IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CIVIL ACTION NOS.:
15-335(JBS); 14-667(JBS);
14-4149(JBS); 14-5144(JBS)

SENJU PHARMACEUTICAL CO., LTD.,
BAUSCH & LOMB INCORPORATED, and
BAUSCH & LOMB PHARMA HOLDINGS
CORP.

Plaintiffs,

vs.

LUPIN, LTD. AND LUPIN
PHARMACEUTICALS, INC.,

Defendants.

SENJU PHARMACEUTICAL CO., LTD.,
BAUSCH & LOMB INCORPORATED, and
BAUSCH & LOMB PHARMA HOLDINGS
CORP.,

Plaintiffs,

vs.

INNOPHARMA LICENSING, INC.,
INNOPHARMA LICENSING, LCC,
INNOPHARMA, INC., and
INNOPHARMA, LLC,

Defendants.

Job No. NJ 2238419

Transcript of deposition taken by and before Lisa Forlano, CCR, CRR, RMR, Certificate No. XI01143, at the offices of Alston & Bird, LLP, 90 Park Avenue, New York, New York, on Friday, February 26, 2016, commencing at 10:38 a.m.

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I N D E X

E X H I B I T S

E X H I B I T S (CONTINUED)

VIDEO OPERATOR: Good morning, we're now on the record. Please note that the microphones are sensitive and may pick up whispering and private conversations. Please turn off all cellphones or place them away from the microphones, as they can interfere with the deposition audio. Recording will continue until all parties agree to go off the record.

My name is Jim Roberts representing Veritext, with offices in Livingston, New Jersey.

Today's date is February 26, 2016.

The time is approximately 10:38 a.m. The deposition is being held at Alston & Bird, located at 90 Park Avenue, New York City, New York, and is being taken by counsel for the Plaintiff.

The caption of the case is Senju Pharmaceuticals, et al. versus Lupin, LTD., et al. The case is held in the US District Court, District of New Jersey. The name of the witness is Robert C. Cykiert.

Counsel will please state their

appearances for the record.

MR. DINER: Bryan Diner with the law firm of Finnegan Henderson, representing the Plaintiff, Senju, et al. With me is my colleague, Terrence Kim.

MR. JANUSZ: Joe Janusz of Alston & Bird, representing the Innopharma defendants and the witness, today.

VIDEO OPERATOR: Our court reporter, Lisa Forlano, also of Veritext, will please swear in the witness.

ROBERT C. CYKIERT, M.D., having been duly sworn, was examined and testified as follows:

BY MR. DINER:

Q Good morning, sir.

A Good morning.

Q How are you today?

A All right. Good. How are you doing?

Q Fine, thank you. Can you please state your full name and address for the record?

A Sure. Robert Cykiert, 345 East 37th Street, New York, New York 10016.

Q Dr. Cykiert, have you been deposed before?

A Yes, I have.

Q Have you been deposed in an IP case before? By IP, I mean intellectual property.

A No, not that I recall.

Q Okay. I'll just go over a few ground rules for today's proceeding, if that's fine with you.

A Sure.

Q I kind of break them down into three parts; my questions, your breaks, perhaps, or any questions you have. So first with regard to my questions. My job is to ask the questions, your job is to answer them, and to answer them truthfully and accurately.

Does that sound fair?

A Yes.

Q Okay. With regard to breaks, any time you feel you need a break, it's fine with us, just let us know. If there is a question pending, however, I would just ask that you answer that question and then we can take a break afterwards.

Is that fine?

A Yes.

Q Okay. And to the extent that you have any questions of a question that I've asked or are

unclear about something, please let me know and I'll be happy to either clarify or rephrase the question.

Is that okay?

A Yes.

Q And if I ask a question and you answer it, I'll assume that you understood the question.

Is that fine?

A Yes.

Q Okay. Is there any reason why you cannot testify today truthfully and accurately?

A No, no reason.

Q I'd like to mark the first exhibit.

(Responsive Expert Report of Robert C. Cykiert, M.D., on Objective Indicia of Non-Obviousness was marked Cykiert-1 for identification.)

BY MR. DINER:

Q Okay. Now, Dr. Cykiert, the court reporter has just handed you a document that is entitled, Responsive Expert Report of Robert C. Cykiert, M.D., on Objective Indicia of Non-Obviousness.

Is what has been marked as Cykiert Exhibit 1 your expert report, including any exhibits or appendices that you have submitted in this case?

A What's the question? I'm sorry.
Q Is this the expert report that you have submitted in this matter?
A Yes, it looks like it.
Q Okay. Can you please turn to the page in your expert report after page 31.
A Okay.
Q On that page do you see the signature at the top?
A Yes.
Q Is that your signature?
A Yes, it is.
Q Now, on the next page, which actually doesn't have a page number, there's another signature. Is that your signature as well?
A Yes.
Q Now, if you hold these two pages open together, I think as you are doing presently, the page after page 31 has a date of February 3 at the top.
Do you see that?
A Yes.
Q The next page actually has a date of February 1, 2016 at the top.
Do you see that?

A Yes.

Q Do you know why you have two signature pages with two different dates.

A Yeah, apparently I signed it without looking at the date and later I was told it was the wrong date, so I had to re-sign it again with the correct date.

Q And which one is the correct date that you re-signed?

A I believe it was February 1.

Q Okay. So you signed the report on February 1, but February 3 was the date indicated when you signed it?

A Apparently it was the wrong day. I believe I signed it actually on February 1, but I didn't notice that it had the wrong date printed on it, February 3, so I was asked to re-sign it with the correct date.

Q Okay. Thank you.

Who prepared your expert report in this case?

A I prepared it.

Q Did you prepare it by yourself?

A I prepared it with the attorneys.

Q Okay. Now, at the end of your report,

does it contain a copy of your CV?

A Yes, it does.

Q And is this CV current and accurate as of today?

A I think it's accurate to within probably about six months or so.

Q Okay. Is there anything that you would like to add to your CV that's not presently in it?

A Nothing right now that I can think of.

Q Okay. And your curriculum vitae lists your current, relevant professional experience, correct?

A Yes.

Q Dr. Cykiert, in what areas do you consider yourself an expert?

A I'm an ophthalmologist and I have special expertise in what's called the anterior segment of the eye, which is the front of the eye, which includes things like cataract surgery, cornea, external disease, any diseases, conditions, problems or complications or surgeries of the front part of the eye.

Q You're not an expert on any of these conditions in the posterior part of the eye?

A The posterior part of the eye is

connected to the front of the eye, so I'm also, as an ophthalmologist, an expert on all parts of the eye, front to back, but I have specific fellowship training in the anterior segment of the eye. So many conditions that affect the front of the eye also have an effect on the back of the eye, which I'm an expert on as well.

Q Any other areas of ophthalmology that you would consider yourself an expert in other than what you just stated?

A Basically it depends how you define expert. What do you mean by "expert"?

Q Well, do you have an expertise in any other areas of ophthalmology other than what you just described?

A I have numerous areas of expertise within ophthalmology. Again, depending on how you define "expert," I have special super expertise in the front part of the eye, but I'm also an expert on the back of the eye, the middle the eye, the sides of the eye and every disease and condition of the eye.

Q Okay. Are you an expert in the field of pharmacy?

A That I'm not an expert in, no.

Q Have you ever practiced pharmacy?
A No, I have not.
Q Are you an expert in the area of pharmacology?
A No, I'm not an expert in pharmacology.
Q And neither are you an expert in pharmacokinetics?
A I am not an expert in pharmacokinetics.
Q Nor are you an expert in pharmacodynamics, right?
A I'm not an expert in pharmacodynamics. But I should say that I know certain things about all those things that you mentioned simply because part of ophthalmology is treating conditions, diseases with various drugs which required me to know a bit about pharmacy, pharmacokinetics and pharmacodynamics.
Q But as you stated, you don't consider yourself an expert in those areas, correct?
A Again, depending on how you define "expert," I would say with my definition of expert, I'm not an expert in those, as I previously stated.
Q That's fine.
Dr. Cykiert, have you ever conducted any research on any bromfenac-containing product?

A No, I have not.
Q Have you ever conducted any research on any tyloxapol-containing product?
A No, I haven't.
Q Are you an expert in chemistry, using your definition of an expert?
A Well, I majored in chemistry in college, so I do have basic fundamental knowledge of chemistry, especially how it applies to the eye and diseases of the eye, but I wouldn't consider myself an expert in that.
Q Thank you. Would you consider yourself an expert in chemical stability testing of aqueous liquid preparations?
A That I'm not an expert in.
Q Have you ever conducted any chemical stability testing on an aqueous liquid preparation?
A No, I haven't.
Q Are you an expert in patent law?
A No, I'm not.
Q Are you a named inventor on any U.S. Patent?
A Yes, I am.
Q How many, approximately?
A One patent.

Q And what does it deal with?
A It's a patent that blocks radiation from cellphones.
Q So not involved in ophthalmology, then?
A No, it's not.
Q Are you a named inventor on any pending U.S. Patent applications?
A Could you repeat that?
Q Sure. Are you a named inventor on any pending U.S. Patent applications?
A No.
Q You mentioned you have at least one patent. Are you comfortable reading patent claims?
A What do you mean by am I comfortable?
Q Let me back up a minute. Do you know what I mean by a patent claim?
A Sure.
Q Okay. When you read patent claims, do you feel you understand them?
A Yes.
Q So, then, are you comfortable in reading patent claims?
A I can read them, certainly.
Q And can you read them and understand them?

A It depends what the patent is about.
Q Okay.
A If it's a patent in ophthalmology or related to ophthalmology I feel very comfortable reading it and understanding it.
Q Very good. Thank you.
Are you an expert in clinical testing?
A No, I'm not.
Q Have you ever conducted any clinical testing with a pharmaceutical product?
A No, I don't believe I have.
Q And so that would include not having conducted any testing, clinical testing with an ophthalmic product, correct?
A Correct.
Q In connection with your opinions in this matter, did you conduct any testing comparing a bromfenac -- comparing bromfenac-containing compositions?
A No, I did not.
Q And you understand that Prolensa is a bromfenac-containing composition, correct?
A Yes.
Q And you understand that Xibrom is a bromfenac-containing composition?

A Yes.

Q And you also understand that Bromday is a bromfenac-containing composition, correct?

A Yes.

Q You did not conduct any comparative testing between Prolensa and Bromday, correct?

A That's correct, I did not.

Q Nor did you conduct any comparative testing between Prolensa and Xibrom, correct?

A I did not.

Q Were you instructed not to conduct any comparative testing among bromfenac-containing compositions?

MR. JANUSZ: I'll caution the witness not to reveal the substance of any communication with counsel. I think that -- let me just read the question.

MR. DINER: I'll agree that if he answers it yes or no it's not a waiver of any privilege.

MR. JANUSZ: That's fine.

THE WITNESS: I'm sorry, could you repeat that question.

BY MR. DINER:

Q Were you instructed not to conduct any

comparative testing among bromfenac-containing compositions?

A No.

Q Would you please turn to page 3 of Cykiert Exhibit 1, which is your expert report.

I'd like to refer you to the bottom of the prior testimony section.

Do you see that?

A Yes.

Q Go to the first bullet point. I think it indicates cases in the last five years in which you have provided expert testimony; is that correct?

A Yes.

Q The first case in the first bullet point, Chery versus Malik.

Do you see that?

A Yes.

Q What was your role in that case?

A I believe that was a medical malpractice case.

Q And what was your role?

A I was an expert.

Q And what was your role as an expert in that case?

A I don't remember the details of that

case right now.

Q Do you remember, generally, what kind of expert opinions you provided in the case as a general matter?

A That case I don't recall.

Q Thank you. That was in 2015, correct?

A Right.

Q Okay. How about the next case, Gallimore versus Allison. What was that case about?

A That's a medical malpractice case as well.

Q And you appeared as an expert in that case?

A I don't think I appeared in that.

Q You provided testimony in that case, correct?

A Yes.

Q In what capacity?

A As a defense expert.

Q Did you provide testimony at trial?

A No, not at trial.

Q Did you provide deposition testimony?

A No.

Q So what kind of prior testimony did you offer in this case that led you to list this in this

category?

A I don't know exactly the name, but it's a court document that's submitted to the Court. It might be perhaps a summary judgment document or some attestation type of document. I don't recall the details of it.

Q Such as a Declaration perhaps?

A Right, a Declaration, correct.

Q Okay. And did you say that this case dealt with medical malpractice as well?

A Yes.

Q Okay. There are six more cases on your list, beyond the Gallimore versus Allison case. Were all of those medical malpractice cases?

A Yes.

Q And let's just go to this Cifuentes versus Staciu case. Do you recall what your role was in that case?

A Yes, that one I appeared in court.

Q And were you testifying in court as an expert?

A Yes.

Q And what generally was the subject matter of your testimony?

A It was a complication during cataract

surgery.

Q Okay. And which side in the litigation did you represent?

A I represented the doctor.

Q So you were offering your opinions in defense of a malpractice suit brought against the doctor?

A Yes.

Q Dr. Cykiert, is CME an abbreviation for cystoid macular edema?

A Yes, it is.

Q If I refer to cystoid macular edema today as CME, will you understand what I mean?

A Yes.

Q And that will be easy for both of us, I presume?

A Yes, that's a nice abbreviation.

Q Is it correct that Prolensa is approved for post-operative treatment of inflammation and pain after cataract surgery?

A Yes.

Q Now, Prolensa is not approved for treatment of CME, correct?

A That's not the official approval, that's correct.

Q It doesn't have any approval, official or otherwise for CME, correct?

MR. JANUSZ: Objection, vague.

THE WITNESS: Well, approval by whom?

BY MR. DINER:

Q By the FDA.

A Not by the FDA, no.

Q Does it have approval by anyone for the treatment of CME?

A It has approval by many doctors who use it for that purpose off label, which is perfectly acceptable.

Q Administering compounds off label is acceptable?

A Yes.

Q Is that what you're saying?

A Right.

Q What is your basis for that?

MR. JANUSZ: Objection, calls for speculation.

THE WITNESS: That's commonly understood that certain medications have uses other than the official FDA approval.

BY MR. DINER:

Q And do you often administer ophthalmics

off label?

A It depends on what you mean by "often." It depends on the ophthalmic, it depends on the patient's condition. It depends on numerous factors.

Q Have you administered ophthalmics off label before?

A Yes, I have, as have thousands of other ophthalmologists every day.

Q Are you familiar with the ophthalmic Voltaren?

A Yes.

Q Is it approved by the FDA for the treatment of CME?

A No, it's not.

Q In fact, there are no ophthalmic NSAIDs that are approved by the FDA for the treatment of CME, correct?

A Correct.

Q And there are no ophthalmic NSAIDs approved by the FDA for the prevention or prophylaxis of CME, correct?

A Correct.

Q Do you draw a distinction between treatment in prophylaxis with respect to CME?

A Yes, there is a distinction.
Q What is it?
A Well, broadly, prevention means putting a patient on a drug to try to prevent a condition from occurring. And treatment is the condition or disease already exists and you're using a drug to try to cure or treat that disease or condition.
Q And the explanation you just gave as between prophylaxis and treatment would similarly apply to the prophylaxis and treatment of CME?
A That's correct.
Q Other than for the treatment post-operatively of inflammation and pain after cataract surgery, Prolensa is not approved for anything else, correct?
A I'm not aware of anything but those two things you mentioned.
Q Now, the approved indication on the Prolensa label is not limited to cases where the patient is unable to receive corticosteroid treatment due to allergy, correct?
A Could you repeat that again?
Q Sure. The approved indication on the Prolensa label is not limited to cases where the patient is unable to receive corticosteroid

treatment due to allergy; is that correct?

A That's correct.

Q And the approved indication on the Prolensa label is not limited to cases where the patient has diabetes, correct?

A That's correct.

Q Are you familiar with the term "sulfite sensitivity" with regard to ophthalmics?

A Yes.

Q Are asthmatics a class of people that could have sulfite sensitivity?

A Asthmatics can and so can anybody else. Some people are allergic to sulfites.

Q When someone is allergic to sulfites, how does that manifest itself clinically?

A Just like any allergy, there are various manifestations. Sometimes it could just be itching of the skin. Some people can get hives. Some people can get respiratory problems, they have difficulty breathing, and in the most severe cases they can have what's called anaphylaxis, which is a severe life-threatening reaction where they can't breathe, their blood pressure drops, their heart may even stop. So there's a broad spectrum of allergic reactions that can occur with sulfite.

Q And in the context of ophthalmics, this issue of sulfite sensitivity, was that known for sometime?

MR. JANUSZ: I'll just object to the scope. Go ahead.

BY MR. DINER:

Q You can answer.

A That's been known for a while. Several drops contain that, and we know some patients have sulfite allergies.

Q Was it known prior to 2003 that there -- some people who were sulfite sensitive in the context of taking ophthalmics, for example?

MR. JANUSZ: Same objection.

THE WITNESS: I can't tell you specifically what year the sulfite allergy issue came up with in ophthalmics. I'm not sure why you picked 2003, but I couldn't tell you exactly what year, so I can't answer that accurately.

MR. DINER: I'd like to mark the next document, please.

(Adverse reactions to sulfites article was marked Cykiert-2 for identification.)

THE WITNESS: Thanks.

BY MR. DINER:

Q Now, Dr. Cykiert, the court reporter has just handed you a publication to Yang, et al., and it is entitled, Adverse Reactions to Sulfites. It's a couple-page document. You can take a look at it and let me know when you're ready and I'll ask you some questions.

A Do you want me to read the entire document before you ask me questions?

Q Well, how about I ask you some questions, and to the extent you need to refer to the document in greater detail you should feel free to do so.

A Okay.

Q Now, just a few moments ago you were talking about anaphylactic shock, I believe.

Do you recall that?

A Yes.

Q You see in that first paragraph of this article on the first page, left-hand column, it says -- second sentence, In the United States more than 250 cases of sulfite-related adverse reactions, including anaphylactic shock, asthmatic attacks, urticaria and angioedema, nausea, abdominal pain and diarrhea, seizures and death have been reported.

Do you see that passage?

A Yes.

MR. JANUSZ: Object to scope here as well.

BY MR. DINER:

Q Now, in the context of what we were talking before about sulfite sensitivity and some of the manifestations of sulfite sensitivity, does the list that I just read include some of the manifestations that you were aware of for sulfite sensitivity?

MR. JANUSZ: Same objections.

THE WITNESS: I mentioned earlier all these things that are listed in this article before I saw the article.

BY MR. DINER:

Q Okay. And at the bottom of the first page it indicates that this article was published on November 1, 1985; is that correct?

A Right.

Q Uh-huh. And if you look at the paragraph bridging the first and second page -- sorry, strike that.

If you look at the second column of the first page, you see where it identifies six

sulfiting agents?

MR. JANUSZ: Same objection.

THE WITNESS: What do you mean by sulfiting --

BY MR. DINER:

Q Let me refer you to the second column, second full paragraph on the first page. There it talks about a number of different sulfites identified in various products.

Do you see that, the different sulfites?

A Yes.

Q Okay. And sodium sulfite is listed there, correct?

MR. JANUSZ: Same objection.

THE WITNESS: Where is sodium sulfite listed?

BY MR. DINER:

Q The fifth line down.

A Could you point to the paragraph? I'm not sure --

Q Sure.

A That paragraph.

Q Yeah.

A Yeah. It says six sulfiting agents.

Q And one of the six sulfiting agents includes sodium sulfite, correct?

MR. JANUSZ: Same objection.

THE WITNESS: Yes, that is listed there.

BY MR. DINER:

Q And you're familiar with the ophthalmic Bronuck, correct?

A Yes, I am.

Q And Bronuck contains sodium sulfite; is that correct?

MR. JANUSZ: Same objection.

THE WITNESS: I'd have to see the packet insert to be sure.

(Bronuck Ophthalmic Solution document PROL0333509 - PROL0333513, was marked Cykiert-3 for identification.)

BY MR. DINER:

Q Now, Dr. Cykiert, the court reporter has just handed you a document marked as Cykiert Exhibit 3, bearing Bates numbers PROL033509 through 513. Following up on my last question and your last answer, I would direct you to the second page of Cykiert Exhibit 3, the left-hand column at the top. You see the box that identifies the composition of

Bronuck?

A Yes.

Q Okay. And back up a minute. Would you agree that this translation appears to be the package insert information concerning the ophthalmic formulation known as Bronuck?

A Are you asking me to vouch that the translation is correct?

Q No.

A Oh.

Q I'm asking you to let me know if you agree that this appears -- that Cykiert Exhibit 3 appears to be the prescribing information for Bronuck.

A Yes.

Q Okay. And back to the left-hand column of the second page, do you see that box towards the top identifying the ingredients in Bronuck?

A Yes.

Q Do you see next to additives a list of additives in Bronuck?

A Yes.

Q Do you see that it -- strike that.

Bronuck, according to this document, contains sodium sulfite, correct?

MR. JANUSZ: Objection, scope.

THE WITNESS: It says dry sodium sulfite.

BY MR. DINER:

Q Okay. Can you go back to Cykiert Exhibit 2, please? Now, Cykiert Exhibit 2 identifies that sulfites, such as sodium sulfite, can be used in ophthalmics. And if it will help you to answer the question I'll refer you to the bottom of page 1 and the paragraph bridging the right-hand column to the top of the second page of Cykiert Exhibit 2.

MR. JANUSZ: Objection, scope.

THE WITNESS: Yes, I see that.

BY MR. DINER:

Q Okay. And it indicates that -- strike that.

So this document indicates that it was known in November of 1985 that adverse reactions to sulfites, such as sodium sulfite, could occur in ophthalmic eye drops, correct?

MR. JANUSZ: Objection, scope and to the extent it mischaracterizes the document.

THE WITNESS: Yeah, I didn't read the whole document, but it says in the first

paragraph that you mentioned that you can have reactions to it, which we know, we discussed. And then later it mentions that it's present in eye drops. I don't know if there's a discussion about the risks of eye drops, which you just said, so I'd have to extensively read this document and see if it says that. Otherwise I'm reaching for conclusions that may not be there.

BY MR. DINER:

Q Okay. But this document would establish that there was knowledge of sulfur sensitivity with regard to ophthalmics prior to 2003, correct?

MR. JANUSZ: Same objections.

THE WITNESS: No, what you just said is wrong. You said sulfa sensitivity. This is sulfites.

BY MR. DINER:

Q Oh, pardon me. Thank you very much. So to rephrase the question, this document establishes that it was known in the art prior to 2003 that ophthalmics containing sodium sulfite could have sulfite sensitivity issues, correct?

MR. JANUSZ: Same objections.

THE WITNESS: Again, you're asking me to reach a conclusion by reading two separate paragraphs that are unconnected, so I think that would be a far reach. If you want me to read the document, I can read it and then give you my interpretation of it. But --

BY MR. DINER:

Q Well, let's try it from this angle. Sulfur sensitivity was something that was known in the art prior to 2003, correct?

MR. JANUSZ: Same objections.

THE WITNESS: You again said sulfa, and there's a difference between sulfa and sulfite. Can I assume when you say "sulfa" you mean sulfite?

BY MR. DINER:

Q I'll restate the question. Thank you, Doctor. Sulfite sensitivity was something that was known in the art prior to 2003, correct?

MR. JANUSZ: Same objections, asked and answered.

THE WITNESS: This article is 1985. It mentioned adverse reactions to sulfites, it's in a journal that I'm not familiar with, but I assume it was in a journal that people read,

so I assume it was known about at that time.
BY MR. DINER:
Q Thank you. You can put those aside now.
A Thanks.
Q You're welcome.
Okay. Let's go back to Prolensa. Shall we?
A Sure.
Q Okay. Back to the approved indication for Prolensa. Now, the approved indication on the Prolensa label is not limited to cases where the patient has a diagnosis of a retinal disorder, correct?
A Correct.
Q And an FDA-approved indication for a drug is a clinically-verified reason for prescribing that drug, correct?
MR. JANUSZ: Objection, vague.
THE WITNESS: Not necessarily. It just says that's one of the uses. It doesn't mean you have to use it.
BY MR. DINER:
Q My question is a little different. By virtue of the fact that the drug is FDA approved,

that approval is based on the submission of clinical studies, correct?

A To the FDA?

Q Correct.

A Right.

Q And so is it fair to say, then, that an FDA-approved indication for a drug is clinically -- is a clinically verified reason for prescribing that drug?

MR. JANUSZ: Objection, vague.

THE WITNESS: I think you're saying it incorrectly.

BY MR. DINER:

Q Why is that?

A From what I'm understanding that you're saying is that if the FDA approves a drug for treating one and two, that means for disease one or disease two, if you have a patient with disease one and two you have to use that drug. That's my understanding of what you said. That's not the case. That's up to the physician to determine, depending on numerous factors whether, indeed, the physician should use that drug to treat that condition in that patient at that time.

Q When the FDA approves a drug for use,

that approval was based on the fact that it would be clinically acceptable for doctors to prescribe that drug to a patient, correct?

A Yes.

Q Okay. So is the treatment of post-operative inflammation and reduction of ocular pain in patients who have undergone cataract surgery a clinically-verified reason for prescribing Prolensa?

MR. JANUSZ: Objection, vague.

THE WITNESS: It is, but there are other factors that come into play to determine if you should use it in a patient.

BY MR. DINER:

Q Okay. But the fact that the FDA has approved Prolensa means that you could use it in a patient, correct?

A Yes.

Q In a clinical setting, correct?

A Yes.

MR. JANUSZ: I'll object to vague, to the last question.

BY MR. DINER:

Q Now, when cataract surgery is performed, Dr. Cykiert, an incision is made in the

eye, correct?

A Yes.

Q And there is typically post-operative inflammation associated with that surgical incision, correct?

A Yes.

Q There's also post-operative pain associated with that surgical incision, correct?

A Not always.

Q But typically there can be, correct?

A I would say in a minority of patients.

Q But there can be post-operative pain associated with the surgical incision as part of cataract surgery, correct?

A There can be.

Q Okay. Now, inflammation in a patient post-cataract surgery would require medical treatment, correct?

A Yes.

Q And pain in a patient after cataract surgery would require medical treatment as well, correct?

MR. JANUSZ: Objection, vague.

THE WITNESS: Yes.

BY MR. DINER:

Q Inflammation is a major factor in the development of CME following cataract surgery, correct?

A The current thinking is that that is the case.

Q And Prolensa is indicated for treatment of both operative inflammation after cataract surgery, correct?

A Yes.

Q Not treating inflammation can increase the chances of development of CME; is that correct?

MR. JANUSZ: Objection.

THE WITNESS: It's variable from patient to patient.

BY MR. DINER:

Q But in some patients it can occur that CME develops if the inflammation is not treated, correct?

A In some patients, but not all patients.

Q CME can lead to blindness in some cases, correct?

A You have to explain what you mean by blindness. You have to define blindness. Blindness is not a specific word or term.

Q Okay. It's a term of art, blindness; is that correct?

MR. JANUSZ: Objection, vague.

THE WITNESS: I'm not sure what you mean by a term of art.

BY MR. DINER:

Q You have an understanding of blindness, correct?

A I do.

Q Okay. Let's use your definition of blindness. Can CME lead to blindness?

A No. According to my definition. But you didn't ask me what my definition is.

Q So tell me your definition.

A Blindness, from our perspective as ophthalmologists, is total loss of vision in an eye. CME doesn't cause that.

Q Okay. Could CME cause something less than total blindness?

A Yes.

Q And what can it cause that would be something less than total blindness?

A It can cause mild blurry vision or moderate blurry vision.

Q Can it cause severe blurry vision?

A In rare cases it can.

Q And in those cases where it can cause severe blurry vision, would you consider that a severe complication?

A Yes.

Q Now, Dr. Cykiert, are corticosteroids and NSAIDs two different types of drugs?

MR. JANUSZ: Object to form.

THE WITNESS: Yes, they are different.

BY MR. DINER:

Q And do they act by different mechanisms?

MR. JANUSZ: Same objection.

THE WITNESS: Yes, they have different mechanisms.

BY MR. DINER:

Q And what are the differences in their mechanisms?

A Well, that's a complicated question and answer, but, in general, the steroids inhibit inflammation by inhibiting what's called the COX-2 pathway, whereas I think you asked NSAIDs is the other one, they inhibit COX-1 and COX-2 pathways.

Q And so these drugs inhibiting different mechanisms can have a different side effect profile,

correct?

MR. JANUSZ: Object to form.

THE WITNESS: Yes, they can.

BY MR. DINER:

Q Now, we spoke a moment ago about blurry vision. Do you recall that discussion?

A Yes.

Q So in the context of the next few questions I'm going to ask, I'm going to ask you to be thinking about that concept of blurry vision as we discussed before. Rehabilitation of vision in the days immediately after cataract surgery is an important clinical measure; is that correct?

MR. JANUSZ: Objection, vague.

THE WITNESS: It's one of the important clinical measures.

BY MR. DINER:

Q Okay. What are some of the other important clinical measures?

MR. JANUSZ: Same objection.

THE WITNESS: There are things like preventing infection, making sure the incision is healing properly, making sure the intraocular lens implant is in good position, making sure the anterior chamber is deep.

There are numerous factors. Those are some of the major ones.

BY MR. DINER:

Q The time to heal -- strike that.

The time to obtain visual rehabilitation following cataract surgery can impact patient satisfaction with the surgery, correct?

A It varies from patient to patient actually.

Q So can you give me some examples in which it can, or visual rehabilitation can impact patient satisfaction with the surgery?

A Sure. If you start somebody with a severe cataract where they can't even see the eye chart, you operate on them, and the next day they can read the eye chart, to them that's an incredible, remarkable improvement even though their vision may not be great the next day, they think it's incredible.

On the other hand, if you start with somebody who's got only a moderate cataract with mild blurring, if they don't have 20/20 vision the next day they may be upset because I just had the surgery, I'm not a perfect 20/20 yet. So we basically educate them, let them know that the time

to get perfect vision is very variable from patient to patient. So a lot of it has to do really with patient expectations. Some people think the surgery is almost magical and you have perfect vision the next day. Other patients understand that with surgery there may be time that it takes to get better. It could be anywhere from days to weeks or months. So it's a complicated question and answer because there are numerous extrinsic factors, and it's extremely variable from patient to patient.

Q With regard to both subgroups of patients that you just described, when they get their vision back, that impacts favorably their quality of life, would you agree?

MR. JANUSZ: Objection, vague.

THE WITNESS: When they get their vision back is, as he said, a very vague term. What do you mean by getting your vision back? It depends what your vision was. It depends where you are. It depends what your needs are. It depends if you're going back to work the next day. It depends if you're retired. It depends how old you are. It depends on the vision in the other eye. I could go on for another hour or two, but I don't think you

want me to.

BY MR. DINER:

Q How about if the person needs his vision to drive, okay, with that qualification, when that person gets his vision back, is that an improvement in that person's quality of life?

A If the individual is unable to drive because of poor vision and then after surgery they achieve the vision that's required by law to drive again, then, yes, they would be satisfied with that.

Q And that would be a positive effect on their quality of life, correct?

A Yes.

Q Now, NSAIDs are effective in reducing CME soon after surgery, correct?

MR. JANUSZ: Objection. Object to form.

THE WITNESS: That's not necessarily the case.

BY MR. DINER:

Q Some NSAIDs have been shown to be effective in reducing CME soon after surgery, correct?

MR. JANUSZ: Objection, vague.

THE WITNESS: Shown by who?

BY MR. DINER:

Q The authors of the article that you cited in your expert report. The name is Kim, et al.

A If you're referring to a specific article, if I could look at it, I'd appreciate it.

Q Sure.

(Topical Nonsteroidal Anti-inflammatory Drugs and Cataract Surgery Article, 2159 - 2168, was marked Cykiert-4 for identification.)

BY MR. DINER:

Q Dr. Cykiert, the court reporter has just handed you what has been marked as Cykiert Exhibit 4. Cykiert Exhibit 4 is -- appears to be an article from the Ophthalmic Technology Assessment or from the American Academy of Ophthalmology. It is entitled, Topical Nonsteroidal Anti-inflammatory Drugs and Cataract Surgery. A report by the American Academy of Ophthalmology.

Now, Dr. Cykiert, have you seen this article before?

A Yes, I have.

Q And is this an article that you rely on -- cite and rely on in your expert report?

A Yes, I did.

Q Okay. And so you reviewed this document as part of providing your opinions in your expert report, correct?

A Yes.

Q Okay. I'd like to refer you to the first page of this document, Cykiert Exhibit 4, in the section entitled Results.

Do you see that?

A Yes.

Q Can you read the very first sentence of that subsection into the record, please?

A Sure. Non-steroidal anti-inflammatory drug therapy was effective in reducing CME detected by angiography or optical coherence tomography, OCT, and may increase the speed of visual recovery after surgery when compared directly with placebo or topical corticosteroid formulations with limited intraocular penetration.

Q So the authors of this article, Cykiert Exhibit 4, concluded that NSAIDs are effective in reducing CME soon after surgery when compared to placebo or topical corticosteroid formulations, correct?

MR. JANUSZ: Object to the extent it

mischaracterizes the document.

THE WITNESS: Yeah, what you just said is totally wrong.

BY MR. DINER:

Q What's wrong with it?

A Because that's not what it says, and I'll point it out to you exactly. It's effective in reducing CME detected by angiography or OCT. That's a very subtle testing of CME, which often is clinically insignificant. So the CME detected by those two tests is not necessarily significant. In fact, in most cases it's not. And you missed the word and "may" increase the speed. "May." It doesn't say it will increase, it says may. May means maybe it does, maybe it doesn't. And when compared directly with placebo. Well, if you compare anything to placebo it might be better placebo because placebo is nothing. So maybe it's better than placebo. To me that's not a big deal. Or topical corticosteroid formulations with limited intraocular penetration. Well, if you take a corticosteroid that doesn't penetrate the eye well that's almost like placebo. It doesn't have an effect because you need intraocular penetration. So saying that it may be better if you're testing OCT

or angiography means it probably isn't, and if it increases the speed of visual recovery compared to placebo, that doesn't mean anything, and if you're comparing to it a steroid that doesn't penetrate the eye, it's better than that. That doesn't mean anything. So basically what they're saying here is that it has no significant clinical effect. And if you read their conclusion section it says that very clearly.

Q And so you're relying on this document in support of your opinions, correct?

A This is one of the things. This isn't the sole thing, but this is an important document. It's a report by the American Academy of Ophthalmology, which is the leading ophthalmology association in the USA and the world. And when they come out with a report, it's something that is very researched in a rigorous way by a panel of experts in the field. So this is an extremely reliable document.

Q And -- but they're relying on an extremely insensitive method for detecting CME?

A No, that's not what the article says.

Q But that's what you said, though.

A No, no. You're putting words in my

mouth. That is not what I said. What I said, and I'll say it again, is that it may be helpful if you're comparing it to this test which is not clinically very relevant, and it may be helpful if you're comparing it to placebo, and it may be helpful if you're comparing it to a weak steroid. That's what they're saying.

Q So the clinical test that they're relying on may not be clinically relevant; is that correct?

A The OCT testing and fluorescein angiography testing showing CME is often not clinically relevant because it will pick up extremely subtle CME that is not clinically relevant. I'll give you an example. This table appears pretty smooth to you, right?

Q Okay.

A Okay. The table is very smooth. If I magnify the surface of this table with a hundred power microscope it will look like Mount Everest or the Himalayas or the Rocky Mountains, because under high magnification you will see tiny bumps and crevices and it will look unsmooth. However, that's not relevant because this table is very smooth. You can put your paper on it, you can write on it. If

you pass your hand on it, it's very smooth.

So when you do OCT testing you can pick up what's called subclinical CME, which means it's not relevant to the patient or doctor. If you do fluorescein angiography, you can pick up subclinical CME, which is not relevant to the patient or doctor. What we're talking about really is clinical significant CME where the patient has blurry vision and the doctor can detect it. So what this basically says is there's no benefit that's been shown or proven for clinically significant CME.

Q But this very reputable journal that you referred to still relied on the OCT in reaching it's conclusion that non-steroidal anti-inflammatory drugs may be effective in reducing CME compared to placebo and topical steroids with limited intraocular penetration, correct?

MR. JANUSZ: Object to form.

THE WITNESS: No, you're misinterpreting the document and what it says. If you read the conclusion section, which if you'd like me to read in, it clearly explains what they're saying. So your interpretation of that is incorrect.

BY MR. DINER:

Q Now, you referred to the use of the word "may" before in that sentence that we've been discussing --

A Correct.

Q -- and you said that your understanding is that NSAIDs may, or they may not, based on this sentence, reduce CME, as determined by OCT compared to a placebo or the corticosteroids that are identified there; is that correct?

A Yeah. It says may.

Q Okay. And your interpretation of "may" is what again in the context of this sentence?

A Maybe yes, maybe no. We know what may means.

Q Okay. So in your view they're equivocating, to some extent; is that correct?

MR. JANUSZ: Objection, calls for speculation.

THE WITNESS: No, not at all. Again, you're misinterpreting the article. If you let me read the conclusion section it will really verify it so we all can understand it clearly.

BY MR. DINER:

Q Well, let's go to 2165 of Cykiert

Exhibit 4 under the conclusions. And there, the left-hand column, please, Dr. Cykiert. You see it?

A Yes. Thanks.

Q There it says that NSAIDs clearly are effective in reducing the incidence of angiographic or OCT-based CME in hastening visual recovery in the short term (less than three months) when compared with placebo and topical corticosteroid formulations that have poor corneal penetration, correct?

A Right.

Q It didn't use the word "may" in that sentence, did it?

MR. JANUSZ: Objection, mischaracterizes the document.

THE WITNESS: Why don't you read what it says after the comma.

BY MR. DINER:

Q I'm just asking you.

A Well, you're taking a fragment of a sentence to try to prove a point, which is incorrect, not valid.

Q But what I'm asking you specifically there is that's an affirmative statement using the affirmative form of the verb "to be," in this case the word "are" to say that they are effective under

these conditions, correct?

MR. JANUSZ: Same objection.

THE WITNESS: They left out the word "may" here, for whatever reason, but again I'll bring to your attention that in reducing incidence of angiographic or OCT-based CME, that's what's called subclinical CME, that's me magnifying the surface of this table 100 power and showing you it looks like the Himalayas or Rocky Mountains, when, in fact, it's perfectly smooth and flat. And again, they're saying compared to placebo, compared to nothing, okay. Compared to a steroid that's weak, okay. But it's not clinical significant CME. That's what they're saying, it's effective for clinically insignificant CME. That's what they're saying here.

BY MR. DINER:

Q When a product is approved by the FDA for marketing, it can be approved on its basis of efficacy and safety versus placebo, correct?

A Could you repeat that?

Q When a product is approved by the FDA for marketing, it can be approved on the basis of that product's efficacy and safety versus placebo,

correct?

A That's correct.

Q Okay.

A But you're mixing two things, because it's approved for pain and inflammation. This article here deals with CME, which is not identical to pain and inflammation. So you're making a side point, but it's not valid for what we just discussed.

Q You talked about this as being subclinical CME, correct?

A Right.

Q But it's still CME, nonetheless, correct?

MR. JANUSZ: Objection. Object to form.

THE WITNESS: There's a difference between CME, that's clinical and subclinical CME. Now, to you it may seem like it's the same thing, it's CME, CME. But to ophthalmologists it's totally different. And to patients it's totally different, because I can do -- I could take 100 post-operative cataract patients who have 20/20 vision, yet if I do fluorescein angiography or OCT on

them, maybe 30 or 40 percent will have an abnormality of that. So they have what's called subclinical CME. But you know what, those patients are thrilled because they have 20/20 vision. They don't know they have subclinical CME, only the ophthalmologist who does those tests knows it, but they're clinically insignificant.

BY MR. DINER:

Q But those patients that are nonetheless thrilled that their vision has improved, even though they may have had subclincal CME, correct?

MR. JANUSZ: Objection, mischaracterization.

THE WITNESS: I don't understand. You're summarizing what I just said?

BY MR. DINER:

Q Yes.

A I don't know if your summary is accurate. I think what I said stands for itself.

Q Let me ask you: You said there may be patients who have subclinical CME, correct?

A Correct.

Q And they may have their subclinical CME treated in a way that they are satisfied with,

correct?

MR. JANUSZ: Objection, mischaracterizes prior testimony.

THE WITNESS: There's no reason to treat subclinical CME. And so I can't answer your question. Why would you treat something that's subclinical?

BY MR. DINER:

Q Well, I'm just going on what you said a moment ago. You said that someone with subclinical CME may be thrilled to have their vision back, correct?

MR. JANUSZ: Same objection.

THE WITNESS: Right.

BY MR. DINER:

Q Okay. So then that person with subclinical CME who is thrilled to have their vision back received the benefit from whatever treatment that person received in receiving back their vision, correct?

MR. JANUSZ: Object to form.

THE WITNESS: Are you implying they're on an NSAID, is that what you're saying?

BY MR. DINER:

Q No, I'm just saying generally?

A Well, in general, people are happy to get their vision back.

Q And if they had subclinical CME and got their vision back, they would be happy, correct?

A That's correct.

Q And that would be a benefit to them, correct?

A That's correct.

Q Now, Cykiert Exhibit 4 recognizes the benefits, even in the short term, soon after surgery in administering NSAIDs to reduce CME, correct?

MR. JANUSZ: Objection, mischaracterization.

THE WITNESS: No, that's incorrect. We just went over that. It's subclinical CME. And if you read the paragraph it's very clear after the comma. There is no Level I evidence to suggest that prophylactic use of NSAIDs reduces longer term, greater than three months vision loss from CME after cataract surgery. The body of Level II evidence supports the same conclusion. The claim made by several authors that use of an NSAID and corticosteroid is synergistic with the implication that the combined effect of each

drug class exceeds the additive effect of each drug is not supported by the literature. This clinical impression of synergy remains unproven and seems unlikely, given the overlapping mechanisms of the drugs.

That really says it all.

BY MR. DINER:

Q We'll get to that actually, but I want to go back to my question, which was slightly different. So I'll articulate it again. Cykiert example -- excuse me, strike that.

Cykiert Exhibit 4 recognizes the benefits, even in the short term, soon after surgery in administering NSAIDs to reduce what you call subclinical CME, correct?

MR. JANUSZ: Same objection.

THE WITNESS: Only if you compare it to placebo, nothing, or compare it to a weak steroid, which is nothing. So yes, if you compare the NSAID to zero it may be a little bit better, but if you compare the NSAID to a true steroid that is universally used by all doctors who do cataract surgery, then it's probably worthless, is what this article says because there is no Level I or Level II

evidence.

BY MR. DINER:

Q There is also no Level I or Level II evidence that steroids other than the ones talked about here can reduce CME, correct?

A That's not the case at all.

Q It doesn't say that in this article, does it?

A This article doesn't deal with corticosteroids. This is an article about NSAIDs, as the title says. There's endless documentation that steroids are beneficial for the eye, a proper steroid, not a weak steroid, after cataract surgery.

Q Okay. Beneficial for the eye for treating inflammation, correct?

A Yes.

Q Okay. But this article that you characterized as coming from a very reputable journal in your field of medicine doesn't support the fact that steroids can be used to reduce CME, correct?

MR. JANUSZ: Object to form.

THE WITNESS: This article doesn't deal with that subject, so I can't comment on that. The article has nothing to do about that.

It's dealing with NSAIDs.

BY MR. DINER:

Q Now that we've established that NSAIDs can reduce subclinical CME, let's talk about Prolensa. Prolensa --

A I'm sorry to interrupt, but you said something, we've established it. We haven't established that. You maybe have established it, I have not.

Q Okay.

A So you have to start that question a little bit differently because I haven't established it.

Q Okay. So let's start it this way. With respect to what you called subclinical CME, Cykiert Exhibit 4 recognizes the benefits in administering NSAIDs to reduce what you call subclinical CME, correct?

MR. JANUSZ: Objection, mischaracterization.

THE WITNESS: You didn't finish the sentence. You're taking half the thought because you're leaving out the placebo or poorly penetrating topical corticosteroids. So you have to be complete in the question.

BY MR. DINER:

Q I will rearticulate the question. So in the context of what you call subclinical CME, Cykiert Exhibit 4 recognizes the benefits in administering NSAIDs to reduce subclinical CME compared to placebo and corticosteroid formulations with limited intraocular penetration, correct?

MR. JANUSZ: Same objection.

THE WITNESS: Yes.

BY MR. DINER:

Q And Prolensa is indicated for treating inflammation post-operatively, correct?

A Yes.

Q And so Prolensa, as an NCE formulation, could also reduce subclinical CME as compared to placebo and corticosteroids with limited intraocular penetration, correct?

MR. JANUSZ: Objection, vague as to NCE.

BY MR. DINER:

Q NSAIDs.

A Oh, I'm sorry. I heard NCE, also.

Q My apology. I will repeat the question.

So Prolensa could -- strike that.

Prolensa is indicated for use in treating post-operative inflammation, correct?

A Yes.

Q And so as an NSAID-containing formulation, Prolensa could be used to reduce subclinical CME as compared to placebo or corticosteroids with limited ocular penetration, correct?

MR. JANUSZ: Object to form.

THE WITNESS: That's what it says here, but that's clinically irrelevant because we all universally use steroids with good penetration post-operatively after cataract surgery. So it's basically a clinically irrelevant fact. The only exception would be in the incredibly rare exception where a patient may have an allergy to corticosteroid drops. Then you're left with an NSAID alone. So maybe that's one out of tens of thousands or hundreds of thousands of patients.

BY MR. DINER:

Q Okay. Let's go to paragraph 39 of your report. And you can take a moment if you'd like to read that paragraph just to refresh yourself on what that paragraph says.

A Thank you. Okay, I read it.

Q Now, in paragraph 39 of your report you cite to what has been marked as Cykiert Exhibit 4, which I referred to as the Kim article. And in your report you state that -- the second sentence -- Ophthalmologists have "reported the impression that there is a pharmacologic drug synergy from the use of both an NSAID and a corticosteroid" resulting from the use of an NSAID post-operatively following cataract surgery to prevent the development of CME.

Do you see that?

A Yes.

Q Okay. Now, the drug synergy that you referred to, that would result from the use of an NSAID and a corticosteroid together, correct?

MR. JANUSZ: Objection, mischaracterization.

THE WITNESS: That's what synergy means, when you use two things together and you get an effect.

BY MR. DINER:

Q So just for the record, for synergy there to be present it means that the combined effect of the two drugs together exceeds the additive effect of each drug alone. Is that

reasonable?

A That's a definition of synergy, but that's not what this paragraph says.

Q Well, --

A Well, the keyword is, reported "the impression." Maybe we can bold or underline the word, the impression. So what happens is doctors use two drugs and they get the impression, wow, you know, maybe things are better with these two drugs. But basically what this article, from the American Academy of Ophthalmology says is that that's just an impression. There's no Level I or Level II evidence to document that or to prove that. That's just an impression people have. People often get impressions, but there's no proof of that in this case.

Q So effectively there is no proof of synergy of the two compounds working together to obtain a synergistic result, correct?

A Right.

Q And there was no evidence of synergy between those two compounds in preventing CME, correct?

A Right.

Q So just to say that two drugs are not

synergistic doesn't mean that the drugs may not individually be effective in treating CME, correct?

MR. JANUSZ: Objection, vague, calls for speculation.

THE WITNESS: Yeah, synergy doesn't break down that way. You're kind of going backwards from synergy. It doesn't work that way.

BY MR. DINER:

Q What I'm saying is that when you referred to drug synergy and quoting from this article and that there was no synergy, it doesn't mean that the individual compounds, the corticosteroid and the NSAID individually didn't have some effect in addressing CME, correct?

MR. JANUSZ: Object to form.

THE WITNESS: Synergy doesn't discuss that at all. You're drawing conclusions that can't be drawn from this. You can't say -- if A and B are not synergistic that means that A itself is good and B itself is good. That doesn't work that way. Going backwards doesn't work.

BY MR. DINER:

Q Okay. But now I understand. That

wasn't exactly my question. My question was: When this article refers to the possible synergistic effect of these two drugs, does it effectively debunk that possibility that the two drugs were -- could be synergistic in treating CME?

A I just said that. It's not synergistic. There's no evidence.

Q Okay. And -- but there is evidence, at least as to the NCEs, as you testified earlier, that they could be used to effectively treat what you called subclinical CME as compared to placebo and some specific corticosteroids, correct?

MR. JANUSZ: Object to form.

THE WITNESS: That's a long compound question, and you said again NCE. I think you mean NSAIDs when you say that, so I'll assume you mean NSAIDs. But, again, I think we've covered this. You can't go backwards from synergy and say that each drug itself works well. It doesn't work that way. So -- and we've already discussed 15, 20 minutes of the fact that the NSAIDs, there's no Level I or II lefts evidence there are any benefit.

BY MR. DINER:

Q Lack of any Level I or Level II

evidence that there's no benefit in treating CME is looking at it at a period of greater than three months, correct?

A Let me look at the article.

Q And while you're doing that, I'll refer you to the conclusions on the left-hand column of page 2165.

A Yes, it refers to after three months.

Q Okay. And what it does, though, say in that same passage in the conclusion on page 2165 is that the NSAIDs are clearly are effective in reducing, in your words, subclinical CME when compared to placebo or corticosteroids of poor corneal penetration, correct?

A We've gone over that, I think, many, many times already.

Q And so your answer is yes, then?

A My answer is the same as it was before. I've said it about half a dozen times, I think.

Q Okay. So I'll ask it again just to be clear.

A Uh-huh.

Q In the conclusion here on page 2165 it does say that NSAIDs clearly are effective in reducing what you call subclinical CME when compared

with placebo or topical corticosteroids having poor corneal penetration, correct?

A You left out less than three months.

Q Okay. So they're effective at less than three months in that context, correct?

A They're effective -- let me summarize it for you. They're effective from treating non-clinically significant CME in under three months when you're comparing them to zero.

Q And I think we established earlier that someone with subclinical CME, as you called it, who got their vision back would consider that to be a benefit, correct?

MR. JANUSZ: Objection, mischaracterizes.

THE WITNESS: Patients are not aware that they have subclinical CME. It's just a test that we could do. Again, this table looks like the Himalayas, if you magnify it a hundred times. It's not as perfectly smooth. So it's basically a test used for research purposes, but it's not clinically significant.

BY MR. DINER:

Q Nonetheless, that person with what you call subclinical CME getting his vision back would

be satisfied with the return of his vision, correct?

MR. JANUSZ: Same objection.

THE WITNESS: But that would have happened most likely anyway if they weren't on NSAIDs, because the eye usually heals and the subclinical CME is insignificant and usually goes away. And on top of that, since we universally use a potent steroid that penetrates well it's an irrelevant fact or point that you're making.

BY MR. DINER:

Q In those cases where it doesn't spontaneously correct itself and that person who had what you called subclinical CME and got his vision back would be satisfied with the return of his vision, correct?

A Anybody who gets their vision back is satisfied, whether they have subclinical CME or not. So your question is kind of vague, and I don't understand what the question is.

Q I think you've answered it. So thank you.

A Okay.

MR. DINER: Is this a good point for a break?

MR. JANUSZ: Yeah.

VIDEO OPERATOR: Off the record, 12:08. This is the end of disc 1 of the deposition of Robert C. Cykiert.

(Lunch recess.)

VIDEO OPERATOR: Going back on the record, 12:58 p.m. This is the beginning of disc 2 in the deposition of Robert C. Cykiert.

BY MR. DINER:

Q Welcome back from lunch, Dr. Cykiert.

A Thank you. Thanks.

Q Dr. Cykiert, you're familiar with the ophthalmic Xibrom, correct?

A Yes, I am.

Q Okay. Are you also aware that the prescribing label for Xibrom indicates that 2 to 7 percent of the patients -- strike that. Let me go to a document instead.

(Document, PROL0080486 - PROL0080492, was marked Cykiert-5 for identification.)

BY MR. DINER:

Q The court reporter has just handed you Exhibit 5, bearing Bates numbers PROL0080486 through 492.

Have you seen this document before?
A Yes, I have.
Q I apologize for the small print.
A No problem.
Q Does this document appear to be highlights of prescribing information for Xibrom?
A Yes.
Q Okay. Would you look at the first page of Cykiert Exhibit 5, the right-hand column under adverse reactions?
A Yes.
Q Does this document indicate that Xibrom reported adverse reactions in 2 to 7 percent of the patients, which included eye irritation?
A Yes.
Q And is burning and stinging indicated in Cykiert Exhibit 5 to be a type of eye irritation?
A Yes.
Q Okay. You can put that aside.
And you're also familiar with the product Bromday, correct?
A Yes.
Q I believe we spoke about that a little bit today.
MR. DINER: Let me mark the next

exhibit.

(Document, PROL0080493 - PROL0080497, was marked Cykiert-6.)

BY MR. DINER:

Q Now, the court reporter, Dr. Cykiert, has handed you Cykiert Exhibit 6, bearing Bates numbers PROL0080493 through 497.

Have you seen this document before?

A Yes, I have.

Q Okay. And does this document appear to be highlights of prescribing information with regard to Bromday?

A Yes.

Q And this first page, right column of this document, does it indicate that one of the adverse reactions for Bromday is eye irritation?

A Yes.

Q And does that document report that it would have occurred in 2 to 7 percent of the patients?

A Yes.

Q And eye irritation in this document for the prescribing information highlights for Prolensa -- pardon me, for Bromday also indicates that it includes burning and stinging, correct?

A Yes.

Q You can put that aside.

Are you familiar with the product Acular?

A Yes.

Q Does the product -- prescribing information for the product Acular indicate that 40 percent of patients report burning and stinging after using Acular?

A Do you have that document?

Q I'll show it to you. You can also refer to, if you like, paragraph 56 of your expert report.

(Acular information document, PROL0332429 - PROL0332439, was marked Cykiert-7 for identification.)

BY MR. DINER:

Q Okay. The court reporter has handed you Cykiert Exhibit 7, having Bates numbers PROL0332429 through 439.

Dr. Cykiert, have you seen this document before?

A I have.

Q Does it appear to be describing information for the product Acular?

A Yes.

Q Would you please turn to the fourth page into Cykiert Exhibit 7, bearing Bates number PROL0332432. And take a look at the bottom of the page under adverse reactions.

A Yes.

Q Does this indicate that Acular has adverse events that include transient stinging and burning on installation?

A What's the page number you're on? If you could give me --

Q The Bates number at the bottom, Dr. Cykiert, is PROL0332432.

A Right, I have that. Which paragraph?

Q The first paragraph under adverse events -- sorry, adverse reactions.

A Okay. Got it. I'm there.

Q Does this document, Cykiert Exhibit 7, indicate that Acular reported adverse events, including transient stinging and burning on installation?

A Yes.

Q Okay. And did that adverse event occur up to -- in up to 40 percent of the patients participating in the clinical trials for Acular?

A Yes.
Q Okay. You can put that aside as well. Dr. Cykiert, are you familiar with the product Voltaren?
A Yes, I am.
Q You prescribe that on occasion?
A Yes.
Q Does Voltaren have adverse events that include burning and stinging upon installation?
A Could I just see the package insert again?
Q Sure.
(Voltaren Ophthalmic information document, PROL0332414 - PROL0332418, was marked Cykiert-8 for identification.)
BY MR. DINER:
Q Now, looking at the page numbers across the top of Cykiert Exhibit 8, can you flip to page 6, please. There's a crosscheck, the last three numbers of the Bates number at the bottom is 417.
A Got it.
Q Can you go to the subsection, adverse reactions?
A Okay.
Q And beneath that, ocular, do you see

that?

A Yes.

Q Does this document indicate, that is, Cykiert Exhibit 8, that Voltaren Exhibit exhibited transient burning and stinging in approximately 15 percent of the patients across the clinical studies submitted for Voltaren?

A Yes.

Q Okay. You may put that aside. Now, Dr. Cykiert, would you agree that patients should use medication as prescribed for it to be effective?

A Yes.

Q And would you agree that it is important that -- that it is important for patients to use the medications they have been prescribed after cataract surgery as prescribed?

A Yes.

Q Now, is it your position that the industry has recognized -- strike that.

Is it your position the industry has recognized that burning and stinging -- that removing burning and stinging is beneficial to patients?

A I don't see where it states that, that the industry has recognized that.

Q Would you agree that there is a trend in the industry to reformulate NSAID treatments to reduce burning and stinging?

MR. JANUSZ: Object to form.

THE WITNESS: I haven't seen that trend. I don't know. Do you have any documentation of that anywhere?

BY MR. DINER:

Q Yeah. Can you refer to paragraph 37 of your expert report at page 12? Five lines down from the top of page 12, beginning with the word "Additionally."

A Okay.

Q Can you read that sentence from your report into the record, please?

A Additionally, the trend in the industry has been to reformulate ophthalmic NSAID treatments to reduce or remove potential irritants and thereby potentially reduce any burning and stinging.

Q So is the removal of -- pardon me, strike that.

Is the reduction of burning and stinging a trend that is recognized in the industry for ophthalmic NSAID treatments?

MR. JANUSZ: Object to form.

THE WITNESS: It's the trend in the industry. That's what this sentence says.

BY MR. DINER:

Q So on that basis, is it fair to say that the industry has recognized that removing burning and stinging is beneficial to patients?

MR. JANUSZ: Objection, vague.

THE WITNESS: It doesn't say anything about beneficial to patients specifically. It just says the trend in the industry has been to reformulate to reduce potential irritants.

BY MR. DINER:

Q And it goes on to say, and potentially reducing any burning and stinging, correct?

A Yes.

Q So would the reduction of burning and stinging associated with ophthalmic NSAID formulations be considered a benefit to patients taking those formulations or taking those ophthalmics?

MR. JANUSZ: Same objection.

THE WITNESS: It depends on the degree of burning and stinging and other factors. You'll notice in the package inserts that you gave me the word "transient" is used

frequently. So it turns out that transient burning and stinging is common for most, if not all, eye drops for some individuals.

BY MR. DINER:

Q Okay. And so in the case of those individuals, is it a benefit to them to reduce the transient burning and stinging in the ophthalmic formulations that they may take?

A If it's a mild burning and stinging that lasts for just a few seconds, then it's insignificant, patients won't even mention it. If it's a significant burning and stinging that burns and stings a lot and it goes on for half a minute or a minute or two, then that's different, then that they will complain about.

Q And, in your experience, have you ever seen that with any patients, that they complain of the burning and stinging?

A Yes, some patients do.

Q Okay. And so the removal, reduction of burning and stinging associated with the ophthalmic formulations that they may be treated with would be a benefit to them, correct?

MR. JANUSZ: Object to form.

THE WITNESS: The ones who have

significant burning and stinging for a prolonged period of time, those would benefit. The ones who have mild transient burning or stinging, really there's not much difference because they don't object to it much, it doesn't bother them, it doesn't prevent them from using their drops. They may just mention it in passing or it may come about in conversation somehow with their doctor or with me.

BY MR. DINER:

Q But even if they mentioned it in passing, the removal of that burning and stinging still would have been a benefit to those patients, correct?

MR. JANUSZ: Same objection.

THE WITNESS: If somebody is not complaining about something, they're just mentioning it, and you remove it, then that's of no benefit. If they're complaining about it and you remove it, then that's a benefit.

BY MR. DINER:

Q So it's your position that only if they complain of the burning and stinging that removing it is a benefit?

A That's correct. If it's a complaint, a significant complaint, you can get rid of that, and that's a benefit. If they just have it, but it doesn't bother them, then it doesn't really make much difference.

Q Dr. Cykiert, is the reducing of the number of daily installation of eye drops a benefit to patients?

A It's of benefit to some patients and not others, and there are other factors that come into significant consideration in answering that question.

Q Has the industry recognized, to some extent, then, the benefit of reducing the number of daily installations of ophthalmics as beneficial to patients?

A I would say in general, yes, but it's not an across-the-board benefit for all patients. It depends on other factors. For example, expense is a very significant factor. So there are some patients who won't mind taking a drop three or four times a day if it's one-tenth or one-twentieth the cost of a drop that's only taken once a day. In other words, the severe burning and stinging in their wallet or pocket may be more significant than

the transient mild burning and stinging that they get once or twice or three or four times a day.

Q So referring now, then, to the industry trend. As you mentioned in paragraph 37 of your report, is the industry's focus on removing burning and stinging an indication that there are therapies available on the market that don't meet the need of reduced burning and stinging?

MR. JANUSZ: Object to form.

THE WITNESS: Did you say paragraph 37? I'm sorry, I'm trying to find that.

BY MR. DINER:

Q Yeah. Back to where we were before in paragraph 37 in your statement about the trend in industry.

A Which part of paragraph 37 are you directing me to?

Q So on page 12, go about five lines down.

A Right. Yes, we already discussed that.

Q So is the industry's focus on trying to remove burning and stinging an indication that there are therapies available in the market that actually don't meet the need to remove burning and stinging?

MR. JANUSZ: Object to form.

THE WITNESS: It doesn't say that there --

BY MR. DINER:

Q Well, I'm asking you --

A -- it just says that the industry trend is to reduce it.

Q Okay. But I'm asking you, then, beyond your statement there --

A Right.

Q -- in light of that statement, does the industry's focus on trying to remove burning and stinging indicate that of the therapies that are available, they do not meet the need to remove burning and stinging?

MR. JANUSZ: Same objection.

THE WITNESS: They may be trying to improve it, but that doesn't mean what's currently out there is bad.

BY MR. DINER:

Q And trying to improve it and reduce the burning and stinging could ultimately lead to benefits for the consuming public, correct?

A Again, it depends on the severity and duration of the burning and stinging. If the burning and stinging is mild and transient, then

it's really of no significance because most eye drops have some burning and stinging transiently that's mild. If it's moderate or severe burning and stinging that's for a prolonged period of time, then I would say, yes, that should be improved upon by the industry, where possible.

Q Okay. Thank you. Now, is it fair to say that many cataract surgery patients are elderly?

A I would say that's correct.

Q And as people age they can sometimes become forgetful, correct?

MR. JANUSZ: Objection, calls for speculation.

THE WITNESS: Sometimes yes and sometimes no. I have some 90-year-olds who are really sharp and on the ball.

BY MR. DINER:

Q And I suspect that you have some people younger than 90 that can be quite forgetful, correct?

MR. JANUSZ: Same objection.

THE WITNESS: That's correct. So it's extremely variable.

BY MR. DINER:

Q Now, I think you mentioned that

Voltaren is a medication that is prescribed four times a day; is that correct?

A In general, it is.

Q Okay. According to the label it's prescribed four times a day; is that right?

A I'd have to specifically look at that, if you want me to look at it. Do you want me to?

Q No, I think it's in your report anyway.

A Yes, in general, it's used four times a day, but sometimes it's used only two or three times a day in some patients if what you're treating is a milder case of what they have.

Q So let's say we're dealing with the prescription of Voltaren four times a day to a patient who has just had cataract surgery, okay? We'll set that up as the facts that we're going to be talking about.

A Okay.

Q Acceptable? And let's also say that that person is elderly. Okay?

A Okay.

Q For that person having to remember to take medication four times a day, could that increase the likelihood that the patient could forget to use the medication as prescribed?

MR. JANUSZ: Object to form, calls for speculation.

THE WITNESS: Just because a patient is elderly doesn't mean they're forgetful. They don't necessarily go hand in hand.

BY MR. DINER:

Q And for those patients that you have had that are elderly and forgetful, would having to take an ophthalmic such as Voltaren four times a day increase the likelihood that they could forget to take the medication as prescribed?

MR. JANUSZ: Same objections.

THE WITNESS: My patients who are forgetful, regardless of their age, there's some young ones, some old ones and in between, if they're forgetful they forget to take their drops once a day or four times a day. In fact, interestingly, the opposite occasionally occurs because if you're supposed to take something four times a day you reinforce it to yourself because you're doing it frequently and so you actually remember to take it two or three or four times a day because it's a repeated habitual thing almost. Whereas, if it's once a day it kind of may slip your mind

overnight. So the answer is, it's extremely variable, as I just gave you that example.

BY MR. DINER:

Q But it can occur that for an elderly forgetful person, they could miss taking their medication, if prescribed, four times a day, they could miss one of those installations, correct?

MR. JANUSZ: Same objections.

THE WITNESS: It's possible. But I have, for example, glaucoma patients who are on one drop a day of a glaucoma eye drop and I won't see them for two or three months for a checkup and they come in, and I say are you taking your drop and they go, what drop? And it was only once a day. I go, remember, I prescribed that, you have glaucoma, you're supposed to take it. They go, oh, you know, I forgot all about that. You're right.

BY MR. DINER:

Q Okay. Now, if that medication in our scenario, elderly patient, forgetful, taking medication four times a day as prescribed, for that patient if that medication were to cause burning and stinging could it increase the likelihood that that patient may not use the medication as prescribed?

MR. JANUSZ: Same objections, calls for speculation; if not already stated.

THE WITNESS: Again, it really depends on the severity and duration. If it's a mild burn or sting, it has really no effect, and if it's a moderate or severe burning or stinging, then there is an effect and they may not take it and may call me. So it kind of is variable. There is no one set answer to that.

BY MR. DINER:

Q Would you agree that it is impossible to predict which patients will experience burning and stinging?

A I wouldn't say it's totally impossible because it depends on the patient and their history and your previous experiences with them.

Q Is it fair to say, then, it's sometimes hard to predict which patients may experience burning and stinging?

MR. JANUSZ: Object to form.

THE WITNESS: Again, it's very variable. I have patients who complain of burning and stinging with every drop I ever give them and then other patients never complain about anything. So it has to do a

lot with tolerance of burning and stinging or pain or discomfort. It has to do with the patient's mental status as well. It has to do a lot with patients' expectations of what eye drops are supposed to feel like. There are numerous factors.

BY MR. DINER:

Q And so I'll refer you to paragraph 37 again of your expert report, page 12, towards the bottom, six lines up beginning with the sentence, Because it is difficult.

A Okay, I see that. Thanks.

Q So then would you agree that it is sometimes difficult or impossible to predict which patients may experience burning and stinging, for example?

A Yeah, that's what I basically just said.

Q Okay. Would you also agree that many cataract patients may have other conditions causing sensitivity in their eyes?

A Yes.

Q Would dry eye be one of those?

A Yes, it would be.

Q Therefore, with such a subgroup of

patients would it make sense to use less irritating ophthalmics as much as possible after surgery with these type of patients?

MR. JANUSZ: Object to form.

THE WITNESS: It's variable. Are you speaking about specifically about the dry eye patients?

BY MR. DINER:

Q Yes. So let's take the dry eye patient. So with a dry eye patient post-cataract surgery, would it make sense to prescribe to that patient an ophthalmic formulation to address inflammation that is less irritating?

MR. JANUSZ: Object to form.

THE WITNESS: Again, it depends on the severity of their dryness, whether it's mild or severe or in between. It depends how much symptoms the patient is having from their dryness. For example, I have patients who have severe dryness on my examination, yet they have near zero symptoms. Then I have patients who have very mild dry findings on my exam of their eye, yet their symptoms are severe, and then there is people in between. So the symptoms of the dryness and my exam

findings of the dryness don't always correlate well, and so it's difficult to predict sometimes how they will respond to another eye drop.

BY MR. DINER:

Q Well, let's stay with that example of the person with, say, severe dry eye problems. Would it make sense to administer to that person or to prescribe to that person an ophthalmic NSAID that had reduced irritation as one of its side effect events?

MR. JANUSZ: Same objection.

THE WITNESS: What do you mean by "irritation"?

BY MR. DINER:

Q Burning and stinging.

A The dry eye symptoms are different than the burning and stinging symptoms. So they don't correlate. They're two separate different things.

Q So someone who has dry eye, they wouldn't be negatively affected by an ophthalmic NSAID that was known to cause burning and stinging?

MR. JANUSZ: Object to form.

THE WITNESS: No, because burning and stinging are different than dry eye. The

symptoms of a dry eye patient generally are foreign body sensation. Whereas the symptoms of burning and stinging are not foreign body sensations. So they're two different things.

BY MR. DINER:

Q Now, Bromday and Prolensa, they have the same active ingredient, correct?

A Yes, that's correct.

Q And that ingredient is bromfenac, right?

A Right.

Q And it's your view that Bromday and Prolensa have the same efficacy and safety profiles; is that right?

A Bromday and Prolensa, yes.

Q Prolensa is more expensive to the customers than Bromday; is that right?

MR. JANUSZ: Objection, foundation.

THE WITNESS: Well, Bromday I don't believe is currently available.

BY MR. DINER:

Q Is there a generic Bromday out there today?

A There's a generic bromfenac.

Q Okay. Prolensa is more expensive than

generic bromfenac; is that right?

A Yes.

Q By a large margin?

MR. JANUSZ: Same objection.

THE WITNESS: From what I know, from what patients tell me, it's often a huge difference.

BY MR. DINER:

Q A huge difference in price as between Prolensa and generic bromfenac?

A Right.

Q With Prolensa being the more expensive one?

A Yes, Prolensa being much more expensive than the generic bromfenac.

Q And because of the price differential, do you prefer to prescribe generic bromfenac over Prolensa?

A Yes. Because it's essentially the same in efficacy and safety and how it works, and if it's a lot cheaper for the patient, then I think that's preferable, since patients complain a lot about expensive medications, and healthcare in general.

Q Okay. So physicians would not prescribe a new drug that used the same active

ingredient as the prior drug if that new drug did not deliver any benefits over the prior drug; is that right?

MR. JANUSZ: Objection, foundation, calls for speculation, vague.

THE WITNESS: That's a very broad generalization, what you just said. Physicians have different reasons for prescribing medications.

BY MR. DINER:

Q How about for you?

A For me?

Q Yeah.

A If I have a generic drug that's less expensive and a brand drug that's a lot more expensive and they have equal efficacy and safety, then I'll usually prescribe the generic, cheaper brand for the patient.

Q Do you believe that your view, as you just expressed it, is shared by other doctors?

A I believe my view, as I just said it, is shared by the vast majority of ophthalmologists.

Q So then a new more expensive drug with no benefits to consumers compared to the old drug is probably not likely to succeed; is that right?

MR. JANUSZ: Objection, foundation, outside the scope.

THE WITNESS: That's not necessarily correct because there are other factors that influence prescribing decisions by doctors, including marketing that's done by the company that makes the branded product and other factors such as availability of the generic, cheaper brand.

For example, unfortunately, sometimes the generic bromfenac is not available. So I'll write a prescription for it, the patient goes to the drugstore and either the patient or the pharmacist calls me and says they don't have this generic, what do I do? So that may force me to write a more expensive drug because the patient has to have this drug, and I have no choice, or I may go with another branded drug that's essentially the same in efficacy and safety made by a different company, if I can get that cheaper.

MR. DINER: I'd like to mark the next exhibit, Lisa.

(Prolensa information document, PROL00802189 - PROL0080224, was marked

Cykiert-9 for identification.)
BY MR. DINER:
Q Okay. Dr. Cykiert, you've been presented with Cykiert Exhibit 9, bearing Bates numbers PROL0080219 through 224. Are you familiar with labeling approval at the FDA level?
MR. JANUSZ: Objection, vague.
THE WITNESS: I'm familiar with it, but what specifically are you referring to?
BY MR. DINER:
Q Well, when the FDA approves a label for a product that's going to get market approval, does it approve that label based on the clinical studies that have been submitted by the applicant for that product?
A That's my understanding of how the FDA works, correct.
Q Okay. And when they fill out the portion of the label dealing with adverse reactions, that's also based on the clinical studies that have been submitted by the applicant, right?
A That is correct.
Q And so Cykiert Exhibit 9 appears to be the highlights of prescribing information for the product Prolensa. Would you agree with that?

A Yes.
Q And you've seen this document before, right?
A Yes, I have.
Q Under adverse reactions on the first page, right-hand column, does it indicate burning and stinging as an adverse reaction of Prolensa?
A It doesn't specifically say that on this document.
Q And it doesn't indicate eye irritation either for Prolensa, correct?
A Well, it depends how you define "eye irritation." Notice that it says foreign body sensation and eye pain and photophobia. And I would put that under the category of eye irritation.
Q But there's no indication here, as we've established, as to burning and stinging, correct?
A Specifically it does not say burning and stinging. Although I do know from experience that patients do have burning and stinging from Prolensa.
Q Now, this label for Prolensa was approved without an indication that burning and stinging is an adverse reaction to Prolensa,

correct?

MR. JANUSZ: Object to form.

THE WITNESS: Well, what this label means is in the clinical trials that they did and submitted to the FDA, burning and stinging did not appear at a certain percentage of patients below a certain number. So they excluded it from here. But we shouldn't think for a moment that this includes every possible adverse reaction that can occur. Just because it doesn't say that here doesn't mean it doesn't occur in real life.

And I'll bring to your attention the paragraph below that which says, to report suspected adverse reactions, contact Bausch + Lomb, Incorporated, at an 800 number, or the FDA at an 800 number, or the FDA website, which basically says that the FDA knows that there can be other adverse reactions that occur after a drug is approved by the FDA. And it's asking doctors to report those adverse reactions to the FDA so that the FDA can, from time to time, amend the package insert to include other adverse reactions. And as you know, sometimes there are black box

warnings, which are more serious adverse reactions, that come out after a drug is approved.

BY MR. DINER:

Q Are you aware of any amendments being made to the product label for Prolensa with regard to adverse reactions?

A I'm not aware of any now, but as I mentioned, that can occur at any time. There are many medications that come out with subsequent adverse reaction warnings, or even black box warnings, which are more severe, that can come out months, or even years after a drug is approved.

And I'll also bring to your attention in Section 6.1 of this document. It says that because clinical trials are conducted under widely varying conditions and adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in clinical trials of another drug and may not reflect the rates observed in clinical practice. That last phrase, and may not -- "and may not reflect the rates observed in clinical practice." What they're saying there is that this is not the end of it.

There can be things that you find in

your clinical practice which are not reported in a package insert. And so that basically explains that this is very preliminary findings based on the clinical trials and a limited number of small patients in the clinical trials. Later on when a drug is used on thousands of patients, tens of thousands of patients over years, other adverse reactions can come out. And, in fact, there is documentation in many places that Prolensa does have burning and stinging other than what I just said. There's documentation of that.

Q But focusing on Cykiert Exhibit 9, and what's on the label, Prolensa is the only NSAID approved for the treatment of post-operative inflammation and reduction of ocular pain after cataract surgery, which does not have burning and stinging listed as an adverse event on its label, correct?

A Currently that's the case.

Q Okay. You can put that aside.

A Thanks.

Q Is it advantageous when formulating ophthalmics, or any pharmaceuticals, to try to use the lowest effective dose of an active ingredient?

MR. JANUSZ: Objection, foundation.

THE WITNESS: In fact, there's no evidence of that.

BY MR. DINER:

Q Is it preferable to use the lowest effective dose of a particular active ingredient in an ophthalmic, for example?

MR. JANUSZ: Same objection.

THE WITNESS: Not necessarily.

BY MR. DINER:

Q Is it beneficial to identify what the lowest effective dose is for an ophthalmic?

A Not in all cases. It's variable. It depends what the ophthalmic is and for what purposes its used.

Q But it can be, correct?

A In some cases, depending on the drug and what you're using it for that may be the case. But that's not a general broad statement that covers all ophthalmics, and specifically it doesn't cover NSAID ophthalmics at all.

Q Is the benefit of using the lowest effective dose the idea that the pharmaceutical could have a minimum of side effects?

MR. JANUSZ: Objection, foundation.

THE WITNESS: Theoretically, that would

kind of seem like, hey, maybe that's logically correct, but, in fact, that's not the case. And the evidence is in all these package inserts that you sent me here that I have in front of me. If you look at the Prolensa warnings and precautions section and then you look at the Xibrom warnings and precautions sections, which in both cases start with Section 5.1 to about 5.6, you'll see that all the serious warnings and precautions by the FDA for both of these drugs are essentially identical, even though Prolensa, 0.7 percent, and Xibrom or Bromday are 0.9 percent. So therefore, in this case, lowering the percentage of the drug to 0.7 percent does not make it in any way safer or better. And there's no change in efficacy, either, by the way.

BY MR. DINER:

Q Well, let's look at -- under Warnings and Precautions -- you have Cykiert Exhibit 9 in front of you for Prolensa?

A Yes.

Q All right. I have to refer to the other one. I think you made a comparison allergic

to sulfites between Prolensa and Bromday; is that right? Were you looking at Cykiert Exhibit 6 for Bromday?

A I don't think I have Bromday. I have Xibrom. Oh, wait, Bromday, I have here.

Q Whatever one you have, it doesn't matter.

A Yeah, they're essentially the same.

Q Which one are you looking at, Xibrom or Bromday?

A I'm looking at Bromday and Xibrom. We can look at all of them. Yeah, the number 5 section in all of them, it appears that it's the same number section in all three drugs.

Q You refer to that in the context of stating that lowering the amount of the active ingredient may have no benefit at all; is that right?

A Yeah, based on what you said earlier, that well, if you lower the concentration of the active ingredient, then isn't that better for the eye or the patient, and that may initially seem like, hmm, that sounds pretty logical, maybe that's right. But, in fact, it isn't because you can see that Section 5 for all three of these drugs is

essentially identical, which means that lowering the dosage from -- I should say lowering the concentration of the drug of the bromfenac from 0.9 percent to 0.7 percent makes no difference. So that really is documented here very clearly.

Q So the first warning in precaution 5.1 is directed to sulfite allergic reactions, correct?

A That's in all three package inserts, that's correct. Prolensa, Bromday and Xibrom.

Q And sulfite is not the active ingredient, correct?

A That's correct. That's an inactive ingredient.

Q Okay. You can put that aside.

I believe you said that you rarely prescribe Prolensa; is that right?

A Not rarely. I used to prescribe it a lot more. Recently it's rarely, and the reason I have decreased my prescriptions over time is that it was very expensive and I received many patient complaints about it. So initially I started prescribing it, but over time I've prescribed it less and less because of the expense, and when I used it, I found no difference in efficacy when I used it, and also I found that there was no

difference in patient symptoms with regard to burning, stinging, irritation between the drugs. So I said why should I be prescribing something that is very expensive and all my patients complain about, or the vast majority of patients complain about, when I can use equivalent generic products that are much cheaper or use a competitor's branded product that comes out much less expensive and has the identical safety, efficacy and side effect complaint profile.

Q You would agree that Prolensa is clinically effective, correct?

MR. JANUSZ: Objection, vague.

THE WITNESS: Clinically effective for what?

BY MR. DINER:

Q Treating post-operatively inflammation and ocular pain after cataract surgery.

MR. JANUSZ: Same objection.

THE WITNESS: It's approved for that, and when needed it can be used for that, but my uses of it are for treating CME, which we discussed earlier, as an off-label, acceptable use for it.

BY MR. DINER:

Q And have your experiences in using Prolensa to treat CME been positive?

A Yes, in patients who have CME, it's been effective in reducing the CME, but it's equivalent to generic bromfenac or Ilevro, or previously when I used Bromday or Xibrom. They're all basically similarly identical. And in some patients where I've used either Acular generic or Voltaren generic three or four times a day, those are equally effective.

Q Now, as between Prolensa and Bromday, would you agree that they are both equivalent in terms of their ability to treat post-operatively inflammation in ocular pain?

A I would say that it's approximately the same, yeah, correct.

Q Okay.

MR. JANUSZ: Can I interrupt for a moment. I don't think my LiveNote is working here.

VIDEO OPERATOR: Off the record, 1:55 p.m.

(Brief recess.)

VIDEO OPERATOR: We're back on the record, 2:03 p.m.

This is the beginning of disc 3 in the deposition of Robert C. Cykiert.

BY MR. DINER:

Q Dr. Cykiert, before the break I believe we were talking about the clinical efficacy of Prolensa on the one hand and Bromday on the other. And just so the record is clear, is it your view that Prolensa and Bromday are equally effective?

A Yes.

Q Prolensa contains 0.7 percent of -- sorry, strike that. Prolensa contains 0.07 percent bromfenac, correct?

A That's correct. Did you say 0.7?

Q 0.07 percent.

A Right. Right. .07 percent.

Q I'll just say it again so the record is clear. So Prolensa contains 0.07 percent bromfenac, correct?

A Right.

Q And Bromday contains 0.09 percent bromfenac, correct?

A Correct. Right.

Q And so Prolensa achieves the same clinical effect -- efficacy as Bromday at a lower dose, correct?

MR. JANUSZ: Object to form.

THE WITNESS: The percentage of the drug is clearly lower and they're equally effective.

BY MR. DINER:

Q Okay. The pH of an ophthalmic can impact the ocular comfort upon installation of the drug, correct?

A It can in some cases, but there are numerous external extrinsic factors that also influence that. So it's not the pH alone.

Q The pH of Prolensa is indicated in Cykiert example -- pardon me, Exhibit 9 to be 7.8, correct?

A Correct.

Q And if you look at Cykiert Exhibit 6, I believe, for Bromday, it's indicated to be 8.3; is that right?

A Yes.

Q And Exhibit 5 is Xibrom prescribing information, and it indicates that the pH of Xibrom is 8.3 as well; is that correct?

A Right.

Q Okay. So the pH of Prolensa at 7.8 is closer to the pH of natural tears than either Xibrom

or Bromday, correct?

MR. JANUSZ: Object to form, foundation.

THE WITNESS: Not necessarily, because it turns out that the pH of people's tear fluid is variable. So in some cases it may be closer to a person's tear fluid and in other cases not. So it really depends on what the individual person's pH of their tear fluid is.

BY MR. DINER:

Q I believe in footnote 2 of your expert report on page 19 you indicate that the pH of tear fluid can vary between 6.5 and 7.6; is that right?

A Right.

Q So Prolensa at a pH of 7.8 is closer to this range of natural tear fluid, as you've provided in footnote 2, than either Xibrom or Bromday at a pH of 8.3; is that right?

A That's correct, but it's not clinically significant.

Q But it is closer, correct?

A Yes, on a pure number basis I agree with you. It's definitely closer, but again, it's not clinically significant.

Q And pH is on a logarithmic scale,

correct?

A I believe it is, right.

Q Was that the factor of 10 for each movement on the pH scale, correct?

A Right. But again that's not clinically significant, either. As you can see above that there are listed about a dozen different eye drops. One of them has a pH of about 4, Ciloxan eye drop. It's the first one in Table 1. And that's a drop, it's antibiotic. It's commonly used and patients have no symptoms from that and find it to be very comfortable. And so the pH alone doesn't tell you much about the tolerance or side effects from a medication because there are other factors involved.

Q But generally, a pH that is going to be closer to the range for natural tears would be expected to have greater ocular comfort, correct?

MR. JANUSZ: Object to form.

THE WITNESS: No, again, that's one of those logical, assumptions that turns out to be not logical and there's no evidence for that. If that were the case, they'd be making all these other drops at a different pH. So similarly before when you said, well, 0.7 percent -- 0.07 percent is better than

0.09 percent. Again, when you think about it, yeah, it would seem that way, but, in fact, there's no evidence of that. So the statement that pH of an eye drop being closer to the pH of human tear film is better, there's no evidence of that. That's just kind of a supposition with no basis behind it.

BY MR. DINER:

Q Those other formulations that you pointed to in Table 1 of your expert report deal with many different active ingredients, correct?

A Those are the names of the specific drops and each one of those has different active ingredients and also inactive ingredients and also different pHs.

Q Okay. Thank you.

Now, I believe that you said that a pH of an eye drop being closer to the pH of human tear, that there's no evidence that that would mean it would have greater ocular comfort; is that right?

A Right.

Q And that that was supposition with no basis behind it; is that your opinion as well?

A Right. Because there are numerous other factors that contribute to that. So it's not

the pH alone.

Q Did you consider the expert report of Dr. Prausnitz in providing your opinions in this case?

A I saw parts of that report.

Q You saw parts of it in draft form?

A No, in what I was given.

Q When you say you saw parts of it in what you were given, what does that mean?

A I didn't see the entire report.

Q Well, what parts did you see?

A I saw sections of it, which are referred to in my report.

Q Were those draft sections?

A What do you mean by "draft sections"?

Q Non-finalized -- was it sections of a non-finalized report?

A No, those were just sections that I were given that are in my report, that's what I saw. What's in my report is what I saw.

Q Were you told that the sections that you were viewing came from a final and signed report of Dr. Prausnitz?

MR. JANUSZ: Objection. I'll caution the witness not to reveal the substance of any

communication with counsel.

THE WITNESS: Yeah, you're asking me about discussions with attorneys specifically. I don't know -- I have a privileged question about that.

BY MR. DINER:

Q Well, I'll withdraw the question.

Do you recall what sections of Dr. Prausnitz's report -- do you recall what sections of Dr. Prausnitz's report that you reviewed?

A Yes, the sections that are mentioned specifically in my report. That's it.

MR. DINER: I'll mark the next exhibit.

(Expert Report of Mark R. Prausnitz, Ph.D., Regarding Secondary Considerations was marked Cykiert-10 for identification.)

BY MR. DINER:

Q Now, Dr. Cykiert, you've just been handed what has been marked as Cykiert Exhibit 10. This is an expert report of Mark R. Prausnitz, Ph.D., regarding secondary considerations.

Have you seen this document before?

A I don't believe I've seen this entire document before.

Q Would you turn, please, to page 16 of Cykiert Exhibit 10. And I'll direct your attention to paragraph 41, please.

A Okay.

Q Would you read the first sentence from paragraph 41 into the record. I'm sorry, before you do that, does this -- you can take a moment and look at it, if you need to, but the section that we're in of the Prausnitz report begins with page 16d and goes to page 17, the middle of page 17. Can you just take a moment and look at this and let me know if this was the portion of Prausnitz's report that you've seen before?

A I don't recall off the top of my head if I saw it before or not, so I can't tell you for sure whether I did see this section or not before, but I could read it, if you want me to.

Q No, that's fine. If you can't remember, you can't remember.

Let's just go to paragraph 41.

A Okay.

Q Could you read the first sentence into the record, please?

A Even if there were a reduction in pH, it is known in the scientific literature that

stinging and burning of the eye is affected by pH, and a more physiologically pH causes less ocular discomfort.

Q Is a more physiological pH one that is closer to the pH of natural tears?

A That's what that would mean, right.

Q And would you agree that Dr. Prausnitz is saying that a formulation that has a pH closer to natural tears would have less ocular discomfort?

MR. JANUSZ: Objection, mischaracterization, and objection to scope.

THE WITNESS: Give me one second to read that again. Okay. The key two words here, "scientific literature." Which scientific literature is he mentioning? I'm not really sure.

BY MR. DINER:

Q Well, if you read the previous paragraph -- why don't you take a moment to read that and then I can ask you a follow-up question.

A Okay. Okay. I read the paragraph before that. Which basically says that actually it's not 7.8. It's in a range of 7.5 to 8.5, and if you go with the 8.5 it's actually above 8.3. So to me it would seem like in general if you average the

pHs they're about the same.

Q Well, hold on one second. The range of 7.5 to 8.5 is referring to what is called a claimed pH range, right?

A That's what it says there, right.

Q That's not talking about the range of pH for natural tears, correct?

A That's referring to -- let me just read that again. Yeah, what he's saying there is if you look at patent '431, patent claim 10, the actual pH of Prolensa is not limited to 7.8. It's between 7.5 and 8.5. That's in the patent claim. Do we have the patent? We can look that up. And then if that's the case, then the pH range of Prolensa is very broad and in some cases it's identical to the pH of Bromday and Xibrom. So on the average I would say they have the equivalent pH.

Q I think you're misreading the paragraph.

A Oh.

Q And particularly that sentence. That sentence that you are referring to is referring to -- not to Prolensa, but to claims of the '431 patent, right?

A Let me ask you this, just so I'm clear,

is the '431 patent one of the Prolensa patents?

Q It's my job to ask the questions.

A Oh, sorry.

Q Let's go to paragraph 41. So then when Dr. Prausnitz says that a more physiological pH causes less ocular discomfort, is that also supposition on the part of Dr. Prausnitz?

MR. JANUSZ: Objection to form.

THE WITNESS: Not necessarily. He's referring to scientific literature, and I just like to know more specifically which scientific literature he's referring to for me to give you a definitive answer to that question.

BY MR. DINER:

Q But you don't disagree with his statement, correct?

MR. JANUSZ: Same objection.

THE WITNESS: You know, I can't agree or disagree because I don't have enough information right now to answer that accurately.

BY MR. DINER:

Q And you don't know if you relied on this section of Dr. Prausnitz's expert report for

the opinions you've given in your expert report, correct?

A I'm not 100 percent positive, but I can tell you from experience, and from Table 1 in my report, that the pH of an eye drop itself does not determine how comfortable or uncomfortable it is to that patient. There are numerous other external, extrinsic factors that go along with the pH to determine that.

Q And so Dr. Prausnitz hasn't taken that into account when making that statement that he makes in paragraph 41, correct?

MR. JANUSZ: Objection, foundation, calls for speculation.

THE WITNESS: Well, I can't say that for sure because I didn't read this whole document right now, but again, I'm not sure if he's saying if all other parameters are exactly the same, then perhaps reduction of pH to a physiologic level is better. But if all other external factors are different, then it's different. So that's basically what I can't determine, without reading this entire document. So that's really a question, are all other factors kept at a constant and if

it's just reduction of pH then that may be the case. But if you combine the reduction of pH to approximate the tear fluid pH, but other factors change, then you can't really say that. So it depends on other things. Hard to say for sure.

BY MR. DINER:

Q So looking at this, you don't know if Dr. Prausnitz in the statement he makes there, with regard to physiological pH causing less ocular discomfort, is right or wrong?

MR. JANUSZ: Object to form.

THE WITNESS: I'm not saying if it's right or wrong. I just don't have enough information. You're asking me to take one sentence out of context and tell you right or wrong, and I'm saying I can't really do that and give you an accurate assessment of that.

BY MR. DINER:

Q You can put that aside.

A Thanks.

Q Now, with respect to Bromday, you understand that that contains the surfactant polysorbate 80, correct?

A Right. I believe it does. I'd have to

check the package insert for sure, but I believe that it does.

Q And are you aware that the amount of polysorbate 80 used in Bromday is 0.15 percent?

A Well, let me look it up, just to be 100 percent certain. Give me a second.

Q Sure.

A Okay, I have the Bromday. And you're asking me what the polysorbate 80 concentration is?

Q I'm not sure you're going to see it in there, Dr. Cykiert.

A Oh. Well, actually it does have it.

Q Oh, okay.

A If we turn to PROL0080496, the inactive ingredients include polysorbate 80 at a concentration of 1.5 milligrams per ML.

Q Okay. And then if it's based on a weight per volume percent with bromfenac being present at .09, does that get the amount of bromfenac -- sorry, the amount of polysorbate 80 at about 0.15 weight percent per volume?

A I'm sorry, that question I need repeated because I think there were some --

Q Let's do it this way. How about I represent to you that the amount of polysorbate 80

used in Bromday is 0.15 weight percent per volume, will you accept that representation?

A I think so, off the top of my head.

Q And we can proceed on that basis.

A Okay.

Q Do you know what the -- strike that.

And do you understand that in Prolensa the surfactant used is tyloxapol?

A Right.

Q Okay. And are you aware that the amount of tyloxapol is 0.02 weight percent per volume?

A I believe that's the number, but -- I'll take your word for it that's the number.

Q Okay. So as between Bromday at 0.15 weight per volume percent for polysorbate 80 and Prolensa with 0.02 weight per volume percent for tyloxapol, that represents about a seven and a half times difference, right, approximately?

A That's a misleading comparison because they're two completely different chemical compounds and substances. So comparing the percentage is completely irrelevant. You have to compare apples and apples. If they both had polysorbate 80 and you told me that Prolensa only has this much, very

little, and that Bromday has a huge amount, 10 times that, then I would say that's a valid comparison. But when you tell me drug A has only one apple in it as a preservative and drug B has 10 oranges in it, isn't drug A better because I only need one apple to preserve it, whereas the other one I need 10 oranges. That's not a valid comparison, and it's not technically correct to discuss it that way, from a chemistry point of view.

Q Now, you said that they are two completely different chemical compounds and substances, right?

A Right.

Q What did you mean by that?

A Well, Tyloxapol is not polysorbate 80.

Q Are they chemically dissimilar then?

A They are different substances, different chemicals, that's correct.

Q Are they vastly chemically dissimilar?

MR. JANUSZ: Objection, vague.

THE WITNESS: As I mentioned in the beginning, I'm not a chemistry or a pharmacology expert, so I can't tell you exactly what the differences are, but clearly they're different because they have different

names. So while apples and oranges are both fruits, they're very different from each other. So these are both fruits, but polysorbate 80 is an apple, tyloxapol is an orange, or maybe even a watermelon.

BY MR. DINER:

Q And so as a result they are very chemically different, right?

MR. JANUSZ: Objection, asked and answered, vague.

THE WITNESS: They're different chemicals, correct. Otherwise if they weren't different they'd have the same name, right?

BY MR. DINER:

Q And would different chemicals, such as polysorbate 80 and Tyloxapol, they have different chemical -- they have different properties as a result of their differences in chemical structure, right?

MR. JANUSZ: Objection, foundation.

THE WITNESS: That, I wouldn't know. That, you'd require a chemistry expert or a pharmacology expert or an expert in inactive ingredients to tell you. I can tell you they're different. So that comparisons of

percentage or weight volume is not a valid comparison. The exact differences of those two compounds, I'm not an expert at, unfortunately, so I can't comment in any depth on that.

BY MR. DINER:

Q I believe earlier, Dr. Cykiert, you testified that there's information in the public that Prolensa can cause some burning and stinging; is that right?

A Yes, I did say that.

MR. DINER: I'd like to mark the next exhibit.

(WebMD document on Prolensa Ophthalmic was marked Cykiert-11 for identification.)

BY MR. DINER:

Q Dr. Cykiert, the court reporter has handed you what has been marked as Cykiert Exhibit 11, which appears to be a WebMD publication with regard to Prolensa ophthalmic.

Have you seen this document before?

A I've seen this on the website.

Q And is this the document that you were referring to which would allegedly indicate that Prolensa has, on occasion, caused burning and

stinging?

MR. JANUSZ: Object to form.

THE WITNESS: Give me a moment to look at it.

BY MR. DINER:

Q Sure. Dr. Cykiert, I'll withdraw the question.

A Okay.

Q But I just have a question about WebMD. Are you familiar with WebMD as a service, a publication service?

A Yes, I am.

Q Is the content of WebMD regulated by the FDA, do you know?

MR. JANUSZ: Objection, vague.

THE WITNESS: I doubt it, but I'm not 100 percent sure. I don't think the FDA regulates the site in general, but if they have any advertisements on the websites for pharmaceuticals or drugs, then the appearance and contact of those ads may be partially regulated by the FDA. So the answer is kind of yes and no.

BY MR. DINER:

Q Okay. With regard to the content

outside of advertisements, is the content of WebMD peer reviewed?

MR. JANUSZ: Same objection.

THE WITNESS: I'm not sure of the answer to that, if it's peer reviewed or not. But the point is, this article, which by the way, you gave me Anne incomplete version of, because the significant portion of this article would be under the side effects section, which this is only the uses section and excludes the side effects section, mentions that there's burning and stinging as a result of Prolensa. But you asked me earlier is this the example. This is just one of many.

I found about eight different websites from very reputable, reliable sources that Prolensa causes burning and stinging. For example, the Kaiser Permanente program in California, which insures hundreds of thousands or maybe millions of lives has a section on Prolensa where it mentions burning and stinging as a side effect. Memorial Sloan Kettering Cancer Center here in New York, which is the top cancer center in the USA, if

not in the world, or maybe in the top two, also has a Prolensa section where it says it causes burning and stinging. The University of Maryland Medical Center has a Prolensa website where it says Prolensa causes burning and stinging. Syracuse University medical center has a website with a section on Prolensa where it causes burning and stinging. So -- and there are a few others I don't recall off the top of my head, but that's present in many websites of reliable sources.

BY MR. DINER:

Q Now, none of those organizations that you just mentioned that allegedly report Prolensa as having burning and stinging are cited in your expert report, correct?

A The only one I cited was this as an example.

Q Okay.

A I could have cited the other ones, though.

Q But you didn't, correct?

A I did not.

Q Okay. Now, the WebMD, it's not -- it's not a peer reviewed journal or anything, correct?

MR. JANUSZ: Objection, vague.

THE WITNESS: I think I answered earlier that I'm not 100 percent sure whether it's peer reviewed or not.

BY MR. DINER:

Q Okay. That's fine. Now, do you know a Dr. Silverstein?

A Are you referring to the Dr. Silverstein mentioned in Dr. Trattler's reports?

Q Yes.

A I don't know that Dr. Silverstein, no. I never heard of him before reading that.

Q How about Dr. Thomas Walters, do you know him?

A I don't know him, and I never heard of him before reviewing these documents.

Q Okay.

MR. DINER: I would like to mark the next exhibit, please.

(Bromfenac Ophthalmic Solution 0.07% Dosed Once Daily for Cataract Surgery document, PROL0333854 - PROL0333862, was marked Cykiert-12 for identification.)

BY MR. DINER:

Q Dr. Cykiert, the court reporter has

handed you what has been marked as PROL0333854 through 862. This document is entitled, Bromfenac ophthalmic solution 0.07 percent dosed once daily for cataract surgery, results of two randomized control trials.

Have you seen this document before?

A Yes, I have.

Q Okay. And I believe you just said that you do not know the first named author, Dr. Thomas R. Walters; is that correct?

A I don't know him.

Q Do you know any of the other authors that are identified in this article?

A Let me take a look. No, I don't.

Q Are you familiar with the journal in which this article appeared?

A Yes, this is known as ophthalmology or the AAO journal, the American Academy of Ophthalmology journal.

Q Is this a peer reviewed journal?

A Yes, it is.

Q What does it mean to be a peer-reviewed journal?

A It means that before they publish an article the article is reviewed by an editorial

board and the journal who are experts in the field of the article and they feel that the article is worthy of being published.

Q And do you know what kind of review process the article goes through?

A I don't know in exact detail what the editorial board does to make that decision.

Q And I believe you said the editorial board is comprised of experts in the field; ISTA correct?

A Generally that's what they do.

Q And how about for the AAO, is the editorial board for the AAO comprised of experts in the field of ophthalmology?

A Yes.

Q Now, have you reviewed this article as part of looking at it?

A Yes.

Q And is there anything in this article, in terms of its substance, that you would disagree with?

A No, I agree with it.

Q Okay. The type of design for the tests, you see that on the first page? Under the subheading, Design?

A Yes.

Q It says two phase 3 randomized, double-masked, placebo-controlled, multicenter clinical trials.

What does that mean?

A That means they did trials on patients that were randomized, meaning they didn't know which patient got placebo and which didn't. They were double masked so that the doctors didn't know who was getting what, and placebo control, that means some patients got nothing and some got the active drug, and they were done in several centers, multicenter.

Q Is this a proper design for a clinical study?

MR. JANUSZ: Objection, calls for speculation.

THE WITNESS: To my knowledge, this is a proper design, but I think I mentioned earlier if -- if I didn't, I'm not an expert in designing clinical trials. I haven't done that. So I'm not an expert in that area, and if you want my opinion as a non-expert, I think it's okay.

BY MR. DINER:

Q Okay. And the authors of this article, Cykiert Exhibit 12, say that they take responsibility for the data that is presented in this article and for the analysis of that data, correct?

A They do, but they -- the problem here is in their acknowledgments on the last -- next to the last page, which ends in 860. It says, The authors thank Maurico Munoz, PharmD. and Karen Gertz, BA, of Bausch + Lomb, Irvine, California for data review and verification.

In general, when the company that makes the product is involved in the clinical trials, there's a little lightbulb that goes off in every doctor's mind and makes you wonder whether this is completely independent or not. And, in fact, this is an ongoing controversy now in the medical journal publication world as to whether companies that manufacture products should be involved in any way in analysis, supervision, financing, review, verification of the study because it has the appearance of not being valid. And you need to be sure that it's totally valid, that there are no biases or outside influences, and you also need to have the appearance of that. And when I see that

the drug company that makes the product is involved in the process, I question the results of this. That's number one.

You'll notice one of the authors of this is the Bromfenac Ophthalmic Solution .07 Once Daily Study Group. You know, it kind of reminds me of when the tobacco companies did research on cigarettes and said not only weren't they unhealthy, but they were actually good for you.

Q Well, Dr. Cykiert, AAO is a reputable journal, correct?

A Very reputable.

Q And it had an editorial board to review this article, correct?

A Correct.

Q And you stated before that you didn't have any issue or problem with the substance of this article, correct?

A That's correct.

Q And the editorial board that reviewed this journal did not express the same concerns that you just did with regard to appearance of impropriety, did they?

MR. JANUSZ: Objection, calls for speculation.

THE WITNESS: Right. I don't know what they said, but I'm just telling you -- you asked me what I think of it and I'm being honest with you. And it says on the last page, the 862 page, sponsored by Bausch + Lomb, Incorporated, Irvine, California, which participated in the design of the study and data analyses and interpretation and supervised the preparation of the manuscript and approved the final version. The authors had full access to all study data and take responsibility for the integrity, et cetera.

BY MR. DINER:

Q Could you continue to read that, please?

A Sure. Take responsibility for the integrity of data and the accuracy of the data analysis. All authors participated in the interpretation of the study findings and in the drafting or critical revision of the manuscript, or both.

But what I'm telling you is when the company that makes the product is so heavily involved in this, I have a little lightbulb that goes off that says, hmm, and so do many of my

colleagues. I'm just telling you what the facts are.

Q But those are not facts as opposed to just your speculation that something is done here that is improper, correct?

MR. JANUSZ: Object to the form of the question.

THE WITNESS: Not speculation, but I would say it's a very valid opinion that's held by a majority of ophthalmologists.

BY MR. DINER:

Q But you have no basis for believing that anything with regard to this study and the reports in this article were done in any improper way, correct?

A I have no evidence of that whatsoever. I want to state that very clearly. But I'm just telling you what my reservations are about the appearance of this article.

Q Thank you. You can put that aside.

MR. DINER: I'd like to mark the next document, please.

(Volume 14 from the Journal of the American College of Nutrition, Number 3, June 1995, was marked Cykiert-13 for

identification.)

BY MR. DINER:

Q Dr. Cykiert, you've just been handed what has been marked as Cykiert Exhibit 13. It's an article from the Journal of the American College of Nutrition. And do you recall this morning we were talking about the subject of sulfite sensitivity?

A Yes.

Q Okay. Is this -- Cykiert Exhibit 13 indicate that this is a review article entitled, Sulfite Sensitivity: Significance in Human Health?

MR. JANUSZ: I'll object to scope.

THE WITNESS: Yes, that's what it says as the title. I'll agree with that.

BY MR. DINER:

Q Would you turn to the page identified at the bottom of this Exhibit 13, page 230.

A Okay. Got it.

Q And right-hand column of the page.

A Yes.

Q About midway down, the paragraph beginning, The manifestations of sulfite sensitivity.

You see that?

A Yes.

Q In this paragraph, if you would like to take a moment to read it, please do.

A Okay.

Q But the manifestations of sulfite sensitivity that are discussed here, are those similar to the ones we were discussing this morning with regard to sulfite sensitivity?

MR. JANUSZ: Object to scope.

THE WITNESS: Let me read it first before I respond.

BY MR. DINER:

Q Sure.

A Okay, I read it.

Q And so the manifestations of sulfite sensitivity that are discussed here in this paragraph that I've pointed you to of Cykiert Exhibit 13, are those similar to the ones that we discussed this morning with regard to sulfite sensitivity?

MR. JANUSZ: Same objections.

THE WITNESS: Yeah, they look pretty similar to me.

BY MR. DINER:

Q Okay. And the sources of sulfites that give rise to sulfite sensitivity, are they

identified below in that same column in Table 1?

MR. JANUSZ: Same objection.

THE WITNESS: They list several sulfate salts.

BY MR. DINER:

Q And is sodium sulfite listed among several of those sulfate -- sulfite salts?

MR. JANUSZ: Same objection.

THE WITNESS: It's listed there, but I don't know if that's a typo where it says sulfate salts because sulfate and sulfite are different.

BY MR. DINER:

Q Okay. Now, on the next page of this article, page 231, right-hand column, first full paragraph beginning with "Finally," you see that?

A Yes, I see that.

Q And does it indicate that sulfites can be added to pharmaceutical agents as antibiotics -- pardon me, as antioxidants?

MR. JANUSZ: Same objection, and to the extent there's any mischaracterization of the document.

THE WITNESS: Let me read that, please.

BY MR. DINER:

Q Sure.

A Yes, it says they're added to antibiotics and antioxidants.

Q Okay. And they could be added in pharmaceuticals, as for example, an antioxidant, correct?

MR. JANUSZ: Same objections.

THE WITNESS: That's what it says.

BY MR. DINER:

Q If you refer back to page 229, what is the date that this Exhibit 13 was published?

MR. JANUSZ: Same objection.

THE WITNESS: 1995.

BY MR. DINER:

Q Thank you. You can put that aside.

A Thanks.

MR. DINER: Mark the next exhibit, please.

(Article - Adverse reactions to sulfites in drugs and foods, 1077 - 1080, was marked Cykiert-14 for identification.)

BY MR. DINER:

Q Okay, Dr. Cykiert, the reporter has just handed you Cykiert Exhibit 14. Cykiert Exhibit

14 is entitled, Adverse reactions to sulfites in drugs and foods.

Do you see in the very first paragraph of this article where it identifies sulfites as antioxidants used in drugs?

MR. JANUSZ: Objection to scope.

THE WITNESS: I do see that in the first sentence.

BY MR. DINER:

Q Okay. And a few lines down, does it refer to one of the six sulfites that are used in drugs and foods as being sodium sulfite?

MR. JANUSZ: Same objection.

THE WITNESS: Yes, it says sodium sulfite there.

BY MR. DINER:

Q And what is the publication date of this article?

MR. JANUSZ: Same objection.

THE WITNESS: It says June 1984 at the top of the page.

BY MR. DINER:

Q And if you go two pages into the article, it also identifies that same date, correct, June 1984?

MR. JANUSZ: Same objection.

THE WITNESS: Right.

MR. DINER: You can put that aside.

(Vol. 99, No. 2, February 1997 article from the American Academy of Pediatrics, "Inactive" Ingredients in Pharmaceutical Products: Update (Subject Review) was marked Cykiert-15 for identification.)

THE WITNESS: Thanks.

BY MR. DINER:

Q Okay. Dr. Cykiert, you've just been handed Cykiert Exhibit 15. This is an article from Pediatrics -- American Academy of Pediatrics, entitled "Inactive" Ingredients in Pharmaceutical Products Update. And in parens beneath the title it says, Subject Review.

Now, I refer you to the first page of this document, right-hand column. Under the subheading, sulfites, do you see that, sulfiting agents are used as antioxidants?

MR. JANUSZ: Object to scope.

THE WITNESS: I see that, right.

BY MR. DINER:

Q And then one of the six identified sulfite antioxidants can be sodium sulfite?

MR. JANUSZ: Objection, scope, and mischaracterization of the document.

THE WITNESS: I see it says that.

BY MR. DINER:

Q And then in the bottom of that same paragraph it indicates that the sulfites can be used in ophthalmic administration of sulfite-containing drugs; is that correct?

MR. JANUSZ: Same objections.

THE WITNESS: Let me read that. That's not exactly what it says, unless I misunderstood your question.

BY MR. DINER:

Q Does it indicate that sulfites are used in ophthalmic formulations?

MR. JANUSZ: Same objections.

THE WITNESS: It says children have had serious reactions after ophthalmic administration of sulfide-containing drugs.

BY MR. DINER:

Q Okay. And on the next page, does it discuss what some of those reactions were?

MR. JANUSZ: Same objections.

THE WITNESS: Yes, it mentions some.

BY MR. DINER:

Q And does that include some of the manifestations of sulfite sensitivity that we discussed earlier this morning?

MR. JANUSZ: Same objections.

THE WITNESS: It appears to repeat some of those.

BY MR. DINER:

Q And what is the publication date of this article, Cykiert Exhibit 15?

A February 1997.

Q Thank you. You may put that aside.

MR. JANUSZ: Bryan, we've been going for, I think, about an hour. Is this a good time for a break?

MR. DINER: Actually, I think I'm done. I have no further questions.

MR. JANUSZ: We have nothing further as well.

VIDEO OPERATOR: Going off the record, 3:09 p.m.

This is the end of disc 3. and completes the deposition of Robert C. Cykiert.

C E R T I F I C A T I O N

I, LISA FORLANO, a Certified Realtime Reporter, Certified Court Reporter and Notary Public, do hereby certify that I reported the deposition in the above-captioned matter, that the said witness was duly sworn by me; that the foregoing is a true and correct transcript of the stenographic notes of testimony taken by me in the above-captioned matter.

I further certify that I am not an attorney or counsel for any of the parties, not a relative or employee of any attorney or counsel connected with the action, nor financially interested in the action.

LISA FORLANO, CRR, CCR #XI01143

DATED: March 1, 2016

ATTACH TO DEPOSITION OF: Robert C. Cykiert
IN THE MATTER OF: Senju vs. Innopharma
DATE TAKEN: February 26, 2016

E R R A T A S H E E T

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_____, 2016

To: JOSEPH M. JANUSZ, ESQUIRE

Case Name: Senju Pharmaceutical Co., Ltd v. Lupin Limited And Lupin Pharmaceuticals

Veritext Reference Number: 2238419

Witness: Robert C. Cykiert Deposition Date: 2/26/2016

Dear Sir/Madam:

Enclosed please find a deposition transcript. Please have the witness review the transcript and note any changes or corrections on the included errata sheet, indicating the page, line number, change, and the reason for the change. Have the witness' signature at the bottom of the sheet notarized except in California where they are signing under penalty of perjury and forward the errata sheet back to us at the

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Sincerely,

Production Department

Encl.

Cc: BRYAN C. DINER, ESQUIRE
SARAH FINK, ESQ

Federal Rules of Civil Procedure

Rule 30

(e) Review By the Witness; Changes.

(1) Review; Statement of Changes. On request by the deponent or a party before the deposition is completed, the deponent must be allowed 30 days after being notified by the officer that the transcript or recording is available in which:

(A) to review the transcript or recording; and

(B) if there are changes in form or substance, to sign a statement listing the changes and the reasons for making them.

(2) Changes Indicated in the Officer's Certificate. The officer must note in the certificate prescribed by Rule 30(f)(1) whether a review was requested and, if so, must attach any changes the deponent makes during the 30-day period.

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