you now know that all limitations of Claim 1 now appear in Claim 2?

A. Yes.

Q. Does your analysis of Claim 1 apply to those same limitations that are now incorporated into Claim 2?

A. Yes.

Q. How does Claim 2 of the '258 patent differ from Claim 2 of the '463 patent?

A. I see no difference in the text.

Q. Okay. Would one of ordinary skill in the art interpret these claims differently?
A. No.
Q. Does DeSantis disclose all limitations of Claim 2 of the '258 patent?
A. Yes.
Q. And how did you reach this conclusion?
A. By means of the same analysis that I applied to Claim 2 of the '463 patent.
Q. To wrap this up, Dr. Laskar, is it your opinion that DeSantis discloses all the elements of Claim 2 either explicitly or inherently of the '258 patent?
A. Yes.
Q. Now, let's focus on --
MR. RUZICH: If I could get that box checked, please. Oh, no, we didn't get to obviousness yet.
Q. (By Mr. Ruzich) With regards to Dr. Laskar's -- Dr. Laskar, with regards to your opinion as to obviousness, with regards to Claim 2 of the '258 patent, do you have an opinion?
A. Yes.
Q. And what is that opinion?
A. That DeSantis as well as information available

to a person skilled in the art in April of 2002 would render Claim 2 of the '258 patent obvious.

Q. And is it fair to say, then, that your analysis of Claim 2 of the '463 patent is also readily applicable to Claim 2 of the '258 patent?

A. Yes.

Q. Okay.

MR. RUZICH: And if we could check Claim 2, both those boxes, please.

We have a technical glitch, Your Honor, again, but -- there we go. Fantastic.

So let's now move to Slide 35, please.

Q. (By Mr. Ruzich) Can you read for the Court Claim 3, please?

A. Yes. Claim 3 of the '258 patent reads: The composition of Claim 2 comprising about 0.005% Benzalkonium Chloride.

Q. And now do you understand that Claim 3 depends from Claim 2, which in turn depends from Claim 1?

A. Yes, I do.

Q. And is it your understanding that all limitations that can be found in Claim 1 and Claim 2 are now incorporated into Claim 3?

A. Yes, I do understand that.

Q. And does your analysis -- based on that

understanding, does your analysis of Claim 1 and Claim 2 still apply to those same limitations that are now incorporated into Claim 3?

A. Yes.

Q. How does Claim 3 of the '258 patent differ from Claim 3 of the '463 patent?

A. There appears to be no difference.

Q. Would one of ordinary skill in the art interpret these claims differently?

A. No, they would not.

Q. Does DeSantis disclose all the limitations of Claim 3 of the '258 patent?

A. Yes.

Q. And how did you reach that conclusion, sir?

A. Using the same analysis that I applied in analyzing Claim 3 of the '463 patent.

Q. Dr. Laskar, is it your opinion that DeSantis discloses all the elements of Claim 3, either explicitly or inherently, of the '258 patent?

A. Yes.

Q. In your opinion, does DeSantis anticipate Claim 3 of the '258 patent?

A. Yes.

Q. Turning now to obviousness, do you have an opinion as to obviousness with regards to Claim 3?

A. I do.
Q. And what is that opinion?
A. My opinion is that DeSantis and information available to one skilled in the art in April of 2002 would render Claim 3 obvious.
Q. And is that conclusion with regards to anticipation of Claim 3 of the '258 patent -- I'm sorry -- the '463 patent and your obviousness analysis of Claim 3 of the '463 patent readily applicable to Claim 3 of the '258 patent?
A. Yes.
Q. I hope I said that right.
A. I had to parse that kind of carefully.
Q. I appreciate it. Okay.
MR. RUZICH: Let's move on now to Claim 4 of the '258 patent, Slide 37, please.
Q. (By Mr. Ruzich) Okay. Can you read Claim 4 to the Court, please?
A. Yes. Claim 4 of the '258 patent reads: The composition of Claim 1 wherein Brimonidine is Brimonidine Tartrate and Timolol is Timolol Maleate.
Q. And, again, Claim 4 depends from Claim 1.
Do you see that?
A. Yes.
Q. And do you understand now that all limitations

of Claim 1 are now in Claim 4?

A. I do.

Q. Does your analysis of Claim 1 apply to those same limitations that are now incorporated into Claim 4?

A. Yes, it does.

Q. How is this claim different than the other composition claims that we've been through, such as Claim 1?

A. Claim 4 of the '258 patent makes the distinction between Brimonidine in general and -- and defines Brimonidine as being Brimonidine Tartrate, and in an analogous fashion, defines Timolol as Timolol Maleate.

Q. Okay. What exactly is Tartrate and what exactly is Maleate?

A. Tartrate and Maleate are the counter-ions used in the formation of a salt of Brimonidine and a salt of Timolol, respectively.

Q. And does DeSantis disclose all limitations of Claim 4?

A. Yes, it does.

Q. Would a person of ordinary skill in the art have understood DeSantis to disclose the salt forms you just testified to?

A. Yes. A person of ordinary skill would

immediately envision in April of 2002 that when Brimonidine is referred to, that, in fact, Brimonidine Tartrate is referred to -- is meant, and that when Timolol is referred to, that Timolol Maleate is the object of that referral.

Q. Is that knowledge set forth in the publications we discussed earlier, specifically the PDRs for the Alphagan and Timoptic labels?

A. Yes. Both those pieces of information are present in the monograph for Alphagan and the monograph for Timoptic that appear in the PDR.

Q. Okay. So this is the Alphagan PDR.

MR. RUZICH: Next slide, please.

Q. (By Mr. Ruzich) And this is the PDR for Timoptic?

A. Yes.

Q. Great.

MR. RUZICH: Slide 40, please.

Q. (By Mr. Ruzich) Dr. Laskar, is it your opinion that DeSantis discloses all the elements of Claim 4, either explicitly or inherently, for the '258 patent?

A. Yes.

Q. And does DeSantis, in your opinion, anticipate Claim 4 of the '258 patent?

A. Yes.

Q. Let's now turn to your obviousness review.
Do you have an opinion as to whether Claim 4 is rendered obvious?
A. Yes.
Q. And what is that opinion?
A. That DeSantis, together with information available to one skilled in the art in April of 2002, would render Claim 4 of the '258 patent obvious.
Q. Okay. And as to your analysis with regard to anticipation and obviousness of Claim 1 of the '258 patent, would that analysis also be applicable to your analysis of Claim 4 here?
A. Yes.
Q. So address Claim 5 of the '258 patent, Dr. Laskar. What does Claim 5 recite?
A. Claim 5 of the '258 patent states: The composition of Claim 1, which is useful for treating ocular hypertension.
Q. And you notice that Claim 5 depends from Claim 1?
A. I do.
Q. And do you understand that all those limitations that are in Claim 1 can now be found in Claim 5?
A. Yes.

Q. And does your analysis, Dr. Laskar, of Claim 1 apply to those same limitations that are now incorporated into Claim 5?

A. Yes.

Q. Dr. Laskar, in your opinion, does DeSantis disclose Claim 5?

A. Yes, it does. In Column 1, beginning Line 13 where the highlighted -- as indicated in the highlighted section, treatment of ocular hypertension.

Q. And that's Column 1, 13 through 24?

A. Yes.

MR. RUZICH: Next slide, please.

Q. (By Mr. Ruzich) Dr. Laskar, is it your opinion that DeSantis discloses all the elements of Claim 5, either inherently or explicitly, of the '258 patent?

A. Yes.

Q. Does DeSantis anticipate Claim 5, in your opinion, of the '258 patent?

A. Yes.

Q. Let's now focus on your obviousness review of Claim 5.

Do you have an opinion as to whether Claim 5 has been rendered obviousness?

A. Yes.

Q. And what is your opinion?

A. That DeSantis and information available to one skilled in the art in April 2002 would render Claim 5 of the '258 patent obvious.

Q. And the knowledge of a person having ordinary skill in the art at that time was what? Are there any publications that you can point to that would show what the knowledge of one of ordinary skill in the art had at that time?

A. In this case, yes. The information concerning ocular hypertension is contained within the monographs for Alphagan and Timoptic, such as those that which -- those that appear in the PDR.

Q. So now let's focus on the Claim 6 of the '258 patent.

Can you please recite the claim for the Court?

A. Claim 6 of the '258 patent reads: The composition of Claim 1, which is useful for treating glaucoma.

Q. Okay. And, again, Claim 6 depends from Claim 1, correct?

A. Yes.

Q. And do you understand now that all limitations of Claim 1 can now be found in Claim 6 of the '258 patent?

A. Yes.

Q. And does your analysis of Claim 1 apply to those same limitations that are incorporated into the Claim 6?

A. Yes.

Q. Dr. Laskar, does DeSantis disclose Claim 6?

A. Yes, it does. It does so in Column 1, beginning in Line 13, in which it notes that the invention relates to the treatment of glaucoma.

Q. Okay. And just for the Court's sake, it's Column 1, Lines 13 through 24?

A. Yes.

Q. Okay. Thank you.

MR. RUZICH: Let's go to the next slide.

Q. (By Mr. Ruzich) Dr. Laskar, is it your opinion that DeSantis discloses all the elements of Claim 6, either explicitly or inherently, of the '258 patent?

A. Yes.

Q. Does the DeSantis anticipate Claim 6 of the '258 patent?

A. Yes, it does.

Q. And now let's turn to --

MR. RUZICH: Put a check in that box.

Q. (By Mr. Ruzich) Now let's turn to your obviousness opinion.

Do you have an opinion as to whether Claim 6

has been rendered obvious?

A. Yes, I do.

Q. And what is that opinion?

A. My opinion is that DeSantis and information available to a person skilled in the art in April of 2002 would render Claim 6 of the '258 patent obvious.

Q. Thank you.

Let's focus now on Claim 7. We have three more claims to go of the '258 patent.

MR. RUZICH: Slide 45, please.

Q. (By Mr. Ruzich) And you'll notice, Dr. Laskar, that Claim 7 is an independent claim.

A. Yes, I noticed that. Thank you.

Q. Would you please read Claim 7 of the '258 patent for the Court?

A. Would you like it in its entirety or section-by-section?

Q. Section-by-section. I think the Court would appreciate that.

A. Okay. The first element of Claim 7 of the '258 patent is an article of manufacture comprising packaging material and a composition within said packaging material.

Q. Okay. And we're going to make a comparison to the Claim 4 of the '463 patent, Dr. Laskar.

How does Claim 7 of the '258 patent differ from Claim 4 of the '463 patent?

A. The first element of Claim 7 of the '258 patent and the first element of Claim 4 of the '463 patent are identical in wording.

Q. And the differences are pointed out by the bolded language on the right-hand side?

A. Except there is no bolded language in that particular element.

Q. Okay. Fair -- okay. Fair enough. We'll get to that in a moment.

Would one of skill in the art interpret these claims differently?

A. No.

Q. And why not?

A. Because the words are identical in -- in exactly identical order.

Q. Okay. And in your opinion, Dr. Laskar, does DeSantis disclose all the limitations of Claim 7 of the '258 patent?

A. It certainly discloses element 1 insofar as we've analyzed that claim thus far of the '258 patent.

Q. Okay. And what about the other elements?

A. I have -- the second element of Claim 7 has the -- the difference between that and Claim 4 of the

'463 patent are the modifiers about preceding .2% of Brimonidine, .5% Timolol.

And Claim 3 of the -- of Claim -- excuse me -- element 3 of Claim 7 of the '258 patent is identical in wording to the third element of Claim 4 of the '463 patent.

And therefore, my analysis of Claim 4 in its entirety, as well as of the elements of the '463 patent, is identical to what I would -- I would apply to Claim 7 in its entirety of the '258 patent.

Q. Thank you.

MR. RUZICH: Okay. Next slide, please. Slide 47.

Great.

Q. (By Mr. Ruzich) Dr. Laskar, is it your opinion that DeSantis discloses all the elements of Claim 7, either inherently or explicitly, of the '258 patent?

A. Yes, it does.

Q. And does DeSantis anticipate Claim 7 of the '258 patent?

A. Yes, in its entirety.

Q. Fantastic.

Now, let's turn to your obviousness review. Do you have an opinion as to whether Claim 7 of the '258 patent has been rendered obvious?

A. Yes, I do.
Q. And what is that opinion?
A. My opinion is that DeSantis and information available to one skilled in the art in April of 2002 would render all elements of Claim 7 of the '258 patent obvious.
Q. We understand that your analysis that you applied to Claim 4 of the '463 patent would be readily applicable to Claim 7 of the '258 patent when discussing and opining on anticipation, correct?
A. When opining upon anticipation and obviousness.
Q. Okay. Thank you.
Claim 8.
MR. RUZICH: Can we go to Slide 48, please?
Q. (By Mr. Ruzich) Dr. Laskar, can you read Claim 8?
THE WITNESS: Perhaps 49.
MR. RUZICH: We can punch it to 49.
THE WITNESS: No, the next one.
MR. RUZICH: There we go. Thanks.
Q. (By Mr. Ruzich) Can you read Claim 8 to the Court, please?
A. Yes. Claim 8 of the '258 patent reads: The

article of manufacture of Claim 7, wherein the composition further comprises from 0.001% to 0.01% Benzalkonium Chloride.

Q. Okay. And you notice that Claim 7 depends -- I'm sorry -- Claim 8 depends from Claim 7?

A. I do.

Q. And do you understand that all the limitations of Claim 7 are now in Claim 8?

A. I do.

Q. And does your analysis of Claim 7 (sic) still apply to the same limitations that are now incorporated into Claim 8?

A. I think you meant to say Claim 8. And my analysis of Claim 8 of the '258 patent is the same.

Q. Thank you.

MR. RUZICH: Let's go to the next slide. Let's go back. I'm sorry. Let's go back to 49.

Q. (By Mr. Ruzich) Let's take a look at Claims 8 and 9 of the '258 patent as to the claims of 5 and 6 of the '463 patent.

Would one of ordinary skill in the art interpret these claims differently?

A. Not at all.

Q. And does DeSantis disclose all limitations of Claim 8 of the '258 patent?

A. Yes, it does.
Q. And how did you reach that conclusions?
A. Using the same analysis that I performed on Claim 5 of the '463 patent, that analysis I applied to Claim 8 of the '258 patent.
Q. Okay. And, Dr. Laskar, is it your opinion that the DeSantis discloses all the elements of Claim 8?
MR. RUZICH: If we could have the next slide, please.
A. Yes.
Q. (By Mr. Ruzich) Is it your opinion that DeSantis anticipates Claim 8 of the '258 patent?
A. Yes.
Q. Now, let's turn to your obviousness opinion.
Do you have an opinion as to whether Claim 8 has been rendered obvious?
A. Yes, I do.
Q. And what is your opinion?
A. That DeSantis, together with information available to one skilled in the art in April of 2002, would render Claim 8 of the '258 patent obvious.
Q. And that information that was available to a person of ordinary skill in the art as of April of 2002 included the PDRs that we discussed?
A. Yes. That would be one of the references they

could use.

Q. Okay. And to be specific, the PDR of the Alphagan label?

A. It would be the Alphagan monograph and the Timolol monograph in that volume.

Q. And by the Timolol monograph, you're referring to the Timoptic?

A. Yes, Timoptic.

Q. I know it's getting late in the day.

Claim 9, let's address that next. Can you please read that for the Court?

A. Yes. Claim 9 of the '258 patent reads: The article of manufacture of Claim 7, wherein the composition further comprises about 0.005% Benzalkonium Chloride.

Q. And you understand that all the limitations of Claim 7 are now in Claim 9, because Claim 9 depends from Claim 7?

A. Yes, I do understand that.

Q. And does your analysis of Claim 7 still apply to those same limitations that are incorporated in Claim 9?

A. Yes.

Q. And let's take a look at Claim 9 of the '258 with Claim 6 of the '463 patent.

Do you have that?
A. Yes. It's a typo --
Q. Yeah.
A. -- in that box.
Q. Okay. How does Claim 9 compare to Claim 6 of the '463 patent?
A. The wording is identical, except for the number 7 in Claim 9 of the '258 patent, and 5 in Claim 6 of the '463 patent. But those claim referentials refer to identical text in their respective documents.
Q. Would one of skill in the art interpret these claims differently?
A. No.
Q. Does DeSantis disclose all limitations of Claim 9 in the '258 patent?
A. Yes.
Q. How did you reach that conclusion?
A. I reached that conclusion on Claim 9 of the '258 patent using the same analysis that I performed on Claim 6 of the '463 patent.
MR. RUZICH: Next slide, please.
Q. (By Mr. Ruzich) Dr. Laskar, is it your opinion that DeSantis discloses all the elements of Claim 9, either explicitly or inherently, of the '258 patent?
A. Yes.

Q. And in your opinion, Dr. Laskar, does DeSantis anticipate Claim 9 of the '258 patent?
A. Yes.
Q. As to obviousness, have you rendered an opinion as to Claim 9 of the '258 patent is obvious?
A. Yes.
Q. And what is that opinion?
A. My opinion is that DeSantis and one skilled in the art, having information available such as that from the respective monographs of Alphagan and Timoptic, would render Claim 9 of the '258 patent obvious.
Q. Okay. Dr. Laskar, with respect to the '258 patent, you know that that was cited to the Patent Office, correct? I'm sorry?
A. That DeSantis -- the '052 was cited within the body --
Q. Let me rephrase. You know that DeSantis was cited to the Patent Office during the prosecution of the '258 patent, correct?
A. Yes, I do.
Q. You also know that DeSantis was not cited to the Patent Office during the prosecution of the '463, the '149, and the '976, correct?
A. I am aware of that.
Q. As to the '258 patent, as to the fact that

DeSantis was provided to the Patent Office, does it impact your opinion as you testified in Court today?

A. Not at all.

Q. Okay.

MR. RUZICH: I just have a couple of wrap-up questions, Your Honor.

Q. (By Mr. Ruzich) Dr. Laskar, have you read Dr. Noecker's reports?

A. I have.

Q. And have you read what Dr. Noecker -- have you read what Noecker defines as a person of ordinary skill in the art?

A. I have.

Q. And do you agree with his statements regarding the level of knowledge of one skilled in the art?

A. I do not.

Q. And why is that?

A. I believe that Dr. Noecker does not give sufficient credit to a person skilled in the art at the time of April of 2002.

MR. RUZICH: Your Honor, I have nothing further, and I pass the witness.

THE COURT: Okay. Ms. Brooks, cross-examination?

MS. BROOKS: Thank you, Your Honor.

CROSS-EXAMINATION

BY MS. BROOKS:

Q. Good afternoon, Dr. Laskar.

A. Good afternoon, Ms. Brooks.

Q. Am I correct, if I did my math right, that you have not worked for Allergan for approximately 18 years? Is that right?

A. That sounds about right, yes.

Q. And since that time, you've worked for various startup companies at various points in your career?

A. I hardly describe Santen or Dey as startup companies. They're very well-established. Santen, I think, began business early in the 20th century. Dey began business in the late 1980s.

Q. I'm sorry. Perhaps you misunderstood my question.

Dr. Laskar, have you worked for various startup companies during the course of your career?

A. Yes.

Q. Okay. And I think you told us about some of them on direct examination; is that right?

A. Yes.

Q. And at the present time, you have your own consulting company called Laskar & Associates; is that correct?

A. Laskar Associates, yes.
Q. Laskar Associates. And are you also on the management board for a company called Amalyte Pharmaceuticals?
A. I am.
Q. And is that also a startup company?
A. Yes, it is.
Q. Are you also on the management board of a company called G2B Pharmaceuticals?
A. Yes, I am.
Q. And is that also a startup company?
A. Yes, it is.
Q. Now, both of those companies have scientific advisory boards, but you are not on their scientific advisory boards, correct?
A. That is correct.
Q. In addition to working for various startup companies, you've also assisted generics on occasion in formulating generic copies of branded products; is that right?
A. I have assisted one company.
Q. And, in fact, is it fair to say, Dr. Laskar, that the only combination ophthalmic glaucoma treatment that you have worked on was a generic version of Cosopt?
A. No, that's not correct.

Q. So at your deposition, when you were asked this question -- it's at Page 17, Line 18:

So then, Dr. Laskar, is it correct that the only combination ophthalmic glaucoma treatment that you worked on was the generic version of Cosopt?

And your answer was: Yes.

Was that inaccurate?

A. Yes, that was.

Q. So you want to change that answer to no?

A. Yes.

Q. All right. Have you worked on other generic versions of other combination ophthalmic products?

A. No.

Q. So is it correct, then, that the only combination ophthalmic glaucoma treatment that you worked on was a generic version of Cosopt?

A. No.

Q. Okay. What other combination ophthalmic glaucoma treatments have you worked on?

A. As I mentioned in -- in direct examination, I assisted Santen's finished subsidiary in their ready-to-use version of a combination of Timolol and Pilocarpine.

Q. Did that ever make it to market?

A. No, it did not.

Q. Now, when you're assisting a generic in the case of the generic who was copying Cosopt, you would agree that the formulation, then, had already been achieved by the branded company, correct?
A. The formulation had been achieved by the branded company, that's correct.
Q. And you would agree that the branded or the innovator company had already gone through its preformulation efforts, correct?
A. Yes.
Q. And the innovator company would have already gone through its formulation efforts, correct?
A. That is correct.
Q. And it would have already gone through its Investigational New Drug Application, correct?
A. Yes.
Q. It would have already gone through its Phase 1 clinical trials, correct?
A. Yes.
Q. It would have gone through its Phase 2 clinical trials, correct?
A. That's correct.
Q. It would have gone through its Phase 3 clinical trials, correct?
A. That is correct.

Q. It would have already submitted its New Drug Application to the Food and Drug Administration, correct?

A. Of course.

Q. And it would have already received approval for that drug, correct?

A. Yes.

Q. And so would you agree with me, Dr. Laskar, that when working for a generic who is copying an innovator's formulation, that hindsight is 20/20?

A. It is -- no, I would not agree with that.

Q. Would you agree that it's a lot easier to be able to just copy an innovator's formulation than to have to start from scratch?

A. Yes, I would agree with that.

Q. Now, let's turn to your analysis in this case of the Timolol and Brimonidine combination that is Combigan. You started your testimony by showing us a page from your expert report, DTX98, and specifically Page 10 -- excuse me.

MS. BROOKS: And if we could pull that back up, Mr. Exline.

And at Page 10, if we could blow up that chart that you showed us.

Q. (By Ms. Brooks) Now, on this chart, this is

showing Timoptic in one column and Alphagan in another column; is that correct?

A. Yes.

Q. And it appears that the buffer in Timoptic is something called a monobasic and dibasic sodium phosphate; is that right?

A. Those are the components of that buffer system.

Q. The buffer system for Alphagan was a citric acid and sodium citrate, correct?

A. Yes, it is.

Q. And as a formulator, you would agree that those are two different buffer systems, are they not?

A. Yes, they are.

Q. In fact, the phosphate is toward the alkaline end of the pH scale, and then the acid or citrate would be more toward the acid end?

A. It depends on the ratio of those two phosphate salts, sodium phosphate --

Q. You would agree -- I'm sorry. I didn't mean to interrupt.

A. No, I was incomplete in my sentence, and I tried to correct.

Q. And you would agree as a formulator that the Alphagan formulators must have chosen the citric acid

and sodium citrate buffer for a reason?

A. Yes.

Q. Now, we move down to the BAK. In Timoptic, the amount of BAK was .01%, correct?

A. That is correct.

Q. And in Alphagan, the amount of BAK was .005%, correct?

A. That is correct.

Q. Now, again, as a formulator, you would agree that there must have been a reason for the formulators of Timoptic to choose the .01% BAK, correct?

A. I would believe so, yes.

Q. And, in fact, we've heard testimony that there is cytotoxicity to BAK; is that right?

A. Yes.

Q. And so, one, as a formulator, you would want to try to use the lowest amount of BAK possible.

Would that be a fair statement?

A. That's what I've said before, yes.

Q. And so we can assume that the formulators of Timoptic used the .01% BAK, because they believe that that was necessary for that formulation.

Would you agree with that?

A. I -- I would agree that they had some reason to do so. I have no idea what that reason might be. I

can't get inside the Merck formulator's head.

Q. Now, if it we come down to the tonicity agent, for Timoptic, there is no tonicity agent; is that right?

A. There is no tonicity agent.

Q. But for Alphagan, there is a tonicity agent called sodium chloride; is that correct?

A. Correct.

Q. And, again, as a formulator, I think you mentioned that a formulator would want to try to use the minimum amount of excipients possible.

Did I hear your testimony correctly?

A. That is correct.

Q. So the fact that there is this tonicity agent in Alphagan would lead you as a formulator to believe that it is there for a reason; is that right?

A. Yes, it would have to be there for a reason. Otherwise, it would not be there.

Q. And there is under viscosity agent in the Timoptic formulation, there's nothing listed under viscosity agent; is that right?

A. Not in Timoptic. That's correct.

Q. But in Alphagan, there's polyvinyl alcohol listed; is that correct?

A. Yes, there is.

Q. And, again, as a formulator wanting to use the

least amount of excipients possible, you would agree that the formulators of Alphagan must have been using polyvinyl alcohol for a reason?

A. Yes, absolutely.

Q. And then we come down to the pH adjusting agent, and both Timoptic and Alphagan have pH adjusting agents of sodium hydrochloride, or in the case of Alphagan, also hydrochloric acid?

A. I think you misstated. Within Timoptic it's sodium hydroxide, not hydrochloride.

Q. My apologizes. You're right. It is late in the day for everybody.

Timoptic has sodium hydroxide as a pH adjusting agent; is that right?

A. Yes.

Q. And Alphagan also has sodium hydroxide as a pH adjusting agent, correct?

A. It has sodium hydroxide as one of the pH adjusting agents, yes.

Q. Correct. And it says: Or hydrochloric acid; is that right?

A. Yes. And actually, I think there may be a typo there, because I believe the labeling may say and/or.

Q. So it could be both. In fact, the

hydrochloric acid and the sodium hydroxide might be present in the Alphagan formulation?

A. In one batch and it may be one or the other in another batch. I can't postulate what happens in the manufacturing for Allergan.

Q. Would you agree that the formulators of Combigan would have been aware of the excipients that were contained in the Alphagan formulation when they began their formulation efforts?

A. I would hope so.

Q. And you would agree that the formulators of Combigan would have been aware of the excipients contained in Timoptic when they began their formulation efforts?

A. They would have known at least the qualitative version, and perhaps more, given the generic version of Timolol, that Allergan, through their specific pharma markets are marketed.

Q. Now, let's talk for a minute about pH. You don't have this in your report, but the pH of Timoptic, the target pH, is approximately 7; is that right?

A. That's correct.

Q. And that is right at neutral on the pH scale; is that correct?

A. As you instructed us yesterday.

Q. And did I get it right?
A. As you instructed, so, yes, you were right.
Q. Thank you. I just like people to say that. Alphagan, the pH of Alphagan is 6.3; is that right? The target pH?
A. No. It appears -- as I read the label, that the lower limit of the target is 6.3, and the upper is 6.5 or 6.6. I don't recall exactly.
Q. All right. So there is a range of pH for Alphagan; is that right?
A. That's what I recall from the labeling.
Q. And it's a range of probably 6.3 to 6.5. Does that sound about right?
A. You probably have better access to that information immediately than I do, so I'll accept that.
Q. And you would agree that those are two different pHs, 7.0 versus 6.5 or 6.3?
A. Absolutely.
Q. And was I -- was I right that the pH scale is a log scale?
A. Yes.
Q. So there -- it would be between 7.0 pH and 6.3 pH, a sevenfold difference; is that right?
A. No.
Q. Okay. What would be the difference between

6.3 and 7?

A. About fivefold.

Q. A fivefold difference?

A. Yes.

Q. What would be the difference between 6.5 and 7?

A. About three or fourfold.

Q. So we have anywhere from a three to fourfold to a fivefold difference between the two pHs in this case; is that right?

A. Yes. That's what I said.

Q. And, again, the formulators would be aware of that, also?

A. Yes.

Q. Now, would you agree that when formulating ophthalmic formulations, a formulator would, if possible, try to get the formulation as close to the pH of the eye as possible?

A. Other things being equal, yes.

Q. Exactly. Other things being equal.

So can we assume, then, that the formulators of Alphagan were unable to formulate Alphagan at higher than a pH of 6.5?

A. I don't know that with certainty, given the information that in 2001 or 2002 would have been

available, I believe, publicly and certainly within the frame -- the laboratories of Allergan.

Q. Well, at the time that Alphagan was formulated, the conventional thinking was that Brimonidine would fall out of solution at higher pHs; isn't that right?

A. I don't know that that's common knowledge.

Q. Do you know that?

A. Do I know that?

Q. Yes.

A. I know from the information that's publicly available and has been for quite some time that that would not be the case.

Q. Well, we're talking now about -- we're going to get to Alphagan-P in a minute. We're talking about --

A. No, I'm talking about Alphagan.

Q. Pardon me?

A. I am talking about Alphagan.

Q. Would you agree that Alphagan was indeed, though, formulated at a pH of approximately 6.3 to 6.5?

A. I've not disputed that at all.

Q. Okay. Now, let's talk for a minute about Alphagan-P.

Are you familiar with that drug?

A. Somewhat.
Q. And Alphagan-P does not use BAK as a preservative; is that correct?
A. Yes, that is correct.
Q. It uses Purite as a preservative, correct?
A. Yes, it does.
Q. But the active ingredient in Alphagan-P is Brimonidine; is that right?
A. Brimonidine Tartrate, yes.
Q. And it is the same active ingredient that is in Combigan, correct?
A. Yes, it is.
Q. And were you here when Mr. Beck testified that the formulators of Combigan attempted to use Purite as the preservative in Combigan?
A. Yes.
Q. And were you here when Mr. Beck testified that those formulation efforts failed?
A. Yes.
Q. And did you understand his testimony to be that the reason that they failed was the Purite ended up oxidizing with the Timolol?
A. Yes.
Q. And as a formulator, you are familiar with that type of phenomenon occurring, are you not?

A. I am.
Q. Where you might put two ingredients together and together something happens that wouldn't -- wouldn't occur if you kept them apart?
A. I think in the -- in this particular case that given the information that would be publicly available, that that reaction would have been one that one would be suspicious about; that is, that there would be the suspicion that that could happen.
Q. So the formulators at Allergan were just wasting their time when they tried to formulate Timolol and Purite?
A. No, I did not say that.
Q. Well, you seem to have quite a working knowledge of Brimonidine, where it does or doesn't fall out of solution.
But isn't it true, sir, you don't have any experience working with Brimonidine?
A. Not in a hands-on fashion. That is absolutely correct.
Q. And, in fact, you don't have any experience working with Alpha-2 adrenergic agonists; is that correct?
A. Given that Brimonidine is -- is -- occupies 90-plus percent of the market, then you are absolutely

correct.

Q. Well, you don't have any hands-on experience working with Apraclonidine, do you?

A. No. You're correct. I was being a little bit facetious.

Q. Now, you said on direct examination that in looking at the patents, the formulators appear to have no problems in formulating, and then you said this formulation, and you were pointing to the formulation in the patent; is that right?

A. Yes.

Q. Now, when you say, in looking at the patent, you're talking about then starting with the patent and confining your observations to the patent to determine whether or not there appear to be formulation problems; is that right?

A. Yes. That's the information that I have available.

Q. For example, you did not look through Allergan's laboratory notebooks of their formulation efforts on Combigan, did you?

A. I would have no way of having access to that information.

Q. Well, actually, aren't you, Dr. Laskar, approved under the protective order in this case?

A. I -- I -- when I speak of that, I speak of that as a formulator outside the realm of this particular -- and I did not -- I did not have -- I was not given access to the notebooks.

Q. My question, Dr. Laskar, was -- is it your understanding you're approved under the protective order in this case to see Allergan confidential information?

A. Yes.

Q. And --

A. That's my understanding.

Q. I take it you didn't ask to see the lab notebooks?

A. That would be correct.

Q. Okay. So it's not like you asked and your counsel refused to let you see them?

A. That's correct.

Q. So your opinion on whether the formulators did or did not have any formulation issues is based solely on the patent; is that right?

A. Yes, it is.

Q. Now, if we look at JTX3, which is the '463 patent -- and specifically at the bottom of Column 3 and over to the top of Column 4, is the formulation that you referred to.

Do I have that right, Dr. Laskar?

A. Yes. I don't recall whether I referred to this one or to the same table that appears in the '258 patent.

Q. Okay. So it's -- the same table appears in both patents you're opining on; is that right?

A. That's correct.

Q. And you refer to this as the starting formulation, if I heard you correctly.

A. I -- I said what -- no, I don't think -- I may have misstated or perhaps you misheard.

What I said was, as a formulator of a fixed combination of Brimonidine and of Timolol, I would start with one of the monotherapies. And my first preference would be to start with the monotherapy whose formulation had the fewest number of excipients, and by virtue of that assessment, I would have started with the Timolol formulation.

Q. But you're aware, are you not, Dr. Laskar, that this formulation that's up on the screen wasn't the starting formulation in this case but the finished formulation.

A. I don't know whether it's the beginning or the end. It is the one that appears in the patent.

Q. Well, you were here when Mr. Beck testified, were you not?

A. I was.
Q. And did you hear Mr. Beck testify about the formulator's efforts in using Synergel as a vehicle in Combigan?
A. Yes.
Q. And you heard how those efforts failed?
A. Yes.
Q. Did you hear Mr. Beck testify about using their efforts to use Purite as the preservative in what would become Combigan and how those efforts failed?
A. Yes.
Q. Did you hear Mr. Beck testify on how the formulators attempted to use carboxymethylcellulose in the formulation and how those efforts failed?
A. Yes.
Q. And you heard Mr. Beck testify that the formulators ran multiple tests at different pHs before they came to the pH that would ultimately become the Combigan pH?
A. I don't recall having heard that testimony that they -- that Allergan ran multiple formulations using a composition that would be qualitatively the same as the composition in this table.
Further, as a formulator, a fixed combination --

Q. I think you answered my question, actually.
A. Okay. Fine. Thank you.
Q. So, Dr. Laskar, you did see Mr. Beck put up on the screen, lab notebooks that showed tests of various formulations at various pHs, did you not?
A. Yes, I did.
Q. Okay. And you also saw Mr. Beck put up on the screen various tests that showed different amounts of BAK being tested, correct?
A. Yes.
Q. And you also heard Mr. Beck testify that even after they went through the Synergel formulation, the Purite formulation, the CMC formulation, and decided on the aqueous formulation, they found that unique degradants were appearing.
You heard Mr. Beck testify about that, correct?
A. I did.
Q. And that they had to stop moving forward on the project until they could determine whether or not those degradants were toxic.
A. I heard -- I heard that they needed to do some work to evaluate the impact of those degradants, yes, I did.
Q. Now, you would have only known about all of

that listening to Mr. Beck here in the courtroom, correct?

A. Yes.

Q. Because you didn't go through the lab notebooks prior to rendering your opinion in this case; is that right?

A. That's correct. That's correct. Sorry to step on your words.

Q. Now, you also mentioned, in relation to the '463 patent, that there was nothing in the claims about the FDA. Did I hear that correctly?

A. Yes.

MS. BROOKS: Now, if we could pull up, please, Claim 4 of the '463 patent, which is going to be at the top of Column 10.

Q. (By Ms. Brooks) Now, this claim doesn't go specifically to a composition, does it?

A. I'm sorry. Would you repeat your question?

Q. Sure. This claim, Claim 4 of the '463 patent, doesn't go to a composition, does it?

A. It -- as I read it, it refers to both an article of manufacture and a composition.

Q. And a composition within the packaging material; is that right?

A. That is contained within the packaging

material.

Q. And you've described the packaging material as being not only the box and the label but what's called the package insert; is that right?

A. Yes.

Q. And you are aware, are you not, as a formulator that eventually, before a package insert can get to market, that package insert or label, as we call it, has to be approved by the FDA.

MR. RUZICH: Objection, Your Honor. It's outside the scope of his expert report. He's not an expert on FDA approval.

THE COURT: Overruled. It's cross-examination. Go ahead.

Q. (By Ms. Brooks) If you know, Dr. Laskar, since you said you didn't see anything in the claims that would require FDA involvement, do you know whether or not, in fact, a label has to be approved by the FDA?

A. It is my understanding that the text of the label is a requirement for FDA approval.

Q. And then the '258 patent, I think you said the same thing, that you didn't see anything in the claims that would involve the FDA. But if we can go to JTX4 and pull up Claim 7, which is at Column 10, that, too, is referring to, at least in part, the package insert or

label, correct?

A. Yes.

Q. And it is your understanding that at some point in time, the FDA would need to approve the contents of that label, correct?

A. What I -- what I said was that they need to approve the text of that label. The fact that a label and package insert is used is -- is a requirement for usual pharmaceuticals, whether it be ophthalmic or otherwise. It is merely the words contained therein that have FDA review.

MS. BROOKS: And now, while we're on the '258 patent, if we can go to the front page, Mr. Exline.

Q. (By Ms. Brooks) And this has already been shown, and I know you don't dispute it.

MS. BROOKS: If we could blow up, please, under References Cited.

Q. (By Ms. Brooks) The fifth reference down is the DeSantis reference upon which you base your anticipation opinion, correct?

A. Yes.

Q. And it is also the reference upon which you base your obviousness opinion combined with what one of skill in the art would have known; is that right?

A. That's correct.

Q. And so we know that the Examiner had DeSantis before him at the time that he approved Claims 1 through 9 of the '278 patent, correct?

A. Yes.

Q. Thank you.

Now, speaking of DeSantis, let's move on to that. I won't reinvent the wheel with the questions that I asked Dr. Tanna, but just very quickly, would you agree that DeSantis discloses 56 beta-blockers?

A. If that's the number that you've counted, I agree with it.

Q. Would you agree that DeSantis discloses 18 alpha-agonists?

A. If you counted it to be that, I accept your counting.

Q. And then would you agree that DeSantis incorporates by reference Timmermans?

A. Yes, absolutely.

Q. And would you agree that Timmermans discloses 197 alpha-agonists?

A. That's what they -- a counting does, yes.

Q. And that Timmermans is not discussing the reduction of intraocular pressure, correct?

A. It does not.

Q. What it is disclosing is the use of

alpha-agonists for cardiovascular use; is that right?

A. Let me read the title again.

Q. And if you would like to look at DTX124, that's Timmermans, specifically at Bates Stamp No. 210.

A. Right. As I read the title of -- and it's Bates 210, yes -- Roman IV: Structure-Activity Relationships in Clonidine-Like Imidazolidines and Related Compounds.

I don't see that the title refers to cardiovascular effects.

MS. BROOKS: Well, if we can blow up, it will say -- actually, it's up higher. It should say: The first part of this charter deals with the structure-activity relationship --

Q. (By Ms. Brooks) Okay. That's what you read.

MS. BROOKS: Now let's go on to the intravenous administration. Here we are. DTX124. Ah, right here. Right here. Thank you.

Q. (By Ms. Brooks) Intravenous administration of Clonidine provokes a biphasic effect on arterial pressure.

So what Timmermans was looking at was arterial pressure; is that correct?

A. With Clonidine in that quote -- or in that piece of text, yes.

Q. And also intravenous administration, correct?
A. Yes. That's what he was talking about.
Q. Would you agree also that DeSantis discloses nine preservatives?
A. Yes, that sounds about right.
Q. Now, Counsel, on direct examination, said: Well, you're not here to do math, Dr. Laskar, and you admitted that there could be, if you looked at all these various combinations, literally millions of combinations that one could take away from DeSantis in light of Timmermans.
A. Depending on how you -- what items you put together, yes.
Q. But Counsel then asked you -- or you said: But DeSantis discloses only one potential combination, and that's Brimonidine and Timolol.
Did I understand you correctly, Dr. Laskar?
A. When considered -- when done under the view of a person of skill in the art reviewing that information, on or about April of 2002, having as part of their knowledge information about Allergan's brand of Brimonidine, known as Alphagan, and knowing information about Timoptic.
Q. Well, you understand that for an anticipation reference, all of the elements of the claims must be

present in one reference --
A. Yes, I do.
Q. -- or a reference incorporated by -- by reference, for example, Timmermans, correct?
A. Yes.
Q. So for your anticipation analysis, you understand that one could not look to the Alphagan label or the Timolol label. You understand that?
A. Yes. Perhaps I misunderstood your question, but I thought I heard the word obviousness within the text of that question.
Q. Okay. What I asked you was: Did I hear you correctly that DeSantis discloses only one potential combination, Brimonidine and Timolol?
A. It -- it -- it is the combination of an alpha-agonist and Timolol that it discloses, yes.
Q. Well, let's see if that's actually accurate then, if we could, Dr. Laskar.
MS. BROOKS: If we can go to DeSantis DTX123 and go to Column 6, Lines 20 through 29.
Q. (By Ms. Brooks) Now, isn't it true, Dr. Laskar, that what we're looking at here is the only formulation disclosed in DeSantis?
A. It is.
Q. And the --

A. And the leading text says: It is typical of aqueous ophthalmic solutions of the present invention.

Q. And the only formulation disclosed in DeSantis is a formulation combining Apraclonidine and Betaxolol; is that correct?

A. That is the text -- that is the only example that it gives of -- wherein a quantitative description is provided.

Q. Thank you.

Let's turn now to your opinions regarding the amount of BAK as disclosed in the claims.

MS. BROOKS: Mr. Exline, if you could pull up Slide 12 of Dr. Laskar's.

Q. (By Ms. Brooks) Now, you showed this to the Court, and even though DeSantis discloses a very wide range of BAK, from .001% to 1.0% by weight, that -- I think your words were, a person of skill in the art would go immediately to the .01% in Claim 2 for the BAK in the formulation; is that right?

A. That's what I said.

Q. Now, let's go back and look at Slide 10 that was used in opening statement.

MS. BROOKS: And if you could, Mr. Exline. No. This is -- oh, I'm sorry. In Defendants' opening statement. Or I can try to go to

the ELMO, if we can't find it. There we are.

Q. (By Ms. Brooks) Now, this is a chart that you prepared; is that right?

A. Yes, it is.

Q. And if I look here, I see that Travatan has a BAK of .015; is that right?

A. Yes.

Q. And would you agree with me that that is more than .01?

A. Yes.

Q. And do I see that Xalatan has a BAK of .02?

A. Yes.

Q. And would you agree with me that that is more than .01?

A. Yes.

Q. Lastly, Dr. Laskar, I want --

MS. BROOKS: Thank you.

Q. (By Ms. Brooks) Lastly, I just want to make sure I understand your obviousness opinion.

Is it your opinion that because Brimonidine was already on the market as Alphagan and Timolol was already on the market as Timoptic, that it would have been obvious to put the two of them together in one bottle?

A. It would be obvious to be motivated to put

those two drugs together in a single formulation.
Q. And are you saying that when that is done, then those claims are not new or novel or inventive?
A. That -- that having -- can you rephrase the question?
Q. Sure. Are you saying that just because Alphagan was already on the market as a monotherapy and Timolol was already on the market as a monotherapy, the fact that the formulators were able to put them together in one bottle and the clinicians were able to get FDA approval for that, that that was still not new or novel or nonobvious?
A. The -- the fact that you have monotherapy of Alphagan, monotherapy of Timoptic would motivate one to put those -- those two together and that having achieved that is -- is a matter of routine experimentation and not -- and not a matter of -- of supreme creativity or extraordinary creativity as a part -- the creativity required is no more than that which would be required of a person of ordinary skill in the art --
Q. So, Dr. Laskar, I take --
A. -- in putting that formulation together, is my --
Q. I take it, sir, that you would not claim that something was new and novel and non-obvious if you

didn't think that it was; would that be fair?
A. I think -- I think that's fair, yes.
Q. You certainly wouldn't sign a declaration of inventorship that something was new and novel and non-obvious if you didn't believe that it was new and novel and non-obvious; is that fair?
A. Yeah, that is fair.
Q. So let me ask you this, Dr. Laskar: Have you ever heard of an acne treatment that is made up of Benzoyl Peroxide?
A. Yes.
Q. Have you ever heard of an acne treatment that is made up of Clindamycin?
A. In a combination, yes.
Q. Well, I'm not getting to combination yet.
A. As individual agents, yes, absolutely. I thought I heard the word and in there.
Q. So you've heard way back when -- let's see -- all the way back in 1992, you're familiar -- you were familiar with the fact that Benzyl Peroxide was being used as a monotherapy for the treatment of acne, correct?
A. That is correct.
Q. And you knew, way back in 1992, that Clindamycin was being used as a monotherapy for the

treatment of acne; is that correct?

A. That is correct.

Q. Yet you and your fellow inventor, Dr. Nadkarni, filed a patent where you claimed: A method of treating acne vulgaris in human patients comprising topically administering to said patients a composition comprising a therapeutically effective amount of Benzyl Peroxide and Clindamycin; is that correct?

A. Yes, it is.

Q. And you believed at the time that your ability to combine those two monotherapies was new and novel and patentable, correct?

A. Yes, I -- I did and I do, inasmuch as there were some formulation hurdles in order to stabilize the Clindamycin in the presence of the Benzyl Peroxide.

Q. But you don't discuss those formulation hurdles in your patent application, do you, sir?

A. No, I did not. I guess that's the way Allergan chooses to write their patents.

Q. Thank you very much.

MS. BROOKS: No further questions, Your Honor.

THE COURT: Mr. Ruzich?

REDIRECT EXAMINATION

BY MR. RUZICH:

Q. Dr. Laskar, do ophthalmic drugs in Europe contain labels?

A. Yes. There is -- there is a patient leaflet. My recollection of the information that's provided in European products is slightly different than the information contained in the U.S. one, but it is -- it contains information about the composition and the manner of use of the product.

Q. Okay. So the labeling requirement, if there is one, would not be limited to the United States, correct?

A. Absolutely not.

Q. Okay. And then based on your experience, is it at all unusual to try parallel formulations along with simpler formulations?

A. Depends on the intent, but yes. It is routine, in my opinion, to take several formulations forward. Hopefully, if you have manpower enough in parallel in order -- because it is routine and normal for things to drop away for one reason or another.

And, in fact, through many scars, I've learned to always have a back-pocket formulation even as late as Phase 3.

Q. I wasn't able to review the patent that Ms. Brooks had up in front of here. Did you secure a

patent for that product?
A. I believe it still remains a patent application. You'd have to ask the Allergan legal department concerning its status, because I am unaware of it. And, in fact, I thought it had never been pursued and was only informed at a previous deposition that Allergan appears to be prosecuting it.
Q. Have you ever testified in court before as an expert?
A. No, I have not.
MR. RUZICH: Nothing further, Your Honor.
MS. BROOKS: Nothing further. Thank you, Your Honor.
THE COURT: Wait just a minute.
THE WITNESS: Okay.
THE COURT: You used a term I don't know how many times. I ran out of counting. You said that in April of 2002, that one of ordinary skill in the art would immediately envision. You kept using that term.
What did you mean by that exactly?
THE WITNESS: It means -- and I think it's a parallel term or an analogous --
THE COURT: I want to know what you meant when you kept using the term immediately --
THE WITNESS: That the information --

that the information -- if -- if -- if somebody referred Alphagan to me, it would, to me, cause me to think Brimonidine .2%, that's a citrate buffer, the polyvinyl alcohol for corneal residence and Benzalkonium Chloride as a preservative. That's what -- those are pieces that would come popping up immediately.

THE COURT: Okay. Thank you.

THE WITNESS: You're welcome.

THE COURT: You may step down.

MR. RUZICH: Your Honor, just to clarify, we're holding Dr. Laskar for potential rebuttal.

THE COURT: Okay. Who's your next witness?

MR. DAVIS: Your Honor, at this time, the Defense rests.

THE COURT: Okay. How much more you got, Ms. -- how long you need tomorrow? I'm talking to Ms. Brooks now. He just rested.

MS. BROOKS: Yes, Your Honor.

THE COURT: The ball is in your court.

MS. BROOKS: Thank you.

We will be making a judgment as a matter of law, Your Honor, on the Defendants' defenses of anticipation and obviousness as to all asserted claims.

They have not met their burden by clear

and convincing evidence on any of the claims.

With that, Your Honor, we would move -- unless Your Honor grants the judgment, we would move into our rebuttal case, and we have two witnesses we will be calling, I believe.

And so I would think we would be about -- I don't want to underestimate -- a couple of hours, Your Honor, at most.

THE COURT: All right. We'll recess until the morning.

Your motions are denied.

COURT SECURITY OFFICER: All rise.

THE COURT: 8:30.

(Court adjourned.)

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CERTIFICATION

I HEREBY CERTIFY that the foregoing is a true and correct transcript from the stenographic notes of the proceedings in the above-entitled matter to the best of my ability.

/s/_____ _____
SUSAN SIMMONS, CSR Date
Official Court Reporter
State of Texas No.: 267
Expiration Date: 12/31/12

/s/_____ _____
SHELLY HOLMES Date
Deputy Official Court Reporter
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