why would they need to discuss anything about the structure.

Q So you would agree with me that in the context of this patent discussion of the problem of NSAID-BAC complexation, there's no discussion of the degree of lipophilicity of different NSAIDs, right?

MS. LEBEIS: Objection. Mischaracterizes the document, asked and answered, and to the extent it mischaracterizes prior testimony.

A There's no reason why they would discuss the lipophilicity -- about a problem that they don't experience.

Q In talking generally about the problem of NSAID-BAC complexation, whether or not it's experienced in this patent, the authors of the patent don't discuss differences in lipophilicity between different NSAIDs; is that right?

MS. LEBEIS: Objection, same objections.

A Well, I don't think that I've seen any evidence that the problem exists anywhere

let alone in this patent so --

Q Again, Dr. Davies, we're going to be here a long time if you don't answer my questions. So I've heard you testify now that you don't believe there's a problem. We got that. I'm trying to get you to answer the questions I'm asking you.

MS. LEBEIS: Counsel, he's answering your questions.

Q And, again, my question to you is that in the context of this paragraph that's discussing a general problem of NSAID-BAC complexation, is there any discussion in this patent in that section of differences between NSAIDs in terms of their lipophilicity?

MS. LEBEIS: Objection, asked and answered. Mischaracterizes the document and mischaracterizes -- to the extent it mischaracterizes prior testimony.

A There's no discussion because there's no problem experienced in this patent.

Q And you would agree that in this paragraph that talks about the problem of NSAID-BAC complexation, there's no discussion

of the degree of hydrogen bonding among different NSAIDs; is that right?

MS. LEBEIS: Objection. Mischaracterizes the document.

A There's no discussion because the problem isn't observed in this patent, and that's not the aim of the patent.

Q Now, you would agree with me that we're talking here about the "Background of the Invention" section of this '876 patent, right?

A Yes.

Q And you would agree with me that the "Background of the Invention" section generally doesn't talk about problems that are -- or experimental data that are observed in the context of the patent, right?

MS. LEBEIS: Objection. Calls for a legal conclusion. Calls for speculation.

A I would think that depends on patent to patent.

Q Well, certainly when you publish a paper, when you have a background section of your paper, that's not the section in which you report your experimental data, right?

STEPHEN G. DAVIES, D.PHIL.

MS. LEBEIS: Objection. No foundation.

A You might report the result.

Q But, generally, that section is directed to concepts that are known in the background in the relevant field, right?

MS. LEBEIS: Objection, no foundation. Asked and answered.

A In one of my papers, every statement we would make in the background section would have a reference to it to substantiate whatever comment we were making.

Q And those would be comments or concepts that were known in the field already, not new data that you generated in your laboratory, right?

MS. LEBEIS: Objection to the form of the question. Vague and ambiguous. No foundation.

A I think we would try to put references to everything.

Q And those references would reflect what was known in the field already prior to the publication at issue, right?

STEPHEN G. DAVIES, D.PHIL.

MS. LEBEIS: Objection. Asked and answered. Same objections.

A It would be substantiating what we were saying in the background introduction section.

Q And that background introduction section would detail information that was known in the relevant field, right?

MS. LEBEIS: Objection, no foundation. Asked and answered.

A It would show substantiate -- substantiatable data, properly referenced -- describe substantiatable data with properly referenced.

Q And, again, that substantiatable data, properly referenced, would be information that was known in the field, right?

MS. LEBEIS: Same objections.

A We wouldn't be able to substantiate it if it wasn't known in the field.

Q So it would be information that was known in the field then.

MS. LEBEIS: Objection.

A It would be --

STEPHEN G. DAVIES, D.PHIL.

MS. LEBEIS: Same objections.

A It would be known in the field because we could put a reference to it.

Q So a person of ordinary skill in the art reading a patent would understand that the "Background of the Invention" section often sets forth information that's known in the field, right?

MS. LEBEIS: Objection to the extent it calls for a legal conclusion. Asked and answered. Calls for speculation.

A I don't think that's necessarily true. So I haven't seen any evidence in this case that there is a problem of an insoluble complex.

Q Let's see if you can answer the question I'm asking, which is, would a person of skill in the art, reading a background section of a patent, generally understand that that section will include information that's known in the field?

MS. LEBEIS: Objection. Calls for a legal conclusion, asked and answered, and calls for speculation.

STEPHEN G. DAVIES, D.PHIL.

A I'm not sure, if it's not referenced, they would be able to tell whether it was speculation or fact.

Q So if a statement in a patent has no reference, in your view, a person of skill in the art would just read it and move on and not pay any attention to it. Is that your testimony?

MS. LEBEIS: Objection --

A No.

MS. LEBEIS: -- to the extent it mischaracterizes prior testimony. Calls for a legal conclusion and speculation.

A I think if a person of ordinary skill in the art knew references themselves that substantiated a statement, then that would be fine.

MS. RAPALINO: Let's look at another reference, if we could. Let's mark as Davies Exhibit 3 U.S. Patent 5,603,929.

(Exhibit 3 was marked for identification and attached to the deposition transcript.)

BY MS. RAPALINO:

Q Now, Exhibit 3 is another U.S. patent

that you considered in forming your opinions, right?

A Yes.

Q This patent indicates that the date of the patent is February 18th, 1997, right?

A That's what it says.

Q The patent is entitled "Preserved ophthalmic drug compositions containing polymeric quaternary ammonium compounds," right?

A Yes.

Q If you turn to column 1 of the '929 patent, Exhibit 3 --

A Yes.

Q -- and you look at the paragraph that begins at line 27 --

A Okay.

Q -- you would agree that the patent reports that benzalkonium chloride is widely used in ophthalmic solutions, right?

A That's what it says, yes.

Q And it goes on in that paragraph in the next sentence to say that BAC and other quaternary ammonium compounds are generally

considered incompatible with ophthalmic compositions of drugs with acidic groups like NSAIDs. Do you see that?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A It makes that general statement.

Q And then it goes on to make the general statement that this is because the preservative BAC loses its ability to function because it forms complexes with the charged drug compounds. Do you see that?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A It's a general statement without any reference.

Q And that general statement about BAC forming complexes with acidic NSAIDs is not limited to any particular NSAID, right?

A Well, it doesn't even give one example.

Q Right. So it's not limited to even one example, right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

Mischaracterizes the document.

A It doesn't give any evidence that there's a problem with even one. It's just a general statement without any foundation.

Q And that general statement is not limited to any particular NSAID. It's about NSAIDs generally, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document. Asked and answered.

A Without even giving an example of one occurrence, a person of ordinary skill would have -- wouldn't know on what basis that was being made.

Q But you would agree that the general statement itself is not limited to any particular NSAID, right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony. Asked and answered.

A This is not informing a person of ordinary skill of any instance where there actually is a problem between a carboxylic acid and NSAID and benzalkonium chloride. The

actual patent itself is about preservative action, again.

Q And this general statement that we just looked at in column 1 ties the formation of complexes between BAC and NSAIDs to the issue of preservatives losing their ability to function, right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A Well, it doesn't give any evidence that that's true. There would be other ways that preservatives could lose their function.

Q But this suggests that one way could be that the preservatives lose their ability to function as they form complexes with the charged drug compounds, right? That's what it suggests?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A But since it doesn't give any examples where it actually happens, it's a meaningless statement.

Q It may be true that complexes form which cause the preservatives to lose their

efficacy, right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony, and asked and answered. Mischaracterizes the document.

A Without any examples, it may never be true.

Q And it may be true, right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A Without examples, you cannot just make the assumption. Otherwise you would have to assume millions of things, billions of things. You need to have a problem that's concrete before you have to worry about it.

Q But this patent at column 1 suggests that the problem of complexation leads to preservatives losing their ability to function, right?

MS. LEBEIS: Objection, asked and answered. Mischaracterizes the document.

A It suggests without any evidence that that might be the case, but unless a person of ordinary skill sees the problem in reality,

then it's irrelevant.

Q But you can't know with certainty whether or not these complexes form without seeing the test data, right?

MS. LEBEIS: Objection. Vague and ambiguous. To the extent it mischaracterizes prior testimony.

A You have -- you would not assume there was a problem until you've done a test and found the problem existed.

Q You wouldn't know with certainty whether or not a complex formed between a particular NSAID and benzalkonium chloride until you saw the test data, right?

A Sorry, I missed the first part of that question.

(Record read.)

A You would not know, no.

Q In this patent, the '929 patent, Exhibit 3, there is no discussion in this section that talks about this potential problem of complexation about differences between NSAIDs in terms of their chemical structure, right?

STEPHEN G. DAVIES, D.PHIL.

MS. LEBEIS: Objection, no foundation. Mischaracterizes the document.

A There isn't, nor would one expect there to be when the problem isn't actually observed.

Q There's also no discussion in this section of the patent that talks about the potential problem of complexation between NSAIDs and BAC of the differences in electron density between different NSAIDs, right?

MS. LEBEIS: Same objections.

A There isn't, nor would a person of ordinary skill expect there to be when the problem isn't presented.

Q There's also no discussion in this '929 patent of the differences between NSAIDs in terms of whether they're primary, secondary, or tertiary amines as being relevant to this issue of potential complexation, right?

MS. LEBEIS: Same objection.

A The patent is not about potential complexation so there would be no discussion.

Q There's also no discussion, in this section of the patent that talks about the

problem of potential complexation between NSAIDs and BAC, of the differences between NSAIDs in terms of the presence or absence of halogenation on the compounds?

MS. LEBEIS: Objection to the form of the question.

A There wouldn't be because that's not the problem being addressed by the patent.

Q And there's also no discussion in this patent, in the section that talks about the potential complexation between NSAIDs and BAC, about differences in lipophilicity between different NSAIDs, right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A I lost the end of the sentence, end of the question.

(Record read.)

MS. LEBEIS: Objection.

A There isn't because it's irrelevant to what the main part of the patent is about.

Q And there's also no discussion in this patent in the section that talks about potential complexation between NSAIDs and BAC

of differences between NSAIDs in terms of their degree of hydrogen bonding, right?

MS. LEBEIS: Objection. Mischaracterizes the document.

A There wouldn't be because such facts are irrelevant to the rest of the patent and what it's actually dealing with.

Q What do you think this patent is directed to, this Exhibit 3, '929 patent?

MS. LEBEIS: Objection, vague and ambiguous.

A Well, the data that's presented has to do with preservative action.

Q So this patent is directed to ophthalmic pharmaceutical compositions with good preservative efficacy?

MS. LEBEIS: Objection to the extent it mischaracterizes the prior testimony and mischaracterizes the document.

A As I said, the data that is presented has to do with preservative action.

Q In what kind of formulations?

A (Document review.)

In diclofenac formulations. This is

another one, sulfacetamide and suprofen. Those three are formulated.

Q So this patent provides a formulation that's suitable for use with those three compounds; is that right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A (Document review.)

The results seem to be on formulation A, which is sodium diclofenac, in terms of its preservation activity.

Q In your view, is the subject of the patent then limited to formulations of diclofenac sodium?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A That's a legal question. It's not for me to say. But the data is only presented for, as far as I can see, for formulation A, which has diclofenac in it.

Q So you don't have an opinion one way or another on whether this patent is limited to formulations of diclofenac sodium or includes other formulations?

STEPHEN G. DAVIES, D.PHIL.

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A The data presented and what a person of ordinary skill would see is data on sodium diclofenac.

Q Now, if we go back to the paragraph in column 1, starting at line 27.

A Yes.

Q So if you can keep that open and then go back to Exhibit 2.

A Okay.

Q And look at the paragraph we looked at in column 1 of Exhibit 2, the '876 patent that starts at line 10.

A Starts at line --

Q 10.

A 10?

Q Column 1.

A Okay.

Q You would agree that the statements in Exhibit 2, the '876 patent, in column 1, are consistent with the statements in Exhibit 3, the '929 patent, at column 1?

MS. LEBEIS: Objection to the form of

the question. Vague and ambiguous.

A They're broadly consistent. They're from the same -- both patents are from the same company. There's no evidence in either of them that they're true or not.

Q I think you pointed out, they're both from Alcon Laboratories, Inc., right, both of those patents?

A That's correct.

MS. RAPALINO: Let's mark as Davies Exhibit 4 European Patent 0306984.

(Exhibit 4 was marked for identification and attached to the deposition transcript.)

BY MS. RAPALINO:

Q Dr. Davies, this is a European patent you considered in forming your opinions in this case?

A Yes.

Q Is it okay if we refer to that as EP '984?

A That's fine.

Q This patent has a date of publication of March of '89; is that right?

A That's correct, yes.

STEPHEN G. DAVIES, D.PHIL.

Q This patent is -- indicates that the applicant is Syntex, Inc., right?

MS. LEBEIS: Objection. Mischaracterizes the document.

A It says, "Applicant, Syntex, Inc."

Q That's a separate company from Alcon Laboratories, right?

MS. LEBEIS: Objection. Calls for speculation.

A I don't know.

Q Well, it doesn't list Alcon as the applicant, right?

A It does not.

MS. LEBEIS: Objection, argumentative.

A It doesn't say Alcon.

Q And the inventors listed on this patent are not the same inventors as the -- those on Exhibits 2 and 3 that we looked at earlier, right?

A They're not, no.

Q Now, if we look at page 2 of EP '984, Exhibit 4.

A Page 2.

STEPHEN G. DAVIES, D.PHIL.

Q Page 2.

A Okay.

Q You see that in the paragraph beginning at line 10, EP '984 describes an earlier patent, U.S. Patent 4,454,151?

A Yes.

MS. LEBEIS: Is that a question? Is there a question?

MS. RAPALINO: Yes, I think we just got an answer to it.

A I see the patent number there, yes.

Q Yes. And then it goes on to say that "While the formulations described in the '151 patent were efficacious, an insoluble complex was found to form between the NSAID and BAC." Do you see that?

A That's what it says.

Q And if you go down to page 2, line 31 --

A Yes.

Q -- you see there's a sentence that says, "Benzalkonium chloride, a quaternary ammonium compound, has been widely used in ophthalmic solutions and is considered to be

the preservative of choice"?

A That's what it says.

Q You don't disagree that benzalkonium chloride had been widely used in ophthalmic formulations and was a preservative of choice, do you?

MS. LEBEIS: Objection. Calls for speculation.

A I haven't done that analysis.

Q So you don't have an opinion one way or another?

A Since I haven't done the analysis.

Q So you don't have an opinion one way or another?

MS. LEBEIS: Asked and answered.

A I haven't done the analysis so I don't. I don't know. And I suspect it depends on the ophthalmic solution as what the preservative of choice is. I've seen others that don't have the benzyl ammonium, the quaternary ammonium compound.

Q But you haven't done the analysis one way or another to know when benzalkonium chloride would be a preservative of choice,

right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A I haven't done the analysis, and I suspect it depends on which formulation we're talking about as to which would be the preservative of choice.

Q That suspicion that you have is not based on any analysis that you've done; is that right?

MS. LEBEIS: Objection, asked and answered. Argumentative.

A I've not done a detailed analysis, but I have seen formulations that don't contain benzalkonium chloride as a preservative.

Q Which formulations are those?

A I think we saw some earlier in one of the patents we've already looked at.

Q Do you want to tell me which formulation that was?

A (Document review.)

In the '929 patent.

(Document review.)

Q Apart from the formulation that

you've seen in the '929 patent, are you aware of any other formulations for ophthalmic use that don't contain benzalkonium chloride as the preservative?

MS. LEBEIS: Dr. Davies, you can take your time looking at the '929 patent in answering counsel's question.

Q Just to be clear, though, my question is, apart from the formulations in the '929 patent, are you aware of any ophthalmic formulations that don't contain benzalkonium chloride as the preservative? I don't think you need to look at the '929 patent to answer that question. But if you feel you do, please feel free.

A I believe I've seen other formulations, yes.

Q Can you point to any of those formulations?

A Not sitting here at this moment.

Q Let's go back to Exhibit 4, the EP '984 patent.

Okay. If you look at page 2 again, at line 33, you see that the EP '984 patent

STEPHEN G. DAVIES, D.PHIL.

goes on to say that "BAC has typically been considered to be incompatible with anionic drugs, forming insoluble complexes which cause the solution to become cloudy or turbid."

Do you see that it says that?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A That's what it says.

Q It goes on to say that such complexation between an anionic drug and BAC can cause a decrease in the pharmaceutical activity of the drug.

Do you see that?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A It's the same as the previous cases. I don't see any evidence that that's true, that there is a problem.

Q You would agree, though, that EP '984 asserts that that's a problem, right?

MS. LEBEIS: Objection to the form of the question, asked and answered, to the extent it mischaracterizes prior testimony.

A It makes a broad statement without

any evidence.

Q And that broad statement is that there's a problem of complexation between anionic drugs and BAC, right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony and mischaracterizes the document.

A It doesn't give any evidence that such a complex would form.

Q But the EP '984 nonetheless makes the broad statement that there is a problem of complexation between anionic drugs and BAC, right?

MS. LEBEIS: Objection. Asked and answered, mischaracterizes the document, and to the extent it mischaracterizes prior testimony.

A Without any evidence, a person of ordinary skill wouldn't be able to take anything from that.

Q Let's look at paragraph -- the paragraph on page 2 just below the one we were looking at.

A Okay.

STEPHEN G. DAVIES, D.PHIL.

Q Do you see that it says "In the past, as in the case with other ophthalmic drugs that contain a carboxylic acid group, anti-inflammatory solutions of NSAIDs for ocular use have proven to be incompatible with quaternary ammonium compounds such as BAC."

MS. LEBEIS: Objection. Mischaracterizes the document.

Q Do you see that it says that?

A It says those words, but there's no evidence to allow person of ordinary skill to understand if they're correct or not.

Q Okay. But those are the words that the patent uses, right?

MS. LEBEIS: Objection. Asked and answered.

A The words are written down in the patent, but, without any evidence, a person of ordinary skill can't take anything from them.

Q And it goes on to explain that this incompatibility is due to the fact that the carboxylic acid group can form a complex with the quaternary ammonium compound, rendering the preservative less available to serve its

function and reducing the activity of the active ingredient, right? That's what it says?

MS. LEBEIS: Objection, mischaracterizes the document.

A That's an assumption for which there is no evidence.

Q So this EP '984 patent talks about the general problem of complexation between drugs, ophthalmic drugs in the carboxylic acid group and benzalkonium chloride consistent with the way that that problem was discussed in Exhibits 2 and 3, the '876 and '929 patents, right?

MS. LEBEIS: Objection. Mischaracterizes the document. Asked and answered.

A In none of the patents is there any evidence that this problem actually exists.

Q You would agree, though, that the statement of this problem in EP '984 at the paragraph from line -- on page 2, lines 29 through 44 is consistent with the statement we looked at in the '876 patent, Exhibit 2, at column 1, lines 10 through 24, right?

STEPHEN G. DAVIES, D.PHIL.

MS. LEBEIS: Objection to the form of the question and to the extent it mischaracterizes prior testimony.

A They describe the same general purported problem for which there is no evidence being presented. So a person of ordinary skill wouldn't be concerned about it unless they faced it.

Q And the discussion in EP '984 of this general problem of complexation between carboxylic-acid-containing compounds and BAC does not mention any differences between different NSAID compounds, in terms of their chemical structure, as being relevant to that problem, right?

MS. LEBEIS: Objection. Mischaracterizes the document.

A Well, it wouldn't, though, because it's not what the rest of the patent is about. So they wouldn't need to discuss those things.

Q There's also no discussion in the EP '984 of any differences between NSAID compounds in terms of their electron density, right?

MS. LEBEIS: Same objection.

STEPHEN G. DAVIES, D.PHIL.

A It wouldn't discuss such matters because they're irrelevant to what the rest of the patent is discussing.

Q There's also no discussion in EP '984 of differences between NSAIDs in terms of whether they're primary, secondary, or tertiary amines, right?

MS. LEBEIS: Same objection.

A They wouldn't do because it's not what the patent goes on to discuss.

Q There is also no discussion in EP '984 of the impact of the presence or absence of halogenation on NSAIDs as relevant to the issue of complexation, right?

MS. LEBEIS: Same objection and objection to the form of the question.

A It wouldn't discuss that because it's not relevant to the rest of the patent.

Q So there's no discussion, right?

MS. LEBEIS: Same objection.

A Nor would a person of ordinary skill expect there to be a discussion.

Q So there is no discussion in the patent of presence or absence of halogenation

STEPHEN G. DAVIES, D.PHIL.

of different NSAIDs, right?

MS. LEBEIS: Same objection.

A There is no discussion because it's irrelevant to the rest of the patent.

Q There's also no discussion in the patent of the differences between NSAIDs in terms of their degree of lipophilicity with respect to this problem of complexation, right?

MS. LEBEIS: Same objection.

A There is no discussion because it would be irrelevant to the rest of the patent.

Q There's also no discussion in the patent regarding the degree -- differences in the degree of hydrogen bonding as between different NSAIDs as it relates to the issue of complexation.

MS. LEBEIS: Same objection.

A No, because it's irrelevant to the rest of the patent.

Q And there's also no discussion about the degree of solvation of any of the NSAIDs in this patent in relation to the problem of complexation, right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A I don't believe so because it would be, well, irrelevant to the rest of the patent.

Q Now, let's look at page 4.

A Yes.

Q And there are some examples given of formulations according to the invention of this patent, right? Do you see the tables?

A I see the boxes, yes.

Q And each of those formulations on page 4 and over to the top of page 5 lists the active ingredient as NSAID. Do you see that?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A It said these are preferred formulations. They're not actual formulations unless they release the NSAID in that formulation.

Q Right. So these just say generically NSAID for these preferred formulations, right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A Well, it says "NSAID." It could be one particular NSAID. You have to read the

whole of the rest of the patent to determine whether it's one or any one.

Q And then if we look at page 6 of the EP '984, Exhibit 4 --

A Yes.

Q -- there are some more preferred ophthalmic NSAID solutions listed on page 6. Do you see that?

A Yes.

Q And each of those lists the active ingredient as NSAID, right?

A Yes. But, again, that could be one or more. You have to read the whole patent.

Q Then if we look at the examples in the EP '984 patent, Exhibit 4, starting at page 7, and going on to page 8 --

A Yes.

Q -- there are examples of representative pharmaceutical formulations. Do you see that?

A Yes.

Q The active ingredient in some of those formulations is ketorolac tromethamine. Do you see that?

STEPHEN G. DAVIES, D.PHIL.

A In the first three, which is consistent with the statement underneath the general boxes on page 8, where it says the "most preferred is the ophthalmic solution according to the above formulation wherein the NSAID is ketorolac tromethamine or an isomer thereof," yes.

Q And ketorolac tromethamine is an NSAID, right?

A Yes.

Q It's a carboxylic acid containing NSAID?

A Yes.

Q And it's an NSAID that's anionic at pH 7 to 9, right?

A Yes.

Q Each of these formulations in EP '984, Exhibit 4, contain octoxynol 40. Do you see that?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A It's listed in them, yes.

Q Have you ever worked with octoxynol 40?

STEPHEN G. DAVIES, D.PHIL.

A I personally haven't, no.

Q Octoxynol 40 is an ethoxylated octylphenol compound, right?

A Yes.

Q On page 9 of EP '984, under example 5, the EP '984 patent compares formulations of ketorolac tromethamine, benzalkonium chloride, and three different surfactants in three different formulations, right?

A Yes.

Q If you look at line 11 on page 9, it describes the experiment of example 5, and it says, "Three surfactants were evaluated for their ability to dissolve the ketorolac-benzalkonium chloride complex and maintain a physically clear solution over an extended period of time."

Do you see that?

A Yes.

Q The three surfactants that were tested in example 5 were octoxynol 40, polysorbate 80, and Myrj 52. Do you see that?

MS. LEBEIS: Objection.

Mischaracterizes the document.

STEPHEN G. DAVIES, D.PHIL.

A I see that. It says tween on -- in the actual table, but ...

Q Tween 80 is the same as polysorbate 80, right?

A As it says above, yes.

Q The results presented in the table in example 5 show that the ethoxylated octylphenol surfactant, octoxynol 40, was the best among those tested in that it provided a clear solution at all the time points and conditions tested, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A It says it was superior, yes.

Q For the formulations tested in EP '984, the ethoxylated octylphenol surfactant, octoxynol 40, provided the superior results in terms of solubilization at all of the test conditions, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A Well, to the extent that it remained clear all the time, yes.

Q For ophthalmic solutions, it's

STEPHEN G. DAVIES, D.PHIL.

desirable to have a solution that remains clear, right?

MS. LEBEIS: Objection. Calls for speculation.

THE WITNESS: Can you repeat the question, please.

(Record read.)

THE WITNESS: I didn't get the first two words.

(Record read.)

A Yes.

MS. LEBEIS: We've been going about an hour. Do you think it's a good time to take a lunch break?

MS. RAPALINO: Can I do one more document and then we'll break? Are you okay with that?

THE WITNESS: That's fine, yes.

MS. LEBEIS: Yes, that's fine.

BY MS. RAPALINO:

Q In your view, do the results presented in example 5 provide any evidence of complexation between an NSAID and benzalkonium chloride?

STEPHEN G. DAVIES, D.PHIL.

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A There's no analytical data to suggest what is making some of these solutions turbid.

Q So something is making some of the solutions turbid. You would agree with that, right?

A But there's no indication as to what that might be. So you can't assume and you wouldn't assume that it's a ketorolac-benzalkonium chloride complex.

Q EP '984 doesn't provide any suggestion about what else that precipitate or turbidity might be, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A It doesn't give you any indication what it is in fact. There's no data produced.

Q And just to be clear, EP '984, even if it has no data to back it up, certainly suggests that these surfactants were being evaluated for their ability to dissolve the ketorolac-benzalkonium chloride complex. Do you see that?

STEPHEN G. DAVIES, D.PHIL.

A Objection to the extent it mischaracterizes the document.

A person of ordinary skill reading that would not -- and reading the experimental that's been done would not be able to understand the experiment because it says "were evaluated for their ability to dissolve ketorolac-benzalkonium chloride complex." That would imply that there is solid ketorolac-benzalkonium chloride complex available as solid form and that it was being dissolved. That is not what is -- that is not the experiment that they do.

Q So, in your opinion, a person of skill in the art wouldn't understand this experiment in example 5 of EP '984, Exhibit 4?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A I've told you what the words would mean to a person of ordinary skill. When you dissolve something, you take a solid, and you add a liquid, and you watch the solid dissolve in a liquid.

Q So with that semantic definition of

dissolve, a person of skill in the art then would be at a loss to understand what was being done in this experiment in example 5 of EP '984. Is that your testimony?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A They could go back and look at the actual experimental, which is also -- no, that is not a proper description.

Q Where do you see the actual experimental?

A Well, it lists the ingredients, none of which are ketorolac -- any ketorolac-BAC complex. So they would -- they would -- they would know that -- so this is on page 7 under the box.

It says, "The above ingredients," none of which are ketorolac-benzalkonium chloride complex, "are mixed, adding purified water until they're dissolved, and the pH adjusted to 7.4," then the balance made up with purified water. So they can read the actual experiment that was done.

Q So then they would understand what

experiment is being done in example 5?

A And, therefore, that it isn't what's written above the quote you gave to me, which was the ability to dissolve ketorolac-benzalkonium chloride.

Q Now, you don't actually think that the formulations that were tested in example 5 were all the formulation that you pointed to on page 7, right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A It's given the general experimental of how these solutions were being made up.

Q Okay. So you're just pointing to page 7 to show how they're manufacturing the -- how they're making the formulation, right, that they're mixing the ingredients and adding purified water until they're dissolved? Is that what you mean?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony or the document.

A What I'm trying to illustrate is that they really are not starting from

ketorolac-benzalkonium chloride complex and trying to dissolve that, which is what is implied in lines 11 to 12 on page 9.

Q Okay. But in the context of the rest of the patent, a person of ordinary skill in the art reading example 5 would understand that example 5 is intended to evaluate the ability of these different surfactants to solubilize any complexes that are formed between ketorolac and benzalkonium chloride, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A There is not -- there is nothing in -- no data produced to say that the turbicity is -- turbidity, rather, is due to a complex between ketorolac and benzalkonium chloride.

Q That's just what's being suggested by the author, right, without any data, that what's being evaluated here is the ability to solubilize those complexes?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A Well, there's no -- there's no --

without any evidence as to what this precipitate or the turbidity is due to, you can't tell what is being solubilized.

Q What else, in your view, could cause the turbidity in this solution?

MS. LEBEIS: Objection. Vague and ambiguous, incomplete.

A Any --

MS. LEBEIS: One second. Also incomplete hypothetical.

A Without experimentation, you can't tell what the turbidity is due to.

Q So you don't have a view, one way or the other, whether there's anything else that could be causing the turbidity in this composition?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A Until you know what the turbidity is due to, you can't possibly tell what is causing it.

MS. RAPALINO: Let's mark as Davies Exhibit --

MS. LEBEIS: We went another 10

STEPHEN G. DAVIES, D.PHIL.

minutes on this reference. Would it be okay to take a lunch break now?

MS. RAPALINO: Dr. Davies, do you need a lunch break?

THE WITNESS: Yes, can we?

MS. RAPALINO: Sure.

THE VIDEOGRAPHER: We're going off the record at 12:36 p.m.

(A lunch recess was taken.)

THE VIDEOGRAPHER: We're going back on record at 1:20 p.m. This is the start of disc number 4 in the deposition of Stephen Davies.

MS. RAPALINO: I'm going to ask the court reporter to mark as Davies 5 an international patent application WO 94/15597.

(Exhibit 5 was marked for identification and attached to the deposition transcript.)

BY MS. RAPALINO:

Q Is this an international or PCT patent application you considered in forming your opinions in this case?

A Yes.

Q It was published in July of 1994; is that right?

A That's the international publication date, yes.

Q And you see that it's entitled "Ophthalmic compositions comprising benzyl-lauryl-dimethyl-ammonium chloride."

A Yes.

Q Now, benzyl-lauryl-dimethyl-ammonium chloride is sometimes abbreviated LAC, or L-A-C, right?

A I believe so.

Q That's a different preservative from BAC; is that right?

A It's a similar type.

Q So they're similar preservative?

A They're similar in the sense that they're benzyl ammonium salts.

Q Okay.

If you look at page 2 of this PCT application -- and if it's okay with you, I'll refer to it as the WO '597 application; is that right?

A Okay.

STEPHEN G. DAVIES, D.PHIL.

Q So let's turn to page 2 of WO '597. And if you look at the first paragraph on page 2, WO '597 reports that "BAC is a quaternary ammonium compound that has been widely used in ophthalmic solutions, right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A That's what it says.

Q And then it goes on to say in the second sentence in that first paragraph on page 2, "It is also well-known that BAC is considered incompatible with anionic drugs, forming insoluble compounds which cause the solution to turn cloudy."

Do you see that?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A I read the words, yes.

Q If you go back to the cover page of WO '597, Exhibit 5, you see that the applicant for this international application is Allergan, Inc., right?

A Yes.

Q That's another pharmaceutical company

that specializes in ophthalmic products, right?

MS. LEBEIS: Objection. Calls for speculation.

A I don't know that.

Q You're not familiar with Allergan?

A I've heard of it, but I don't know that its speciality is ophthalmic.

Q Okay. You know it's a pharmaceutical company?

MS. LEBEIS: Objection. Calls for speculation.

A I believe it to be a pharmaceutical company, yes.

Q Then if you look at -- going back to page 2 of WO '597, the next two paragraphs on page 2 go on to describe the reason for the complexation phenomenon that was discussed in the first paragraph, right?

MS. LEBEIS: Objection. Mischaracterizes the document.

A Well, it doesn't give any evidence in those paragraphs so it's speculation.

Q Right. So it provides some speculation about the reason behind the

STEPHEN G. DAVIES, D.PHIL.

formation of insoluble precipitates of NSAIDs and quaternary ammonium compounds, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document. Calls for speculation.

A It doesn't give any evidence that any cloudiness or precipitate is due to the interaction of the positively charged preservative with the negatively charged active.

Q WO '597 here is positing a theory as to what might lead to insoluble compounds due to the association between benzalkonium chloride and a negatively charged acidic drug, right?

MS. LEBEIS: Objection. Mischaracterizes the document. Calls for speculation.

A They're making -- they put those words in the introductory paragraph without any backup. So I don't know what a person of ordinary skill would take from it in terms of fact.

Q But they're positing a theory, right,

as to what might lead to insoluble complexes due to the association between benzalkonium chloride and a negatively charged acidic drug, right?

MS. LEBEIS: Objection. Mischaracterizes the document, calls for speculation, and asked and answered.

A It's what it says in the introductory part for this prep.

Q And what it says in these first three introductory paragraphs of WO '597, that's consistent with what we saw in Exhibit 4, EP '984, and Exhibit 3, the '929 patent, and Exhibit 2, the '876 patent, right?

MS. LEBEIS: Objection, form of the question. You should feel free to go back and look at those other documents if you need to.

A Well, it's not exactly the same wording. This has different suggestions than the other patents.

Q The concept, though, is the same, is consistent between this patent, the WO '597, and the earlier Exhibits 2, 3, and 4 that we

looked at in terms of the description of the general phenomenon of an insoluble precipitate forming between an acidic NSAID and benzalkonium chloride, right?

MS. LEBEIS: Objection. Mischaracterizes the documents. Calls for speculation. Asked and answered.

A There can't be a general phenomenon if there's no evidence that it's actually occurring.

Q You would agree, though, that this WO '597, consistent with the prior three exhibits that we looked at, Exhibits 4, 3, and 2, provides a general description of a phenomenon even without evidence, but they all provide a consistent description of the phenomenon of the formation of an insoluble precipitate due to the formation -- due to the interaction of benzalkonium chloride and an acidic drug or NSAID, right?

MS. LEBEIS: Objection. Mischaracterizes the documents, calls for speculation, asked and answered, and objection to the form of the question.

STEPHEN G. DAVIES, D.PHIL.

A A phenomenon is something that actually exists that needs an explanation. I haven't seen that -- any evidence that you get a precipitate from benzalkonium chloride and carboxylic acid.

Q So your issue is with the word "phenomenon"? Is that the problem?

A That's one of the issues, I suspect.

Q So why don't we try this. You would agree with the description of this potential problem in WO '597 of interaction between benzalkonium chloride and anionic drugs is consistent with the description of that same problem we looked at in Exhibits 4, 3, and 2, right?

MS. LEBEIS: Objection. Mischaracterizes the documents, calls for speculation, asked and answered, and objection to the form of the question.

A I don't think in any of the cases it's a problem because it hasn't been shown to exist.

Q The speculation in each of these references about a potential problem in the

formation of a complex between benzalkonium chloride and an NSAID is consistent as between WO '597 and the other references that we looked at, EP '984, U.S. patent '929, and U.S. patent '876, right?

MS. LEBEIS: Objection. Mischaracterizes the documents, calls for speculation, objection to the form of the question, and asked and answered. He's answered this question. You've asked it now several times.

A Without some evidence, you don't know the problem exists. And in none of the previous cases we looked at did whatever was being suggested have anything to do with the bulk of the patent.

Q Let's look at EP '984 at Exhibit 4.

A Yes.

Q You would agree with me, would you not, that on page 2 of EP '984 at line 31, the European patent says that "benzalkonium chloride has been widely used in ophthalmic solutions," right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A That's what it says there, but --

Q Then if you look at --

A -- I have no way of knowing that that's --

Q I didn't ask about what you know. I just asked whether that's what the patent said. Do you understand the question?

A That is what the patent says, yes.

Q Then if you look at Exhibit 5 that we were just looking at, the WO '597, at page 2 --

A Yes.

Q -- you see at the top of the page 2, the first sentence also says, "Benzalkonium chloride has been widely used in ophthalmic solutions."

Do you see that?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A That's what it says in the document, yes.

Q So those two statements in the two patents we just looked at are consistent with one another, right?

STEPHEN G. DAVIES, D.PHIL.

MS. LEBEIS: Objection to the form of the question.

A Well, that single sentence is they're consistent with one another, but you have to read them in context in each of the patents.

Q Okay. Let's look at some more of the context then. If you could go back to Exhibit 4, the EP '984.

A Yes.

Q And let's look at the next sentence on page 2 that starts at line 33.

A Yes.

Q It says that "BAC has typically been considered to be incompatible with anionic drugs, forming insoluble complexes which cause the solution to become cloudy."

Do you see that?

MS. LEBEIS: Objection. Mischaracterizes the document.

A Well, it actually quotes as the anionic drug salicylates and nitrates.

Q Okay. So with that amendment, you agree that's what it says in EP '984?

MS. LEBEIS: Objection to the extent

STEPHEN G. DAVIES, D.PHIL.

it mischaracterizes prior testimony.

A There's no evidence that --

Q I'm not asking about evidence now.

MS. LEBEIS: You need to let him finish answering the question.

MS. RAPALINO: He needs to answer my question.

MS. LEBEIS: You need to let him finish answering the question and give his full answer to your question before you start with another question.

BY MS. RAPALINO:

Q Dr. Davies, you would agree that EP '984, starting at line 33, says, "BAC has typically been considered to be incompatible with anionic drugs (e.g., salicylates or nitrates, et cetera), forming insoluble complexes which cause the solution to become cloudy or turbid."

Do you see that?

A I can see the words written there.

Q And then if you look at --

MS. LEBEIS: He wasn't finished answering the question.

STEPHEN G. DAVIES, D.PHIL.

MS. RAPALINO: That was the answer to the question.

MS. LEBEIS: He had not finished answering the question.

Dr. Davies, you can finish answering.

BY MS. RAPALINO:

Q Could you turn, Dr. Davies, to --

A But there was -- there's no evidence provided that that is a real phenomenon.

Q Did you think that was the answer to the question about whether the words were written on the page?

MS. LEBEIS: Objection to the form of the question. Argumentative.

A I'm giving you the answer I think is the answer I wish to give to the question you asked me.

Q You've got to answer the questions I ask, not just give the testimony you wish to give. Do you understand that?

A I believe I'm answering the questions you ask.

Q So let's go on to my next question. Let's see if you can answer the question I ask.

STEPHEN G. DAVIES, D.PHIL.

If you look at WO '597, which is Exhibit 5, do you see that in the second sentence, it says, "It is also well-known, however, that benzalkonium chloride is considered incompatible with anionic drugs, forming insoluble compounds which cause the solution to turn cloudy."

Do you see that it says those words?

A Those are the words that are written down, yes.

Q You would agree that that sentence is consistent with the sentence that we just read from EP '984 on page 2, lines 33 through 35.

MS. LEBEIS: Objection to the form of the question. Asked and answered.

A They're not exactly the same words.

Q Right. So which words do you think are different?

A So which were the lines you were asking me about on the '984?

Q Page 2, lines 33 to 35.

A That says, "BAC has typically been considered to be incompatible with anionic drugs (e.g., salicylates or nitrates, et

cetera)," so it's qualified, "forming insoluble complexes which cause the solution to become cloudy or turbid." So the one in '984 is qualified.

Q When you say it's "qualified," you mean that there are examples that are provided of anionic drugs?

A Yes.

Q And other than the fact that one patent provides examples of anionic drugs and the other one doesn't, those sentences are consistent with one another, right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A What's written in the two patents is consistent between the two patents but is meaningless to the person reading it on their own.

Q Now, if we look at page 5 of Exhibit 5, the WO '597 patent.

A Yes.

Q The first sentence under "Detailed Description" says that "Flurbiprofen is a classic example of an acidic drug that forms an

insoluble ion pair with benzalkonium chloride."

Do you see that?

A Yes.

Q And flurbiprofen is an acidic NSAID with a carboxylic acid moiety, right?

A That's correct.

Q Bromfenac is also an acidic NSAID with a carboxylic acid moiety, right?

A It is an NSAID, and it has a carboxylic acid group, yes.

Q And I think we might have established this earlier. Bromfenac is also an anionic drug at the relevant pH for ophthalmic solutions, right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A I've said it before, yes.

Q Now, if you look at table 1 on pages 6 and 7 of WO '597, this is example 5, there are -- this table, table 1, provides two -- the ingredients of two different formulations of sodium flurbiprofen, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

STEPHEN G. DAVIES, D.PHIL.

A Sorry, you have to repeat the question, please.

Q If you look at table 1 on pages 6 and 7 of the WO '597 in Exhibit 5, table 1 provides the ingredients of two different formulations of sodium flurbiprofen, right?

MS. LEBEIS: Same objection.

A That's what it looks like, yes.

Q Example A in table 1 contains sodium flurbiprofen and benzalkonium chloride, right?

A That's correct.

Q Example B in table 1 contains sodium flurbiprofen and lauralkonium chloride, right?

A That's correct.

Q Under the table -- under table 1 on page 7, the patent reports -- the patent application reports that example A, that's the example with benzalkonium chloride, "results in a cloudy solution with precipitate and loss of antimicrobial efficacy."

Do you see that?

A Yes.

Q And example B, the one that contained the lauralkonium chloride but no benzalkonium

chloride, remained as a solution and the solution maintains its antimicrobial efficacy. That's what's recorded there, right?

A That's what's written down.

Q The only difference between example A and example B, in terms of the formulations presented in table 1, is the identity of the preservative, right?

A Yes, that's true.

Q So in the formulation with the benzalkonium chloride and the acidic NSAID, the patent reports that it became cloudy with a precipitate and loss of antimicrobial efficacy, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A It just says it's cloudy. It doesn't say what the cloudiness is due to, but it says it's cloudy.

Q Right. And then in the other formulation, example B, where the only difference in that formulation was substituting lauralkonium chloride for benzalkonium chloride, it reports that the solution remained

clear, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A It doesn't say it's clear.

Q It says it remains a solution, right?

A Yes.

Q Okay. And it maintained its antimicrobial efficacy, right?

A That's what it says. I don't see the results on that table that it's done so.

Q I'm sorry, what is it that you said you don't see?

A In that table it just says the words "it maintained."

Q If you turn the page to table -- I'm sorry, to page 8, do you see table 3?

A Yes.

Q That table reports the results of a -- microbiology results on the example B formulation, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A It doesn't actually say for table 3 it's example B. It just says lauralkonium

chloride itself is able to maintain its antimicrobial efficacy of a period of up to one year or more.

Q Then on page 7, line 13, the patent reports that example B passes the British Pharmacopeia preservative effectiveness test, right?

A That's what it says, yes.

Q You're not an expert in preservative efficacy, are you?

A No.

Q You're not an expert in any of the pharmacopeial methods for evaluating preservative efficacy?

A No.

Q You yourself have never evaluated a formulation for its preservative efficacy, have you?

A I have not.

Q You would agree that a person of skill in the art reading the information in WO '597 about the sodium flurbiprofen and benzalkonium chloride formulations would conclude that the presence of benzalkonium

chloride in example A is responsible for the cloudiness and precipitate formation in the example A formulation, right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A I don't think I can agree with that because we don't know the result of what happens if you leave out the benzalkonium chloride altogether. So you have a -- if you look at example B, you have a non-cloudy solution that does contain lauralkonium chloride. You take that out, and it goes cloudy. That does not mean it's responsible for the thing you've added, which is benzalkonium chloride.

Q Okay. So you can't conclude one way or another from that data whether or not benzalkonium chloride is responsible for the cloudiness of example A?

A I can't, no.

Q It's certainly possible that the presence of benzalkonium chloride is responsible for that cloudiness, which is -- and removal -- or replacement of benzalkonium

with lauralkonium chloride resolved that issue, right?

MS. LEBEIS: Objection. Mischaracterizes the document, calls for speculation, asked and answered.

A You can't make the conclusion that it is responsible from that.

Q Right. But without making any conclusion, it's possible, that's one explanation for what's observed here, that it's the presence of benzalkonium chloride that's responsible for that cloudiness, right?

MS. LEBEIS: Same objections.

A I don't -- I wouldn't speculate without the proper experimental data.

Q Let's look at your expert report at page 5. This is in Exhibit 1.

A Sorry, which page?

Q Page 5.

A Page 5. Okay.

Q You have a footnote 1 there at the bottom. Do you see that?

A Yes.

Q And in the second sentence of your

STEPHEN G. DAVIES, D.PHIL.

footnote, you write, "An NSAID and a quaternary ammonium compound, however, cannot form a complex and can only potentially form a salt."

Do you see that?

A Yes.

Q So you agree that an NSAID and benzalkonium chloride can potentially form a salt, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A I'm talking about chemical differences between what a complex is and what a salt is.

Q Right. And you wrote, "An NSAID and a quaternary ammonium compound can only potentially form a salt, right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A It's defining what a salt is and what a complex is. There's no -- I don't see how a complex can be formed between an NSAID and a quaternary ammonium complex -- compound.

Q But you do see how a salt could be formed between an NSAID and a quaternary

ammonium compound?

MS. LEBEIS: Objection, asked and answered.

A These are definitions of what a salt and a complex are, and an NSAID itself can't form a salt, and a quaternary ammonium compound can't form a salt with something else directly.

Q Right. But an interaction of the NSAID and the quaternary ammonium cation could form a salt, right?

MS. LEBEIS: Objection to the form of the question.

A In principle, anything with a negative charge can form a salt with something with a positive charge. Whether or not it ever does depends on the particular circumstances and what the positive and the negative charge are. If you put them into solution, then essentially you have a solution of a salt, but whether it will ever form a solid salt is -- you can't predict.

Q So it might, but it might not?

MS. LEBEIS: Objection to the form of the question. Asked and answered.

STEPHEN G. DAVIES, D.PHIL.

A You have no way of telling unless you do the experiment.

Q Now, this point you're making in footnote 1, that's a -- I think you said before it's a definitional point, right? You're defining what a complex is and what a salt is?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A What I'm showing is that under the definition of complex and salt, NSAIDs and quaternary ammonium compounds won't form complexes.

Q Because of -- you wouldn't use the terminology "complex" to refer to the potential entity that would be formed through interaction of an NSAID and a benzalkonium chloride ion; is that right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A Well, I've written down in this footnote exactly what a complex and a salt is and what a person of ordinary skill would understand a complex and a salt is, and Dr. Lawrence's defini- -- use of complex is not

correct.

Q Let's go back again just for a moment to Exhibit 2, the '876 patent.

If you look at column 1, line 16 --

A Sorry, I've got the wrong exhibit.

Q We're in Exhibit 2, '876.

A Okay. Column 1?

Q Column 1.

MS. LEBEIS: Make sure that you're there before answering.

Q Line 16.

You would agree that the authors of the '876 patent, right or wrong in your view, right or wrong, they refer to whatever is -- whatever they're hypothesizing is the interaction between BAC and NSAIDs as insoluble complexes. Do you see that word "complexes" on line 16?

MS. LEBEIS: Objection to the form of the question.

A Well, they're using the word "insoluble complexes" but without any evidence that they would actually form. Since they can't form complexes, I'm not -- I don't expect

STEPHEN G. DAVIES, D.PHIL.

them to be formed, and a person of ordinary skill reading this wouldn't expect complexes to be formed.

Q Okay. So we've established that the '876 patent uses that term "complexes," right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

Q Would you agree with me that the '876 patent uses the term "complexes"?

A The word "complexes" is written in the '876.

Q Then let's look, if you would, at the -- Exhibit 3, the '929 patent.

A Yes.

Q And if we can go in Exhibit 3 to column 1, line 34.

A Yes.

Q And you would agree that the '929 patent also uses the word "complexes" in describing this phenomenon, right?

MS. LEBEIS: Objection to the form of the question.

A Well, I don't think there is a phenomenon, and maybe it is because they can't

form complexes.

Q Okay. But you see that it uses the term "complexes" there to describe the interaction between NSAIDs and BAC?

MS. LEBEIS: Objection to the extent it mischaracterizes the document and to the extent it mischaracterizes prior testimony. Objection to the form of the question.

A It uses the word "complexes," but there's no evidence that an interaction between an NSAID and benzalkonium occurs.

Q Then if you look at Exhibit 4, which is the EP '984 patent we were looking at earlier --

A Okay.

Q -- and we look at page 2, line 34 --

A Yes.

Q -- the EP '984 patent also uses the word "complexes" to describe the interaction between BAC and anionic drug compounds, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A Well, without any evidence it's a hypothetical interaction. They use the word

"complexes," but there's no evidence that complexes or salts form.

Q So it's your view that a person of skill in the art -- and, again, a person of skill in the art related to these patents that are at issue, that person wouldn't use the word "complex" in talking about the interaction of NSAIDs and benzalkonium chloride even though each of the prior art references that we looked at just now all use that word in referring to that interaction --

MS. LEBEIS: Objection.

Q -- is that right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony. And objection to the form of the question.

A Whatever the personal people writing these patents are using for a term to describe the precipitate or whatever, there's no evidence that such a precipitate exists.

Q But in your view, all these people writing these patents, they're all wrong to refer to it as a complex, right?

MS. LEBEIS: Objection.

STEPHEN G. DAVIES, D.PHIL.

Mischaracterizes prior testimony and argumentative.

A It's not -- it does not fit within the absolute definition of a complex or a salt.

Q From a chemist's perspective.

A From any scientist's perspective.

Q Except for these scientists who wrote these patents, right?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony. Argumentative. Asked and answered.

A There's no evidence what the precipitate is so they may well think it is a complex, but I can't see how one forms.

Q Could you envision a way in which a salt might form between an NSAID and benzalkonium chloride?

MS. LEBEIS: Objection. Calls for speculation.

A I can envisage a way that a salt can be formed in solution. Well, as I said previously, potentially a salt can form from anything that has a plus charge with anything that has a minus charge. And whether it does

STEPHEN G. DAVIES, D.PHIL.

requires experimentation to find out.

Q So, potentially, a salt could form between the plus charge of the benzalkonium ion and the minus charge of an NSAID compound at pHs relevant to ophthalmic solutions?

MS. LEBEIS: Objection to the form of the question. Calls for speculation. Improper -- incomplete and improper hypothetical.

A It's a theoretical possibility, but without any evidence, you don't know it's going to happen.

MS. RAPALINO: Let's mark as Davies Exhibit 6 U.S. Patent Number 5,110,493.

(Exhibit 6 was marked for identification and attached to the deposition transcript.)

BY MS. RAPALINO:

Q Exhibit 6 is another U.S. patent you reviewed in forming your opinions in this case?

A (Document review.)

I don't recall looking at it at this moment. Can you refresh my memory?

Q Okay. We'll just take a look at the patent, and maybe, as we look at it, that will

refresh your memory. This patent issued in May of 1992, right? That's the date of the patent?

MS. LEBEIS: Objection calls for a legal conclusion.

A It says the date of the patent is May 1992.

Q It's entitled, "Ophthalmic NSAID formulations containing a quaternary ammonium preservative and a nonionic surfactant," right?

A And a nonionic, yes.

Q The first sentence of the abstract on the cover page of the '493 patent, Exhibit 6, describes the invention as directed to a "stable, clear, antimicrobially effective ophthalmic formulation," right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A So that's the first part of the first sentence, yes.

Q Right. And the rest of that sentence more specifically describes the subject of the patent as formulations including "especially a carboxylic acid group-containing drug or an NSAID, a quaternary ammonium preservative, and

a nonionic surfactant all in an aqueous vehicle," right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A Well, that's what it says in the abstract. Whether that's what it does in the rest of it, we would have to have a look.

Q That's what the abstract says anyway, right?

A You've just read from the abstract, so yes.

Q If you look at column 1, starting at line 36 --

A Okay.

Q -- the patent says, "While the formulations described in the '151 patent were efficacious, a complex was found to form between the NSAID and BAC." Do you see that?

A That's what it says, yes.

Q And, again, this patent uses the term "complex" to describe the interaction between NSAID and BAC, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

STEPHEN G. DAVIES, D.PHIL.

A Well, I assume it's quoting from the '151 patent rather than using it itself.

Q But it repeats then what the '151 patent -- what you suppose the '151 patent says, which is that it's a complex that forms between the NSAID and BAC?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony.

A We would have to look at the '151 patent to see what it actually says. I haven't seen any evidence that precipitate forms between an NSAID and BAC.

Q Again, just to be clear, this patent, the '493 patent, refers to a complex. It uses the word "complex" when talking about the interaction between NSAID and BAC, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document and prior testimony and asked and answered.

A Well, the word "complex" is there, but looks like it's a quote from the '151 rather than the authors of the '493 using it.

Q And if we look at the bottom of column 1, line 65, in the '493 patent, which is

STEPHEN G. DAVIES, D.PHIL.

Exhibit 6 --

A Okay.

Q -- it says, "Benzalkonium chloride, a quaternary ammonium compound, has been widely used in ophthalmic solutions and is considered to be the preservative of choice."

Do you see that?

A That's what it says there, yes.

Q That's consistent with the descriptions of benzalkonium chloride that we've seen in some of the other patents we've looked at, right?

MS. LEBEIS: Objection to the form of the question.

A Similar statements have been made but without any substantiation.

Q Then the next sentence goes on to say, "However, BAC has typically been considered to be incompatible with anionic drugs (e.g., salicylates or nitrates, et cetera), and can be inactivated by surfactants."

Do you see that?

A That's what it says there.

STEPHEN G. DAVIES, D.PHIL.

Q If you go to column 2, line 8, the '493 patent also says that "These NSAIDs have proven to be incompatible with quaternary ammonium compounds such as BAC because they can form a complex with them, rendering the preservative less available to serve its function, as is the case with other ophthalmic drugs that contain a carboxylic acid group."

Do you see that?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A Well, you're reading from the patent so I can see the words.

Q So that statement in the '493 patent, that's consistent with statements we've seen in the prior -- each of the prior patents that we've looked at, right?

MS. LEBEIS: Objection to the form of the question.

A Well, similar statements have been made in other places but without demonstration that it forms a complex.

Q And if we look at column 4 of the '493 patent --

A Yes.

Q -- you see that there's a paragraph that begins at around line 20 that starts, "NSAIDs useful in the practice of this invention"?

A Yes.

Q That paragraph lists a number of NSAIDs for use in the formulations of this invention, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

THE WITNESS: Can you repeat the question, please.

(Record read.)

A It lists some NSAIDs, yes, none of which are bromfenac. But it lists some.

Q And the patent here doesn't describe any structural differences between these different NSAIDs that would affect their use in this formulation, right?

A Well, it just names them, so -- and in context of the patent, they wouldn't need to.

Q And there's no discussion in this

patent of any differences in electron density between those different NSAIDs that would be relevant to the use of these patents in this formulation?

A Such a discussion wouldn't be relevant to this patent so they wouldn't need to discuss them.

Q There's also no discussion in here of any differences between any of those listed NSAIDs in terms of whether they're primary, secondary, or tertiary amines as relevant to whether they would be useful in this formulation?

A They obviously didn't think it was necessary to do so, no.

Q There's also no discussion here of the presence or absence of halogenation of the different NSAIDs listed here as being relevant to their use in this formulation, right?

A They don't need to in the context of the patent.

Q There's likewise no discussion here of differences in lipophilicity as between these different NSAIDs listed in column 4 with

respect to their usefulness in the formulation of the patent, right?

A There's no discussion because they wouldn't need to.

Q And, likewise, there is no discussion here about the differences in degree of hydrogen bonding as between the different NSAIDs set forth in this patent as useful in this formulation?

A The same answer. They don't need to discuss it in the context of the patent.

Q The nonionic surfactants that are called out as useful in the formulations in this patent at column 4, starting at line 32, include preferably polyoxyethylated surfactants, right?

A That's what it says, yes.

Q And I think you -- is that the same as saying polyethoxylated octylphenol surfactant?

A Yes.

Q And I think you said earlier that octoxynol 40 is one such surfactant, right?

A Yes.

Q Tyloxapol is another polyoxyethylated surfactant, right?

A It's one of a very large family of such compounds, each of which have their own properties.

Q So tyloxapol is in the family of polyethoxylated surfactants?

A It has chains of polyoxyethylated groups attached to it. In that sense, yes.

Q And it's actually a polyethoxylated octylphenol surfactant, right?

A Well, you say oligomer of -- not an oligomer. It's a co- -- it's got a group -- it's got seven such head groups and seven chains.

Q You wouldn't want to call it an oligomer, would you?

A It's not an oligomer.

Q Okay.

A I misspoke.

Q And it's an -- the head group -- the head groups in tyloxapol are octylphenol head groups, right?

A It has -- tyloxapol has seven such

head groups.

Q By "such," you mean seven octylphenol head groups?

A Substituted octylphenols, yes.

Q So you would agree that it's in the family of polyethoxylated octylphenol surfactants?

A It's one of a very large number of such things, each of which will have its own properties.

Q As of 2003, how many polyethoxylated octylphenol compounds have been used in approved ophthalmic solutions?

MS. LEBEIS: Objection. Calls for speculation.

A I haven't done that analysis.

Q So you didn't consider how many ethoxylated octylphenol surfactants were in use in approved pharmaceutical products in reaching your opinions in this case?

MS. LEBEIS: Objection, asked and answered, form of the question.

A I didn't do the analysis of how many there were.

STEPHEN G. DAVIES, D.PHIL.

MS. RAPALINO: Let's mark as Davies Exhibit 7 U.S. Patent 5,504,113.

(Exhibit 7 was marked for identification and attached to the deposition transcript.)

BY MS. RAPALINO:

Q This is another U.S. patent, right?

A It's a United States patent, yes.

Q Do you recall whether you considered this patent in forming your opinions in this case?

A I believe I did, yes.

Q It's a patent that the date of the patent is April of 1996, right?

A That's correct.

Q It's entitled "Enhancement of benzalkonium chloride preservative activity in formulations containing an incompatible drug," right?

A That's what the title says, yes.

Q What did you understand incompatible drug to mean in that title?

A Well, I didn't know when I read the patent precisely because they don't -- don't they give an example of the -- I'll have to

check -- of an incompatible drug?

Q Are you familiar with The Merck Index?

A Yes.

Q Is that a reference that you use in your work?

A I have used it, yes. It's on my shelf.

Q And is it a reliable reference?

MS. LEBEIS: Objection. Calls for speculation.

A It's what it is. It gives you a very brief summary of a somewhat random list of properties of biologically active molecules.

Q When you say it's on your shelf, is it a book that you consult and rely upon in the course of doing your work?

MS. LEBEIS: Objection, asked and answered.

A I use it very infrequently. It's on my shelf because they gave it to me.

Q Who gave it to you?

A Whoever publishes The Merck Index.

Q Okay. Is it a -- is it a common

reference text for chemists to use?

A It used to be before Google arrived.

Q As of 2003 -- I guess Google was probably around, but was it something that was in use in around 2003?

A I would think so.

Q If we look at -- going back now to Exhibit 7, the '113 patent --

A Okay.

Q -- the abstract of this patent describes the patent as covering a formulation that includes an acceptable drug, including flurbiprofen or ketorolac tromethamine that is interactive with benzalkonium chloride, right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A Sorry, what was the question that you asked me.

Q The abstract of this patent describes the patent as covering a formulation that includes an acceptable drug including flurbiprofen or ketorolac tromethamine that is interactive with benzalkonium chloride, right?

A That's what it says in the abstract,

but you have to read the body of the patent to see what they're actually doing.

Q We'll get there.

And the abstract specifies that interactive with benzalkonium chloride means that the drug forms a precipitate with benzalkonium chloride, right?

A I don't think they give any evidence that that's the case.

Q That's what the abstract says, right?

MS. LEBEIS: Objection, asked and answered.

A That's what the words in the abstract say. It's meaningless unless there's some evidence produced.

Q And then if we look at column 1 of the '113 patent, and I'm looking now starting at line 31 --

A Okay.

Q -- it says, "Therefore, benzalkonium chloride, which is a quaternary ammonium compound, has been widely used in ophthalmic solutions."

Do you see that?

STEPHEN G. DAVIES, D.PHIL.

A That's what it says.

Q That's consistent with prior statements we have seen in other patents we've looked at?

MS. LEBEIS: Objection to the form of the question.

A The words are consistent, but nowhere is any evidence produced.

Q And then it goes on to say, "It is also well-known, however, that benzalkonium chloride is considered incompatible with anionic drugs, forming insoluble complexes which cause the solution to turn cloudy."

Do you see that it says that?

A The words are there, yes.

Q And those words are also consistent with the prior statements we've seen in the other patents we've looked at, right?

MS. LEBEIS: Objection to the form of the question.

A It's consistent with the words in other patents, but in no case has it been demonstrated that any cloudiness is due to insoluble complexes.

STEPHEN G. DAVIES, D.PHIL.

Q Then the next paragraph starting at line 37 goes on to say, "This is because of the fact that many anionic drug entities carry a negative charge at physiological pH. In fact, all acidic drug entities will carry a negative charge at all pHs above their PKAs."

Do you see that?

A I can read that, yes.

Q Okay. And you agree that anionic drug entities -- I'm sorry, acidic drug entities will carry a negative charge at all pHs above their PKAs?

A That is correct, yes.

Q Then the next sentence goes on to say, "In the case of benzalkonium chloride, which is a positively charged preservative, insoluble complexes can be formed with acidic drug entities causing the drug to precipitate out of solution."

Do you see that?

A I read those words, yes.

Q You agree that benzalkonium chloride is a positively charged preservative, right?

A Well, it contains the benzalkonium

cation that is positively charged, and it's a preservative, I agree with that.

Q And given that benzalkonium -- the benzalkonium ion is a positively charged ion and that acidic drug entities will be negatively charged at pHs above their PKAs, you agree that insoluble salts may form between an acidic drug and benzalkonium chloride, causing the drug to precipitate out of solution, right?

MS. LEBEIS: Objection to the form of the question, calls for speculation, and to the extent it mischaracterizes the document.

A It's possible that a salt could be formed under certain circumstances between anything that has a positive charge and anything that has a negative charge, but I have seen no evidence to suggest that it happens in the cases that are being discussed here.

Q And then if we look down to the paragraph that begins just after that chemical structure in column 1, so we're about line 57 --

A Yes.

STEPHEN G. DAVIES, D.PHIL.

Q -- it says, "As hereinbefore noted, it is well-known that benzalkonium chloride is generally incompatible with anionic detergents or anionic drug compounds."

Do you see that?

A That's what the words say there, yes.

Q For that proposition, the patent cites The Merck Index, 11th Edition, Merck & Company, Inc., 1989, right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A It says "See The Merck Index." The Merck Index isn't a primary source of results. So I doubt there's any data in The Merck Index.

Q Okay. But it cites The Merck Index for the proposition that BAC is "generally incompatible with anionic detergents or anionic drug compounds," right?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A The Merck Index is cited in that paragraph, yes.

MS. RAPALINO: Let's mark as Davies Exhibit 8 U.S. Patent 6,265,444.

STEPHEN G. DAVIES, D.PHIL.

(Exhibit 8 was marked for identification and attached to the deposition transcript.)

BY MS. RAPALINO:

Q Exhibit 8 is a U.S. patent that you considered in forming your opinions in this case; is that right?

A It is, yes.

Q It issued, or the date of the patent is July 2001, right?

A The date of the patent is, yes, July 2001.

Q It's entitled "Ophthalmic composition"?

A Yes.

Q And it's assigned to InSite Vision, Incorporated, right?

A Yes, it is.

Q Then if we look at column 2, starting at line 34, the '444 patent at Exhibit 8 says, "Additionally, preserving an ophthalmic composition that contains an NSAID can be problematic."

Do you see that?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A That's what it says in the introductory part to this patent without any evidence, yes.

Q And then the next sentence goes on to say, "Conventional broad spectrum antimicrobial agents like BAC tend to interact with the NSAID agents over time and thereby reduce the efficacy of the medication."

Do you see that?

MS. LEBEIS: Objection.

Mischaracterizes the document.

A That's what it says in this introductory part of the patent without any data to back it up.

Q And those statements are consistent with the statements that we've seen in the prior patents that we looked at, right?

MS. LEBEIS: Objection to the form of the question. Vague and ambiguous.

A We've seen similar statements, but there's never anything to back it up.

Q If you look for a moment at the claims of this patent, the '444 patent,

starting at column 15 and going on to column 16.

A Yes.

Q Do you see that this patent is generally directed to compositions that are suspensions?

MS. LEBEIS: Objection. Calls for a legal conclusion.

A Where do I see that?

Q So, for example, if we look at claim 1, it talks about compositions wherein from "about 80 mole percent to less than 100 mole percent of said agent is in the form of a precipitate."

Do you see that?

A I see that, yes.

Q And do you understand that to be a suspension formulation?

A Not without reading the bulk of the patent.

Q Do you see, in claim 29 at column 16, that the composition being claimed explicitly describes it as an aqueous suspension?

A Well, it says, "An ophthalmic

composition comprising an aqueous suspension of a crosslinked carboxyl-containing polymer, solid diclofenac in free acid form, dissolved diclofenac, and dissolved magnesium two plus or calcium two plus cations." So that says it's a suspension.

Q Okay.

Then if you look at column 7 of the '444 patent at line 55.

A Line what, say, 65?

Q Line 55.

A 55.

Q Do you see that the patent says, "It should be noted that BAC was found to be unexpectedly compatible with diclofenac in the present ophthalmic composition"?

A That's what it says, so that means, presumably, there was no complex or precipitate formed.

Q Could you point me to the experimental data that shows that in this patent.

A I'm just reading the words you just read to me.

STEPHEN G. DAVIES, D.PHIL.

Q Okay. So in this instance you feel that you can just read the words without the experimental data?

MS. LEBEIS: Objection, argumentative, and to the extent it mischaracterizes prior testimony.

A Well, as I read it, it implies -- well, I better look at the -- read the whole thing again. But it says it's unexpectedly compatible, presuming nothing untoward is going on. So there's no adverse event.

Q So when it says that -- when the statement in the patent is that it was unexpectedly compatible, you just take that at face value, but statements that say that benzalkonium chloride and NSAIDs are incompatible, for those you would need some experimental data? Is that your position?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony, argumentative, and asked and answered.

A This is in -- I'm reading it in the Detailed Description of the Invention.

Q Oh, so because it's in the section

STEPHEN G. DAVIES, D.PHIL.

"Detailed Description of the Invention," you don't need experimental data to believe it; is that right?

MS. LEBEIS: Objection to the extent that it mischaracterizes prior testimony, argumentative, and asked and answered.

A Well, I think there's a difference between assuming there's a problem in some instances and being told there is no problem in another instance. That's different.

Q Is there any difference between being told there is a problem and being told there isn't a problem?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony, argumentative, and asked and answered.

A I would say there's no -- there's only a problem when you encounter one. If you don't encounter a problem, that's fine.

Q And you'd take at face value a statement that no problem was encountered, but you wouldn't take at face value a statement that a problem was encountered? Is that your view?

STEPHEN G. DAVIES, D.PHIL.

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony, argumentative, and asked and answered.

A I've seen no evidence that a problem exists with an acid precipitating or causing turbidity with benzalkonium salts whereas this is describing a nonproblem.

Q So to believe a statement about a nonproblem, you don't need experimental data to show that?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony, argumentative, and asked and answered.

A A problem only exists when it occurs. If something works the way it is supposed to work and there is no problem, why invent one.

Q What do you understand the authors to mean when they say that BAC was unexpectedly compatible with diclofenac? What do you understand to be unexpected about that?

MS. LEBEIS: Objection to the extent it calls for speculation. Mischaracterizes the document.

A I don't know is the answer, but what

you take out of that is BAC is compatible with diclofenac.

Q And you don't take out of that that the authors didn't expect BAC to be compatible with diclofenac?

MS. LEBEIS: Objection to the extent it mischaracterizes prior testimony. Argumentative.

A The sentence says what it says. What I take out of it is that BAC is compatible with diclofenac. What they're expecting or not is irrelevant to the fact that BAC is compatible with diclofenac. It does not precipitate.

Q Now, the authors of this patent hypothesize a theory as to why this -- why BAC is unexpectedly compatible with diclofenac in the formulations discussed in this patent, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A You'll have to show me where that is.

Q I'm looking at column 7, starting at line 57.

A Well, they're basically saying they

haven't got a clue because they say "the reasons are not entirely clear, and without wishing to be bound by any theory, the presence of the divalent cation is believed to prevent BAC from complexing the diclofenac out of the system." There's no basis for that.

Q So what is the theory they're proposing here as to why the BAC here is unexpectedly compatible with diclofenac?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A They haven't really got one. They're just basically saying that because there's some divalent cations in there, maybe that's got something to do with it, but they don't want to be bound by it at all because they have no experimental evidence that that's true.

Q Right. So they're just proposing a theory as to what might be preventing the BAC from complexing with the NSAID, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A They're not really proposing a theory because they say they don't want to be bound by

it.

Q Right. But they say that's what they believe is happening.

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A You have to read the whole sentence. It's obvious that they are completely unsure what's going on.

Q Right. They're not sure, but they say "the presence of the divalent cation is believed to prevent the BAC from complexing the diclofenac out of the system," right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document. Asked and answered.

A A person of ordinary skill reading that sentence would understand they don't know what's going on.

Q Right. And a person of skill in the art would understand that they believe that the presence of the divalent cation is preventing the BAC from complexing the diclofenac out of the system, right?

MS. LEBEIS: Objection to the extent

it mischaracterizes the document and to the extent it mischaracterizes prior testimony, asked and answered.

A If you read the whole sentence, it's clear they don't know what's going on.

Q They don't know for certain what's going on, right?

MS. LEBEIS: Objection, asked and answered.

A They don't know what's going on, and that's why they say that they don't want -- that it's not clear and they don't want to be bound by anything they're talking about.

Q But then they postulate a theory, right?

MS. LEBEIS: Objection, asked and answered.

A If you read the whole sentence, as I read the whole sentence, it's clear they don't know what's going on.

Q You haven't seen any prior art bromfenac formulations that contain magnesium chloride or calcium chloride, have you?

MS. LEBEIS: Objection. Calls for

STEPHEN G. DAVIES, D.PHIL.

speculation. Vague and ambiguous.

A I don't recall any.

MS. LEBEIS: I think it might be a good time for a break. We've been going for about an hour and a half. Short break?

MS. RAPALINO: Sure, take a break.

THE VIDEOGRAPHER: We're going off the record at 2:41 p.m.

(A brief recess was taken.)

THE VIDEOGRAPHER: We're going back on the record at 2:51 p.m. This is the start of disc number 5 in the deposition of Stephen Davies.

MS. RAPALINO: Let's mark as Davies Exhibit 9 U.S. Patent 5,597,560.

(Exhibit 9 was marked for identification and attached to the deposition transcript.)

BY MS. RAPALINO:

Q Is this a patent you considered in forming your opinions in this case?

A Yes.

Q The date of the patent is January of 1997, right?

A That's correct.

STEPHEN G. DAVIES, D.PHIL.

Q It's entitled, "Diclofenac and tobramycin formulations for ophthalmic and otic topical use," right?

A Yes.

Q If we look at column 2, starting at line 18 --

A Yes.

Q -- do you see that the patent describes that "Fu, et al., reports that the use of nonionic surface active agents, especially polyoxyethylene alkylphenol surfactants, avoids the unacceptable interactions between NSAID and quaternary ammonium compounds, wherein the NSAID and quaternary ammonium compound form a complex that is either insoluble or retards the absorption of the NSAID"?

A That's what it says there, yes.

Q This reference to "unacceptable interactions between NSAID and quaternary ammonium compounds" is consistent with the statements we've seen in the other patents we looked at regarding those interactions, right?

MS. LEBEIS: Objection to the form of

the question. Vague and ambiguous.

A It's consistent with some of the other things we've seen, but yet again, there's no evidence that the problem actually exists.

Q This statement also refers to the use of polyoxyethylene alkylphenol surfactants as a way of avoiding unacceptable interactions. Do you see that?

A Well, it's -- that's what it said, but since we haven't seen any evidence that there are unacceptable interactions between an NSAID and quaternary ammonium compounds, it's hard to see what's been avoided.

Q Then if we look at column 6, comparative example C, toward the bottom -- do you see that?

A Yes.

Q And it describes in comparative example C that two comparative controls were prepared, one with sodium diclofenac as the active and the other with tobramycin as the active ingredient. Do you see that?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

STEPHEN G. DAVIES, D.PHIL.

A That's what it says.

Q And those were compared to another formulation that had diclofenac, tobramycin, benzalkonium chloride, and octoxynol 40, right? I'm just reading at the beginning of comparative example C now.

A Oh.

Okay, yes.

Q So then you would agree with me the comparative controls were the same as that formulation of sodium diclofenac, tobramycin, benzalkonium chloride, octylphenol 40, but just each of those controls had just a single active ingredient, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A (Document review.)

I'm sorry, what was the question, please?

Q I'm just trying to make sure we both -- we're on the same page in terms of what they're doing in comparative example C.

A Yes.

Q So you would agree that there was one

STEPHEN G. DAVIES, D.PHIL.

formulation that contained sodium diclofenac, tobramycin, BAC, and octoxynol 40, right?

A Yes.

Q Then there were two controls, each of which contained either diclofenac or tobramycin along with those other ingredients that were in that first formulation, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

Dr. Davies, you should feel free to read the entirety of comparative example C and not just the portions that counsel has directed you to.

A (Document review.)

It doesn't specifically say that all of the other components were the same.

Q Is that your understanding of what a control is?

A I guess in this case we can take that.

Q And you would agree that the formulation that contains diclofenac, BAC, and tyloxapol after 41 days at 4 degrees did not develop a precipitate, right?

STEPHEN G. DAVIES, D.PHIL.

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A Repeat the question --

Q Sure.

A -- please.

Q The control formulation containing diclofenac, BAC, and octoxynol 40 did not develop a precipitate after storage for 41 days at 4 degrees, right?

A After 41 days they didn't develop a precipitate.

Q Right.

You agree with that?

A That -- I agree with that, yes.

I note that a precipitate that was formed isn't anything to do with BAC.

Q Right. There was a precipitate that formed in the presence of octoxynol 40, but that was a precipitate between the two active ingredients, right?

A Right. So BAC isn't involved, wasn't involved.

Q Right. So octoxynol 40 successfully prevented the precipitate -- any precipitate

from forming in the formulation of diclofenac, BAC, and octoxynol 40, right?

MS. LEBEIS: Objection to the extent it mischaracterizes the document.

A I wouldn't come to that conclusion because -- well, there was no precipitate, but you don't know that it -- anything is preventing the formation of a precipitate. It's not evidence that a precipitate would have been formed between BAC and either of the active ingredients.

Q If you keep this Exhibit 9 open in front of you but also pull out Exhibit 4, which is the EP '984 patent.

A Okay.

Q If you would turn to page 9 of the EP '984 patent, Exhibit 4.

A Okay.

Q You would agree that in Exhibit 9, the '560 patent, we see a report of no precipitate in a formulation of diclofenac, BAC, and octoxynol 40, right?

A Where do I see that?

Q We're looking now back at the '560