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UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD

ARGENTUM PHARMACEUTICALS LLC,)	
)	
Petitioner,)	Case No.
)	IPR2017-00807
v.)	
)	U. S. Patent No.
CIPLA LIMITED,)	8,168,620
)	
Patent Owner.)	

DEPOSITION OF WARNER WESTOVER CARR, M.D.
IRVINE, CALIFORNIA
WEDNESDAY, FEBRUARY 7, 2018

REPORTED BY:
LINDSAY PINKHAM
CSR NO. 3716

1 Deposition of WARNER WESTOVER CARR, M.D.,
2 taken on behalf of Petitioner, commencing at 9:02 a.m.,
3 Wednesday, February 7, 2018, at 15785 Laguna Canyon
4 Road, Suite 100, Irvine, California 92618, before
5 LINDSAY PINKHAM, CSR 3716, CCRR 17.

6

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I N D E X

WITNESS	EXAMINATION BY	PAGE
WARNER WESTOVER CARR, M.D.		
	MR. HOUSTON	4, 291
	MR. LaROCK	290

E X H I B I T S

EXHIBIT NO.	DESCRIPTION	PAGE
Exhibit 1010	Printout of December 1998 Flonase label, 9 pages	297
Exhibit 1055	Copy of a portion of a document labeled "Dr. Accetta Patient Record," 1 page	12

INSTRUCTIONS NOT TO ANSWER

(None)

INFORMATION REQUESTED

(None)

1 IRVINE, CALIFORNIA; WEDNESDAY, FEBRUARY 7, 2018

2 9:02 A.M.

3

4 WARNER WESTOVER CARR, M.D.,

5 having been first duly sworn,

6 was examined and testified as follows:

7

8 EXAMINATION

9 BY MR. HOUSTON:

10 Q Good morning, sir. Could you start by stating
11 your full name for the record.

12 A Yes. My full name is Warner Westover Carr.

13 Q And is "Dr. Carr" okay for me to refer to you
14 as today?

15 A Sure.

16 Q Good morning, Dr. Carr. My name is Michael
17 Houston. I'm an attorney with Foley & Lardner, and we
18 represent the petitioner in this case, Argentum
19 Pharmaceuticals. And I understand you're a witness here
20 today on behalf of the patent owner Cipla. Is that
21 right?

22 A That is correct.

1 Q And I believe you've been deposed at least one
2 other time in the proceeding on this same patent and on
3 another patent in a case that was Cipla and Meda versus
4 Apotex. Is that correct?

5 A Yes, that's correct.

6 Q So I'm going to assume that you're familiar,
7 generally familiar with the rules of the deposition, but
8 I'll just highlight a couple of things this morning for
9 you, and you can let me know if you need further
10 explanation.

11 But you understand that you're under oath now,
12 and that I'm going to ask you a series of questions,
13 you're going to answer them to the best of your ability,
14 unless your attorneys instruct you not to, and the court
15 reporter's going to try to record my questions and your
16 answers as best she can. You understand that?

17 A Yes, I do.

18 Q And also, because of your familiarity with this
19 general subject matter, particularly in regards to the
20 prior case, I will sort of tend to assume a level of
21 knowledge on your part, familiarity with the material on
22 your part. So I might tend to use acronyms and things

1 like that. I'm certainly not an expert like you are,
2 and so I may misstate things from time to time.

3 But if I do either one of those things, use
4 acronyms or misstate things, please feel free to correct
5 me or ask for clarification if you're not sure what I
6 mean. Fair enough?

7 A Thank you.

8 Q Dr. Carr, as of 2002 -- and when I say 2002,
9 what I'm really referring to is as of the filing date of
10 the '620 patent in this proceeding, okay? As of 2002,
11 it's true that you and other doctors in your profession
12 had prescribed the drugs Astelin and Flonase nasal
13 sprays for sequential administration by your patients;
14 correct?

15 MR. LaROCK: Objection. Outside the scope.

16 THE WITNESS: So as of -- that's like 15 years
17 ago. It would be difficult for me to pull my records
18 from that time. So I would say that that is incorrect.

19 Q BY MR. HOUSTON: So incorrect as to you, or
20 incorrect as to doctors in your profession in general?

21 A Well, the practice as of 2002 was not to
22 administer azelastine or, for that matter, other

1 antihistamines, and a nasal steroid. You mentioned
2 fluticasone, which is one of the numerous number of
3 nasal steroids. The practice was not to administer them
4 sequentially, no.

5 Q All I'm asking is whether some doctors did in
6 fact do that as of 2002.

7 MR. LaROCK: Object to the form of the
8 question.

9 THE WITNESS: Okay. Well, again, it would be
10 hard to pull all doctors' records from 10, 15 years ago,
11 so I would have to basically rely on how, in my medical
12 community and the parameters that we used at that time,
13 those medicines were not recommended to be administered
14 sequentially, no.

15 Q BY MR. HOUSTON: Dr. Carr, I'm going to hand
16 you what's been marked as Exhibit Cipla 2021. And what
17 this is, this is a portion of the transcript from the
18 trial that I referenced earlier. And this includes some
19 of your testimony given at the trial, and I apologize
20 that it's such a big exhibit. That's the way it was
21 filed by Cipla in this proceeding.

22 So I'm going to ask you to turn to page 110 of

1 this document. Are you on page 110, Dr. Carr?

2 A Yes.

3 Q At line 10 you were asked by counsel in the
4 trial -- and by that point in time, and we're referring
5 to 2002, you see that right above; correct? So counsel
6 asked you:

7 "And by that point in time, you had
8 patients that received, your own
9 patients that received both Astelin and
10 Flonase nasal sprays administered
11 sequentially; correct?"

12 You answered:

13 "For a variety of reasons, yes. "

14 Did you testify to that effect in trial?

15 A Let me read the context that this question was
16 asked. So for clarification, on page 110, line 13, my
17 answer to the question actually was, "For a variety of
18 reasons, yes. "

19 Q Right. Which is what I read, wasn't it?

20 A I can't recall exactly what you read. But I
21 don't believe that was your question, no.

22 Q So the answer includes a "yes." Correct? So

1 that is true that your patients had received both
2 Astelin and Flonase nasal sprays administered
3 sequentially as of 2002. That's how you testified;
4 right?

5 MR. LaROCK: Object to the form of the
6 question. Also objection, outside the scope of this
7 declaration.

8 THE WITNESS: So look, again, these are
9 complicated issues, because I don't believe in my
10 declaration I referenced any of my patient charts or
11 records from 10, 15 years ago.

12 Patients are complicated. I have written
13 probably every single medication that there is to
14 prescribe for allergic rhinitis over the years. And
15 inevitably, inevitably, I'm sure if you ask any person
16 that was prescribing medicines, that their patients may
17 have ended up on these medications at the same time. So
18 it's very difficult to give a definitive "no" to that
19 question. So you have to realize the context.

20 The issue --

21 Q BY MR. HOUSTON: Dr. Carr, all I'm asking --
22 Dr. Carr, please, I have limited time today. I can't

1 let you go on indefinitely.

2 A I want to answer your question.

3 Q That wasn't my question, my question is simply,
4 is that how you testified? Did you say yes to that
5 question? And I believe the answer is that you did,
6 right. At trial in the testimony, as we see right here
7 on line 13, you testified "yes." Correct?

8 MR. LaROCK: Object to the form of the
9 question. Objection, mischaracterizes the document.

10 And Mike, if you can let the witness answer.

11 MR. HOUSTON: We have limited time, you know
12 that, Adam, so I'm not going to let him go on and on and
13 on, especially when I'm asking a very clear question. I
14 will of course try to defer to the witness when it's
15 appropriate.

16 MR. LaROCK: He was answering the question. I
17 think he was trying his best --

18 MR. HOUSTON: Well, we disagree about that.

19 THE WITNESS: So again, line 13 says, "For a
20 variety of reasons, yes." And I would say probably the
21 most common thing, and the standard that we would use
22 those medicines was it was on demand. So if those

1 patients were to sequentially get those medicines, it
2 would be an on-demand. So it's not something I would
3 have them do every day for long periods of time. It
4 would be on demand.

5 Q BY MR. HOUSTON: Okay. And we'll get to that
6 aspect of it later. I'm just asking if it occurred.
7 And you testified there that it did. Are you changing
8 your testimony today?

9 MR. LaROCK: Objection. Mischaracterizes the
10 document. Mischaracterizes what he previously said
11 also.

12 THE WITNESS: I will just recapitulate. I
13 think that the answer I gave in this document is
14 actually a good answer. So for a variety of reasons,
15 yes. But the caveat is, it's not a scheduled thing.

16 Q BY MR. HOUSTON: It wasn't for you.

17 A I don't think it was for anybody.

18 Q Okay. Did you sit through the whole trial, the
19 whole trial that was conducted between Meda and Cipla
20 and Apotex?

21 A I missed the very last little couple of
22 minutes, as I was heading off to catch a plane. But I

1 was there for pretty much the whole trial.

2 Q Were you there in the beginning, towards the
3 beginning?

4 A Yes.

5 Q Do you remember a Dr. Accetta testifying?

6 A Dr. Accetta?

7 Q Accetta, excuse me.

8 A I do remember him testifying, yes.

9 MR. HOUSTON: I'm going to ask the court
10 reporter to mark that as Exhibit 1055.

11 (Deposition Exhibit 1055 was marked
12 for identification.)

13 Q BY MR. HOUSTON: Dr. Carr, my review of the
14 transcript from the trial reveals that Dr. Accetta
15 testified that he did in fact prescribe Flonase and
16 Astelin together to his patients who had been diagnosed
17 with allergic rhinitis, and he referenced as one example
18 the patient record that you see sort of an extract from
19 here in Exhibit 1055. And he showed this and discussed
20 this at trial. Do you recall that?

21 MR. LaROCK: Object to this document as being
22 incomplete. Not quite sure what this document is.

1 Mischaracterizes the document. Also an objection,
2 mischaracterizes the trial testimony.

3 THE WITNESS: I don't believe this is part of
4 my declaration. So you're asking me to recall something
5 quite some time ago with just a small highlighted piece
6 of the document. Do you actually have the full document
7 for me to review so I could appropriately comment on it?

8 Q BY MR. HOUSTON: So you may or may not know
9 that Argentum, the petitioner here, was not a party to
10 that proceeding. And you may also see this document in
11 the bottom left was stamped "Highly Confidential." And
12 so these exhibits are not available to Argentum. None
13 of the exhibits other than these demonstrative exhibits
14 like the one you're viewing here are available to us.
15 So no, we don't have that.

16 So I'm simply asking if you recall Dr. Accetta
17 discussing this and testifying that he in fact
18 prescribed Flonase and Astelin. And if you don't
19 recall, that's fine. We have the trial testimony, so it
20 speaks for itself. I'm just asking for your
21 recollection.

22 MR. LaROCK: Object to the form of the

1 question.

2 THE WITNESS: Well, perhaps, if I may, I could
3 try to read the document behind rather than just what
4 you've highlighted.

5 Q BY MR. HOUSTON: Yes, please.

6 A I note the date of what appears to be an
7 encounter with a patient is March 26 of 2001.

8 Q Yes.

9 A And I notice that he has a physical exam listed
10 here, and it says the patient's physical examination is
11 normal. And I notice at the bottom that it says
12 "medicines," and the thing that's blown up. And the
13 first medicine, No. 1, says Flonase, two sprays b.i.d.,
14 which is double the approved dose of Flonase, very high
15 dose. And the start date there is 1-17-2000.

16 So then it says medicine No. 2, "plus Astelin,"
17 two sprays b.i.d. And that is the same day as this
18 encounter, 3-26-01. So it's unclear to me why
19 Dr. Accetta would say that the patient has a normal
20 physical exam but add another medication. You're just
21 going to get more side effects. And it's not clear to
22 me how this medication was used, because it's an

1 incomplete record, and I wasn't present for the visit,
2 so I don't know if he told to take the medication on a
3 demand basis or not. So that would be my best
4 characterization of this document.

5 Q Dr. Carr, I'm going to ask you again to try to
6 answer my questions. That was a whole bunch of review
7 and testimony that was not in response to my question.

8 My question was simply whether you recall
9 Dr. Accetta's testimony on this document. Do you recall
10 it from trial? That's a "yes" or "no" question, and if
11 you need to caveat it, you can, but I don't need the
12 whole analysis of the entire document.

13 So if you continue to do that, as I mentioned
14 earlier, I have a limited time here today, but if you
15 continue to do that, I'm going to have to call the board
16 and ask for extra time, and we're all going to stay here
17 longer. So that's the reason. I'm not trying to be
18 mean to you. Your counsel will have a chance to ask you
19 whatever questions they want when I'm done, and you can
20 testify all you want within those time limits.

21 So I'm just putting it on the record right now
22 that this is at least the second time that you're not

1 answering my question. So I just would ask you or
2 remind you to please try to do that going forward.

3 So let me ask again. Do you recall Dr. Accetta
4 testifying during trial that he prescribed Flonase and
5 Astelin to some of his patients that presented with AR?

6 MR. LaROCK: Objection, asked and answered.
7 Objection, outside the scope.

8 THE WITNESS: So again, it's taking me a little
9 bit of extra time, because this is not part of my
10 declaration, and you're asking me to recall things.

11 I do recall Dr. Accetta testifying. He was
12 present. I would need time to review the transcript to
13 refresh my memory, to recall all of the intricate
14 details of his testimony. So beyond that, that's the --
15 I tried to analyze the document, because, like I said,
16 it's outside of my declaration. But if you want me to
17 answer these, then I would need time to review this
18 stuff so I could give you the best possible answer. So
19 that's my caveat.

20 Q BY MR. HOUSTON: Okay. So you would agree that
21 at least this document seems to indicate that
22 Dr. Accetta did in fact prescribe those two medications

1 to one of his patients presenting with AR. Correct?

2 MR. LaROCK: Objection. Mischaracterizes the
3 document.

4 THE WITNESS: Dr. Accetta, like myself, and as
5 you referred to earlier, multiple doctors that prescribe
6 medicines, undoubtedly in a given patient probably
7 prescribed Flonase and Astelin to a given patient. But
8 how those medicines were used is a different story.

9 Q BY MR. HOUSTON: When you say "how they're
10 used," you mean what the patient ultimately does with
11 them? Is that what you mean when you said that, by
12 "how they're" -- I'm sorry, you said, "but how those
13 medicines were used is a different story." What did you
14 mean by that?

15 A Well, if you go back to your original question,
16 your question was to me, I believe -- and we can pull it
17 up if we need to -- the sequential use of these
18 medicines. So what I mean is what the instructions were
19 to the patient. The caveat here again is a presumption,
20 and that is that the instructions in this patient,
21 because the patient's exam was normal, was, here's some
22 Astelin, you can use it as needed, and you can do two

1 sprays twice a day on demand, because their exam was
2 normal. So I couldn't imagine him telling them to take
3 it sequentially. That's not what the standard of care
4 was at that time. And using this medicine was on
5 demand.

6 Q Oh, so what significance are you attaching to
7 the word "sequentially"? What does that mean to you?

8 MR. LaROCK: Objection to the form of the
9 question.

10 THE WITNESS: Well, perhaps in order to answer
11 your question initially about sequential use, could you
12 clarify to me, so we could be on the same page, what you
13 mean by "sequential use."

14 Q BY MR. HOUSTON: Well, I only used that word
15 because that's the word that was used in the question
16 that was presented to you during your trial testimony.
17 Did your own patients receive both Astelin and Flonase
18 sprays administered sequentially?

19 And you said, for a variety of reasons, comma,
20 yes. So what was your understanding of "sequentially"
21 when you gave that testimony?

22 MR. LaROCK: Object to the form of the

1 question.

2 THE WITNESS: Well, in sequence. So one after
3 the other, but, like I said in my testimony, for a
4 variety of reasons. So there could be a time
5 difference, there could be a day difference, there could
6 be a season difference. So that's why there's that
7 caveat, "for a variety of reasons."

8 Q BY MR. HOUSTON: If Dr. Accetta testified at
9 trial under oath that he instructed the patients to use
10 both of these sprays, whether they're applied one after
11 another or whether there's some time delay in between,
12 you wouldn't have any reason to dispute his testimony,
13 would you?

14 MR. LaROCK: Objection. Outside the scope of
15 his declaration.

16 THE WITNESS: I guess if you could point to me
17 specifically in here where you're referencing, again, my
18 declaration didn't go into his testimony at trial. But
19 if you show me what you're talking about, I'd be happy
20 to comment on it.

21 Q BY MR. HOUSTON: As you can see, this is
22 already a large document, and this is only about

1 one-fourth of it. I didn't bring the whole thing. So I
2 don't have his testimony.

3 All I'm asking is, do you have any reason, as
4 you sit here today, to dispute his testimony about
5 co-prescribing these two drugs?

6 MR. LaROCK: Objection. Asked and answered.

7 THE WITNESS: I believe I've already answered
8 that.

9 Q BY MR. HOUSTON: And your answer was what?

10 A Could we pull that, what my answer was?

11 MR. HOUSTON: I don't think he answered it
12 before.

13 Q I'm just asking if you have a reason to dispute
14 Dr. Accetta's testimony at trial regarding his
15 co-prescription of these two drugs. And if you tell me
16 that all you can give me is the answer you already gave
17 me, that's fine, we can move on. Is that your answer?

18 MR. LaROCK: Object to the form of the
19 question. Objection, mischaracterizes his testimony and
20 also the trial record.

21 THE WITNESS: I will try to answer again to the
22 best of my ability, and I apologize if I don't use

1 exactly the same words as I used previously.

2 But like I said, at that time all of us
3 doctors, we probably have written every medicine. So
4 inevitably, there would be patients that ended up on
5 Flonase and Astelin. Typically those patients were told
6 to use the Astelin on demand.

7 Q BY MR. HOUSTON: Okay. So that's the extent of
8 any dispute you might have with Dr. Accetta's testimony
9 that he prescribed both of these two drugs to at least
10 some of his patients presenting with AR. Is that fair?

11 MR. LaROCK: Objection. Mischaracterizes
12 Dr. Carr's testimony.

13 THE WITNESS: No, I don't believe it's fair.
14 Like I said before, I would need to -- his testimony was
15 not in my declaration, so I would need to review his
16 testimony again. I would say my answer was a component.
17 It's not the full extent.

18 Q BY MR. HOUSTON: And all I'm asking you is, as
19 you sit here today, do you have any reasons to dispute
20 his testimony on that topic, as you sit here today?

21 MR. LaROCK: Objection. Asked and answered.

22 Q BY MR. HOUSTON: Any reasons that you're aware

1 of right now.

2 MR. LaROCK: Objection. Asked and answered.

3 And object to the form of the question.

4 THE WITNESS: So I think I just answered that
5 question a moment ago, and I could try to recap it if
6 you would like, or we could go back and read my answer
7 again.

8 Q BY MR. HOUSTON: Okay. Anything else --
9 there's nothing else to add to the testimony you've
10 already given; right?

11 A Well, we're going to be here for seven hours,
12 so there's a lot more to add to my testimony.

13 Q Okay, Dr. Carr, I suppose we'll move on, since
14 you don't want to give me a yes-or-no answer to that.

15 We did establish that at least in some
16 instances, as of 2002, you have prescribed to at least
17 some patients a steroid together with an antihistamine.
18 Correct?

19 MR. LaROCK: Objection. Mischaracterizes his
20 testimony.

21 THE WITNESS: Again, I've prescribed numerous
22 medications. I guess I would need you to be more

1 specific as to indications and so forth.

2 Q BY MR. HOUSTON: I'll get to indications in a
3 minute. I'm just asking -- I think you did testify
4 earlier, in fact, several times you said virtually all
5 doctors have at one time or another prescribed these two
6 drugs at the same time. Right?

7 MR. LaROCK: Objection. Mischaracterizes his
8 testimony.

9 THE WITNESS: No, that's not what I said. I
10 said inevitably -- I mean, I'd have to, again, I
11 apologize, I'd have to pull up the exact language. It
12 may not be exactly the same. But what I said was
13 inevitably, we prescribe all these different
14 medications -- leukotriene modifiers, et cetera, et
15 cetera. So inevitably, patients perhaps would have
16 ended up on these medications. But patients end up on
17 Tylenol at the same time.

18 And so there's a rationale, there's a practice
19 of medicine that we're talking about here. It's not a
20 knee-jerk reflex to prescribe those two drugs or any two
21 drugs at the same time.

22 Q BY MR. HOUSTON: I understand, Doctor. I'm

1 just asking whether or not you did it, at least, in some
2 instances, for whatever reason, as of 2002, as your
3 answer here on page 110 of Exhibit 2021, line 13,
4 suggests.

5 A For a variety of reasons, yes.

6 Q So the answer is yes, you have done it; right?

7 A For a variety of reasons, yes.

8 MR. LaROCK: Objection. Mischaracterizes the
9 document and his testimony.

10 Q BY MR. HOUSTON: Okay. So among those reasons,
11 was one of the reasons ever to treat AR?

12 A For which class of medicine?

13 Q Well, I'm just limited to your testimony here.
14 Because that's the only testimony that I have from you.
15 That's the only recollection that you apparently have,
16 is the question here is asking about patients that
17 receive both Astelin and Flonase nasal sprays
18 administered sequentially. And your answer was, "For a
19 variety of reasons, yes."

20 So now I'm asking you about the reasons. Was
21 one of the reasons ever for the treatment of AR?

22 A I would say each patient is complicated, and so

1 you're asking me to speculate. And the reasons could be
2 a multitude of reasons. So could perhaps a patient end
3 up on azelastine and Flonase for AR in my practice?
4 Again, I don't have my records in front of me, so I
5 can't give you firm data behind it. And you're asking
6 me to recall something over ten years ago. I would say
7 yes, but those patients would not use the Astelin on a
8 continuous basis. It would be on demand.

9 Q And so in those instances where the patients
10 were using the Astelin -- they were using Flonase
11 continuously and using Astelin on demand, was it your
12 belief that that combination worked better at relieving
13 AR symptoms than just the Flonase by itself?

14 A I can't answer that with a simple yes or no.
15 So I'll try to explain it to you. Over time our
16 understanding of how medicines work and treat patients
17 changes. So I'm trying to answer this question with
18 pre-2002 up to 2002 knowledge.

19 At that time, the thought process was that
20 there was no improvement over a nasal steroid alone with
21 the addition of an antihistamine. So I would say my
22 general thoughts at the time were that no, adding

1 azelastine on demand to fluticasone continuous probably
2 would not have improved AR that much.

3 Q Why would you have instructed your patients as
4 of that time to have done that, to have used Astelin on
5 demand in conjunction with the Flonase, if it wasn't to
6 improve the AR?

7 A Well, again, same caveats of recalling over 15
8 years ago. In general, these allergic rhinitis patients
9 are complicated. And they will -- I'm sure maybe
10 outside of legal proceedings, just in regular life,
11 you've had a friend or a relative that said, "Hey, you
12 know what, don't take Zyrtec, it doesn't work. But you
13 know what, Allegra really works." And then another
14 person will say exactly the opposite: "No, no, Allegra
15 doesn't work. Use Zyrtec. That really works."

16 So here's two different antihistamines and two
17 different patients that are giving two different
18 outcomes. And patients will cycle through all these
19 different medications. And in the setting of AR alone,
20 in the setting of AR alone, cycling through those
21 medicines usually ends up in the same result, no
22 improvement.

1 But every once in a while, a patient may have
2 something else. For instance, in Dr. Accetta's
3 document, which I'm looking at in front of me, the
4 patient has two diseases. The patient has allergic
5 rhinitis; the patient has chronic rhinitis. And we
6 don't have the whole document. They may have had other
7 diseases for which the nasal spray would have been
8 beneficial.

9 So it's a case-by-case thing, a
10 patient-by-patient thing. And patients are complex.
11 They're not just noses with allergies.

12 Q So certainly I'm intending to, at least at this
13 stage, caveat my questions for at least some patients,
14 because I would agree with you, I think I appreciate
15 that there is a lot of patient variation in terms of how
16 they might respond to drugs or what they may need in
17 order to get the response they're looking for.

18 So I'm just asking about whether there are any
19 patients in which you added the Astelin to a continuous
20 Flonase in the hopes of improving their AR symptoms.
21 Appreciating that the Astelin is added on demand, only
22 as needed.

1 MR. LaROCK: Object to the form of the
2 question.

3 THE WITNESS: So I want to make sure I answer
4 this question correctly. Again, patients and doctors,
5 for that matter, myself, that's the context of the
6 question, myself, would cycle patients through these
7 medications.

8 Our primary treatment would be to start them
9 actually on neither drug. Our primary treatment would
10 be to start them on an oral antihistamine. Those were
11 probably the most commonly used drugs at that time.

12 And then if that failed, we would typically try
13 another oral antihistamine, the whole Allegra-Zyrtec
14 example I gave you a moment ago. Then we would start
15 them on some kind of nasal steroid therapy.

16 But realize, even just like today, there's a
17 lot of steroid phobia. People don't -- they're worried
18 about taking a steroid. If that failed, we would
19 probably try another steroid or double the dose.

20 If that failed, typically we'd give an oral
21 steroid or an oral decongestant, something like Sudafed.
22 If they had really bad allergies, we might add a

1 chromone or an antileukotriene.

2 The use of azelastine was tiny, probably around
3 1 percent or less of all patients. So it's very
4 difficult for me to recall that small of a number of
5 patients over 10, 15 years ago. And I'm not trying to
6 be evasive. So I will give you a firm "perhaps." That
7 would be the best recall I could give you for something
8 that long ago for that specific of an indication for
9 that specific of a patient. But I think I've outlined
10 kind of what my treatment approach would be in general.

11 Q BY MR. HOUSTON: Okay. So -- and you said a
12 "firm 'perhaps.'" Is that what you said? I'm just
13 asking, because the transcript has it "form," and I just
14 want to clarify.

15 A Oh, I'm sorry.

16 Q That's okay. You said "firm 'perhaps'"?

17 A Another way to say it would be "maybe." Like I
18 said, it's hard to say yes or no to that question. So I
19 tried to kind of give you a glimpse into what our
20 treatment algorithm would be for those patients.

21 Q As of 2002, had you heard of anyone else in
22 your profession talking about the potential benefits of

1 prescribing -- or I should say of adding an
2 antihistamine such as Astelin to a steroid such as
3 Flonase for treating AR?

4 MR. LaROCK: Objection. Outside the scope of
5 his declaration.

6 THE WITNESS: I would say --

7 MR. LaROCK: And object to the form of the
8 question.

9 THE WITNESS: If I understand your question,
10 you asked, have I heard of anybody discussing the
11 potential benefit of combining those two medications.
12 And the answer I would give is yes, people have
13 evaluated the potential benefit. And what they found
14 was that there was no benefit of the combination of an
15 antihistamine and a nasal steroid over the nasal steroid
16 alone. And in fact, in some studies, which were the
17 best questions, I would say, there were increased side
18 effects.

19 So people had explored it prior to that time,
20 and so they had asked that question. And that was the
21 answer to their question. No, there is no benefit.

22 Q BY MR. HOUSTON: Let me limit the question to

1 the specific combination of fluticasone as the steroid
2 and azelastine as the antihistamine. So with that
3 limitation, let me ask it again.

4 As of 2002, had you heard of anyone in your
5 profession talking about the potential benefits of
6 prescribing those two specific drugs together for
7 treating AR?

8 MR. LaROCK: Object to the form of the
9 question. Objection, outside the scope.

10 THE WITNESS: In my declaration I have sections
11 where I review studies that look at the combination of
12 an antihistamine and a nasal steroid --

13 Q BY MR. HOUSTON: Different antihistamines and
14 steroids; right?

15 A What I was going to say is, I can't recall the
16 dates of all of the publications. So if you have a copy
17 of it, we could run through it real quick and see if
18 there was a good study prior to 2002 that looked at
19 those exact two combinations.

20 Q So to clarify --

21 MR. LaROCK: Are you done?

22 THE WITNESS: Yeah.

1 MR. HOUSTON: And I'm interrupting him, Adam,
2 because I think maybe he misunderstood my question, so
3 I'll try to clarify.

4 Q I'm not asking about studies. I'm just asking
5 about anyone in your profession. Another doctor.
6 Somebody speaking at a conference. It could be over
7 coffee. Whatever it is. Do you recall anyone as of
8 2002 discussing the potential benefits of using those
9 two specific drugs together to treat AR?

10 MR. LaROCK: Object to the form of the
11 question. Objection, asked and answered.

12 Q BY MR. HOUSTON: For the purposes of this
13 question, I will concede, for the purposes of this
14 question, that there aren't any studies. I'm not aware
15 of any studies. If there were, I probably would be
16 discussing that instead. So let's just assume for
17 purposes of this question that there aren't any formal
18 studies. I'm just talking about general discussions
19 among doctors at conferences, whatever it might be.

20 MR. LaROCK: Same objection.
21 You can answer.

22 THE WITNESS: So again, I'm going to focus on,

1 just in a general time that you asked me about.

2 Q BY MR. HOUSTON: But you are going to focus on
3 those two drugs; right?

4 A Yes, sir. Let's say we're in the doctor's
5 lounge getting a cup of coffee. If a conversation broke
6 out -- that's what you're talking about --

7 Q I'm not asking if you have any recollection of
8 it. I'm not hypothetical. I'm just saying, do you have
9 a recollection of it, yes or no?

10 A The recall that I have about using azelastine
11 really focused around its adverse event profile.

12 So to clarify, the medication has a lot of side
13 effects. And usually, if we had a conversation about
14 using that particular medicine, it would usually focus
15 around the adverse event profile, how bad the medicine
16 tastes, how sedating it is, my patients don't like this
17 medicine, those types of questions.

18 We would not -- I can't recall a time where we
19 were sitting around the coffee pot saying, yay, let's
20 use those two medications together. It would usually
21 focus immediately on the adverse event profile
22 associated with azelastine.

1 Q BY MR. HOUSTON: In your opinion going right to
2 the adverse event profile, is that because there was
3 some kind of understanding or presumption that they
4 could be efficacious together, and so therefore you were
5 concerned about the negative effects? Why would you
6 even be talking about it if there wasn't some hope or
7 belief or understanding that they had a potential
8 benefit? You wouldn't even consider it, would you?

9 MR. LaROCK: Object to the form of the
10 question. Objection, outside the scope.

11 MR. HOUSTON: Let me strike that question and
12 start again.

13 Q You wouldn't prescribe a combination of drugs
14 to a patient unless you thought it would at least
15 potentially provide a benefit to the patient; right?

16 A So to clarify, I mean, why would we even be
17 discussing these strategies? It was an FDA-approved
18 medication, so it would be something that would come up
19 as options.

20 But the reason we went right to adverse events
21 is because the experience from patients was quite
22 profound. And if you read the label, the adverse event

1 profile -- so it's a risk versus benefit, you know, so
2 it would be more like a risk-versus-benefit profile.

3 Yes, in the clinical studies that were
4 conducted to support the approval, it did show efficacy
5 in the population that it was studied in. But it also
6 had an unfavorable adverse event profile. So that's why
7 we would go right to the adverse events.

8 Q I just want to make sure that I'm clear. I'm
9 asking about the potential benefits of prescribing them
10 at the same time, for patient use at the same time.
11 Whether it's for a day, a week, I don't care about the
12 time period.

13 You're talking to me about FDA approval and the
14 benefits of one specific drug, Astelin. I understand
15 that that's been approved, so it must have some clinical
16 benefit for whatever its indications are. Otherwise
17 they wouldn't approve it. But I'm talking about for the
18 specific combination of those two drugs, there was never
19 a discussion about any potential benefit they might
20 provide to AR patients in prescribing them together that
21 you can recall?

22 MR. LaROCK: Object to the form of the

1 question. Objection, outside the scope.

2 THE WITNESS: I would say no.

3 Q BY MR. HOUSTON: That's fine. If you don't
4 recall, that's fine.

5 MR. LaROCK: Are you done? Did you finish?

6 THE WITNESS: That's okay.

7 Q BY MR. HOUSTON: I want to hand you an exhibit
8 that has been previously marked Exhibit 1045 in the
9 proceeding. Do you recognize that document?

10 A Yes.

11 Q It's what's, I think, referred to in your
12 declaration as the Ratner 2008 reference; is that right?

13 A That's correct.

14 Q I'd like to direct your attention to the first,
15 the very first line up in the first page under the
16 heading -- subheading "Background." And there this
17 article says:

18 "To our knowledge, there are no
19 published studies that evaluated the
20 efficacy of azelastine hydrochloride
21 nasal spray in combination with an
22 intranasal corticosteroid, although

1 anecdotal reports of the use of these
2 agents in combination are common."

3 Do you see that?

4 A I see that.

5 Q Do you have any reason to dispute this
6 reference's report that anecdotal report of the use of
7 these agents in combination are common?

8 A So just to be clear, previously you were asking
9 me about pre-2002.

10 Q That's correct.

11 A Now we're talking about 2008. Right? This is
12 a 2008 paper.

13 Q Yeah, I believe we can say that it published in
14 2008. It looks like the final revision to the
15 manuscript was sent in July 26, 2007. But if your
16 question is, are we moving forward in time, obviously,
17 that's when this paper was submitted.

18 And so as of the time of this paper, they're
19 saying that these reports are common. Right?

20 A My understanding of this sentence is that by
21 2008, there were anecdotes, yes.

22 Q And I'm just asking, do you have any reason to

1 dispute that?

2 MR. LaROCK: Objection. Asked and answered.

3 THE WITNESS: That's what they wrote.

4 Q BY MR. HOUSTON: Okay. Similarly, when Meda
5 submitted its package to the FDA in 2008, they also
6 reported to the FDA that this was a common practice
7 among allergists; right? Would you like to review that?

8 A I would.

9 Q You've got your trial testimony right there in
10 front of you. And I'll ask you to turn to page 114.
11 Now, Dr. Carr, this is again a situation where Argentum
12 doesn't have access to the underlying document. So
13 unfortunately, I can't put that document in front of
14 you. But you were asked about it here at trial.

15 (Examining document) If you need to go back
16 just a little bit for context to see that what you're
17 testifying about here is the package that Meda sent to
18 the FDA, you can do that. For example, page 113 around
19 lines 6 and 8, there's a reference to it. And then
20 again at 11 you refer to it as a "meeting packet." Do
21 you see that?

22 A Yeah. There's several meetings. Let me read

1 it real quick, if that's okay.

2 I'm up to page 114, and I'm at line 19.

3 Q Great. So I'll back you up just a little bit
4 to get on the record what we're looking at here,
5 starting on that same page, 114 of Exhibit 2021, at line
6 8.

7 A What was that?

8 Q Starting at 114, line 8. You were asked:

9 "What Meda, in consultation with
10 you, told the FDA was: 'Reports from
11 many of the physicians who co-prescribe
12 Astelin with topical nasal
13 corticosteroids state that patients
14 respond with substantial relief of their
15 allergies.'"

16 End quote. So would you agree that that's a
17 statement that was in at least one of the packages that
18 Meda sent to the FDA?

19 MR. LaROCK: Objection. Mischaracterizes the
20 trial testimony and likely the underlying documents.

21 Q BY MR. HOUSTON: Just to clarify, Adam, are you
22 suggesting I misquoted the quote here?

1 MR. LaROCK: Well, I guess that --

2 MR. HOUSTON: I just want to know if I
3 misquoted, did I read it wrong. Because sometimes I
4 make a mistake reading.

5 MR. LaROCK: I didn't line these up word for
6 word. So what is the question? Did you misquote it? I
7 don't know if you did --

8 MR. HOUSTON: Okay, fine. If I misquoted it, I
9 was going to try to fix it. If it's some objection
10 different from that, then that's fine. I'm just trying
11 to understand the basis for your objection.

12 MR. LaROCK: No, I don't think you misquoted.

13 MR. HOUSTON: Okay, thank you.

14 Q So Dr. Carr, do you see that testimony, and
15 would you agree that that was a statement that was made
16 to the FDA?

17 MR. LaROCK: Same objection.

18 THE WITNESS: I would just read the transcript
19 as it is. And so that's what this says. You didn't
20 read everything that they said, but --

21 Q BY MR. HOUSTON: I was going to get to that. I
22 was just trying to break it up.

1 A Okay. What we see here in front of us,
2 starting at line 8 through line 12 on page 114, is a
3 representation of what's written on this document. So
4 yes, that's what they said.

5 Q Okay. And then the second quote I want to
6 confirm starts at line 15, where you were asked:

7 "And that Meda went on to say: 'In
8 fact, among allergists, this seems to be
9 a widespread practice, even in the
10 absence of large, well controlled
11 trials.'"

12 End quote. So would you agree that was also a
13 statement that Meda made to the FDA as part of whatever
14 package this was that they sent to the FDA?

15 A So again, just to clarify, I think the
16 transcript from this trial stands on its own, and what
17 we're doing is just reading a question, and that is what
18 the question says.

19 Q Okay. Fair enough. Except that you answered
20 the questions in both cases, and you confirm that yes,
21 you see that written in those reports. Right?

22 A I think for sake of clarity, I started to

1 answer it, and I was cut off, and I basically said, I
2 see a sentence.

3 Q Well, you say, "I see that sentence." Correct?
4 As long as we're being precise about it.

5 A I said, "Yes, sir" -- actually, if we go back
6 to 19, I said, "That is," then I was cut off, and then
7 the question was, "Do you see that, sir?"

8 And then back onto 21, I say, "Yes, sir, I do.
9 I see that sentence."

10 Q Okay. So all I'm asking, is that a
11 confirmation that in fact those two passages apparently
12 appeared in the package that Meda sent to the FDA?

13 MR. LaROCK: Objection. Mischaracterizes the
14 underlying documents.

15 THE WITNESS: Honestly, I would need to see
16 the -- because I could see something was going on here
17 where I was trying to make a clarification, but they
18 were trying to pin me down. So I would need to see the
19 actual document to say that this testimony, that the
20 question that the guy asked me is a line for line
21 verbatim of what the actual meeting request or meeting
22 minutes were. So I will just rely on the content of

1 this question from the attorneys that were asking me
2 this question. And so I will confirm that that is what
3 it says in this transcript.

4 Q BY MR. HOUSTON: Including your answers where
5 you say, yes, I see those two quotes. You did answer
6 that way at trial; right? In both instances. Correct,
7 Dr. Carr?

8 MR. LaROCK: Object to the form of the
9 question.

10 THE WITNESS: I believe on line 14 I said,
11 "Yes, I do," and I believe on line 21 I said, "Yes, sir,
12 I do. I see that sentence."

13 Q BY MR. HOUSTON: So do you have any reason to
14 dispute the notion that those were statements that were
15 contained in one of the packages Meda sent to the FDA,
16 as you sit here today, other than the fact you don't
17 have that package in front of you, nor do I?

18 A Well, again, you know, I can't firmly say
19 something exists if I don't have it in front of me. So
20 I have no reason to disbelieve that these trial
21 transcripts are accurate. I believe that these trial
22 transcripts are the actual trial transcripts, and that

1 they reflect the discussion that we had.

2 Q And I'm asking a further question, which is, do
3 you have any reason to dispute, as you sit here today,
4 to dispute your answers, where you confirm that you're
5 viewing those actual sentences in the package? Do you
6 have any reason to dispute your responses that you gave
7 there at trial?

8 MR. LaROCK: Object to the form of the
9 question.

10 THE WITNESS: These were my responses. So I
11 don't disagree that these were my responses.

12 Q BY MR. HOUSTON: That's not what I'm asking,
13 Dr. Carr. I'm asking, do you have any reason to give a
14 different response today, to think that those weren't
15 the sentences in those packages?

16 A Again, I would need to have the exact document
17 in front of me to give you 100 percent degree certainty.
18 But I'm telling you, I don't dispute that this was the
19 context of our conversation during that time.

20 Q Did you still have these materials in your
21 possession?

22 A Which materials?

1 Q Like the package that this is referring to.

2 A I believe all those are very highly
3 confidential documents and are maintained by the
4 company.

5 Q I'm just asking if you have them in your
6 possession.

7 A No.

8 Q You don't have access to them?

9 A Not that I know of.

10 Q Did you have access to them at the time of
11 trial?

12 A The documents, I think if you go earlier in
13 here, you can see that we were actually reviewing the
14 documents, and that they were marked confidential, so I
15 believe that the company maintains them or -- the
16 company has been since sold, it's a different company
17 now, but --

18 Q All I'm asking, did you have access to them at
19 the time of trial?

20 A I believe that the attorney that was asking
21 these questions handed me a copy of these confidential
22 documents, and so at the trial he was directing me to

1 look at particular sentences. And so I had access to
2 them at the time of this question. I was looking at
3 them.

4 Q And is that the only time you had access to
5 them?

6 A I believe I was present, as the testimony says,
7 for the meeting, but I don't recall if I reviewed the
8 minutes that the FDA sent. So perhaps after the meeting
9 happened, we may have discussed some of the content of
10 it --

11 Q I'm asking about the package itself that this
12 is quoting from.

13 A I'm getting confused. I'm sorry. Can you
14 restate your question?

15 Q The package that Meda sent to the FDA that was
16 a lead-up to the meeting that I think you're referring
17 to. Your name was on that, wasn't it, as a consultant?

18 A Yes.

19 Q And does that imply or -- whether it implies it
20 or not, did you have access to that package that your
21 name was on?

22 MR. LaROCK: Object to the form of the

1 question.

2 THE WITNESS: Perhaps it would be best if I
3 clarify what my role was as a consultant.

4 Q BY MR. HOUSTON: If you have a recollection of
5 whether you had access or not, that's all -- I can't go
6 into --

7 A So in general, pharmaceutical companies do not
8 give access to confidential information at whim to
9 people who are not employed by the company. I was an
10 independent, outside consultant, and I did not have
11 visibility to all of their confidential conversations or
12 communications. They would ask me questions and ask me
13 to help them with certain things, and it was their
14 decision what to give to me. I did not have open access
15 to everything, no.

16 Q Again, that wasn't my question. I'm asking
17 specifically about this package that got sent to the FDA
18 that had your name on it. Do you recall reviewing
19 that -- were you given a chance to review it before it
20 was sent in with your name on it?

21 MR. LaROCK: Object to the form of the
22 question. Objection, asked and answered.

1 THE WITNESS: I believe the night before the
2 meeting, the company received comments from the FDA, and
3 it was the day before the meeting I was listed as a
4 consultant with the intent to attend the meeting.

5 So the night before the meeting, I do believe I
6 had access to certain elements. I can't recall which.
7 It was whatever Meda was asking me about. We weren't
8 even in the same room. They would come over and ask me
9 questions, then they would go strategize.

10 So in all honesty, I would say probably the
11 night before the meeting there were a couple of elements
12 that Meda most likely may have discussed with me.

13 Q BY MR. HOUSTON: Okay. These quotes that we
14 read from page 114 of your trial testimony, do you have
15 any reason, as you sit here today, to dispute these
16 statements that Meda was making to the FDA?

17 A So just to be clear, these quotes are not my
18 quotes.

19 Q I understand. I think I made that clear.

20 A Yes, they are not my quotes. They are quotes
21 that is listed as Meda. And this was in 2008. So
22 they're here, so I guess I have no reason to dispute

1 that they were said in 2008.

2 Q Let me try again. I'm asking, do you have any
3 reason to dispute the facts, what they're actually
4 saying? Not that they said it, but do you have any
5 reason to dispute what they're telling the FDA, that
6 that's true?

7 MR. LaROCK: Object to the form of the
8 question.

9 THE WITNESS: Well, I guess it depends on how
10 you define some of these words. For instance, "many."
11 I don't know what that means. "Reports from many of the
12 physicians." I don't know what that means. Does that
13 mean two? Does that mean four?

14 So these again are not my opinions. And it was
15 not the prevailing thought that the combination of these
16 medicines would be better than the steroid alone. In
17 fact, that was the fear, is that the steroid alone was
18 just so much more potent, as all of the other studies
19 had shown, that they would fail.

20 Q BY MR. HOUSTON: Meda is telling the FDA that:
21 "...many of the physicians who
22 co-prescribe Astelin with the topical

1 nasal corticosteroids state that
2 patients respond with substantial relief
3 of their allergies."

4 Do you have any reason to dispute that that's
5 true?

6 MR. LaROCK: Objection. Mischaracterizes the
7 document.

8 THE WITNESS: Many patients respond and get
9 tremendous clinical benefit from placebo. That doesn't
10 necessarily mean placebo is going to be approved by the
11 FDA. So even though Meda says this, it is not data.
12 It's purely uncontrolled anecdote. And that's not
13 really worth much.

14 Q BY MR. HOUSTON: I understand you want to
15 discount it. You want to take your own view of what
16 this means or what the relevance of it is.

17 I'm just asking whether you have any reason to
18 dispute that it's actually true, that this is what many
19 of the physicians reported, whether they're right or
20 wrong. Do you have a reason to dispute that that's what
21 they reported?

22 MR. LaROCK: Object to the form of the

1 question. Objection, mischaracterizes the document.

2 THE WITNESS: In 2008, in 2008, I do not refute
3 that they, being characterized as the people at Meda,
4 believed this as a rationale.

5 MR. LaROCK: Mike, we've been going for about
6 an hour now.

7 MR. HOUSTON: Yeah, we'll take a break just
8 quickly here.

9 Q And then similarly the second quote, where Meda
10 says:

11 "...among allergists, this seems to
12 be a widespread practice..."

13 Do you dispute Meda's statement there?

14 MR. LaROCK: Objection. Mischaracterizes the
15 document. Objection, foundation.

16 THE WITNESS: I think I could answer that
17 question. There's something in my declaration I think
18 that I discussed a study in there. I just need to look
19 at a date on the study.

20 Q BY MR. HOUSTON: The Ratner 2008 study;
21 correct?

22 A No, not the Ratner 2008 study. Do you have a

1 copy? I could give it to you. It will just take me a
2 second.

3 Q (Handing document) I hand you a copy of
4 Exhibit 2147.

5 A (Examining document) A list of all the
6 supporting -- what I'm looking for is the date that Meda
7 would know the results of the Hampel study. If you go
8 to page 5 on my declaration, it's listed as Cipla
9 Exhibit No. 2045. I think that's the study. If we
10 could just look at that. Do you happen to have that?

11 Q I don't know that I have that one.

12 A It -- this is to the best of my recall, and I
13 apologize if I make a mistake on the date. I believe it
14 was in '07 that they had the results of that. 2007.

15 So Frank Hampel and his co-authors were all
16 allergists, they had conducted a double-blind,
17 placebo-controlled study of azelastine and fluticasone
18 in a single nasal spray device that is eventually the
19 embodiment of Dymista. And it was compared to
20 fluticasone, a generic form, and it was compared to
21 azelastine, their own formulation, and it was compared
22 to placebo. And this study was paid for by Meda. And I

1 believe that the top-line data was that this was
2 conducted in '97, and they had the top-line data for
3 that.

4 So this is part of the confidentiality that
5 pharmaceutical companies have. They don't always have
6 to publish data. They can just give it to the FDA. And
7 that was part of the discussion at the FDA, because the
8 FDA didn't like this study, because it used commercially
9 available Flonase and Astelin. But this was done prior
10 to 2008. I believe it was 2007. So Meda had that
11 top-line data, and this was when they actually showed
12 that Dymista -- at the time they called it "MP2902" --
13 they showed that when compared to azelastine and
14 fluticasone, the commercial embodiments, and placebo,
15 that this combination was better.

16 So if you fast-forward to the meeting that they
17 had with the FDA, and they had given the FDA
18 confidential information about the company so the FDA
19 could review, my suspicion is those are the allergists,
20 and the allergists that they worked with and that had
21 visibility to the studies.

22 They say in the absence of large,

1 well-controlled studies. This was just one single
2 study.

3 Q Right. But it says widespread practice. So
4 you're saying that by widespread practice among
5 allergists, that's just referring to the people who had
6 access to this confidential study? That's widespread
7 among allergists in your view?

8 A We'll say multicenter, multistate -- it's all
9 across the United States. And so it's not just the
10 authors. It's numerous study sites. I would have to
11 actually go back and look at the actual number of study
12 sites.

13 But in general, you're looking at at least 100
14 study sites. At a given study site there could be
15 anywhere from two to four investigators. So that could
16 be up to 200 to 400. There are only about 4,000
17 allergists. So we're talking 10 percent. That to me
18 would be widespread.

19 Q As you were testifying, Dr. Carr, I think I
20 found the article. It seems to have been produced under
21 a different exhibit number as well. So my copy is
22 marked Exhibit 1043. And you can take a minute to

1 confirm, but I believe this is the same article that you
2 refer to in your declaration that you were just talking
3 about, 1045. You see that? Would you agree?

4 A I believe that this is the study, yes. This
5 data was available, I believe, in 2007 and shared with
6 the FDA at the time of this meeting. And the FDA said
7 you cannot go forward and use azelastine and fluticasone
8 in the commercially available. You have to use them in
9 the same formulation as MP2902, or Dymista.

10 Q Do you have any evidence that that in fact
11 occurred, that this is the data reported in this article
12 that was shared with the FDA?

13 A You asked my opinion, and --

14 Q Now I'm asking if you have any evidence that
15 this was the data that was shared with the FDA. That's
16 my question right now.

17 A Not on me.

18 Q Your counsel asked for a break a little bit.
19 Sorry I went over. We'll take a break now.

20 (Recess 10:13 to 10:30 a.m.)

21 Q BY MR. HOUSTON: Dr. Carr, in 2002, with
22 respect to the issue of whether or not there was a

1 perception that adding azelastine to an ongoing
2 fluticasone therapy in an AR patient provided any
3 benefits to the patient, could there be differences of
4 professional opinion between doctors in your field on
5 that issue?

6 MR. LaROCK: Object to the form of the
7 question.

8 THE WITNESS: I would -- by "doctor," I'm going
9 to say medical doctor, not Ph.D. While in a laboratory
10 setting you may generate a hypothesis, you may test it
11 in a tissue culture, those do not always equate to a
12 clinically meaningful improvement in an actual patient.

13 In my declaration there was a very good review
14 that was done by Neilsen. Are you familiar with it? Do
15 you want me to pull it up?

16 Q BY MR. HOUSTON: I don't really. I'm just
17 asking if it's possible for there to be a difference of
18 opinion among medical doctors in 2002 regarding whether
19 that combination of drugs would have a benefit in AR
20 patients as opposed to the monotherapies. Is that
21 possible?

22 MR. LaROCK: Object to the form of the

1 question. Objection, asked and answered.

2 THE WITNESS: I think opinion is not proof, and
3 that question was asked several times because of
4 people's opinion. And it was studied, actually, quite
5 extensively studied. And the results of the study
6 demonstrated that there was no benefit.

7 Q BY MR. HOUSTON: To prescribing --

8 A The combination of an antihistamine and a
9 steroid.

10 Q No, I said azelastine --

11 A Which is an antihistamine.

12 Q Okay. But my question was azelastine
13 specifically, not just antihistamines in general.
14 Azelastine with fluticasone. Are you suggesting there
15 couldn't be a difference of opinion among doctors in
16 2002 as to whether or not that combination provided an
17 improvement in AR patients as compared to either
18 monotherapy by themselves?

19 MR. LaROCK: Object to the form of the
20 question. Objection, asked and answered.

21 THE WITNESS: I think I will refer back to your
22 early concession where you said, "I concede there were

1 no studies prior to that time with fluticasone and
2 azelastine." So typically, when a doctor or scientist
3 has an embodiment of their question, it's studied. So I
4 would say that would be my answer. It wasn't studied.

5 Q BY MR. HOUSTON: So can you give me a yes-or-no
6 answer to whether or not it's possible that there could
7 be a difference of opinion between doctors as to whether
8 or not that combination of drugs provided a benefit to
9 AR patients? Can you give me a yes-or-no answer to
10 that?

11 MR. LaROCK: Object to the form of the
12 question. Objection, asked and answered.

13 THE WITNESS: So again, doctors express
14 opinions, then they generate a hypothesis, then they
15 test the hypothesis. And you can decide whether or not
16 the opinion was right or wrong.

17 I believe Juniper, while it was not azelastine
18 and fluticasone, is one of the first people to express a
19 concern or question about that opinion. And she studied
20 it, and numerous people studied it afterwards. And
21 again, azelastine is just one antihistamine that was
22 considered --

1 Q BY MR. HOUSTON: Dr. Carr, I'm --

2 MR. LaROCK: Let him finish.

3 MR. HOUSTON: No, I'm not going to let him
4 finish, because I intentionally tried to ask a very
5 specific question to avoid just this sort of extra
6 testimony.

7 Q I'm limiting my drugs to just these two for my
8 question, and I'm just asking if it's possible that
9 there could be a difference of opinion among doctors.
10 And I further ask, can you give me a yes-or-no answer to
11 that. And if your answer is, "No, I can't do that,"
12 then just tell me. Is the answer no, that you can't
13 give me a yes-or-no answer to my question?

14 MR. LaROCK: Object to the form of the
15 question. Objection, asked and answered. Objection,
16 harassing the witness.

17 Dr. Carr's taken time out of his day to come
18 here and give you testimony. When we deposed your
19 witnesses, we gave them respect. We let them answer
20 their questions, let them go on and on and on. You can
21 look at the Schleimer testimony. Dr. Carr's here to
22 answer your questions, and he's doing that.

1 MR. HOUSTON: I would just ask that he do
2 answer my questions, not give testimony that he wants to
3 give. I've made that request once before, and I'll make
4 it again. That's fine.

5 MR. LaROCK: We disagree with your
6 characterization.

7 MR. HOUSTON: That's fine, Adam. I understand
8 that.

9 MR. LaROCK: You can answer. Sorry.

10 THE WITNESS: So I'm getting the impression you
11 don't like my answers, but I'm trying to answer your
12 question to the best of my ability.

13 Could you -- if you could just restate your
14 question again, please, specifically.

15 Q BY MR. HOUSTON: Let me try to key it off of
16 something you said and see if this could help us move
17 forward.

18 You said that sometimes doctors form opinions,
19 develops into hypothesis that eventually gets tested.
20 Right?

21 A In general that would be a characterization of
22 what I just said.

1 Q So is it possible that some doctors formed an
2 opinion as of 2002 that combining azelastine with a
3 fluticasone treatment provided an improvement in AR
4 patients?

5 MR. LaROCK: Objection. Asked and answered.

6 THE WITNESS: I think earlier when we started
7 my deposition, you asked me the same question, did any
8 doctors ever prescribe these two. And so I would say --

9 Q BY MR. HOUSTON: That's a different question.

10 A I would say that my presumption is that they
11 prescribe those two medications, but in 2002, there was
12 no data to support it, and in fact, the practice was to
13 use the azelastine as on demand at that time. So I
14 would guess that that would be their opinion.

15 Q That what would be their opinion? That
16 combining the two would provide an improvement to AR
17 patients?

18 A That their opinion would be to use the
19 azelastine on demand, is what I meant by, that would be
20 their opinion.

21 Q To achieve an improvement in their AR patients.
22 Correct?

1 MR. LaROCK: Object to the form of the
2 question.

3 THE WITNESS: I feel like we're going back to
4 where we kind of went round and round earlier.

5 So again, doctors prescribe numerous
6 medications for allergic rhinitis. Inevitably, they're
7 going to end up on a combination in the same patient
8 where they may have gotten the specific medication
9 fluticasone and the specific medicine for azelastine.
10 However, the azelastine would have been used as a p.r.n.
11 or as needed, on-demand medication. And there are, as I
12 said in my previous testimony, a variety of reasons for
13 that.

14 Q BY MR. HOUSTON: Could one of the reasons for a
15 doctor have been that the doctor believed the addition
16 of azelastine to fluticasone produced an improvement,
17 would produce an improvement in AR symptoms?

18 MR. LaROCK: Objection. Asked and answered.

19 THE WITNESS: I think it's very careful -- we
20 need to be very careful how we characterize AR symptoms
21 and how we characterize improvement.

22 The way allergic rhinitis medications are

1 characterized is by the total nasal symptoms score, not
2 by one symptom. So I do not believe prior to 2002 any
3 doctor would have prescribed fluticasone and azelastine
4 in the same patient with the intent to have an
5 improvement in your total nasal symptom score. That's
6 not what the data supported at the time.

7 Q BY MR. HOUSTON: Do doctors who are seeing and
8 treating patients typically compile and keep track of
9 total nasal scores?

10 MR. LaROCK: Objection to form.

11 THE WITNESS: It's a very common way for us to
12 evaluate our patients, and it's how it's reported. And
13 it is typically questions that are commonly asked of our
14 patients when we're treating those symptoms.

15 Q BY MR. HOUSTON: So when you see your patients
16 who you're treating for AR, you record a TNSS score in
17 their files? You compile the data from the patient
18 necessary to do that?

19 A What year are we talking about?

20 Q 2002 or before.

21 A 2002 or before? Actually, at that time, we
22 would even include other symptoms as well, such as --

1 Q That's fine. I'm asking if you had a TNSS
2 score. That's all I'm asking.

3 A It's a very common practice.

4 Q And so if we go back to my original question,
5 which wasn't asking about TNSS scores, it was simply
6 asking about AR symptoms in general, could one of the
7 reasons for a doctor to have prescribed the addition of
8 azelastine to fluticasone been to try to, in the hopes
9 of seeing an improvement in one or more AR symptom?

10 MR. LaROCK: Objection. Asked and answered.
11 Objection, form.

12 THE WITNESS: Look, it's very difficult to
13 answer that question with a simple yes or no, because
14 these patients are much more complicated.

15 If I could go back to the Accetta patient
16 record, sitting right here on top, this is a patient
17 that you see the two medicines, and they have two
18 different diagnoses. One is allergic rhinitis, one is
19 chronic rhinitis.

20 Is it possible that in a complex patient with
21 multiple medical problems, that has overlapping
22 redundant symptoms that could be manifested by more than

1 one disease, could they be on both fluticasone and
2 azelastine, quote-unquote, for a variety of reasons,
3 like I said in my testimony before, then yes.

4 And this is an example. Patient had chronic
5 rhinitis, had a normal exam, so I don't know why he
6 would prescribe this new medication. Normal exam. But
7 you presented this to me, so this would be possible, as
8 one of those variety of reasons.

9 Q BY MR. HOUSTON: I'm just asking --

10 A I would guess.

11 Q I'm just asking if one of the motivations for a
12 doctor could have been to try to achieve an improvement
13 in one or more of the AR symptoms.

14 MR. LaROCK: Objection. Form. Objection,
15 asked and answered.

16 THE WITNESS: I think I just, to the best of my
17 ability, I think I just answered your question using
18 Dr. Accetta's patient record as an example. I can go
19 through it again if you would like.

20 MR. HOUSTON: I need to go off the record for
21 just a second, please.

22 (Off record)

1 MR. HOUSTON: Back on the record.

2 Q Dr. Carr, the reason that I asked that
3 follow-up question, you were referring to Dr. Accetta's
4 patient record here, but then you pointed out how
5 there's two impressions listed, allergic rhinitis and
6 chronic rhinitis. And so that's why I wanted to
7 clarify.

8 Is it possible that a doctor such as
9 Dr. Accetta, for example, prescribed Astelin in
10 combination with Flonase in the hopes of improving the
11 AR symptoms that this patient was observing?

12 MR. LaROCK: Objection. Form.

13 Q BY MR. HOUSTON: This patient was experiencing,
14 I should say.

15 MR. LaROCK: Same objection.

16 THE WITNESS: I would say, if you look -- I
17 would say no, because if you look under the "Objective,"
18 it says "General: The patient's physical examination is
19 normal." So no, the patient in this case, that has a
20 normal physical exam, would not need another medication
21 to treat something that was normal. They're only going
22 to get side effects from the Astelin in this scenario.

1 So in this case, I would say no.

2 Q BY MR. HOUSTON: So Dr. Accetta would have only
3 added Astelin in that case for what purpose?

4 MR. LaROCK: Objection, form.

5 THE WITNESS: Perhaps we should pull out the
6 transcript and go to Dr. Accetta's testimony, and maybe
7 he could answer that. I don't know what his purpose
8 was. The patient had a normal physical exam.

9 Q BY MR. HOUSTON: As I mentioned before, I don't
10 have that with me. If Dr. Accetta gave his reasons,
11 whatever they were, do you have any reason to dispute
12 his testimony as to what his own reasons were?

13 MR. LaROCK: Objection, form. Objection,
14 outside the scope. Foundation.

15 THE WITNESS: I can't comment on how would I
16 respond to his rationale until I heard it.

17 Q BY MR. HOUSTON: Well, you did sit through
18 trial, right? So you heard all his testimony; right?

19 A You're asking me to recall word for word what
20 his specific patient chart was?

21 Q No.

22 A I can't recall that.

1 Q Okay. As of 2002, had any studies been
2 conducted to test the relative performance of
3 co-administered fluticasone and Astelin versus just
4 either one of those monotherapies by themselves?

5 MR. LaROCK: Objection, form.

6 THE WITNESS: So I'm not 100 percent sure if I
7 understand your question, but I will go back to your
8 concession earlier, where you said, "I concede I don't
9 know of any studies, looking at fluticasone and
10 azelastine being studied prior to 2002." So I'll go
11 back to that.

12 Q BY MR. HOUSTON: Dr. Carr, if we go back to the
13 testimony, you'll see very clearly that I said I concede
14 for purposes of that question. So I'm not conceding
15 that for all of today, and in any event, that was my own
16 knowledge. I'm asking about your knowledge.

17 Are you aware of any studies as of 2002 in
18 which the relative performance of co-administering
19 fluticasone and azelastine was compared with the
20 monotherapies, either monotherapy?

21 MR. LaROCK: Objection, form.

22 Q BY MR. HOUSTON: For those two drugs.

1 MR. LaROCK: Same objection.

2 THE WITNESS: I guess you would have to clarify
3 to me what you mean by "relative performance." That's
4 not a clinical trial term that we typically use.

5 Q BY MR. HOUSTON: Okay. What if I said "an
6 improvement in AR symptoms"? Would you understand what
7 I mean when I ask that question?

8 A My understanding would be that patients
9 demonstrated an improvement in their total nasal symptom
10 score as compared to placebo. That would be my
11 understanding to that. So no, I do not know of any
12 studies prior to 2002 that looked at the combination of
13 fluticasone and azelastine compared to the monotherapies
14 and compared to placebo that showed an improvement.

15 Q Okay. Now, I didn't say "and compared to
16 placebo" in my question. Does that addition in your
17 answer change your answer? Let me start over. Let me
18 ask a different question.

19 As of 2002, are you aware of any studies being
20 conducted that involve the co-administration of
21 fluticasone and azelastine?

22 A Prior to what year?

1 Q As of 2002.

2 A Can I look at my declaration and look at the
3 dates of the things that I've referenced in here?
4 That's 16 years ago, so -- let me pull it up. This
5 one's me; right? Yes. (Examining documents) So if we
6 pull up the studies, they should have the dates on them.
7 Where are the studies?

8 So Neilsen was the best review of those two
9 classes of medication, I will say. And the reason I'm
10 saying this, there's really no difference between any of
11 the intranasal steroids, and there's really no
12 difference between any of the oral or intranasal
13 antihistamines. They're all considered about the same.

14 So Neilsen would be the best review. And that
15 was 2001. Hampel was after that. I believe the study
16 was, top-line data came out, I believe, in 2007.

17 So while you may readily produce an article, I
18 do not believe, prior to 2002, there are any
19 well-conducted clinical trials. And the embodiment of a
20 well-conducted clinical trial is how I described before,
21 placebo-controlled clinical trial that looked at that
22 combination.

1 Q I'm just asking if you're aware of any studies
2 that looked at that combination, whether they're well
3 conducted in your opinion or not.

4 MR. LaROCK: Objection. Asked and answered.

5 THE WITNESS: I can't recall the dates of all
6 the studies. I apologize. If you have one, I'd be
7 happy to review it.

8 Q BY MR. HOUSTON: What's the earliest study that
9 looked at the combination of azelastine and fluticasone
10 that you can think of?

11 MR. LaROCK: Objection, form.

12 THE WITNESS: So again, if I could clarify,
13 when I retrospectively think of a study, I think of a
14 study that is worth remembering. There are numerous
15 studies that are conducted that are not worth
16 remembering.

17 Q BY MR. HOUSTON: Fine. I don't need that
18 opinion, Dr. Carr.

19 MR. LaROCK: Let him finish.

20 THE WITNESS: It would probably be Hampel, to
21 answer my question, it would be Hampel. That would be
22 the first one, because there's numerous studies that are

1 of any value. So Hampel.

2 Q BY MR. HOUSTON: So I want you to expand your
3 answer to even the ones that you think are of no value.
4 I don't care what value that you assign to them. I'm
5 just asking, what's the earliest study you're aware of
6 that looked at those two drugs in combination?

7 MR. LaROCK: Objection. Asked and answered.

8 THE WITNESS: I think the only other study that
9 I would imprint in my memory that would be worth
10 remembering to some degree would be the Ratner study.
11 But it was not a rigorous study, and it was not placebo
12 controlled, so there's a lot of bias in that study.

13 Q BY MR. HOUSTON: Whether worth remembering or
14 not, can you recall any studies that looked at the
15 combination of those two drugs prior to Ratner?

16 A Like I said, if you have one and you'd like to
17 discuss it, then we can. But I don't routinely imprint
18 those in my brain if I didn't feel they had value.

19 Q That's fine. I'm just testing -- I'd like to
20 know what you know, Dr. Carr. I'm allowed to ask what
21 you know or what you remember. I'm allowed to ask that.
22 So I'm just asking any studies you can recall, whether

1 you think they're good, bad, ugly, anything else.

2 A Well, I've tried to tell you what I know, but
3 you keep cutting me off. Go ahead.

4 Q So are you aware of any studies, good, bad, or
5 otherwise, that looked at the combination of azelastine
6 and fluticasone prior to Ratner?

7 MR. LaROCK: Objection. Asked and answered.

8 THE WITNESS: If I could give you some insight
9 into my thought process.

10 I equate azelastine to antihistamines, and I
11 equate fluticasone to nasal steroids. So again, there
12 are studies back in the late '80s and early '90s that
13 looked at combinations of steroids and antihistamines,
14 and I have delineated some of those studies in my
15 declaration.

16 I would use those studies interchangeably with
17 a study that specifically looked at fluticasone, because
18 there's never been a study to show one nasal spray is
19 better than the other. They're all the same. And I
20 would use it to equate it with azelastine. That was the
21 context. Azelastine is as effective as an oral
22 antihistamine, but it has a lot more side effects.

1 So in that context, yeah, there are numerous
2 studies, and I've delineated some of them in my
3 declaration, that would lead me away from ever using
4 that combination.

5 Q BY MR. HOUSTON: Is it your opinion that the
6 combination therapy, whether they're provided as two
7 separate sprays or in a single spray, the combination of
8 azelastine and fluticasone provides an improvement in AR
9 symptoms that is not seen in the combination of
10 antihistamines and steroids in general?

11 MR. LaROCK: Objection, form.

12 THE WITNESS: So two items. First I'd like
13 clarification as to, are we talking in present day, now?

14 And secondly, if you could just be a little bit
15 more -- I didn't quite get the context of the question.
16 Repeat the question, and then in what year are we
17 talking? Because there's advances in medicines. We
18 learn new things.

19 MR. HOUSTON: Let me strike that question and
20 try again. I agree that wasn't a very precise question.

21 Q As you sit here today, you believe that
22 patients taking both fluticasone and azelastine are

1 likely to see an improvement in their AR symptoms as
2 compared to that same patient taking either one as a
3 monotherapy. Right?

4 MR. LaROCK: Objection, form.

5 THE WITNESS: Today? So in --

6 Q BY MR. HOUSTON: As to those two drugs.

7 A I did some of the studies for Dymista. I think
8 Dymista is the embodiment of this whole issue that we're
9 discussing today. And Dymista has both of those active
10 ingredients, fluticasone propionate and azelastine, in a
11 unique novel formulation.

12 And when you compare Dymista to fluticasone and
13 azelastine in the same formulation, it's better than
14 each of the monotherapies. When you compare it to the
15 commercially available formulations of fluticasone and
16 Astelin, it's even so much more better. It was quite
17 unexpected to see that robust of a response. And we
18 published that paper, by the way.

19 Q Are you aware of any studies comparing the
20 performance of Dymista against the administration of
21 fluticasone and azelastine as separate sprays? So
22 co-administration, but as separate sprays. Are you

1 aware of any studies?

2 MR. LaROCK: Objection, form.

3 THE WITNESS: I believe that during the
4 clinical development program, the FDA required Meda to
5 do performance evaluations. They had to look at things
6 such as dose content uniformity; they had to look at
7 plume dimensions; they had to look at a variety of
8 different performance characteristics of the device that
9 they used.

10 I am not a formulation expert. I would refer
11 to the formulation experts to look at the performance of
12 those different molecules with regards to the chemistry,
13 manufacturing, and controls that the FDA requires,
14 otherwise called CMC issues, for the performance
15 characteristics of those devices.

16 Q I can't make sense of that answer. Are you
17 aware of any studies in which Dymista was compared to
18 the co-administration of fluticasone and azelastine?
19 Are you aware of any? Do you know of any that exist?

20 MR. LaROCK: Objection, form. Asked and
21 answered.

22 THE WITNESS: So a device performs a certain

1 way. And in order for the device to be approved, a
2 company has to look at the performance characteristics
3 of the device.

4 So for instance, if you have a nasal spray, it
5 needs to be a spray. It needs to have a plume. It
6 can't be a jet. So the FDA requires those performance
7 characteristics to be conducted on all nasal spray.

8 You can't be squirting a jet into the nose.
9 You'll get a perforation in the nose. So the company
10 had to do those studies to look at the performance of
11 those sprays as part of their chemistry, manufacturing,
12 and controls.

13 And what I'm saying is those are done by CMC
14 pharmacologist experts looking at plume dimensions, how
15 fast it comes out. Those are performance
16 characteristics.

17 Like if you go look at the car, one car is
18 really slow, one car is really fast, one has a higher
19 performance than the other. Those are the performance
20 studies that were done for these devices. And again, I
21 would refer you to the CMC guys for that.

22 Q BY MR. HOUSTON: So for those performance

1 studies, do you think they were looking at the
2 performance of the Dymista device as compared to the
3 Flonase and Astelin device together, co-administered?
4 How could you even do that?

5 MR. LaROCK: Objection. Outside the scope of
6 his declaration. Object to the form of the question.

7 Q BY MR. HOUSTON: You understand my question was
8 about the co-administration of Astelin and fluticasone
9 versus Dymista.

10 A But you have to understand, why would anybody
11 look at the performance? It's all the same -- so in the
12 clinical trials that were conducted, like I said before,
13 in the pivotal studies, it was the same device, it was
14 the same formulation. It's just that in the active
15 treatment arms, they had fluticasone and azelastine, and
16 the monotherapy arms, they had fluticasone in one,
17 azelastine in the other. And then in the placebo,
18 again, it was the same device, it was the same
19 formulation. So there's no reason to believe that the
20 same device would have a different performance
21 characteristic. So I don't see how the performance of
22 the device would change.

1 Q Maybe we're hung up or maybe there's a
2 misunderstanding as to the word "performance." I'm not
3 actually asking about the device performance. I'm
4 asking about the effect on patients in terms of treating
5 their AR symptoms.

6 Are you aware of any study that compares the
7 efficacy of Dymista to the efficacy in patients that are
8 co-administered azelastine and fluticasone as separate
9 sprays?

10 MR. LaROCK: Objection, asked and answered.

11 THE WITNESS: So to be clear, we're talking
12 about clinical efficacy and safety studies now.

13 Q BY MR. HOUSTON: Any study. Any study. I
14 don't care -- good, bad, whether you think they're
15 sufficient, memorable, anything. Any study.

16 MR. LaROCK: Objection, form. Asked and
17 answered.

18 THE WITNESS: Off the top of my head, I cannot
19 think of any randomized double-blind, placebo-controlled
20 trials that had those active treatment arms.

21 Q BY MR. HOUSTON: Any study at all, regardless
22 whether it's randomized, placebo controlled, any of

1 those things. Any study.

2 MR. LaROCK: Same objections.

3 THE WITNESS: Again, off the top of my head,
4 with the caveats I gave before about the kind of studies
5 that I imprint, I can't think of any studies that had
6 those active treatment arms.

7 Q BY MR. HOUSTON: If there had been a study, if
8 you are aware of a study that compared Dymista to the
9 co-administration of azelastine and fluticasone, you
10 wouldn't likely have forgotten that as you sit here
11 today, would you?

12 A Can I give you an anecdote in answer to your
13 question that may give you the answer you're looking
14 for?

15 Q Let's not.

16 I will ask you to look at Exhibit 2021 again,
17 your trial testimony, and turn to page 121.

18 A Yes.

19 Q The question that begins at line 15. You were
20 asked whether any of the studies that you talked about
21 compared Dymista to the co-administration of azelastine
22 and fluticasone. And as part of your answer, you said,

1 "I don't think there is a study that was ever
2 conducted."

3 Is that still your belief today, that you don't
4 think there's a study that was ever conducted?

5 A I believe the answer I've given you already is
6 essentially the same answer.

7 Q Okay. Nothing's changed since you gave that
8 testimony at trial; is that right?

9 A To -- and this was December a year ago?

10 Q A little over a year ago, I believe.

11 A To the best of my knowledge, in the past year,
12 to the best of my knowledge, in the past year, I'm not
13 aware of any additional studies being conducted since
14 then that would fit this.

15 Q That would compare Dymista to the
16 co-administration of azelastine and fluticasone?

17 A I think the best example is my anecdotes
18 treating patients, which is an anecdote. But that would
19 be the closest way that I could answer that question.

20 Q Okay. Well, maybe that will dovetail with my
21 next question, which is, irrespective of whether there
22 are any studies or not, do you have an opinion, a

1 professional opinion, as to whether or not Dymista has
2 better or worse efficacy than the co-administration of
3 Flonase -- sorry, not Flonase -- fluticasone and
4 azelastine?

5 A Yes, I do.

6 Q What is that opinion?

7 A Dymista is better than the co-administration of
8 fluticasone and azelastine.

9 Q When you -- let me add a nuance to that
10 statement right there. When you talk about the
11 co-administration of fluticasone and azelastine, does it
12 matter whether those, fluticasone and azelastine, are
13 formulated as they are in their commercial embodiments,
14 Flonase and Astelin, or is it regardless of how they're
15 formulated, as far as you know?

16 MR. LaROCK: Object to the form of the
17 question.

18 THE WITNESS: Well, as the clinical development
19 program for Dymista demonstrated, there is clearly a
20 formulation effect. And the formulation is very, very
21 important.

22 Q BY MR. HOUSTON: Could I just clarify, when you

1 say "formulation," you mean the --

2 A The Dymista formulation --

3 Q Taking aside --

4 A -- and the monotherapy.

5 Q -- the concentrations of the active
6 ingredients, you mean all the other stuff, the
7 excipients, the things we'd call excipients?

8 A So you asked me about monotherapies versus
9 combination therapy. That's what you just asked me.

10 Q Co-administration.

11 A Co-administration. And you said regardless of
12 formulation. And my point is, you can't disregard
13 formulation. Formulation is very, very important.
14 There's a formulation effect. If you do cross-study
15 comparisons, and you look at the benefit, if you pull up
16 my -- I have actually a very good slide on this. If you
17 go back to my declaration and you pull up that slide
18 that shows Dymista compared to the commercially
19 available monotherapies --

20 Q Which page are you on?

21 A I'm on page 51 down at the bottom. It's right
22 below line 109. If you see Dymista compared to

1 commercially available formulations of fluticasone and
2 azelastine, there is a much bigger difference in the
3 delta here between the two monotherapies. So the delta
4 meaning the improvement between the two monotherapies,
5 and the improvement when the two monotherapies have the
6 same formulation.

7 Q The same formulation as Dymista?

8 A Same formulation as Dymista. And in the
9 clinical trials that were conducted, there was a PK
10 analysis looking specifically at fluticasone during the
11 PK analysis.

12 If you pull the label up for fluticasone,
13 there's 50 percent higher bioavailability of
14 fluticasone, 50 percent higher bioavailability of
15 fluticasone in Dymista, then there is in fluticasone not
16 in Dymista. 50 percent. And there's less side effects.
17 Better efficacy, higher exposure, less side effects.

18 So formulation matters. And there's multiple
19 unexpected findings there.

20 Q So again, I want to clarify, when you say
21 formulation matters, that the unexpected improvements
22 that you will say you see with Dymista, both the alleged

1 increased efficacy and the decreased side effects, you
2 believe that still exists and is still dependent on
3 formulation, even if the dosage of the actives is the
4 same in the two groups. So Dymista here,
5 co-administration of fluticasone and azelastine. If the
6 dosage of the actives is the same, you still think
7 Dymista has the better efficacy, lower side effects, and
8 that that's due to the overall formulation. Is that
9 what you're saying?

10 MR. LaROCK: Object to the form of the
11 question. Objection, mischaracterizes his prior
12 testimony.

13 THE WITNESS: It was a very long question, and
14 you hit me at one point where you said "alleged
15 improvement." The FDA has approved this, and so it's
16 not alleged. It is factually better in efficacy. And
17 it is factually more safe. Because that's what's in the
18 label. So not alleged.

19 Q BY MR. HOUSTON: Hold on, Dr. Carr. You're
20 saying that the FDA has seen data that compares Dymista
21 to the co-administration of these two drugs? I asked
22 you if there were any studies on that, and you said no,

1 you weren't aware of any.

2 A Well, again, your question was very long. And
3 so like I said, it was very long, and you caught me at
4 one point where you said "alleged improvement." It
5 didn't have alleged improvement. It is better. It's
6 FDA approved.

7 Q Just to be clear, when you say it's "better,"
8 you're talking about better as compared to the
9 monotherapies, when you say "better."

10 MR. LaROCK: Objection --

11 Q BY MR. HOUSTON: I'm asking, just to be clear,
12 I'm asking about Dymista as compared to
13 co-administration of these things. And I think we
14 established there weren't any studies on that.

15 MR. LaROCK: Object to the form of the
16 question. Objection, mischaracterizes his prior
17 testimony.

18 THE WITNESS: So to be clear, the
19 word "better," what I mean by that is the following:

20 I gave you my personal anecdote. You said, do
21 you have an opinion about this. And I said, yes, I have
22 an opinion. It's better. So I do believe it is better

1 than the sequential administration of the two drugs in
2 their commercially available embodiment.

3 Then you asked me about formulation, and I said
4 yes, formulation does matter. So fluticasone has 50
5 micrograms, azelastine in Astelin form has 137
6 micrograms. That's the same amount as what's in
7 Dymista. So I'm not sure where you're going with that,
8 but --

9 Q BY MR. HOUSTON: I'm not going anywhere with
10 it. I want to make sure we're comparing apples to
11 apples. When you give your opinion that Dymista's
12 better than the co-administration, I just wanted to
13 clarify that you're talking about the situation where
14 the active ingredients administered in both scenarios is
15 the same, the concentration and the amount that's dosed.
16 I just wanted to make sure that there wasn't any
17 misunderstanding there. That's all I'm trying to get
18 at. I'm not trying to trip you up on that question.

19 A From the available --

20 MR. LaROCK: Object to the form of the
21 question. I don't think there's actually a question
22 pending.

1 THE WITNESS: Okay. Then can you restate the
2 question for me.

3 Q BY MR. HOUSTON: With respect to your opinion
4 that the formulation of Dymista is -- what's a fair way
5 to characterize it? An important component? An
6 important consideration? Is it too strong to say
7 "critical factor"? How would you characterize the
8 importance of the formulation to the performance of
9 Dymista? I just want to use words you're comfortable
10 with.

11 MR. LaROCK: Object to the form of the
12 question.

13 THE WITNESS: So I believe in my manuscript,
14 when I talked about Dymista -- at the time it was
15 MP2902 -- I called it a novel formulation of azelastine
16 and fluticasone in the same bottle. I called it
17 "novel."

18 Q BY MR. HOUSTON: I don't think we're talking
19 about the same thing. Maybe I can get at it a different
20 way.

21 If we have two groups of patients, one takes
22 Dymista, the other does co-administration of Astelin and

1 fluticasone. They can be from Flonase and Astelin, they
2 can be -- whatever. But what I want to just be clear
3 that we're on the same page on is that those groups of
4 patients are given the same dosage of active ingredients
5 in the two studies. Do you have an opinion as to
6 whether or not you believe Dymista would perform better
7 in terms of efficacy and/or side effects as between
8 those two groups?

9 A Yes, I do.

10 Q And I believe your opinion is that you believe
11 Dymista will perform better. Is that correct?

12 A Dymista will have a, using their definition of
13 performance that you elucidated earlier, yes, Dymista is
14 better.

15 Q And that's because -- you believe that's
16 because of the formulation of Dymista.

17 MR. LaROCK: Object to the form of the
18 question. Objection, mischaracterizes prior testimony.

19 THE WITNESS: If I could. This is a
20 hypothetical situation. So using at least some data, it
21 may be helpful to speculate. So if you pull up 109 and
22 you go back to this --

1 Q BY MR. HOUSTON: Just to be clear, you're
2 talking about paragraph 109 of your declaration?

3 A Yes. Page 51. And realize in this chart we've
4 removed the effective placebo just to show the
5 difference as compared to placebo.

6 If you take and you add Flonase and Astelin,
7 you get 2.69. And you -- so that would be hypothetical,
8 because we're having to do hypothetical situations.
9 That's what you asked me. That is less improvement than
10 you're going to see with Dymista, which is at 3.11.

11 So while there is no study to answer this
12 question, my opinion is based upon this data, my
13 clinical experience, and doing the studies with Dymista
14 and the monotherapies to get the drug approved.

15 Q Okay. And then the only thing I'm trying to
16 clarify and follow up -- I understand your opinion. We
17 don't have to argue about it. I'm just trying to
18 clarify, you think that that improvement seen with
19 Dymista is due to the formulation of Dymista being
20 different from the formulation that's used for Flonase
21 and Astelin?

22 MR. LaROCK: Object to the form of the

1 question. Objection, mischaracterizes his testimony,
2 asked and answered.

3 THE WITNESS: If I could be honest with you,
4 just -- it's unexpected. We were so excited when we saw
5 this. It's unexpected. So to this day, I'm still
6 trying to wrap myself around the biology as to why it's
7 so much better. It's unexpected, and I cannot always
8 explain unexpected findings.

9 Q BY MR. HOUSTON: Is one of the reasons for
10 those -- is your belief that one of the reasons for the
11 unexpected finding is due to the formulation? Maybe I
12 can ask it that way.

13 MR. LaROCK: Object to the form of the
14 question, asked and answered, mischaracterizes his
15 testimony.

16 THE WITNESS: I believe there is no clear-cut
17 set of explanations. However, if I could elaborate, the
18 formulation of Dymista, which is the formulation, all
19 the excipients, and then azelastine, and then
20 fluticasone, that is the formulation, has all the
21 actives in there. I believe that that is truly a novel
22 formulation. That's what my paper was about. And we

1 presented these unexpected findings with this novel
2 formulation that has all those components.

3 Q BY MR. HOUSTON: And what I'm trying to get to
4 the bottom of and clarify is just that you think that
5 the novel, unexpected, surprising results, one reason
6 for that is the unique formulation of Dymista as
7 compared to if you were to just take Flonase and Astelin
8 and mix them together in a bottle.

9 MR. LaROCK: Object to the form of the
10 question, asked and answered, mischaracterizes the
11 testimony.

12 THE WITNESS: Again, I'm not a chemist. I'm
13 not a chemistry, manufacturing, and controls expert.
14 But I don't believe you can just take Flonase and
15 Astelin and mix them together. I think there's a lot of
16 problems with that.

17 So yeah, what they did with Dymista is novel.
18 You can't just take azelastine, Astelin and Flonase and
19 throw them together in a baby bottle with a nipple on
20 it. You can't do that.

21 Q BY MR. HOUSTON: Fair enough. That was maybe a
22 bad hypothetical. I want to compare the performance,

1 the efficacy and side effects of Dymista to the
2 co-administration of Astelin and Flonase. And we've
3 clearly established your opinion you think that Dymista
4 will perform better, and one of the reasons you think it
5 will perform better is because of the formula of
6 Dymista. Is that fair? Is that a fair characterization
7 of your opinion?

8 MR. LaROCK: Object to form, mischaracterizes
9 his testimony, asked and answered.

10 THE WITNESS: I think there are a variety of
11 reasons. And I could elucidate some of those other ones
12 if you would like me to.

13 Q BY MR. HOUSTON: Well, that's fine. Actually,
14 I do want to hear that. Can you first start by
15 confirming that one of the reasons is formulation, and
16 then you can tell me about what other ones you think
17 there might be?

18 MR. LaROCK: Objection to form,
19 mischaracterizes his testimony, asked and answered.

20 THE WITNESS: Okay, I'll try to restate it
21 again. I believe I have answered the formulation
22 question before.

1 So in my brain, the formulation of Dymista is
2 fluticasone, azelastine, all the excipients and all the
3 stuff that's in there. I believe that to be a novel
4 formulation, and that the embodiment of that
5 formulation, MP2902, became Dymista. Yes, I believe
6 that that is quite unique and had a variety of
7 unexpected findings. You're asking me to speculate on
8 to the rationale for those unexpected findings, and I
9 believe that there could be many things.

10 Q BY MR. HOUSTON: Let's go through them, what
11 you think they could be.

12 A I can't give you an exhaustive list. I think
13 that that's outside of the scope of my declaration. But
14 I could, you know, list a couple of things if you would
15 like.

16 There's something about the medicine Dymista
17 that there's less volume, okay, and maybe with the,
18 quote-unquote, device performance -- and to be clear, by
19 "device performance," I'm talking about things like
20 plume dimensions -- there may be something to that. So
21 these are all speculations, but those are some examples.

22 Q So formulation, volume, device performance.

1 Those are three potential factors that you think may
2 lead to the better performance of Dymista as compared to
3 the co-administration of fluticasone and azelastine as
4 separate sprays.

5 MR. LaROCK: Object to the form of the
6 question --

7 Q BY MR. HOUSTON: Is that right?

8 MR. LaROCK: Object to the form of the
9 question, mischaracterizes his testimony.

10 THE WITNESS: I don't believe anybody factually
11 knows why we have these unexpected findings. We can
12 hypothesize all we want. My hypothesis may be correct;
13 it may be wrong. You have to test these things.

14 Q BY MR. HOUSTON: That's fair enough. I just
15 want to make sure that I capture what your hypothesis
16 is. Appreciating that you're not trying to give me an
17 exhaustive list, but on the list you gave me, it's
18 formulation, less volume, device performance. Those are
19 at least three things you believe contribute to
20 Dymista's improvement efficacy and lower side effects as
21 compared to the co-administration of azelastine and
22 fluticasone. Is that right?

1 MR. LaROCK: Object to the form of the
2 question, asked and answered, mischaracterizes his
3 testimony.

4 THE WITNESS: There are some unknowns here.
5 And I treat these patients all the time, all day. And I
6 do a lot of clinical trials. There are some unknowns
7 here. And I appreciate you trying to get my theories,
8 but this is complicated. It's complicated. And to this
9 day, they still remain unknown. These are unexpected.
10 And I don't know exactly why you see these unexpected
11 findings.

12 Q BY MR. HOUSTON: Okay. Let me try it this way.
13 We've established, I think, pretty clearly that you have
14 an opinion Dymista should perform better than the
15 co-administration of the two drugs. Here is the example
16 I want to ask you:

17 So in one group, they're treated with Dymista;
18 a second group is treated with a combination of Astelin,
19 the commercial Astelin and the commercial Flonase to
20 give the same dose of actives as in Dymista; and the
21 third group is treated with the comparator formulations
22 that you used in your study for azelastine and

1 fluticasone.

2 Do you have an opinion as to where those would
3 rank in terms of their performance? Better efficacy,
4 lower side effects?

5 MR. LaROCK: Object to the form of the
6 question, calls for speculation, outside the scope of
7 his testimony and declaration.

8 THE WITNESS: So two responses to your
9 question. Please correct me if I misunderstood you or
10 didn't hear you correctly, but you said "should perform
11 better." And that is not what I said. I said it does
12 perform better. That is my opinion. Not "should."
13 "Does."

14 Secondly, I would love to do this study,
15 because I don't know. The devil will be in the details.
16 I would love to do that study. Maybe Argentum would pay
17 to have the study done, because it would be awesome to
18 do that study. Because when you have unexpected
19 findings, you kind of go, "Wow, that was unexpected.
20 Let's do more."

21 Q BY MR. HOUSTON: I just want to be clear. You
22 said you have an opinion that Dymista does perform

1 better. It does perform better as to which group are
2 you talking about? One or both of these?

3 A So --

4 MR. LaROCK: Object to the form of the
5 question. Mischaracterizes his testimony.

6 Q BY MR. HOUSTON: Just for a clear record, let
7 me restate it, just because I want to be clear. Let's
8 just call group 1 Dymista. Group 2 will be the
9 commercial Astelin and Flonase. Group 3 will be the
10 comparative formulations that you used in your study for
11 azelastine and fluticasone.

12 So we're talking about co-administration in
13 group 2 and 3. You have an opinion that Dymista will
14 perform better or does perform better than the
15 co-administration in group 2. Is that fair? That's one
16 of your opinions?

17 A Yes.

18 Q Okay. What about group 1 versus group 3? Do
19 you have an opinion as to which of those would show
20 better performance?

21 MR. LaROCK: Object to the form of the
22 question.

1 THE WITNESS: Again, my opinions sometimes are
2 right, sometimes are wrong when it comes to clinical
3 studies. That is the wonder of doing clinical trials.

4 However, I would love to do this study. I
5 believe -- I alluded to the fact, I think there's
6 something unique about the formulation of Dymista that
7 includes azelastine and fluticasone. Could there be
8 some pharmacodynamic interaction between those drugs at
9 the level of the tissue? I believe that is why the FDA
10 made them break them up and do the studies with the
11 monotherapy formulations that were the same, because the
12 FDA felt that it could be possible that there could be
13 pharmacokinetic and pharmacodynamic differences.

14 We know that in other diseases, like asthma,
15 that taking an inhaled steroid increases and
16 up-regulates the receptors for other drugs, so when
17 those drugs are given concomitantly, they actually work
18 better than you would have expected.

19 So there perhaps is a rationale to form a very
20 early hypothesis that the Dymista would do better than
21 them, given in the same formulation but as
22 monotherapies.

1 Q BY MR. HOUSTON: Given in the same formulation
2 but as monotherapies --

3 A Group 3.

4 Q Just to be clear, when you said
5 "monotherapies," you made me nervous. We're talking
6 about co-administration of these. So it would be the
7 co-administration of those two monotherapies in group 3.

8 And so -- listen, I'm not trying to ask you to
9 go out on a limb. I'm just asking if you have a
10 professional opinion as to whether or not you think
11 group 1 would outperform group 3 or not. And maybe you
12 don't know, and that's fine, too.

13 MR. LaROCK: Objection. Form, asked and
14 answered.

15 THE WITNESS: I would guess group 1 would do
16 better, for the reasons that I just elucidated. There
17 are issues with using two separate monotherapies
18 administered sequentially.

19 Q BY MR. HOUSTON: Okay. Let me ask about as
20 between group 2 and group 3. So now the two groups are
21 group 2 is the co-administration of the commercial
22 embodiments Astelin and Flonase, versus the

1 co-administration of the comparative embodiments using
2 azelastine and fluticasone. Do you have an opinion as
3 to which of those two are likely to perform better?

4 MR. LaROCK: Object to the form of the
5 question, calls for speculation, outside the scope.

6 THE WITNESS: I don't have an opinion.

7 MR. LaROCK: Mike, we've been going for an
8 hour.

9 MR. HOUSTON: Let me see if I have anything I
10 can wrap up on this topic while we're here. Okay, we
11 can go off the record and take a break.

12 (Recess 11:34 to 11:49 a.m.)

13 Q BY MR. HOUSTON: I've got a couple more
14 questions about the topic we were just discussing, where
15 I defined the group 1, group 2, and group 3 categories.
16 Do you recall those, or do I need to go through those
17 again, what each was?

18 A Just to be clear, group 2 commercially
19 available; group 3, what was used in the clinical
20 studies.

21 Q Right.

22 A Okay.

1 Q So it seemed like you had a fairly firm
2 opinion -- and appreciating this is your opinion, but
3 you had a fairly firm opinion that group 1 would perform
4 better than group 2. But you were less sure whether
5 group 1 would perform better than group 3. Is that
6 fair?

7 MR. LaROCK: Object to the form of the
8 question, mischaracterizes the prior testimony.

9 THE WITNESS: No, that's not fair.

10 Q BY MR. HOUSTON: Okay. As between group 1
11 compared to group 2 and group 1 to group 3, is the --
12 are your opinions the same?

13 A I believe, if you did this study and you
14 included placebo, so it's double dummy, right, that
15 group 1 would be better than everything.

16 Q So group 1 would be better than 2 or 3?

17 A And the placebo one.

18 Q And the placebo one. Do you have an opinion as
19 to whether you would expect group 1 to outperform group
20 2 more than it outperforms group 3?

21 MR. LaROCK: Object to the form of the
22 question. Outside the scope.

1 THE WITNESS: That is a very difficult
2 question. Because the formulation of Dymista, like I
3 said before, is novel. It contains both Astelin, or
4 azelastine, and fluticasone in the same bottle. And the
5 groups 2 and group 3 have fluticasone in one monotherapy
6 bottle and azelastine in another monotherapy bottle.

7 So Dymista has both actives in one bottle.
8 That's going to make it, in my opinion, if I were to
9 guess the outcomes of these studies before we did them,
10 better than all of it.

11 And between group 2 and group 3, how much
12 better would Dymista be than group 2 versus group 3?
13 That is very difficult to speculate. I would guess it
14 would be very similar. I don't know. We'd need to do
15 that study.

16 Q BY MR. HOUSTON: Let me ask a housekeeping
17 matter before I go on to my next topic. We've had two
18 breaks so far. I just want to confirm that you haven't
19 discussed with your attorneys the contents of your
20 testimony today or anything about your testimony that
21 you're giving here today or that you've given here so
22 far.

1 MR. LaROCK: I'm going to instruct the witness
2 not to answer on the basis of attorney-client privilege
3 and the work product immunity.

4 MR. HOUSTON: Adam, you're not allowed to
5 instruct the witness to not answer that question. It's
6 clearly prohibited by the rules. I'm just asking if he
7 had conversations about his testimony today. If you're
8 not going to allow him to answer it, then at lunchtime
9 we're going to have to call the board and get a ruling
10 on your objection. That is clearly prohibited by the
11 rules.

12 MR. LaROCK: The issue, Mike, is that your
13 question's really broad, because you've said "anything
14 else about your testimony." But I will, given my
15 objection, I'll let the witness answer to the extent
16 that he doesn't reveal the communications between his
17 counsel, and that he can answer the question that you've
18 posed relating to the contents of his testimony.

19 MR. HOUSTON: Well, the rule says contents of
20 the testimony or anticipated testimony. So I don't see
21 how you could have any conversation with the witness
22 related to his testimony on these breaks that wouldn't

1 be prohibited by the rules. I'm entitled to get an
2 answer from the witness.

3 MR. LaROCK: If you want to rephrase it for the
4 contents or his anticipated testimony, I'll let him
5 answer.

6 MR. HOUSTON: Can I understand why your
7 distinction is, why you think that's okay as compared to
8 my original question?

9 MR. LaROCK: Your original question wasn't
10 limited to the content and his anticipated testimony.
11 Your original question had something to do with "the
12 effect of, and anything else about your testimony."

13 MR. HOUSTON: "About your testimony."

14 Q Have you had any conversations with counsel
15 during the breaks about your testimony, whether it's the
16 testimony you've already given, whether it's testimony
17 that you might anticipate to be given?

18 A We haven't discussed any content of my
19 testimony.

20 Q Well, any instructions to keep doing what
21 you're doing, or to answer faster, answer slower,
22 anything related to your testimony, any instructions

1 related to your testimony, either that you've already
2 done or that might be going forward?

3 MR. LaROCK: You can answer.

4 THE WITNESS: The extent of our conversations
5 at the break where it's related to the deposition have
6 been that there was a fear maybe I was speaking too fast
7 and that she wasn't catching some of the things, so I
8 should try to slow down in some of these sections where
9 there may be real scientific stuff so she can truly
10 capture it.

11 They had felt perhaps you had been rude to me
12 on a couple of occasions and that I should stick up for
13 myself.

14 Beyond that, we talked about, I wish I could
15 still wear a uniform, and some contracting work that's
16 going on at my house. We didn't talk anything else
17 about the case.

18 Q BY MR. HOUSTON: So they instructed you that
19 you should stick up for yourself in response to some of
20 my questioning?

21 MR. LaROCK: Mischaracterizes his testimony.

22 THE WITNESS: No, they said they had felt you

1 had been rude to me by cutting me off so many times and
2 not letting me finish answering your question.

3 Q BY MR. HOUSTON: I want to go -- the second
4 part of what you said. You said that you should stick
5 up for yourself. That's the part I want to understand.
6 What did they say?

7 A That --

8 MR. LaROCK: Objection. Mischaracterizes the
9 testimony.

10 THE WITNESS: I mean, I'm giving -- I can't
11 remember word for word, but the general essence was, you
12 weren't letting me finish, and that that was rude, and
13 that you may not like my answer, but it's okay for me to
14 give my opinion, that I'm here to give my opinion.

15 Q BY MR. HOUSTON: Do you remember anything else?

16 A His wife bought that tie, my wife bought this
17 tie. No, everything else was personal.

18 Q I appreciate you trying to be forthcoming, but
19 yeah, I just wanted to limit it to related to the
20 deposition the testimony.

21 A Nothing else.

22 MR. HOUSTON: Counsel, I do think that probably

1 goes over the line of what the rule is, but we'll just
2 proceed. I would ask you not to have those kind of
3 conversations with the witness going forward,
4 instructing him in any way about the way he should
5 answer questions, the way he should treat this
6 deposition.

7 This deposition has started. You're not
8 allowed to provide those instructions once it's started,
9 under my understanding. We can just proceed, but I
10 would ask you to not do that again going forward.

11 MR. LaROCK: Okay. We didn't instruct the
12 witness to do anything. It was more of logistics, the
13 court reporter's having difficulty.

14 MR. HOUSTON: Okay. The witness just testified
15 the way he testified, so I'm going off of what he told
16 me, and I'm going to assume that's true.

17 (Reporter interruption)

18 MR. HOUSTON: For the record, I would just like
19 to note that the court reporter indicated that she's not
20 having a hard time keeping up with the testimony,
21 perhaps aside from a few times you've asked us to repeat
22 things. Thank you.

1 Q Dr. Carr, you still see patients today and
2 treat them for AR; is that true? "Today" meaning at
3 present, not today necessarily, but --

4 A I have a very busy clinical practice.

5 Q Some of which is treating patients for AR?

6 A That would be correct.

7 Q For a patient that presents with moderate to
8 severe AR, do you have a first-line defense, if you
9 will, do you have a prescription or instructions to the
10 patient that you typically pursue initially?

11 A In 2018? Today?

12 Q Uh-huh.

13 A I have general ways that I approach patients,
14 but every individual patient is unique.

15 Q So patients who present to you with moderate to
16 severe AR, at least, some of the time, do you prescribe
17 to them Dymista?

18 A Yes.

19 Q At least some of the time, do you not prescribe
20 to them Dymista?

21 A Yes.

22 Q Can you give me a rough estimate of about what

1 percentage of patients you prescribe Dymista to versus
2 not prescribing Dymista to as the initial instructions
3 to the patient, initial treatment? Would that be a
4 better word?

5 MR. LaROCK: Objection. Form.

6 THE WITNESS: Each patient is unique, and you
7 have to look at their history. You have to look at
8 their presenting complaints, you have to look at their
9 comorbid conditions, other diseases that they have. You
10 have to look at surgeries that they may have had, in
11 particular, nasal and sinus surgeries. You have to look
12 at their history of allergies. Do they have any
13 hypersensitivity reaction to any of the ingredients that
14 could perhaps be in a medicine you're going to give
15 them? You have to do an environmental assessment.
16 Perhaps if you can modify the environment. So in each
17 individual patient, it is really, really different.

18 So in general, I would say my primary thing
19 that I would do is once I have done a comprehensive
20 history and physical exam, I will try to institute
21 environmental control measures in these patients and see
22 what they've done, what they haven't done. I will see

1 what medicines they have tried and what medicines they
2 have not tried.

3 And then I will perform an allergy specific
4 skin test. And then based on that kind of cohort of
5 data, then I'll formulate a treatment plan along with
6 the patient. And it's different for different ages and
7 different diagnoses.

8 Q BY MR. HOUSTON: So can we focus on patients
9 that have, as at least one of their symptoms, moderate
10 to severe AR? Can we do that?

11 A Sure.

12 Q So as to that set of patients, and for the ones
13 where you proceed to the point of, as you said,
14 formulating a treatment plan, about what percentage of
15 those patients would you say that you prescribed Dymista
16 to, approximately?

17 A So I will keep my answer only to patients that
18 fit the FDA-approved age for Dymista. Because for a
19 three or four-year-old that has severe or moderate to
20 severe allergic rhinitis, I probably would not start
21 with Dymista.

22 So looking at the approved -- let's say it's a

1 15-year-old kid, just for sake of conversation, because
2 that's within that group. I would look at what other
3 medicines that they have had and break them up into two
4 groups: those that have never been on anything, and
5 those that have been cycling through medicines.

6 If they have been on something, I might pay
7 attention for if there were any side effects, like if
8 they've had a nasal ulcer or perforation or something
9 like that from a nasal spray.

10 If there's never been any problems and they
11 haven't been on any medicines or anything like that, I
12 would say in patients that come to me, my first
13 prescription after environmental control, nasal rinses,
14 all that kind of stuff, I would say my first
15 prescription is Dymista.

16 Q And so I'm trying to get at about what
17 percentage of your patients is that true for. Or is it
18 true for all of them?

19 A I would say in all the patients --

20 MR. LaROCK: Hold on. Object to the form of
21 the question, outside the scope.

22 THE WITNESS: I would say in all the patients

1 that meet that description that I gave, so the right
2 age, environmental -- all that kind of stuff, I would
3 say Dymista is my first prescription. It's the one I go
4 to first.

5 Q BY MR. HOUSTON: So in that group it's
6 essentially 100 percent?

7 MR. LaROCK: Object to the form of the
8 question. Mischaracterizes his testimony.

9 THE WITNESS: In that group of patients that
10 I've described, in the office the prescription that I
11 type in, the first thing I will go for is Dymista. That
12 doesn't mean the patient gets it, because now you've got
13 all the issues of insurance and everything.

14 Q BY MR. HOUSTON: Okay. So I just want to make
15 sure I understand. For that group, it's approaching 100
16 percent. I appreciate maybe there's some outliers or
17 something like that. But it's fair to say that in your
18 practice, for that group it's approaching 100 percent
19 that you would prescribe Dymista as the first thing.

20 MR. LaROCK: Object to the form of the
21 question. Outside the scope of his declaration.

22 THE WITNESS: I think a better way to answer it

1 is for that group, it is the treatment of choice.

2 Q BY MR. HOUSTON: Well, that's circumventing
3 what I want to get. Now you're putting the
4 characterization on it that maybe I don't agree with. I
5 don't know. I want to know the numbers. I'll decide if
6 I agree with your characterization. I'm just asking
7 what the numbers are. Do you have a rough idea of what
8 the numbers are, percentagewise?

9 MR. LaROCK: Objection --

10 Q BY MR. HOUSTON: A couple times I've asked you
11 if it's approaching 100 percent, and you won't say yes
12 to that. Why wouldn't you agree with my
13 characterization that it approaches 100 percent for that
14 group?

15 MR. LaROCK: Objection. Outside the scope.

16 THE WITNESS: Well, there's other factors that
17 come to play. So I can't say 100 percent, because
18 there's other factors that come to play. Perhaps the
19 patient has Dymista as a tier 3 medicine and they really
20 don't have a job and they don't have any money, and it's
21 going to be an expensive medicine for them. There could
22 be other extenuating circumstances.

1 So I can't give you 100 percent, but I think
2 it's fairly clear my intent would be, that would be my
3 first prescription medication that I would give to that
4 patient population.

5 Q BY MR. HOUSTON: Well, I think you just
6 described, at least, a hypothetical, where, for whatever
7 reason, you can't do that, or don't do that, because of
8 extenuating circumstances, as you put it. So I'm trying
9 to get a feel for how prevalent is that.

10 Would you say you prescribe Dymista to about 75
11 percent of the patients in that group?

12 MR. LaROCK: Object to the form of the
13 question, asked and answered.

14 Q BY MR. HOUSTON: 50 percent?

15 MR. LaROCK: Object to the form of the
16 question, asked and answered. Mischaracterizes the
17 testimony. Outside the scope.

18 THE WITNESS: It's really difficult for me to
19 give you an exact percentage. If I could just say,
20 again, it's my first prescription that I would give to
21 patients that meet that definition.

22 Q BY MR. HOUSTON: So I'm not --

1 A The majority.

2 Q Okay. So greater than 50. Greater than 50
3 percent, to be clear.

4 A I would guess. I'm not privy to if they get it
5 or not always, but --

6 Q Just your practice.

7 A This is pure speculation. It can vary between
8 my different offices, right, there's different
9 populations and different areas. But in general, across
10 all three offices that I have and in different
11 demographics that I practice within, it would be my
12 first prescription that I would give to patients.

13 Q Well, to be clear, you've established a couple
14 of reasons why you might not do that. And I'm just
15 trying to get a feel for the frequency of one versus the
16 other. So is about 50 percent as fine of a point as you
17 can put on it?

18 A Well, like I said, I can't give you an exact
19 percentage.

20 Q I'm not asking for an exact percentage. I'm
21 asking for a ballpark.

22 MR. LaROCK: Objection. Outside the scope.

1 THE WITNESS: I write it frequently, if that's
2 what you're trying to get at.

3 Q BY MR. HOUSTON: I'm trying to get at how often
4 you write it versus how often you don't write it.
5 That's what I'm trying to get it. Just to say you do it
6 frequently doesn't give me a relative feel for the
7 percentage across this patient population.

8 A Maybe I could answer it in a different way and
9 say if we lived in a pure world where there were no
10 outside forces, insurance companies, payers, money,
11 society, I would write it 100 percent.

12 Q Okay. So roughly how often does it occur that
13 there are these outside influences that something causes
14 you to not write it? Half the time? A third of the
15 time? Quarter of the time?

16 MR. LaROCK: Object to the form of the
17 question, outside the scope.

18 THE WITNESS: Again, look, these are
19 complicated, because, you know, we're sitting here in
20 January, and in January people haven't really met their
21 deductibles yet. They may have a higher cost out of
22 pocket. There may be other extenuating circumstances.

1 You know what it's like to have insurance. And each
2 year your insurance can change.

3 So I think I've answered it to the best of my
4 ability. My intent is to make that my first
5 prescription medication. If the patient goes to the
6 pharmacy and they don't get it, I may not have control
7 over that.

8 Q BY MR. HOUSTON: Sure, and I'm just asking
9 about your --

10 A But my intent is to have that as my first
11 prescription.

12 Q Well, like you said, it's January, a lot of
13 patients haven't met their deductible, so they're paying
14 more out of pocket at this point. So for those
15 patients, would you be less likely to prescribe Dymista?

16 MR. LaROCK: Objection. Outside the scope.

17 THE WITNESS: Again, from a pure approach, I
18 would like to prescribe Dymista to that patient and
19 maybe, perhaps, if they had a very high deductible, I
20 would see if I could give them a sample. Or if we could
21 do some extra work around the office and see if we could
22 possibly get them a prior authorization and get it

1 covered at a better price. There's other things that
2 perhaps we would do more work that we wouldn't have to
3 do, for instance, in August, when people have met their
4 deductible.

5 So those are some of the ways that in clinical
6 practice doctors are under tremendous amount of
7 pressure, where we just want to take care of our
8 patients, but we're being affected by these outside
9 forces. And those are some of the techniques that we
10 can use to get patients on the right medicines.

11 Q BY MR. HOUSTON: So let me ask it this way. If
12 a patient had insurance that's going to cover Dymista,
13 is it fair to say it's more likely that they will end up
14 with a Dymista prescription from you than a patient that
15 doesn't have insurance that covers Dymista? Just
16 relative, relatively speaking.

17 MR. LaROCK: Objection. Outside the scope of
18 his declaration.

19 THE WITNESS: In both patients, I would try to
20 put them on Dymista. I am sensitive to the cost of
21 health care. I think any physician that's working in
22 society today has to be. But I want my patients to get

1 better. And so this medicine is a medicine that will
2 help them get better. And so, like I said, that's my
3 first prescription.

4 Q BY MR. HOUSTON: And all I'm asking is, as a
5 matter of likelihood, is it more likely that a patient's
6 going to come away with a Dymista prescription from you
7 if their insurance covers that drug as compared to if
8 the insurance doesn't cover that drug?

9 MR. LaROCK: Objection. Asked and answered.

10 Q BY MR. HOUSTON: Can you answer that question?

11 MR. LaROCK: Objection. Asked and answered,
12 outside the scope.

13 THE WITNESS: It's very difficult to answer
14 that question. If I could explain why.

15 So I would write the prescription, and then my
16 staff may come back and say, "Hey, Dr. Carr, we just got
17 a message from the pharmacy, and the pharmacy says the
18 patient has not met their deductible yet, and it's going
19 to be \$400," or \$200, or whatever the case may be. And
20 I'll instruct my staff, "See what you can do. See if
21 you can get" -- so this is the second time, in the same
22 patient, that I'm saying, "No, I want Dymista. Get this

1 patient Dymista. See if we can get him a sample. See
2 if we can do a prior authorization. See what we can do
3 to get it covered." And each patient is different. See
4 what medicines they've been on and failed. Because each
5 insurance is different, you know.

6 So for two or three times, I may try to get the
7 patient on Dymista. The insurance company may come
8 back, or the pharmacy may come back and say, "Look, this
9 patient has what's called a step edit. They have to
10 fail X, Y, and Z. Do you have documentation that they
11 failed it?"

12 And if I have it, I'll provide it. If I don't,
13 my staff will call the patient and say, "Your insurance
14 company requires a step edit. We can give you the
15 medicines as a step edit, or you can just buy the
16 Dymista. And we have a sample for you." So each of
17 those scenarios is different, and then it's on the
18 patient.

19 But my side of it is, I have tried numerous
20 times to try to prescribe Dymista for that patient.

21 Q BY MR. HOUSTON: Right. But certainly you
22 would agree that for the patients that go to the

1 pharmacy with their Dymista prescription, it's covered
2 under insurance, they're generally not coming back to
3 you.

4 A No.

5 Q But some of the ones that come back to you, you
6 try all these other things, and in some cases, they end
7 up not getting Dymista. Right? In other words, are you
8 able to 100 percent of the time get those patients
9 Dymista?

10 A Wouldn't that be a perfect world, if the doctor
11 could get their patients medicine that would help them.

12 So obviously, no. It's a commentary on the
13 health care system, really, that sometimes patients
14 cannot get medications that they will benefit from. So
15 it's not 100 percent.

16 Q So that was sort of the first group that you
17 defined, never been on a medicine. I think all the
18 groups are meeting the age requirements, you've tried
19 the environmental assessment, et cetera, and that group
20 has never been on a medicine. Then you defined a second
21 group, where you said they'd cycled through things.

22 A Oh, I'm sorry. Our discussion, that long

1 discussion we just had, was everybody. Looking at the
2 two groups, it's just going into my decision tree, like
3 for instance, if they had been on a spray and they had a
4 perforation because of the spray, I probably wouldn't
5 give them another spray. I'm sorry if I didn't make
6 that clear. But our long discussion that we just had,
7 that was everybody that fit my definition of a patient I
8 would put on Dymista.

9 Q For patients who for whatever reason can't
10 afford Dymista -- I think we've established it can be
11 expensive, if you have to buy it out of pocket -- do you
12 know the approximate cost of, what would be the
13 appropriate way to assess it? A monthly dosage? A
14 yearly dosage? Do you know the approximate cost of
15 Dymista out of pocket?

16 MR. LaROCK: Objection, form. Outside the
17 scope.

18 THE WITNESS: For the life of me, I cannot
19 figure out how insurance companies contract with
20 pharmacies and contract with different pharma companies
21 to set the price and cost. I don't know why one patient
22 can get it for \$18, and another patient it's more than

1 that. So I'm sorry, I'm not an expert in setting the
2 wholesale acquisition cost and negotiating with setting
3 pricing with insurance companies.

4 Q BY MR. HOUSTON: Right. I appreciate the
5 insurance company scenario can get very complicated.

6 But my question was more directed, if I just
7 want to walk into Walgreens with a prescription, and I
8 just want to buy it. Sell it to me. Do you have any
9 sense of what that cost is?

10 MR. LaROCK: Objection. Outside the scope.

11 THE WITNESS: I can give you -- again, my
12 caveat is I'm not an expert in setting the pricing. But
13 I believe the way it works is an individual insurance
14 company sets up a tier system --

15 Q BY MR. HOUSTON: Let me stop you, just because
16 I want to skip all that. I'm talking about somebody
17 that doesn't present with an insurance card. No
18 insurance. Just walks in with a prescription and says,
19 "Sell it to me."

20 A So cash pay patient?

21 Q Cash pay patient. Do you have any sense of
22 what that costs?

1 MR. LaROCK: Objection. Outside the scope.

2 THE WITNESS: Cash pay patients are really
3 super rare. I do not have a significant cabinet of cash
4 pay patients. I don't know how much it would cost if
5 they just walked into a pharmacy, Walgreens. I would
6 presume it would be different for different pharmacies.
7 But I don't know how much it would cost.

8 Q BY MR. HOUSTON: Not even an order of
9 magnitude? Is it more than 100 per monthly dose?

10 A I would say probably. It's pure speculation.
11 But I'd guess perhaps maybe a hundred bucks, something
12 like that.

13 Q So for patients who, based on all the factors
14 you've analyzed on them and that seem suitable for
15 receiving Dymista, so you say, I want to give this
16 person Dymista, but for whatever reason, they cant get
17 it, because it's too expensive, their insurance company
18 won't cover it, whatever it is, and they come back to
19 you and say, "Dr. Carr, you've got to give me another
20 prescription, something else, something that's less
21 expensive," what's your next most popular line of
22 treatment?

1 MR. LaROCK: Objection. Outside the scope.

2 THE WITNESS: Well, again, it's individualized
3 per patient. I think in those patients, I would really
4 at this point encourage them to go into allergy shots.

5 Q BY MR. HOUSTON: Allergy shots?

6 A Yeah, I would encourage them to go into allergy
7 immunotherapy, otherwise termed allergy shots.

8 Q So if they can't afford Dymista, then you don't
9 bother to prescribe any other nasal sprays of any sort?

10 MR. LaROCK: Objection. Mischaracterizes his
11 testimony. Outside the scope.

12 THE WITNESS: Like I said before, you know,
13 there's different presentations of different patients,
14 and there are medicines that are available over the
15 counter that I do not have to write a prescription for.

16 Q BY MR. HOUSTON: Okay. Can I interrupt?
17 Because I think you just mentioned something that helps
18 me clarify. In my question, I might have said
19 "prescribe." And I appreciate that some medicines maybe
20 patients don't have a prescription for. So I want to
21 make sure we're not getting hung up there.

22 So I'm asking about patients that you either

1 have or would generally feel are appropriate to get a
2 Dymista prescription and can't because of the cost or
3 insurance problems or whatever. What's the next line of
4 therapy you recommend, whether it involves prescription
5 or not?

6 MR. LaROCK: Objection. Outside the cope.

7 THE WITNESS: So I would say in the moderate to
8 severe patients, these are motivated people, because
9 they've got moderate to severe disease. And if they're
10 just not going to get it, I would say probably the most
11 common thing I would do next would be a compounded
12 formulation of a nasal rinse with budesonide.

13 Q BY MR. HOUSTON: Budesonide's a steroid?

14 A It's a form of a steroid.

15 Q For those patients that again you think would
16 be appropriate for Dymista, but for some reason can't
17 get it, do you ever instruct them to use a combination
18 of Flonase and Astelin or their generic equivalents?

19 MR. LaROCK: Objection. Outside the scope.

20 THE WITNESS: I think I see what you're trying
21 to ask me. Usually, if I write a prescription for
22 Dymista and the patient comes back at their follow-up

1 visit and they're on Flonase and Astelin, that typically
2 happened at the level of the pharmacy, and they had a
3 substitution at the level of the pharmacy. That's not
4 something that I would typically recommend.

5 Q BY MR. HOUSTON: So in the cases where, for
6 whatever reason, you do have to make a substitution for
7 Dymista, you're saying you don't recommend a
8 Flonase/Astelin or their generic counterpart
9 combination?

10 MR. LaROCK: Objection. Outside the scope.

11 THE WITNESS: Usually the substitutions are
12 done at the level of the pharmacy. So happens all the
13 time, where the doctor will write a prescription, they
14 go to the pharmacy, there's some issue, and at the level
15 of the pharmacy there's a substitution. And the patient
16 will typically come back to me and say, "I got the
17 Dymista sample that you gave me, but when I went to the
18 pharmacy, they gave me two different sprays."

19 And then my anecdote that we talked about
20 earlier is they usually then say, "I want that Dymista,
21 because it worked better than these two sprays." And
22 then we start down that pathway of trying to do what we

1 can. And if we can't do it, then I'll go to the
2 budesonide rinses and I'll try to get them to start
3 allergy shots.

4 Because medicines just treat symptoms. And
5 allergy shots in some patients can induce long-term
6 remission so they don't need the medicine.

7 Q BY MR. HOUSTON: So when patients come to you
8 and report that a given treatment does or doesn't work,
9 that informs your opinion of whether or not it's a good
10 treatment or bad treatment?

11 MR. LaROCK: Object to the form of the
12 question.

13 THE WITNESS: That's a very general question.
14 I do listen to what my patients tell me about their
15 perception of their disease and their perception of
16 their response to therapy. I do listen to that. I
17 think it's very important for doctors to listen to their
18 patients. You've got to have a good relationship with
19 your patient.

20 Q BY MR. HOUSTON: Let me go back to the
21 discussion we were having when we were comparing this
22 group 1 of patients treated with Dymista; group 2,

1 patients treated with Astelin and Flonase. And I think
2 we established that there aren't any formal studies
3 comparing those. You said you'd like to do them.

4 But you said you had an opinion that the group
5 1 patients should see better performance than group 2.
6 Is that based on your anecdotal experience with
7 patients? Is that the basis for your opinion that the
8 group 1 patients would see better results than the group
9 2 patients?

10 MR. LaROCK: Object to the form of the
11 question. Outside the scope.

12 THE WITNESS: Well --

13 Q BY MR. HOUSTON: And again, we're talking about
14 the co-administered.

15 A If you go back to my declaration, back to page
16 51, 109, and you take Astelin and you take Flonase and
17 you add them up, it's still less than the Dymista. So
18 my opinion is based on a multitude of things.

19 Granted, we have established we don't have a
20 double-blind, placebo-controlled prospective clinical
21 trial to answer this question. But if you look at
22 adding the delta here, the benefit as compared to

1 placebo together, it's still less than what you get with
2 Dymista.

3 So there's something novel about this that
4 makes it better than these two given in group 2. That
5 was the basis of my opinion.

6 Q BY MR. HOUSTON: In that instance, where you're
7 adding the results for Flonase and Astelin together,
8 first of all, in doing that, you're assuming just a
9 straight additive effect of those two; is that right?
10 That's why you're adding them together, you're summing
11 those two numbers, you're assuming an additive effect
12 between these two drugs?

13 MR. LaROCK: Objection, form.

14 THE WITNESS: First off, this is very
15 low-quality data, right, by taking this and doing this.
16 You need a well-randomized, double-blind,
17 placebo-controlled trial. And you're asking me to
18 speculate and pinning me down to ask which group is
19 better, one or the other, and then why. And I think
20 we've established there is no real good data, because
21 there are no studies that have been conducted.

22 Q BY MR. HOUSTON: But even with that, you're

1 willing to have some opinions, right, about what you
2 think is going to perform better?

3 A So I think I expressed my opinion earlier that
4 yes, group 1, which is the Dymista group, would perform
5 better than group 2. Part of it is based on this; part
6 of it has been my anecdote which I told you about.

7 Q And I just want to make clear, so you do have
8 that opinion, despite the fact that, as you say, there
9 have been no formal studies done, and even this data
10 here I think you said is low quality, and it's more
11 anecdotal.

12 MR. LaROCK: Hold on. Object to the form of
13 the question. Mischaracterizes his testimony.

14 THE WITNESS: This data, for the purposes of
15 the primary end points of the studies that were
16 conducted, is very high quality data.

17 You're asking me to look at this study, which
18 was done for a different purpose, and speculate about
19 some other question.

20 Q BY MR. HOUSTON: To be clear, I didn't ask you
21 to do that. Hold on. I want to make sure we're on the
22 same page. I didn't ask you to do that. I asked you

1 what your bases were, and you're the one that said,
2 well, if you add these two together.

3 A Okay.

4 Q So I didn't ask you to do it.

5 A I thought you said why.

6 Q That's fine.

7 A So if I could be clear, then, this study is a
8 very good study for the purposes that it was done.

9 Q For what it shows.

10 A For what it shows. When you don't have a
11 double-blind, placebo-controlled study, you can't know
12 the answer.

13 You're asking me to opine on what I think would
14 happen. And so I have given you my opinion, and then
15 you asked me why. And part of it is my anecdote, part
16 of it is like looking at other studies that didn't
17 really answer that question, but I'm trying to glean
18 some data from there. So that's my hypothesis.

19 Q And again, I want to clarify it. I didn't ask
20 you to opine; I asked you if you had an opinion. And if
21 the answer is no, I don't have an opinion, I'm fine with
22 that answer, too.

1 So I just want to be clear, you're changing
2 what I think transpired a little bit. I just want to
3 make sure the record's clear. I just asked if you had
4 an opinion as between group 1 and group 2, and you said
5 you did, and you told me what it was. So just to be
6 clear, I didn't ask you to form an opinion. I asked if
7 you had one. Is that fair? Do you understand that?

8 MR. LaROCK: Objection. Mischaracterizes the
9 testimony.

10 You can answer.

11 THE WITNESS: Yes, I understand it.

12 Q BY MR. HOUSTON: And so based on anecdotal
13 evidence and the situation where you add some of this
14 data together, which makes the data a lot less reliable
15 or -- again, I'm not trying to put words in your mouth,
16 but you used some adjective to say that once you do
17 that, now all of a sudden the data is not nearly so
18 good.

19 So based on your anecdotes and this less than
20 perfect data, that has led you to form an opinion as to
21 the likely outcome as between patients treated with the
22 group 1, being Dymista, versus group 2, being the

1 combination of Astelin and Flonase?

2 MR. LaROCK: Object to the form of the
3 question. Asked and answered. Outside the scope.
4 Mischaracterizes his testimony.

5 THE WITNESS: Are you asking me to opine?

6 Q BY MR. HOUSTON: I'm asking -- well, I think
7 you've established you have an opinion. If you're going
8 to say now you don't, that's fine, you can tell me that.
9 I'm not asking you to do anything. I'm just asking you
10 to tell me whether you have an opinion. And I thought
11 we'd established numerous times that you do have an
12 opinion. Is that wrong?

13 MR. LaROCK: Object to the form of the
14 question. Mischaracterizes his testimony. Outside the
15 scope. Asked and answered.

16 THE WITNESS: To be clear, your question is, do
17 I have an opinion?

18 Q BY MR. HOUSTON: As to whether or not patients
19 in group 1 are likely to see better outcomes as compared
20 to patients in group 2.

21 A I have an opinion, yes.

22 Q And that opinion stems from your anecdotal

1 evidence of what you've observed with patients, as well
2 as manipulating the data that you talk about here in
3 paragraph 109 to add things together in the manner you
4 described; is that right?

5 MR. LaROCK: Objection. Mischaracterizes his
6 testimony. Asked and answered.

7 THE WITNESS: Are you asking me to give you my
8 opinion and opine on this subject? Or are you asking
9 me, do I have an opinion?

10 Q BY MR. HOUSTON: Well, I had asked you if you
11 had an opinion, and you said yes. And I asked what it
12 was. And I believe you told me that you thought group 1
13 would do better than group 2.

14 A So when you said what it was, that was asking
15 me to opine on it.

16 Q I'm asking you to reveal to me what that
17 opinion is that you told me you had.

18 A So you are asking my opinion.

19 Q I'm asking what it is. You already said you
20 had one. I'm just asking you to describe it.

21 A Just so we're clear, you asked me a question
22 earlier, and you said you never asked my opinion. You

1 just wanted to know if I had one. So now you're asking
2 me to give you my opinion.

3 Q To reveal it to me, yes.

4 A Okay. So just for clarification, you've asked
5 me if I have an opinion. I've said yes. Now you've
6 asked me to opine and give you my opinion.

7 So I will repeat what I had previously said,
8 which says there are -- through my anecdote -- and I
9 can't remember the exact words that I said, but through
10 my anecdotes of seeing patients, as well as looking at
11 the results of this clinical trial, and my experience of
12 conducting the studies, I believe group 1 would have a
13 better outcome for clinical efficacy and safety than
14 group 2.

15 Q Okay. In your practice of treating patients
16 with AR over, let's say, the last three years, have you
17 ever instructed a patient to take a combination of
18 azelastine and fluticasone, even if it's for only a
19 short period of time?

20 MR. LaROCK: Objection. Outside the scope.

21 THE WITNESS: Yes, I think we already
22 established that Dymista, which is a combination of

1 azelastine and fluticasone, is my first prescription
2 drug. So I quite commonly recommend it.

3 Q BY MR. HOUSTON: Thank you for catching that.
4 I obviously didn't ask the question the way I wanted to.

5 In the last three years of your practice in
6 treating patients with AR, have you ever instructed
7 patients in such a way that they would be taking
8 fluticasone and azelastine as monotherapy, but
9 co-administered, again, even if it's only on demand or
10 for short periods of time?

11 MR. LaROCK: Objection. Outside the scope.

12 THE WITNESS: If what is on demand?

13 Q BY MR. HOUSTON: Taking one or both of those
14 two monotherapies.

15 MR. LaROCK: Same objections.

16 THE WITNESS: So I prescribe a ton of
17 medications, and I'm certain at some point I have
18 written a prescription of fluticasone and azelastine.
19 And as I stated earlier, it's not a common practice.
20 And you asked about on demand. I'm certain I must have
21 told the patient to take it on demand.

22 Q BY MR. HOUSTON: In those instances, the

1 purpose for those prescriptions would be to treat AR?

2 MR. LaROCK: Objection. Outside the scope.

3 Q BY MR. HOUSTON: Or I should say, one of the
4 purposes?

5 MR. LaROCK: Same objection.

6 THE WITNESS: In 2018.

7 Q BY MR. HOUSTON: I said the last three years --

8 A 2015.

9 Q And if something's changed dramatically,
10 either before or after that, I'd ask you to let me know.
11 I was just trying to pick a -- there's nothing special
12 about that three-year window. I was just trying to pick
13 a window that you might have a decent memory of.

14 A Yes.

15 Q For patients in which, for whatever reason, you
16 end up prescribing or instructing on the use -- for them
17 to use a fluticasone product co-administered with an
18 azelastine product. So again, not in the bottle
19 together like Dymista, but separately. Would you say
20 your preferred steroid in that situation would be
21 fluticasone?

22 MR. LaROCK: Objection. Outside the scope.

1 Mischaracterizes his testimony.

2 THE WITNESS: No.

3 Q BY MR. HOUSTON: What would your preferred
4 steroid in that situation be?

5 A Budesonide.

6 Q And has that always been the case as long as
7 you can remember, or did that change at some point in
8 time?

9 MR. LaROCK: Objection. Outside the scope.

10 THE WITNESS: As medicine changes, doctors
11 change their opinion. I can't point to at one point
12 where budesonide became -- I would say probably as it
13 became an over-the-counter medication, I would choose
14 budesonide. And my sensitivity to women's health.

15 Q BY MR. HOUSTON: So prior to budesonide
16 becoming OTC, would you say budesonide was still your
17 preferred steroid in that situation, or was your
18 preferred steroid something else, like fluticasone?

19 MR. LaROCK: Objection. Outside the scope.

20 THE WITNESS: Preferred steroid for what?

21 Q BY MR. HOUSTON: In the situation we've just
22 been discussing, which is where, for whatever reason,

1 you have provided instructions to a patient to take a
2 steroid and an antihistamine to treat AR. Not in the
3 same bottle, as in Dymista, but as separate
4 administrations.

5 MR. LaROCK: Objection. Outside the scope.
6 Mischaracterizes his testimony.

7 THE WITNESS: So since OTC and, if you recall,
8 I said "and my sensitivity to women's health issues."
9 Prior to that, I probably didn't have a preference.
10 They're all the same. There's never been a study to
11 show one steroid as more efficacious than the other
12 steroid.

13 Q BY MR. HOUSTON: Not even in the situation
14 where the steroid's combined with an antihistamine?

15 A Prior to the studies that we've discussed
16 today. I gave you several examples in my declaration
17 where an antihistamine plus a steroid was no different
18 from a steroid alone. And the unexpected findings we
19 found with Dymista.

20 Q Maybe I could get at it this way. Do you know
21 about when budesonide became OTC and/or was identified
22 as potentially more sensitive to women's health?

1 MR. LaROCK: Object to the form of the
2 question.

3 Q BY MR. HOUSTON: Did that happen before, say,
4 Ratner came out?

5 MR. LaROCK: Object to the form of the
6 question. Outside the scope.

7 THE WITNESS: So budesonide is the only one
8 that has a pregnancy category B. As far as I know, it's
9 always been that way. Which means you can use it in
10 pregnant and nursing mothers. My wife and I tried for
11 five years to have a baby. She has allergies.

12 Q BY MR. HOUSTON: So you're well aware.

13 A So I became much more sensitive to those side
14 effects, and said maybe I should think about these
15 things more from a different perspective.

16 Q Okay. Maybe we could factor out that
17 complication, if you will, if we ask you about your male
18 patients. So patients where you don't have that concern
19 about pregnancy, is budesonide still your preferred
20 steroid in the situation where patients have been
21 instructed to use a combination of a steroid and an
22 antihistamine?

1 MR. LaROCK: Objection. Outside the scope.

2 THE WITNESS: So if our discussion is around
3 efficacy, then there's no difference between any of the
4 other steroids. They're all the same. There's never
5 been a study to show one monotherapy nasal steroid is
6 better than the other. So if a patient says, "Hey, Doc,
7 I got some of this Nasacort at Costco. How's that?"
8 I'll say, "Give that a try first."

9 Q BY MR. HOUSTON: But to be clear, the situation
10 we're talking about here is not monotherapy. It's where
11 a patient, you have instructed a patient for whatever
12 reason to use a combination of a steroid and
13 antihistamine. That's the situation I'm asking about.

14 A Well, I don't usually --

15 MR. LaROCK: Object to the form of the
16 question. It mischaracterizes his testimony. Asked and
17 answered.

18 You can answer.

19 THE WITNESS: So there's other antihistamines I
20 would use, too. I'm not a huge fan of Astelin. Has
21 such a high sedation rate, has such bad taste, patients
22 don't like it.

1 Q BY MR. HOUSTON: I haven't moved to the
2 antihistamines yet.

3 A You just said antihistamine and nasal steroid
4 sprays. So I was responding to that.

5 Q Okay, Dr. Carr, I was clarifying the subset of
6 situation I'm talking about is where there's
7 co-administration of a steroid and an antihistamine.
8 And limit it to male patients, so we can factor out this
9 complication due to pregnancy.

10 A So steroid and antihistamines. I was talking
11 about the antihistamine.

12 Q But that wasn't my question. My question was
13 about the steroid. We'll move to the antihistamine in
14 just a minute. It's not that I'm trying to not let you
15 speak about it; I just want to keep a flow to my
16 questioning.

17 So in that subset, do you have a preference for
18 one steroid or the other?

19 MR. LaROCK: Objection. Outside the scope.

20 Q BY MR. HOUSTON: When there's going to be
21 co-administration?

22 MR. LaROCK: Object to the form of the

1 question. Outside the scope. Asked and answered.

2 THE WITNESS: Not really. They're all the
3 same.

4 Q BY MR. HOUSTON: So as you sit here today, you
5 believe that all of the steroids perform about the same
6 when they're combined with an antihistamine in a
7 co-administration situation?

8 MR. LaROCK: Objection. Mischaracterizes his
9 testimony, outside the scope.

10 THE WITNESS: Was there a question? You just
11 made a statement.

12 Q BY MR. HOUSTON: So as you sit here today, you
13 believe that all of the steroids perform about the same
14 when they're combined with an antihistamine in a
15 co-administration situation; is that right?

16 MR. LaROCK: Objection. Mischaracterizes the
17 testimony. Outside the scope.

18 THE WITNESS: No.

19 Q BY MR. HOUSTON: Okay. The answer before that
20 you said, "Not really. They're all the same." So can
21 you try to explain, when you're co-administering a
22 steroid and an antihistamine, what your -- what is your

1 preference? What's the basis for your preference for
2 choosing a steroid? Again, limited to male patients.

3 A So I think I made it clear before, my
4 preference is Dymista.

5 MR. LaROCK: Objection. Outside the scope.

6 THE WITNESS: That's the co-administration in
7 the same bottle.

8 Q BY MR. HOUSTON: I understand that. We're
9 talking about the situation where, for whatever reason
10 you're not giving Dymista, you're giving the steroid and
11 antihistamine separately.

12 MR. LaROCK: Objection. Mischaracterizes his
13 testimony. Form.

14 THE WITNESS: Can you please restate your
15 question?

16 Q BY MR. HOUSTON: Okay. In those situations
17 that you testified about where you end up with patients
18 who for whatever reason can't take Dymista, and you have
19 instructed to use a steroid co-administered with an
20 antihistamine, and these are male patients, do you have
21 a preference for one steroid over another in that
22 situation?

1 MR. LaROCK: Objection. Asked and answered,
2 outside the scope, mischaracterizes his testimony.

3 THE WITNESS: No.

4 Q BY MR. HOUSTON: So you believe that the class
5 of steroids combined with an antihistamine, all of those
6 steroids will perform approximately equally under those
7 circumstances?

8 A That's not what I said --

9 MR. LaROCK: Objection. Form, outside the
10 scope. Mischaracterizes testimony.

11 Q BY MR. HOUSTON: Why don't you have a
12 preference? There aren't any that work better than
13 others?

14 MR. LaROCK: Objection, form.

15 THE WITNESS: I think I've made it clear, I
16 don't have a preference over one steroid or another in
17 that population. And most of the times, patients just
18 self-select. They're over the counter.

19 Q BY MR. HOUSTON: So in being co-administered as
20 separate sprays with an antihistamine, do you think each
21 of the steroids in that class perform about the same?

22 MR. LaROCK: Objection. Asked and answered,

1 outside the scope, mischaracterizes his testimony.

2 MR. HOUSTON: I'm sorry, Adam, I should
3 clarify.

4 Q When I say "perform about the same," I mean the
5 combination works about the same, not the steroid
6 individually. I'm not sure you could even test that.

7 MR. LaROCK: Same objections.

8 THE WITNESS: Well, that's a totally different
9 question.

10 The combination includes the antihistamine.
11 I've been trying to talk about the antihistamine, but
12 you have been focusing on a mono product, the steroid.

13 So to continue the line of questioning and the
14 answer on the mono product, I'll say again, I don't
15 believe there's ever been a study that shows one
16 monotherapy nasal steroid is better than another
17 monotherapy nasal steroid. Therefore in this population
18 I don't have a preference.

19 Q BY MR. HOUSTON: So the population I'm asking
20 about are the ones that are taking a steroid and an
21 antihistamine at the same time. Not in Dymista, but
22 co-administered as monotherapies at the same time.

1 That's the situation I'm asking about.

2 A That's why I'm ambivalent to the steroid. I'm
3 more interested in the antihistamine. There's no
4 difference.

5 Q So there's no difference among the
6 antihistamines in your opinion when they're being
7 co-administered -- I'm sorry -- there is no difference
8 among the steroids when they're being co-administered
9 with an antihistamine.

10 MR. LaROCK: Objection. Mischaracterizes his
11 testimony. Outside the scope of his declaration. Form.

12 THE WITNESS: So again, I don't know if we're
13 not just connecting on this, but there has never been a
14 study to show there is a difference between one nasal
15 steroid or another nasal steroid such that you should
16 have a preference of one over the other. So I don't
17 really in this scenario care what steroid a patient has.

18 Q BY MR. HOUSTON: Okay. So for example, Ratner,
19 2008, that report -- am I correct to say that reports an
20 azelastine plus fluticasone co-administered
21 monotherapies as one group? Is that right? And it
22 compares that to just azelastine and fluticasone

1 monotherapies by themselves, and perhaps it has a
2 placebo? Is that what Ratner covers?

3 A No. That is not what it covers.

4 Q Maybe I'm misreading. I think you have Ratner
5 in front of Exhibit 1045. In table 1, it reports I
6 guess three different groups.

7 A Yes, it does.

8 Q And the first group is azelastine by itself;
9 right?

10 A No, it's not.

11 Q Okay, what is the first group based on your
12 understanding?

13 A It is azelastine hydrochloride nasal spray
14 group.

15 Q That's the group of patients that are being
16 given a nasal spray that contains azelastine as the
17 active ingredient, isn't it?

18 A Plus placebo. They received two sprays.

19 Q Okay. So it's azelastine plus placebo. The
20 second group, is that fluticasone plus placebo?

21 A Yes.

22 Q And what's your understanding what the third

1 group is?

2 A Azelastine, two sprays each nostril twice a
3 day, and fluticasone, two sprays each nostril once a
4 day.

5 Q And is there any placebo involved in the third
6 group?

7 A This is not a placebo-controlled study. There
8 is not a placebo arm in this entire trial, which makes
9 it biased.

10 Q I'm just asking for the AZ and the FL, the
11 group 1 and the group 2. You said it was azelastine
12 plus a placebo, fluticasone plus a placebo.

13 For the third group, does that also use a
14 placebo in the same way that the first two groups did,
15 or not?

16 A No.

17 Q And you would agree with me that whether you
18 think the data good or bad, that Ratner reports an
19 improvement when azelastine and fluticasone are
20 co-administered as compared to the other two groups.
21 Right?

22 A As compared to the other two groups which

1 involved two different products being sprayed into their
2 nose, yes.

3 Q So if we look at this group 3, where there's a
4 combination of the antihistamine -- an antihistamine and
5 a steroid were co-administered, do you believe -- do you
6 not have a preference or do you not think that -- do you
7 think that any steroid in this class would have worked
8 approximately equally as well as fluticasone did in that
9 group 3?

10 MR. LaROCK: Objection. Outside the scope.

11 THE WITNESS: I believe this study to be a
12 hypothesis-generating study that is not placebo
13 controlled, so you can't take too much away from it.

14 Q BY MR. HOUSTON: I'm just asking whether or not
15 you have an opinion in terms of whether or not any
16 steroid in this class could be substituted for the
17 fluticasone in that group 3 and you would expect similar
18 results, as reported here.

19 MR. LaROCK: Objection. Outside the scope,
20 calls for speculation.

21 THE WITNESS: You'd have to do the study.
22 Because it's not the steroid alone.

1 Q BY MR. HOUSTON: So you don't have an opinion
2 one way or another whether you can sub in or sub out the
3 steroids and expect the same result?

4 MR. LaROCK: Objection. Outside the scope,
5 calls for speculation, asked and answered.

6 THE WITNESS: There's too many other variables
7 that you can't control for in this combination.

8 Q BY MR. HOUSTON: So the improvement that's
9 reported here in Ratner for the group 3, where an
10 antihistamine is co-administered with a steroid, do you
11 have an opinion as to whether or not that improvement is
12 specific to the antihistamine and steroid combination
13 that's reported there, or is it just the fact that an
14 antihistamine is co-administered with a steroid in
15 general?

16 MR. LaROCK: Object to the form of the
17 question. Outside the scope, calls for speculation,
18 asked and answered.

19 THE WITNESS: Well, in this particular study,
20 the combination was azelastine and fluticasone. So the
21 results correlate specifically with them. To make any
22 other opinions, you would need to do those studies,

1 since this is a hypothesis-generating study. If you
2 want me to generate a different hypothesis with a
3 different form other than fluticasone, you've got to do
4 the study.

5 Q BY MR. HOUSTON: So then if we go back to your,
6 I call them prescribing habits -- appreciating it's not
7 always a formal prescription, it might just be
8 instructions, because the medicine's OTC -- you said
9 when you prescribed for those patients where you end up
10 instructing them to use an antihistamine and a steroid
11 co-administered, you don't have a preference for the
12 steroid. Doesn't have to be fluticasone. Right? Could
13 be any steroid?

14 MR. LaROCK: Objection. Mischaracterizes his
15 testimony. Outside the scope. Form.

16 THE WITNESS: Patients will self-select. Those
17 are over the counter, the ones we talked about.

18 Q BY MR. HOUSTON: I'm just talking about your
19 instructions or your references.

20 MR. LaROCK: Same objections.

21 THE WITNESS: I think we've already established
22 this is not my preference.

1 Q BY MR. HOUSTON: Your preference when you find
2 yourself in this limited set of circumstances.

3 MR. LaROCK: Object to the form of the
4 question. Mischaracterizes his testimony, outside the
5 scope.

6 THE WITNESS: So in this circumstance of group
7 3, which is a totally different circumstance than what's
8 going on in Ratner, I don't have a preference to the
9 steroid. I think I already said that.

10 Q BY MR. HOUSTON: Why is that a totally
11 different circumstance than what's good going on in
12 Ratner?

13 A I usually don't give my patients placebo nasal
14 sprays combined with an active. And this difference
15 that was shown is compared to an active plus a placebo.
16 That's an artificial setting. Plus it's not placebo
17 controlled. So that's totally artificial.

18 Q So Ratner, in suggesting that the
19 co-administration of azelastine and fluticasone performs
20 better than these others, are you saying that's not a
21 very reliable study or not a reliable report that would
22 apply to your actual prescription habits?

1 A I think I've said that multiple times. It's
2 not placebo controlled, and at best it's hypothesis
3 generating. I know I've said that multiple times.

4 Q The benefit that Ratner purportedly reports for
5 this group 3, where there's co-administration, do you
6 have any reason to believe that those same benefits
7 would or would not be seen if you just switched among
8 the antihistamines and the steroids in these respective
9 classes?

10 In other words, is that benefit that Ratner
11 says he sees, do you think that's specific to this
12 specific combination, azelastine plus fluticasone, or
13 does it go on to apply more broadly to just a
14 combination of an antihistamine and a steroid?

15 MR. LaROCK: Object to the form of the
16 question. Outside the scope. Mischaracterizes his
17 testimony.

18 THE WITNESS: I think in retrospect it's unwise
19 to make those types of extrapolations. We've just
20 discussed some of the unexpected findings that we saw in
21 the clinical development program for Dymista. So it
22 would be unwise to make those extrapolations.

1 Ratner studied two specific therapies, and he
2 made some conclusions which generated a hypothesis with
3 those two specific therapies. And so it ultimately says
4 what I just said.

5 Q BY MR. HOUSTON: The hypothesis that Ratner
6 generated, did that end up being validated? Was the
7 Ratner paper right?

8 MR. LaROCK: Objection. Outside the scope.

9 THE WITNESS: They didn't study it further.
10 The next study was Hampel.

11 Q BY MR. HOUSTON: So you don't take an opinion
12 as to whether or not Ratner's hypothesis was correct or
13 not correct.

14 A Can you state to me what you mean by "Ratner's
15 hypothesis"?

16 Q BY MR. HOUSTON: You're the one that said that
17 Ratner generated a hypothesis. I'm using your words.
18 You tell me what hypothesis you're talking about.

19 A I didn't say what the hypothesis was. I said
20 that the paper was a hypothesis-generating paper. It's
21 a non-placebo-controlled study. It's a
22 hypothesis-generating paper. I can't opine on his

1 hypothesis. I just said it generated a hypothesis.

2 Q But you don't know what that hypothesis is.

3 MR. LaROCK: Objection. Mischaracterizes his
4 testimony.

5 THE WITNESS: You just asked me if I agreed
6 with it, so I'm asking you to state what it is.

7 Q BY MR. HOUSTON: Okay. And I'm trying to
8 understand. I don't know what it is, Dr. Carr. I'm
9 asking you. Do you know what Ratner's hypothesis was?
10 And if you don't, that's fine. I'm not forcing you to
11 give me an answer. I just want to know whether you know
12 or not know. You said it's a hypothesis-generating
13 paper.

14 A Well, fortunately, we have the paper in front
15 of us. So perhaps let's see if we can find it in here,
16 if the authors, which would include Ratner, tell us what
17 their hypothesis was or is.

18 (Discussion off the record; luncheon
19 recess 1:01 to 1:42 p.m.)

20 Q BY MR. HOUSTON: Dr. Carr, you recall before
21 lunch we were talking about those limited circumstances
22 in which you end up prescribing patients or instructing

1 patients to use simultaneously a steroid and an
2 antihistamine, but where they are administered separate
3 from each other. And I think at one time you had sort
4 of shown a desire to talk about your preferences for the
5 antihistamine piece of that.

6 So in the situations where you, for whatever
7 reason, end up co-administering those two drugs, do you
8 have a preference for the antihistamine that gets
9 co-administered?

10 MR. LaROCK: Objection. Form.
11 Mischaracterizes his testimony. Also outside the scope
12 of his declaration.

13 THE WITNESS: The antihistamines I typically
14 use are the oral antihistamines. And in particular
15 fexofenadine is an antihistamine that has very little
16 sedation. That can actually be given to an airline
17 pilot.

18 So these patients tend to have atopic diseases.
19 And with allergic rhinitis, there's a significant
20 increase of other atopic diseases such as eczema, other
21 itchy skin rashes. So that would be one of the
22 scenarios where I could see using an antihistamine,

1 because it gives me the benefit of helping with other
2 things. You could treat their pruritis from the eczema,
3 so on and so forth. And the very low incidence of
4 sedation with fexofenadine has a very favorable adverse
5 event profile.

6 Q BY MR. HOUSTON: This concept that in the
7 co-administration, the separate but co-administration of
8 a steroid and an antihistamine where the antihistamine
9 might be useful to treat other symptoms in addition to
10 just AR, is that concept known before 2002?

11 A Is your question before 2002, did
12 antihistamines treat other things other than AR?

13 Q Before two thousand -- as of 2002, was it known
14 that if an antihistamine was co-administered with a
15 steroid, separate but co-administered, that the
16 antihistamine could have some additional beneficial
17 effects in terms of treating other symptoms besides just
18 the AR symptoms?

19 MR. LaROCK: Object to the form of the
20 question. Outside the scope.

21 THE WITNESS: So I believe prior to 2002,
22 antihistamines were approved for treatment of other

1 conditions other than AR. So therefore it would be
2 known that the antihistamine has efficacy in that other
3 condition.

4 Q BY MR. HOUSTON: So that knowledge that
5 antihistamines could have efficacy for other conditions
6 could be a motivation for a doctor to prescribe both a
7 steroid and an antihistamine for simultaneous but
8 separate administration, couldn't it be?

9 MR. LaROCK: Objection. Outside the scope.
10 You can answer.

11 THE WITNESS: I think it's possible that there
12 would be a patient that had allergic rhinitis and atopic
13 dermatitis, and they could be on the fluticasone,
14 mometasone or budesonide, or any nasal steroid for their
15 AR, and then they could be on a nonsedating second
16 generation oral antihistamine for the treatment of their
17 itchy skin rash.

18 Q BY MR. HOUSTON: Would nasally administered
19 antihistamine have any effect on these other non-AR type
20 symptoms, if they presented in a patient?

21 A Would nasally administered antihistamine have
22 benefit in eczema? Is that your question?

1 Q Well, I think you've kind of -- I don't know if
2 you've limited it to just eczema. But yeah, these other
3 conditions that you said sometimes accompany AR, eczema
4 being an example.

5 A I'm sorry, what was the question? Would the
6 nasal help the skin?

7 Q Nasal antihistamine, was that known that it
8 could help conditions besides just AR?

9 A So the active molecule was known to help other
10 conditions. As a tablet, I don't know if it was ever
11 studied in the nasal formulation for these other
12 conditions.

13 Q Okay, that's fine. Just to be clear, then, as
14 of 2002, you're not sure whether it was known that
15 nasally administered antihistamines might be useful for
16 treating conditions in addition to AR?

17 MR. LaROCK: Objection. Mischaracterizes his
18 testimony.

19 THE WITNESS: Yeah, I think that does
20 mischaracterize it, because it was approved for other
21 conditions other than AR.

22 Q BY MR. HOUSTON: Even the nasally administered

1 version?

2 A Yes, it was approved for other indications.

3 Q Okay. Please appreciate, Dr. Carr, you know
4 this better than I do. I'm trying to follow your
5 testimony and ask appropriate questions.

6 But that makes me want to go back. So would
7 the fact that it was known that nasally administered
8 antihistamines could have efficacy for conditions in
9 addition to AR, could that be a motivation for a doctor
10 to prescribe both a nasally administered steroid and a
11 nasally administered antihistamine? Again, not
12 necessarily in one bottle, but for co-administration.

13 MR. LaROCK: Objection. Form. Outside the
14 scope of his testimony.

15 THE WITNESS: So I would say, just like
16 patients can have hypertension and diabetes, and they
17 will be given drugs for hypertension and diabetes, two
18 different indications, prior to -- in the context, I
19 should say, in the context of this discussion, it is
20 possible that doctors would have given patients the two
21 separate medications for two separate indications, two
22 separate diseases, like the doctor would treat a

1 diabetic that also has hypertension with two separate
2 medicines.

3 But the benefit is, it gives you the ability to
4 have flexibility in titrating the doses, treating each
5 indication separately. Gives us -- like a doctor may
6 titrate insulin, and as you lose weight, they may
7 titrate your blood pressure medicine.

8 Q BY MR. HOUSTON: In the context of just
9 treating AR, and treating it with both a steroid and an
10 antihistamine, is it important to be able to have the
11 ability to do the dose titration you just referenced?

12 A I'm going to answer your question in the
13 context of 2018. And in general, when you have
14 combination medications, the thought is the benefit of
15 having them separately will allow you to individually
16 titrate. So in a general sense, you could apply that
17 thought to nasal sprays.

18 Q Even in 2018? You said you limited it to 2018.
19 You said in the context of 2018.

20 A Uh-huh.

21 Q Is there some other context where your answer
22 would be different? I'm just trying to understand, why

1 did you add that clarification that you're answering in
2 the context of 2018? Is there something important about
3 that?

4 MR. LaROCK: Object to the form of the
5 question.

6 THE WITNESS: Today we've discussed an evolving
7 practice of medicine over the course of well over a
8 decade. And I just wanted to be sure that you
9 understood what I was -- in what context, what time, in
10 that evolution I was discussing it.

11 Q BY MR. HOUSTON: Is it any more or less
12 desirable today than it was in 2002, to have the ability
13 to do this dosage titration when treating AR with both
14 an antihistamine and a steroid?

15 A Well, prior to 2002, there was no study to
16 support doing that. You've brought up these
17 hypothetical situations that we've discussed. I would
18 point to some of the skepticism from the FDA talking
19 about the practice of medicine, which includes the
20 individual titration of doses.

21 So I would say in all diseases, to include
22 allergic rhinitis, if patients are on multiple

1 medications, one of the practices of medicine is to be
2 able to individually titrate those medicines. When you
3 have a fixed-dose combination, you lose that, which
4 could create problems.

5 Q I want to go back to your treatment practices
6 when I asked you about, again, this limited circumstance
7 where you would end up instructing a patient to use a
8 steroid and an antihistamine simultaneously but
9 separately, administered separately. You made reference
10 to using the orally delivered antihistamine
11 fexofenadine? I might have mispronounced that. Sorry.
12 Do you recall that?

13 A We can call it Allegra.

14 Q Allegra. Fine. Have you ever had a patient
15 that you instructed to use a steroid and an
16 antihistamine, not together in the same bottle,
17 administered separately, where both the steroid and the
18 antihistamine were nasally administered?

19 MR. LaROCK: Object to the form of the
20 question. Outside the scope. Mischaracterizes his
21 testimony.

22 THE WITNESS: Yes.

1 Q BY MR. HOUSTON: Were you treating AR in that
2 patient, or those patients?

3 A I was usually responding to a step edit request
4 from the insurance company.

5 Q You mentioned that before. Can you explain
6 really quickly what step edit requests are?

7 A So a step edit would be the insurance company
8 saying your patient cannot get a drug until they have
9 tried drug X, Y, and Z. So you need to document that
10 they've been on drug X, Y, and Z and that it didn't work
11 before we'll give you the drug that you have prescribed
12 for your patient. So there's a step edit process that
13 you have to go through.

14 So typically, that would be a step edit. I
15 write Dymista, patient goes to the pharmacy, gets
16 switched at the pharmacy, patient takes the sample of
17 the Dymista I've given them, gets better, gets the two
18 separate medicines at the pharmacy, because the
19 insurance company has instituted a step edit, patient
20 comes back to me and says, "Hey, I got these two drugs
21 instead of the one drug that you gave me. The one drug
22 that you gave me was better than the two drugs the

1 pharmacy gave me. Can we do this authorization now,
2 since we've done the step edit?"

3 Q Have you ever in any patients undergoing that
4 step-edit process where the two drugs, the two separate
5 drugs that they took, worked okay, that they didn't come
6 back to you to say, "I really want to be on Dymista"?
7 Has that ever happened?

8 MR. LaROCK: Objection. Outside the scope.

9 THE WITNESS: Well, I have patients that don't
10 come back to me for a variety of reasons all the time.
11 They may move, they may live out of state.

12 When a patient comes back and says, "Hey, this
13 nasal spray combination" -- I mean, in all actuality,
14 trying to make sure I'm very careful with what I'm
15 saying, but in all actuality, if the patient got better,
16 it's because they were compliant with their Flonase.
17 And usually what a patient will say is, "Hey, Doc, I
18 didn't realize that I would do better if I took my
19 medicine every day, and I just stopped that one that
20 tasted bad. And actually, you know, I'm not a hundred
21 percent, but I am better than I was. And I don't get a
22 sinus infection now when I go over to grandma's house

1 and get around the cat."

2 So I think it's a compliance issue.

3 Q BY MR. HOUSTON: So is it fair to say you would
4 have at least some patients who for whatever reason end
5 up taking a steroid and an antihistamine as separate
6 nasal sprays and if they, as you said, if they comply,
7 as they're supposed to, with the recommended dosing,
8 then they adequately control their AR symptoms?

9 MR. LaROCK: Objection. Outside the scope.
10 Mischaracterizes his testimony.

11 THE WITNESS: If I could just clarify your
12 question. I want to make sure I'm not confused. We had
13 been talking about these different groups, and then we
14 kind of just started talking about prescribing patterns
15 in group 3. I still want to just make sure that we're
16 talking about that population of patients which are
17 patients that have moderate to severe AR.

18 Q BY MR. HOUSTON: Would your testimony differ if
19 we were talking about a different patient population
20 besides just those that have moderate to severe AR?

21 MR. LaROCK: Objection. Outside the scope.
22 Mischaracterizes his testimony.

1 THE WITNESS: It would depend on the question.

2 Q BY MR. HOUSTON: So for now let's limit it to
3 those patients that have moderate to severe AR. Are you
4 aware of any of your patients that have ever
5 successfully treated moderate to severe AR by taking an
6 antihistamine together with a steroid but not in the
7 same bottle?

8 MR. LaROCK: Objection. Outside the scope.
9 Form.

10 THE WITNESS: So these patients are
11 complicated. And I gave a good example before of a
12 patient that got better because they were compliant with
13 the nasal steroid.

14 We know that nasal steroids treat patients that
15 have moderate to severe AR. They just don't take their
16 medicine. So I don't know in that hypothetical case in
17 your question if the patient got better because of all
18 the effects of Flonase or budesonide or Nasonex or
19 whatever the steroid was that they got over the counter.

20 Q BY MR. HOUSTON: Versus the antihistamine being
21 added to it?

22 A Versus the combination of the two separate

1 entities.

2 Q Do you have any sense of why, when the pharmacy
3 or the insurance company or whoever it is denies
4 Dymista, why they suggest patients take the combined
5 monotherapies of a steroid and an antihistamine?

6 MR. LaROCK: Objection. Outside the scope.
7 Calls for speculation.

8 THE WITNESS: I think it's because the
9 pharmacies have a relationship with the insurance
10 companies, who have generated these coverages, tier
11 status, and step edits. I don't think that they do it
12 whimsically. I think that there's some kind of
13 motivation, probably financial.

14 Q BY MR. HOUSTON: Let me ask it this way. Is it
15 your understanding that when they won't cover Dymista,
16 that they would push a patient to just using a steroid
17 alone, or do they push them towards using a steroid and
18 an antihistamine in two separate bottles?

19 MR. LaROCK: Objection. Outside the scope.

20 THE WITNESS: Well, the only thing they will
21 cover is an antihistamine. The patient has to go -- the
22 whole cost burden is shifted to the patient. The

1 patient has to go buy a steroid. That's not covered.

2 Q BY MR. HOUSTON: Because that's OTC?

3 A That's OTC. So the only thing that gets
4 covered is the antihistamine. It may seem illogical, it
5 does to me, but that's how they function. And I can't
6 give you the exact rationale, but like I said, my
7 suspicion is that there's a financial incentive.

8 Q Okay, so along those lines, wouldn't that
9 financial incentive be even greater to just tell the
10 patient, go use a steroid, so that they don't have to
11 cover the antihistamine piece of it?

12 MR. LaROCK: Objection. Outside the scope,
13 calls for speculation.

14 THE WITNESS: That could very well be one of
15 the step edits.

16 Q BY MR. HOUSTON: I'm going to switch gears on
17 you for a minutes. Earlier we were talking about, I
18 think the term was "dose titration"? "Dosage
19 titration"? Do you recall that? At least, that topic
20 came up? Am I remembering the phrase correctly?

21 MR. LaROCK: Objection to form.

22 THE WITNESS: In what context?

1 Q BY MR. HOUSTON: Just in our discussion just a
2 few minutes ago.

3 A The flexibility of dosing?

4 Q Yeah. Was the term, is the proper term "dose
5 titration," or just "titration"? I'm just figuring out
6 what the proper term of art is to refer to that.

7 A Well, within the context of prescribing two
8 different medicines in the same patient and being able
9 to maintain the flexibility of up-dosing and
10 down-dosing, I think we could agree on, in this
11 circumstance, using the phrase titration to increase the
12 dose up, or titration to increase it down for each one
13 individual drug.

14 Q Is it generally true or generally expected that
15 when you increase the concentration of a given drug, you
16 would expect the efficacy of that drug to go up?

17 MR. LaROCK: Objection. Outside the scope.
18 Form.

19 Q BY MR. HOUSTON: Let me clarify that, too, so
20 that it's not misinterpreted. Let's say your starting
21 point is the recommended dosage, whatever is recommended
22 on the label. So if we use that as our starting point,

1 is it generally expected that if you increase the
2 concentration, the efficacy will go up, but at the same
3 time, the side effects will go down?

4 MR. LaROCK: Objection.

5 Q BY MR. HOUSTON: I'm sorry. I said that wrong.
6 I saw the puzzled look on your face. Efficacy and side
7 effects, they're both expected to go up when you
8 increase the dosage? Is that right?

9 A If your question is, when you increase the dose
10 above the approved dose, do you always expect both
11 efficacy to go up as well as side effects to go up, my
12 answer is no.

13 Q Well, yeah, and I want to clarify. I didn't
14 say "always," because I appreciate there could be
15 unexpected effects. I'm just saying, is that a general
16 expectation?

17 A It's very specific for the drug. So I would
18 say no.

19 Q Is it true that the general expectation is that
20 as efficacy is increased, side effects are increased?

21 A Can you read me that question again? What was
22 it?

1 Q Is it true that the general expectation is that
2 as efficacy is increased, side effects are increased?

3 A That's a very general question. Very, very
4 vague and general. So I would say no.

5 Q What if we just limit it to the two drugs
6 fluticasone and azelastine? Is that a general
7 expectation as to those two drugs, that as efficacy goes
8 up, side effects go up?

9 A If I may start with fluticasone. Fluticasone
10 is a corticosteroid, which has a dose-response curve
11 that plateaus. So as you get to the top of the plateau,
12 you are not going to get any improvements in your
13 efficacy. However, you can continue to get more and
14 more side effects. That's quite commonly known with
15 steroids.

16 With azelastine, I will focus my discussion of
17 azelastine not as a molecule, but as a nasal spray, as
18 Astelin. If you go above the FDA recommended dosing,
19 two sprays each nostril twice a day, I don't necessarily
20 believe you get improvement in efficacy there, either,
21 but you do get -- you would see more side effects.

22 The only exception would be when azelastine

1 would be given perhaps in a different formulation to the
2 eye. There are examples in the eye, the way the
3 receptors work in the eye, where it's different
4 pharmacodynamically. So you could see improvements in
5 efficacy and improvements in side effects at the same
6 time. But there is this concept, this plateau effect,
7 which is why dose-ranging studies are required by the
8 FDA.

9 Q I think that's what I'm trying to get at.
10 Dose-ranging studies are the studies that are trying to
11 capture the effect of increased efficacy and increased
12 side effects as you raise or lower the dosage; right?

13 A In general, dose-ranging studies look at the
14 efficacy and they look at the safety, and you try to
15 establish a dose-response curve.

16 Q Have you got your declaration in front of you?

17 A Yes.

18 Q Could you turn to paragraph 66. You see there
19 is discussion there of sometimes you call it a stepwise
20 approach, other places you say step-up and step-down
21 approaches? Do you see that?

22 A So I'm reading on page 29, paragraph 66.

1 Q Yes.

2 A Initially on the fifth line down, I'm quoting
3 Dykewicz, where he's talking about the utilization of
4 both step-up and step-down approaches, and then the term
5 "stepwise approach" comes from the ARIA and the asthma
6 guidelines.

7 If you pull up the asthma guidelines, it talks
8 about the stepwise approach to asthma. "ARIA" stands
9 for "allergic rhinitis in asthma." And there was an
10 attempt to kind of use common language, because it's an
11 upper airway and lower airway disease. That's why we're
12 using this verbiage of step-up and step-down therapy.

13 Q What you're talking about here in photograph 66
14 is that the dosage that a patient ends up taking is
15 either going to be increased or decreased in order to
16 try to control symptoms; right? And ideally, you only
17 take as much drug as needed to obtain control of the
18 symptoms. Right?

19 A I think the optimum word here is "control."
20 We're trying to control patients' diseases, and we want
21 to use the least amount of medications to do that. So
22 we may step up a steroid therapy by having them continue

1 their nasal spray at the approved dose, and then giving
2 them an oral steroid, which is a much more potent
3 steroid.

4 Once the patient is under control after a
5 couple days, then they have completed their course of an
6 oral steroid, and they step down to using just the lower
7 dose or exposure to the patient. That would be an
8 example of step up, step down.

9 Q So when you're referring to, in the last
10 sentence:

11 "...the patient that would 'step up'
12 his/her treatment by using the higher
13 dose or second drug 'as needed.'"

14 Could that apply to the situation where a
15 patient is on a nasal steroid medication, and because of
16 a peak in symptoms, the patient steps up by adding a
17 nasal antihistamine?

18 A I guess in this scenario that you're
19 presenting, a good illustrative example is to again use
20 asthma. So fluticasone is approved for asthma. It's a
21 daily controller medicine that patients take every day.
22 And fluticasone is used in allergic rhinitis as a daily

1 controller medicine used every day.

2 For rescue, for step-up in asthma, patients may
3 then add albuterol to be used as needed. And in the
4 hypothetical situation that you've presented with the
5 antihistamine, in that case, then it would be the
6 antihistamine that would be being utilized as the
7 as-needed medication in this hypothetical
8 step-up/step-down scenario.

9 Q I don't think it's so hypothetical. Let's see
10 if we can get to the bottom of this. Go ahead and flip
11 over to the next page, paragraph 67. But it's on page
12 30.

13 A So 67 starts on 29. Yes?

14 Q Go to page 30. The second full sentence at the
15 top of page 30 it says:

16 "In my experience, 'on demand' or
17 'as needed' therapy was the prevailing
18 practice in AR treatment, whereby a
19 patient would take one drug consistently
20 (e.g., a steroid) and use the second
21 drug only when symptoms worsened."

22 Do you see that?

1 A I do see that sentence.

2 Q So you're testifying that based on your
3 experience, the prevailing practice in treating AR was
4 that a patient would be taking one drug consistently,
5 such as a steroid, and then would add a second drug if
6 and when the symptoms worsened. Is that right?

7 A If I could read the sentence prior to that, so
8 you can have my statement in context. It says:

9 "Dr. Schleimer claims that ARIA
10 would have motivated a POSA to develop a
11 fixed-dose combination of Astelin and
12 fluticasone, but this recommendation is
13 contrary to his claim. In my
14 experience, 'on demand' or 'as needed'
15 therapy was the prevailing practice in
16 AR treatment, whereby a patient would
17 take one drug consistently" -- whatever
18 that drug is, example being a steroid --
19 "and use the second drug only when
20 symptoms worsened. "

21 So that is exactly what I said.

22 Q And I'm just asking you, that's what you're

1 talking about there, is the prevailing practice for AR
2 treatment was that a drug such as a steroid would be
3 taken consistently, and then the second drug would be
4 added when symptoms worsened. That's what you're saying
5 in that sentence; right?

6 A What I'm saying here, and what the presumption
7 of this is, is that a second drug that worked would be
8 added when symptoms worsened. And I gave a perfect
9 example a moment ago such as an oral steroid. There are
10 other nasal sprays: oxymetazoline, or Afrin. There were
11 other therapies available. A chromone that they could
12 have used.

13 So the presumption here is that they would use
14 a drug that worked. You don't want to use something
15 that doesn't work. And several studies, as I had said
16 before, had showed that there was no difference between
17 a nasal steroid alone versus the nasal steroid plus an
18 antihistamine.

19 Q So if a doctor, maybe Dr. Schleimer or
20 Dr. Accetta disagreed with you about the effectiveness
21 of adding an antihistamine, if they thought that that
22 would work, then that would at least fall within the

1 prevailing practice in treating AR that you're talking
2 about here. If those doctors thought that second drug,
3 being the antihistamine, would be effective, then the
4 prevailing practice is they would use that, they would
5 add that second drug to treat a bump up in symptoms. Is
6 that fair?

7 A I'd like to respond to the two doctors
8 separately. So Dr. --

9 Q It's a hypothetical, Doctor.

10 A You said Dr. Schleimer and Dr. Accetta.

11 Q I said "for example." A hypothetical doctor --
12 Dr. Carr, you're using up all my time. I can't let you
13 do this. A hypothetical doctor that believes adding an
14 antihistamine will improve the performance.

15 A I would ask that doctor to show me the data.

16 Q So you just don't believe him, is what you're
17 saying.

18 A I don't know who "them" is.

19 Q A doctor who thinks adding an antihistamine
20 would improve performance. An antihistamine to a
21 steroid.

22 A I would direct them to the very large body of

1 evidence that is contradictory.

2 Q Okay. Now, you say that this stepwise approach
3 teaches against developing a fixed-dose combination of
4 azelastine and fluticasone. Is that right?

5 MR. LaROCK: Objection to the extent you're
6 mischaracterizing his testimony.

7 THE WITNESS: I believe what I did was read the
8 sentence. I did not say what you just said I said. I
9 read the sentence, which states:

10 "Dr. Schleimer claims that ARIA
11 would have motivated a POSA to develop a
12 fixed-dose combination of azelastine and
13 fluticasone, but this recommendation is
14 contrary to his claim."

15 I believe that's what I said.

16 Q BY MR. HOUSTON: Well, let's keep going. Then
17 you said:

18 "Accordingly, the two drugs in this
19 practice had to be kept separate. This
20 is similar to the step-up and step-down
21 approach described above -- a POSA would
22 have known that these approaches

1 required varying the ratio of the drugs
2 used. A POSA also would have known that
3 a patient cannot use the azelastine 'on
4 demand' or step it up or down, if it is
5 in the same formulation as the
6 'continuous' treatment."

7 Right? So what you're saying is, you can't do
8 the on-demand therapy or the step-up/step-down therapy,
9 whatever you want to call it. You're saying you can't
10 do that if you have a fixed-dose combination. Right?

11 A You can't step up and step down individual
12 drugs if they are in a fixed-dose combination.

13 Q Could a patient have in his or her medicine
14 cabinet two bottles, one bottle is a steroid,
15 fluticasone, whatever it is, the second bottle is a
16 fixed-dose combination of that steroid with an
17 antihistamine, so when the patient experiences worsened
18 symptoms, couldn't they switch from their steroid-only
19 bottle to the bottle that has the two drugs in it, and
20 then subsequently switch back when their symptoms
21 lessened?

22 MR. LaROCK: Objection. Outside the scope of

1 his testimony. Calls for speculation.

2 THE WITNESS: Prior to the approval of Dymista,
3 a patient could not do that.

4 Q BY MR. HOUSTON: Well, let's leave the FDA
5 approval part of it out. We're just talking about
6 motivation to do this. And you would agree with me that
7 that's in theory possible if the two drugs, as I
8 describe them, are available to the patient; right?

9 MR. LaROCK: Objection. Mischaracterizes his
10 testimony.

11 THE WITNESS: I think I've clearly said in my
12 declaration that a POSA would not have motivation to
13 combine those two medication, unless the patient is
14 different from a POSA. I don't know how you're defining
15 "patient." Are they a chemist? I don't know. But they
16 would not have a motivation prior to the time that we
17 had Dymista on the market.

18 Q BY MR. HOUSTON: Well, that's what I'm trying
19 to get at, Dr. Carr. You're saying the reason they
20 wouldn't have had a motivation is because, according to
21 you, the two drugs would have to be kept separate. And
22 I guess what I'm trying to ask you, that's not strictly

1 true, is it? You could have one bottle that had just
2 the steroid and the second bottle that had the steroid
3 plus the second drug, whatever it is. And when you have
4 worsened symptoms, you switch to the bottle with two
5 drugs, and when your symptoms go back down, you switch
6 to the bottle with the one drug. You could do that,
7 couldn't you?

8 A And in what year are you asking me this
9 hypothetical situation?

10 Q Does it matter?

11 A Yes.

12 Q Why does it matter? I'll ask you to assume
13 that that formulation is available to the patient.

14 A So then we're talking after the approval of
15 Dymista. So after the approval of Dymista, then a
16 patient could do that. Prior to the approval of
17 Dymista, a patient couldn't do that. How could they do
18 it? They didn't exist.

19 Q I'm asking you to assume that it exists, that
20 it's available to them. They could do that; right?

21 MR. LaROCK: Object to the form of the
22 question. Calls for speculation.

1 THE WITNESS: So if you're asking me to assume,
2 then my assumption is it's available on the market. So
3 it would be after the drug is approved and it's on the
4 market, so yes, they could do that. I can't assume
5 something that's not possible to assume.

6 Q BY MR. HOUSTON: This whole paragraph goes back
7 to motivation to try to develop a product to make it
8 available on the market. And so your whole point that,
9 oh, you wouldn't have a motivation because you could
10 never treat this way, that's just not true. You could
11 have the motivation to go ahead and develop that
12 combination product because patients might want to do
13 exactly what I said, use their steroid continuously and
14 when their symptoms worsen, they switch to a second
15 bottle that has that steroid plus a second drug that
16 improves symptom relief. Can you tell me any reason why
17 that's not possible?

18 A I think it's important that we maintain the
19 context of this paragraph. Because you just said this
20 is what this paragraph says. So just to be clear, we're
21 talking about treatment, recommendations, and general
22 practices prior to the date of the invention. With the

1 co-administration studies, findings would not have
2 encouraged a POSA to pursue a fixed dose.

3 And then you jumped down to 67, which starts on
4 page 29. And it's talking about ARIA, and another
5 author, group of authors, which contain the same
6 recommendation, which is specific to azelastine.

7 So we're not talking about combinations in this
8 particular part of the paragraph. We're talking about
9 topical antihistamines, specifically azelastine:

10 "Their use may be therefore
11 recommended for mild organ-limited
12 disease as an 'on-demand' medication in
13 conjunction with a continuous one."

14 That's what they were proposing.

15 Q You go on to say towards the bottom of that
16 paragraph:

17 "A POSA also would have known that a
18 patient cannot use the azelastine 'on
19 demand,' or step it up or down, if it is
20 in the same formulation as the
21 'continuous' treatment."

22 Do you see that, Dr. Carr?

1 A I see that sentence.

2 Q So if the patient were to have bottle No. 1
3 with drug No. 1 in it and bottle No. 2 with drug 1 and
4 2, in fact, a patient could use azelastine on demand or
5 step it up or down, even though it's in the same
6 formulation with the steroid or with drug No. 1. That's
7 possible; right?

8 A No, it's not. You're increasing the dose of
9 drug No. 1, too. It's a fixed dose. As you increase
10 the azelastine, you're increasing the fluticasone.

11 Let's say you need two sprays of azelastine.
12 You're going to therefore get two sprays of the
13 azelastine. Let's say you want to go down to one spray
14 of azelastine. Now you're cutting the daily controller
15 in half.

16 So by being able to add one, you inevitably
17 have to add the second one at the same number of
18 actuations or squirts or dose. So you're changing both
19 drugs. You're not just being able to change one drug.

20 Q Well, you're only changing them if you're
21 changing the dosage each time. You can design bottle
22 No. 1 -- what's the typical instruction for Flonase? Is

1 it two sprays once a day?

2 A That is an indicated dose for Flonase.

3 Q And that provides how much fluticasone? What's
4 the dose of that?

5 A Fluticasone provides 50 micrograms per
6 actuation. So that would be 200 micrograms.

7 Q 200 micrograms if we're counting both nostrils?

8 A Typically patients will put it in both
9 nostrils, or that will be our instructions, at least.

10 Q So that could be the instructions on bottle
11 No. 1, and you could have a concentration and
12 instructions on bottle No. 2 that led you to provide the
13 same dosage of fluticasone, couldn't you?

14 A But it does not allow you to up-dose or
15 down-dose.

16 Q Well, it --

17 A It allows you to give one dose.

18 Q It allows you to switch from a steroid-only
19 bottle to a steroid-plus-antihistamine bottle. That's
20 an example of what you're calling on-demand or
21 step-it-up or step-it-down dosing, isn't it?

22 A For a single dose? I don't call that

1 necessarily a step up/step down. You're going back
2 between bottles? Is that what you're proposing?

3 Q So you're saying that if the patient is on
4 bottle No. 2 that's got the two drugs in it, that
5 patient cannot independently vary the concentrations of
6 the two drugs.

7 A Correct.

8 Q Okay. A patient likewise can't do that with
9 Dymista, can they?

10 A Not per actuation.

11 Q Okay. So is that a critical shortcoming of
12 Dymista, or not?

13 MR. LaROCK: Objection. Outside the scope.

14 THE WITNESS: The inability to individually
15 titrate any combination therapies does limit the
16 practice of medicine.

17 Q BY MR. HOUSTON: And Dymista does not have that
18 ability, correct, as to the two active ingredients?

19 A That would be an example of a fixed-dose
20 combination, that you cannot titrate one active molecule
21 without titrating the other molecule.

22 But we know that Dymista is effective in its

1 exact formulation. So I don't know why anybody would
2 want to do that.

3 Q Right. So there's no reason why a person of
4 ordinary skill in the art couldn't have bottle 1 that
5 has Flonase and bottle 2 that has the active
6 concentrations of fluticasone and azelastine that are in
7 Dymista. They could do that; right?

8 MR. LaROCK: Objection. Form.

9 THE WITNESS: I think maybe in some way you and
10 I just agreed on something, that Dymista is a perfect
11 example of a fixed-dose combination, and a patient would
12 not be able to do that until they had Dymista. Prior to
13 that, okay, prior to that we had unexpected findings
14 with Dymista. There would be no motivation to do that.

15 Q BY MR. HOUSTON: Well, one of your arguments
16 for why there would be no motivation is, oh, a person
17 couldn't dose up or dose down, they couldn't add a
18 second drug or remove the second drug if it's in a fixed
19 dose. And yet that doesn't seem to be a concern of
20 yours when it comes to Dymista. You seem to be fine
21 with that.

22 A Is there a question?

1 Q Is that right?

2 A That is correct.

3 Q Okay. So in the scenario I'm talking about,
4 where you said -- you say right here:

5 "In my experience, 'on demand' or
6 'as-needed' therapy was the prevailing
7 practice in AR, whereby a patient would
8 take one drug consistently (e.g., a
9 steroid), and use the second drug only
10 when symptoms worsened. "

11 That prevailing practice, one could easily take
12 their Flonase, which is the steroid, consistently, and
13 then when symptoms worsen, they could switch to a bottle
14 that has the same amount of fluticasone and has
15 azelastine in it and use that for a time period until
16 their symptoms got better. They could do that; right?
17 That's physically possible, isn't it?

18 A So two responses. First, I clarified the use
19 of the second drug only when symptoms worsened. It
20 would be a second drug that at that time was felt would
21 have additive benefit. Okay? So I clarified that.

22 Secondly, prior to Dymista coming around, I

1 don't believe it was physically possible, because I
2 don't think that they had figured out how to make the
3 two things play nice together and go into a physical
4 formulation where you could physically -- you could not
5 take azelastine and fluticasone and pour them together
6 and then just use them. I don't believe -- I'm not a
7 chemist, that's not my area of expertise, so no, I do
8 not believe it was physically possible.

9 Q So as you just stated, you're not here giving
10 testimony about formulation expertise, right, as a
11 formulation expert?

12 A I said I'm not a chemist. And I did not know
13 if they could mix together. My understanding is you
14 cannot do that.

15 Q Are you a formulation expert?

16 A I think you have my CV. I'm a physician.

17 Q I'm just asking a straightforward question.
18 Are you a formulation expert?

19 A I'm not a chemist --

20 MR. LaROCK: Asked and answered.

21 Q BY MR. HOUSTON: Okay. And would you be
22 willing to accept my request to assume that those two

1 drugs could be formulated together if somebody had
2 wanted to? I'm asking you to accept it. I appreciate
3 it's on the record you don't agree with that assumption.

4 But if I asked to you just assume that, in that
5 scenario, there's no reason why a patient couldn't make
6 use of a fixed-dose, co-formulated drug and still be
7 consistent with what you say is the prevailing practice
8 in AR treatment, which is taking one drug consistently
9 and then adding a second drug when needed.

10 MR. LaROCK: Object to the form of the
11 question. Lacks foundation.

12 THE WITNESS: So in this hypothetical
13 situation, and prior to the approval of Dymista, I would
14 try to convince the patient to use a second drug that
15 actually had shown efficacy.

16 Q BY MR. HOUSTON: So my question was, could a
17 patient do that? Is it possible? Not what your
18 recommendation would be, nothing else. I'm simply
19 asking you, is it possible to do what I described?

20 MR. LaROCK: Object to the form of the
21 question. Lacks foundation. Asked and answered.

22 THE WITNESS: In the sense of hypotheticals,

1 without data, without fact, I guess anything's possible.

2 Q BY MR. HOUSTON: The sentence we've been
3 looking at a lot in paragraph 67, you make reference to
4 using the second drug only when symptoms worsened. In
5 your experience, what might be causes of -- causing of
6 worsened symptoms?

7 A Increased exposure to allergen or increased
8 biological response to a given allergen.

9 Q In your experience, what's a typical time frame
10 that a patient might be exposed to either of those two
11 conditions you just named? Is that typically going to
12 be over the course of a day? A week? A month?

13 MR. LaROCK: Object to the form of the
14 question.

15 THE WITNESS: It's individualized.

16 Q BY MR. HOUSTON: You can't give me any typical
17 time periods?

18 A It's a very broad range.

19 Q Could it be as long as a month?

20 MR. LaROCK: Objection. Outside the scope.

21 THE WITNESS: Perhaps.

22 Q BY MR. HOUSTON: With respect to your

1 prescribing habits as to Dymista, do you ever instruct
2 patients to take more or less Dymista than what's
3 indicated on the label?

4 MR. LaROCK: Objection. Outside the scope of
5 his declaration.

6 THE WITNESS: I never tell patients to take
7 more Dymista than what's on the label. I have told
8 patients to take less than what's on the label.

9 Q BY MR. HOUSTON: And what might prompt you to
10 give that instruction?

11 A There are a multitude of reasons.

12 Q Can you name a few?

13 A Maybe I saw a spot of blood in their mucus.

14 Q Anything else come to mind?

15 A Maybe they're getting ready to have surgery or
16 just have had some nasosinus surgery.

17 Q Anything else?

18 A Maybe it's a woman considering getting
19 pregnant.

20 Q Have you ever made that recommendation based on
21 a patient's complaints about side effects?

22 A The first example I gave, maybe I saw a little

1 blood in the nose, would be an example of a side effect,
2 epistaxis.

3 Q Can you recall any other reported side effects
4 that have led you to suggest taking a lower dose of
5 Dymista?

6 MR. LaROCK: Objection. Outside the scope.

7 THE WITNESS: Yes.

8 Q BY MR. HOUSTON: What would those be?

9 A An example would be nasal irritation.

10 Q Which other side effects do you recall?

11 A Another example would be nasal perforation.

12 Q How about headaches?

13 A Yes, that is a described adverse event of all
14 nasal sprays.

15 Q I'm just asking, can you ever recall a time
16 when a patient complained to you about headaches and in
17 response, you suggested that they take a lower dose of
18 Dymista?

19 MR. LaROCK: Objection. Outside the scope.

20 THE WITNESS: In that scenario, I would
21 probably stop the Dymista.

22 Q BY MR. HOUSTON: So besides the ones you've

1 listed so far, any other side effects you can recall
2 that led you to suggest to a patient to take a lower
3 dose of Dymista?

4 A Again, it would be individualized for each
5 individual patient. We could pull up the Dymista label
6 if you would like and we could go through each of the
7 individual adverse events.

8 Q We could do that, but are you suggesting that
9 each of those events is an example of a reported side
10 effect that has led you to suggest to a patient to use a
11 lower amount of Dymista?

12 MR. LaROCK: Objection. Outside the scope of
13 his declaration.

14 THE WITNESS: What I'm suggesting is we can
15 pull up the label and we can go over each individual
16 adverted events and I can answer each one individually.

17 Q BY MR. HOUSTON: We may get to that label in
18 just a minute. So we can do that.

19 Let me have you flip ahead in your declaration
20 for the moment to paragraph 123.

21 A I'm on page 57, and I see paragraph 123.

22 Q And there's a graph at the bottom of page 57;

1 right?

2 A Yes.

3 Q And that's your reporting of the FDA -- the
4 rates of side effects that are reported on the
5 FDA-approved labels for Astelin, Flonase, and Dymista;
6 is that right?

7 A I think if you look at the sentence right
8 above, it says:

9 "For example, the FDA-approved
10 labels for Astelin (azelastine) and
11 Flonase (fluticasone) show the following
12 side effects:"

13 And in the graph you see Dymista listed there
14 in comparison to those two in green.

15 Q So is the answer to my question "yes"?

16 A Can you restate your question?

17 Q In this graph you're reporting the rates of
18 side effects that are reported on the FDA-approved
19 labels for Astelin, Flonase, and Dymista; right?

20 MR. LaROCK: Objection. Form.

21 THE WITNESS: No, I don't believe so.

22 Q BY MR. HOUSTON: Why don't you agree with my

1 statement?

2 A I believe what I'm showing are the FDA-approved
3 labels for Astelin and Flonase that show all of their
4 following side effects. And for their side effects
5 there, I have, for comparison, how Dymista compares to
6 those two.

7 Q Right.

8 A It's not all-encompassing of all side effects
9 of all three drugs.

10 Q It's not all of the side effects reported on
11 the labels? Is that what you're saying?

12 A I would have to pull the individual labels for
13 each one. It is what I've described it as. For
14 example -- and this is the example -- the FDA-approved
15 labels for Astelin and Flonase show the following side
16 effects. And Astelin is azelastine, fluticasone is
17 Flonase. So those are all the side effects for Astelin
18 and fluticasone. And for these individual ones --
19 epistaxis, headache, and bitter taste -- you see for
20 comparison that Dymista is included in there.

21 Q So are you not reporting all of the side
22 effects reported on the Dymista FDA-approved label?

1 A Shall we pull up the Dymista label and look at
2 it as I suggested with the last line of questioning?

3 Q You don't even cite it here as an exhibit, so
4 no, I'm not inclined to do that. I'm just asking about
5 your testimony. This is your testimony; this is your
6 declaration. I'm asking for clarification of what this
7 is reporting.

8 MR. LaROCK: Objection. Mischaracterizes the
9 document.

10 Q BY MR. HOUSTON: If you can't tell me, that's
11 fine. You say you don't know, that's fine, too,
12 Dr. Carr.

13 A Okay.

14 Q So do you not know if that's reporting all the
15 side effects listed on the FDA label for Dymista?

16 A I will tell you exactly what it is reporting,
17 because I will read the sentence. I'll read the
18 paragraph:

19 "123. While the closest prior art
20 shows an increase in side effects,
21 Dymista unexpectedly shows no increase
22 in side effects as compared to the

1 monotherapies. In fact, it shows
2 a reduced side effect profile as
3 compared to those of either of the
4 individual active ingredients. For
5 example, the FDA-approved labels for
6 Astelin...and Flonase...show the
7 following side effects."

8 That's what I'm saying in totality.

9 Q I understand that's the text there. I'm asking
10 about the graph that comes below that. Is that
11 reporting the incidence of all side effects on the
12 FDA-approved labels for those three drugs? Yes, no, or
13 you don't know?

14 MR. LaROCK: Objection. Form, asked and
15 answered.

16 THE WITNESS: You said, I believe, is that
17 showing "all side effects."

18 Q BY MR. HOUSTON: Reported on the FDA-approved
19 labels.

20 A All side effects reported anywhere in the
21 label. I don't believe so.

22 Q So can you tell me how you arrived at the ones

1 you do report here? Did you choose the ones that would
2 make it look more favorable as compared to Dymista, or
3 less favorable?

4 A I chose common ones.

5 Q What was that?

6 A I chose common ones.

7 Q What do you mean by "common"?

8 A Nearly 20 percent of patients that take
9 azelastine have bitter taste. Everybody that is a
10 prescriber and has prescribed azelastine to a patient is
11 very aware of that. So that would be an important
12 adverse event profile.

13 Q You said you reported common side effects.

14 A I'd like to finish.

15 Headache is also a very common side effect.
16 And so I've shown headache with both azelastine and
17 fluticasone. And then I've shown that. There are
18 uncommon side effects that can occur that are not shown
19 here. So I can't say all are shown here. But common
20 ones are.

21 Q So fatigue is common, dizziness is common,
22 weight increase is common?

1 A Very well described. Close to 2 percent.

2 Q Okay. So that's what I'm asking. What's the
3 threshold for making something common? Is there an
4 incidence number? Is there some other threshold for
5 what makes a symptom common -- a side effect common?

6 MR. LaROCK: Object to the form of the
7 question.

8 THE WITNESS: I would say frequency of
9 occurrence and clinical trials that supported the
10 approval of the drug and generated the label of the
11 drug.

12 Q BY MR. HOUSTON: So you went through for these
13 three drugs and determined which side effects met that
14 criteria, and those are the ones you included in this
15 chart?

16 A These are what was listed in the label. I just
17 put them in this format.

18 Q Well, that takes us back to where we started.
19 So is what you're saying, you're reporting in this
20 chart, are the side effects that are reported in the
21 label? I asked you that and you said, no, just the
22 common ones. I said, okay, what's common. And now

1 you've circled back to saying, oh, it's the ones listed
2 on the label.

3 A That's not what you asked me. You said "all."

4 Q All the side effects listed on the label. Not
5 all side effects. All side effects listed on the label.

6 A Uh-huh, correct. You said "all."

7 Q Is that what you're reporting here?

8 MR. LaROCK: Objection. Form. Asked and
9 answered. Mischaracterizes his testimony and his
10 declaration.

11 THE WITNESS: As I said before, you asked for
12 all side effects listed in the label. And I said this
13 does not include all side effects listed in the label.

14 Q BY MR. HOUSTON: So then my follow-up question
15 was, how did you decide which ones -- which of the ones
16 listed in the label to report here? If you're telling
17 me that it's not all, it's some subset of all, how did
18 you decide on what subset to report here?

19 MR. LaROCK: Objection, form.

20 THE WITNESS: I believe these are the most
21 commonly reported adverse events in the adverse event
22 section of the label for each individual medication, and

1 I have just converted it from a number in a table into
2 these columns format for comparison. So you would have
3 to pull each individual label and pull out the adverse
4 events table, and you could get the individual ones that
5 are listed here.

6 Q BY MR. HOUSTON: Did you personally create this
7 graph that's shown here at the bottom of paragraph 123
8 of your declaration?

9 A This is my declaration. I've reviewed this
10 declaration, and I agree with everything in the
11 declaration.

12 Q I understand.

13 A I'm not an expert in PowerPoint and things like
14 that.

15 Q Okay, so you will adopt it as your own, but you
16 did not create that graph. Is that fair to say?

17 MR. LaROCK: Objection. Mischaracterizes his
18 testimony.

19 THE WITNESS: This graph is a component of my
20 declaration, and I stand by the graph.

21 Q BY MR. HOUSTON: But you won't tell me whether
22 or not you created it?

1 MR. LaROCK: Objection. Form.

2 THE WITNESS: This was my idea, to represent my
3 view for my declaration.

4 Q BY MR. HOUSTON: Have you, as part of doing
5 this, did you review the studies that were conducted
6 that led to the reported side effect data on the
7 FDA-approved Flonase label?

8 A To be clear, your question was prior to. So at
9 some point prior to the production of my declaration, I
10 have reviewed those studies. That's multiple years ago
11 when they first came out.

12 Q Did you review them in preparing your testimony
13 here?

14 MR. LaROCK: Objection, form. Asked and
15 answered.

16 THE WITNESS: As I said, this is a
17 representation of the label. The label is a summary of
18 the studies. So if I have reviewed the label, then I
19 have reviewed the data from the studies presented in the
20 label to prepare this table.

21 Q BY MR. HOUSTON: Well -- and I don't think I
22 got a clear answer to that. So did you review all three

1 labels in preparing the table that's here in paragraph
2 123?

3 A Yes.

4 Q You did?

5 A Yeah.

6 Q Because I thought you told me just a second ago
7 that you reviewed the Flonase label years ago.

8 MR. LaROCK: Objection. Mischaracterizes his
9 testimony.

10 THE WITNESS: No, no, that's not what I said.

11 Q BY MR. HOUSTON: Okay. I mean, the transcript
12 will speak for itself, and maybe I'm misremembering.
13 That's fine.

14 A We can review that so I can clarify it for you
15 so you're not --

16 Q Let's just get to the right answer. The answer
17 is, you did review the Flonase label and the Astelin
18 label and the Dymista label in preparing this testimony.
19 Is that the right answer?

20 A In preparing this testimony, I did look at the
21 Flonase label that was relevant to the time of the
22 patent, as well as the Astelin label. And then I also

1 reviewed the most current label for Dymista.

2 Q Did you review the details of the studies that
3 were conducted for Flonase and Astelin that were used to
4 produce the side effect data reported on those labels,
5 or did you just review the summary, as you mentioned
6 earlier?

7 A What do you mean by "details"?

8 Q Well, I assume there are details that led to
9 the experiments that were run in order to generate the
10 side effect data; right? Let's just back up. How does
11 the side effect data come to appear on the FDA label?
12 Where does that data come from?

13 A Okay, let me explain it to you. And we're
14 talking only right now about adverse events.

15 Q Whatever you're calling these things in this
16 table.

17 A Side effects are adverse events. So a company
18 comes to the FDA and says, we want to get a drug
19 approved, and we would like to do studies to support the
20 approval of it, and we want to show that it is safe and
21 effective.

22 The FDA reviews every single proposed study.

1 Can take several years. The FDA says yes or no, you can
2 do this study. The study is conducted. All of the data
3 from all of the different sites are collated and put
4 into case report forms.

5 Those case report forms then go into top-line
6 data. The top-line data then is locked. The company
7 then submits the top-line data to the FDA. The FDA
8 reviews it.

9 So during the process of a review, one of these
10 boxes that you have right over here, these document
11 boxes, back in the time of Flonase, you would get, as an
12 FDA reviewer, 50 or 60 boxes like that in your office.

13 So you would find the box that showed the
14 top-line data for safety. Then you would pull out that
15 box and you would have ten-plus months to review it, and
16 you would use your internal statisticians, you would see
17 what the company is reporting, you would review the data
18 in great detail, you would use your own internal
19 FDA-approved statisticians, you would run your own
20 analysis. If you saw any big concerns, you may go out
21 and have a site inspection at those sites. You would
22 look at the short-term studies and you would look at the

1 long-term studies.

2 If the drug was shown to be effective and the
3 drug was shown to be safe, then you would start a
4 process of generating a label. You would ask the
5 company to propose a proposed label.

6 The FDA then would review that label and, based
7 on their review of years and years of research in the
8 drug, they would then respond and recommend changes to
9 the label. That goes back and forth until you have a
10 label, and then the FDA approves it.

11 So all of the data to generate a label is not
12 publicly available. A lot of it's confidential. Only
13 what gets published is available. And the publishing
14 process is not the same degree of review as the FDA
15 does. So that's how these tables are generated in
16 general.

17 (Recess 3:02 to 3:15 p.m.)

18 Q BY MR. HOUSTON: Dr. Carr, the data that's
19 reported here in the graph at the bottom of paragraph
20 123, on the left-hand axis, what are those numbers? Are
21 those incidence numbers? Incidence percentages? What
22 am I looking at there?

1 A Percentage.

2 Q Percentage. Okay. So I want to ask you a
3 question just so I understand how these are reported,
4 and to facilitate the question, I'm going to use a round
5 number.

6 Let's just say for one of these side effects,
7 the reported percentage came out to 10. So 10 percent.
8 Does that mean that for the underlying studies, the FDA
9 or the company or whoever does this decided that 10
10 percent of the patients in the study reported that side
11 effect at some point during the study?

12 A It's not quite like that. What happens is,
13 these studies are conducted at numerous sites across the
14 country, and perhaps even the world, depending on the
15 drug.

16 So at the site, patients are enrolled into the
17 study. The patients then interact with what's called
18 the principal investigator for that site. That's the
19 person that's responsible. And the principal
20 investigator then records the adverse event profile for
21 that patient, and then that data is what gets funneled
22 up to FDA and company and so on and so forth. So the

1 capturing of the adverse events occurs at the visit with
2 the patient and the investigator.

3 Q I didn't think that was quite what I was
4 asking. Let me just try again.

5 A And if I can clarify it. So let's say there
6 were 100 patients in the study, and there were 100
7 sites, and every site had one patient. But 10 sites
8 that one patient said, "I'm sedated." Then there would
9 be a 10 percent incidence of sedation.

10 Q I want to follow that. So there's 100 sites
11 and every site had one patient?

12 A I'm just making it up.

13 Q That's what I want to understand. So 10
14 sites -- so at 10 sites, that one patient said, "I'm
15 sedated," so it's basically 10 out of 100.

16 A 10 percent.

17 Q It could have been one site with 100 patients.
18 It means 10 patients reported that side effect over the
19 course of the study.

20 A That would prompt an investigation.

21 Q Well, okay.

22 A It would prompt an investigation, why is it

1 that one site is an outlier for efficacy or safety --

2 Q I'm sorry. I just meant if there were only one
3 site. I suppose what you would say is you would never
4 do it that way, to have a single site.

5 A That's not for an FDA drug, no.

6 Q But what if a patient reports a given side
7 effect like a headache twice over the course of the
8 study? Does that get counted as two reports? Or is
9 that still just, when you're figuring out these
10 percentages, is that just one?

11 MR. LaROCK: Objection. Outside the scope.
12 And form.

13 THE WITNESS: So to kind of explain this with a
14 little bit better degree of granularity, the patient
15 comes in, reports -- there's going to be two visits
16 here. Patient comes in, reports, "I got a headache when
17 I used my spray. I took one spray, gave me a headache
18 this morning. And I've only taken one spray."

19 The investigator says, "Headache. Do you still
20 have the headache?"

21 "No, the headache went away."

22 "How long did it take to go away?"

1 "Four hours."

2 "Did you take medicine?"

3 "Yeah. It really hurt. I took some Tylenol."

4 Then the investigator goes back and says they
5 had the headache, it has resolved, and it was of
6 moderate severity because it required treatment.

7 A month later, patient comes back --

8 Q BY MR. HOUSTON: Still on the study?

9 A Still on the study, and they just got their
10 last dose. No complaints in between. They just got
11 their last dose, and they say, "My last dose I got a
12 headache." The investigator would do exactly the same
13 thing.

14 So in that one patient there will be, in their
15 case report form, two episodes of headache. But that is
16 one patient that got headache. So when it goes back up,
17 it will say, in this patient, it can cause headache.

18 In this example of headache, they don't really
19 look at severity unless it was what's called a "severe
20 adverse event," and it required them to go to the
21 hospital because it was the worst headache of their
22 life. They won't say that one patient got it 10 times

1 and 99 patients got it zero times. So it's 10 percent.
2 It's 10 patients.

3 Q So just to clarify, even if a given patient has
4 two different reports of headache, that's still only
5 going to count as a 1 percent addition to this graph
6 here, if we're assuming 100 patients total? It just
7 gets counted once to figure out the percentage? That's
8 all I was trying to clarify.

9 A Correct. Let's pretend for a moment that it
10 was an adverse event of special interest, whatever that
11 is. So for some reason, the company or the FDA is
12 really concerned about that. Then perhaps in the text,
13 in the descriptions, they may say, yeah, this patient
14 had, you know, there was a 1 percent incidence of
15 headache, it occurred in one patient out of a hundred,
16 but this patient had it numerous times. But it resolved
17 with only this treatment, and there was no permanent
18 sequela when they stopped the drug.

19 Q When they're compiling this data, how do they
20 resolve or how do they combine studies that extend for
21 different periods of time, like if you have one that's
22 two weeks and one that's two months?

1 A So if I could use some terminology. The
2 terminology I would like to use is what's called a
3 "pivotal study." A pivotal safety and efficacy study
4 for allergic rhinitis may perhaps be a two-week study.

5 Now, there is also a long-term safety study.
6 That could be six to twelve months. What they will do
7 is, they will look and summarize in the clinical trials
8 section of the label, they'll summarize the findings for
9 every study. And then they'll generate different
10 tables. So usually the safety and efficacy studies are
11 pretty close to the long-term safety study, and so they
12 just put them all together.

13 If, however, something funny is going on, if it
14 seems like after two weeks nothing happens, but at that
15 three-month mark, people are dropping dead, there could
16 be some accumulation of the drug, then that requires
17 special attention.

18 But if the incidence is 10 percent in the two
19 weeks and the incidence is 10 percent in the one year,
20 then, let's say it's 11 percent, they'll say in the
21 test, in the long-term safety study it was 11 percent.
22 But up here in the thing they'll say these are the

1 pivotal studies, safety and efficacy pivotal studies,
2 and that's what this represents, are the pivotal
3 studies. And that's where the table comes from.

4 Q What I'd like to understand -- and I'd like to
5 use some simple numbers for a hypothetical. Again,
6 we'll just assume 100 sites, one patient each. Let's
7 say we have one study that goes for two weeks, and there
8 was one patient in each week of the two-week study that
9 reported a headache, out of the whole 100. So
10 presumably that would lead to a report in the format of
11 this chart of an incidence of 2 percent.

12 A No, that's not what I said. One patient --

13 Q Two separate patients.

14 A Oh, I'm sorry.

15 Q One in each week.

16 A I thought you said one patient had headache
17 first week and second week.

18 Q Sorry. Thank you for clarifying. I meant two
19 different patients, but one in week 1 and one in week 2.
20 So two patients total in the two-week study. That would
21 presumably give you a number of 2 percent, unless
22 there's something funny or whatever.

1 A So in this hypothetical example, then that
2 would result in a 2 percent. But realize, in order to
3 complete the clinical development program, you need like
4 close to 2,000 patients. 1500 to 2,000.

5 Q You need a large number. I understand.

6 A So things can change over time with 100.

7 Q Now let's say in a four-week study, you have
8 the same situation, where you get a patient, a different
9 patient, but a patient each week that reports a
10 headache. Same number of patients. There that would
11 give you a reported percentage of 4 percent, wouldn't
12 it?

13 A So to dovetail off of the example I gave
14 earlier, let's say that the two-week study is the
15 pivotal study and the four-week study is the long-term
16 safety study. They have differences, and like I said
17 before, if there's differences between the long-term
18 safety study and the two-week safety study, then there's
19 something going on here and they have to further
20 investigate what was going on.

21 So this is probably, they would go and they
22 would pull the individual case report forms for this and

1 try to figure out why there is a difference. Because
2 that's a 50 percent improvement.

3 Q What if it's the case where this study is drug
4 A and this study is drug B? And again, these are much
5 bigger sample sizes, they're all the pivotal studies, et
6 cetera, et cetera, et cetera, we're just simplifying for
7 purposes of the numbers.

8 A So in allergic rhinitis studies, they should
9 all be two-week studies. Now, there may be four-week
10 studies for perennial, and there may be year-long for
11 long-term safety. But in the table, you typically want
12 to do pivotal to pivotal. And comparing two weeks to
13 four weeks could possibly be problematic, depending on
14 the results, because you are comparing apples to oranges
15 here. Here two different drugs, two different clinical
16 development programs, two different patient populations,
17 the inclusion and exclusion criteria could be different.
18 It's very difficult to say what that FDA would do. They
19 usually don't do cross-study comparisons during the
20 conduct of deciding if they can get a label.

21 Q So I just want to make sure I remember a couple
22 of these. You said "patient populations."

1 (Off record)

2 Q BY MR. HOUSTON: You listed some examples. I
3 was hoping to just understand what they were. Patient
4 populations, inclusion and exclusion criteria, okay,
5 that's what you said. Wasn't there a third one,
6 something that could be different? Okay. Well, those
7 are a couple.

8 I guess what I want to ask you now is do you
9 know whether the studies that were used to generate this
10 side effect data reported on the labels for Astelin and
11 Flonase and Dymista were comparable across these types
12 of variables -- time, patient population,
13 inclusion-exclusion criteria, et cetera?

14 A Well, fluticasone was the first to be approved.
15 There were some minor changes at the FDA in their
16 guidance, but it was very similar for azelastine.

17 For Dymista, it was still a two-week safety and
18 efficacy study, and it was still the same number of
19 patients required to have exposure for safety. But it
20 was a difficult development pathway because of the fact
21 that they were combination nasal spray, and there had
22 never been a combination nasal spray studied, and there

1 was not a guidance regulatory document for that.

2 Q So do you know one way or the other whether the
3 three sets of studies that were used to generate this
4 data shown here used comparable time periods, patient
5 populations, inclusion-exclusion criteria, et cetera?

6 A I would say the following. For azelastine and
7 fluticasone, the inclusion criteria were very same.
8 They had to have a 6 out of a 12 for their total nasal
9 symptom score.

10 Dymista was more severe. They had to have an 8
11 out of 12 to be included into the study. So that in and
12 of itself, it's a little bit more severe patient
13 population.

14 As far as exclusion criteria, they're all very
15 relatively comparable, just generally speaking. I'm
16 sure if you look at one study to the other, there may be
17 some fine little nuances, but in a global sense, as far
18 as duration, seasonal allergic rhinitis studies
19 generally speaking are two-week safety and efficacy
20 studies. So the time would have been about the same.

21 Q So you think the time would have been the same.

22 A They're roughly comparable. They're two-week

1 safety and efficacy studies.

2 Q Did you look at them to compare and confirm
3 that, or that's just sort of your understanding of how
4 it would have been done?

5 A That's my understanding of how it would have
6 been done. I mean, I left in 2005. I don't believe it
7 changed.

8 Q Do you know off the top of your head what daily
9 dosage of azelastine a patient would get by following
10 the label recommendation for Astelin?

11 A When it was initially approved?

12 Q As it appears on the label.

13 A The label that's in this document or the
14 current label today?

15 Q I don't know of a label in this document. If
16 you're telling me they changed, then let's talk about
17 both.

18 A Well, the dosage in general is two sprays each
19 nostril twice daily. So that would be 137 micrograms
20 per actuation. So take 137 times 2, and that would be
21 this nose, this nose --

22 Q Nostril.

1 A And then I do that again a second time during
2 the day.

3 Q So the daily dosage of azelastine in Astelin
4 following its recommendations would be 2 times 2 times
5 137. Is that right?

6 A I think that's correct. So we have to do some
7 quick math.

8 Q The number doesn't matter so much. I want to
9 ask the same question about Dymista. If one follows the
10 product label for Dymista, how much azelastine does the
11 patient receive in a day?

12 A Per actuation?

13 Q No, total.

14 A Per day? So Dymista, just to be clear, is one
15 spray each nostril twice a day. And it's the same
16 amount per actuation, so it's 137 micrograms per
17 actuation.

18 Q So it's half. So a patient receives half as
19 much Astelin in a day taking Dymista as in taking
20 Astelin; is that right?

21 A And yet they get better. So that's an
22 unexpected finding. Yes, you are right.

1 Q I believe you have in front of you
2 Exhibit 1043. That's the Hampel article.

3 A I have it in front of me.

4 Q Prior to this proceeding, were you aware of
5 this reference, this report?

6 A Yes.

7 Q Do you know the authors on this reference, the
8 listed authors?

9 MR. LaROCK: Object to the form of the
10 question.

11 THE WITNESS: Some.

12 Q BY MR. HOUSTON: Do you have an opinion about
13 the quality of the study that they report here in
14 Exhibit 1043?

15 MR. LaROCK: Objection. Outside the scope of
16 his declaration.

17 THE WITNESS: This is a double-blind,
18 placebo-controlled study that was a proof of concept
19 study. I actually think that this, relatively speaking,
20 was a pretty good study.

21 Q BY MR. HOUSTON: Let's look at page 3, table 1
22 for just a moment. Are you there?

1 A Yes.

2 Q This table reports the details of four
3 different groups that were tested in this study;
4 correct?

5 A No.

6 Q There's not a placebo group, a fluticasone
7 group, an azelastine group, and an azelastine and
8 fluticasone group?

9 A Page 3, table 1 is the demographic and
10 background clinical characteristics or the
11 intent-to-treat population. Table 1.

12 Q Right. And I'm asking you about what's
13 reported in table 1. There's four groups that are
14 identified there. Right?

15 A I guess maybe I'm not understanding -- are you
16 talking about the demographics of the participants in
17 the study? That's what this is. It's demographics.
18 How many are male, how many are female, how many are
19 white, how many are black, how many are Asian.

20 Q And it's giving those details for four separate
21 groups. One group was given a placebo, one group was
22 given fluticasone, one group was given azelastine, one

1 group was given azelastine plus fluticasone. Right?

2 A I think I understand your question now. This
3 is a study population, an intent-to-treat population.
4 To me, that's one population. There are four different
5 treatment arms that are being discussed here.

6 Q Okay. A lot of times today we've just
7 shorthanded it as "groups." Would you like me to use
8 "treatment arms"?

9 A I just misunderstood you.

10 Q Okay. So whether you call it "treatment arms"
11 or "groups," you would agree there's four identified
12 that are the subject of this study, or four treatment
13 arms that were the subject of this study; right?

14 A Yes.

15 Q Do you have an understanding of what the
16 treatment arm that lists azelastine and fluticasone, do
17 you have an understanding of what exactly drug that was
18 that was provided to these patients?

19 A The azelastine was Astelin, the fluticasone was
20 a generic of Flonase. I don't recall who the generic
21 manufacturer was.

22 Q What about the one that was the combination of

1 azelastine and fluticasone?

2 A I believe this was MP2902, which eventually
3 became known as Dymista. And then let's not forget the
4 placebo group.

5 Q Right. When you're looking at efficacy data
6 for each of these treatment arms, is it your opinion
7 that what you need to be comparing is any improvement
8 that the three active treatment arms have over placebo?

9 A What I would like to see in a study such as
10 this is that the monotherapies with regards to efficacy
11 are better than placebo. And then I would want to see
12 the azelastine, fluticasone, MP2902, the Dymista, I
13 would want to see that better than placebo, as well as
14 better than the individual monotherapies.

15 Q When you say you would want to see it as
16 better, I mean, the data's going to come how the data
17 comes; right?

18 A Yeah.

19 Q This is the first actual report of Dymista
20 being tested, right, so you wouldn't necessarily have a
21 preconception ahead of time, would you?

22 A I'm sorry. I misunderstood your question. I

1 thought you said what would you want to see. I may have
2 misheard you.

3 Q What I'm trying to figure out is when you're
4 trying to compare efficacies among the three active
5 arms, in each case is it efficacy above and beyond
6 placebo? Is that the correct comparison? Or can I just
7 say, okay, for each of these three treatment arms,
8 here's my baseline, and they each improved 25 percent,
9 or 25, 30, and 35 percent. Or do you need to know what
10 the placebo was and somehow account for that to compare
11 the three?

12 MR. LaROCK: Objection. Form.

13 THE WITNESS: The robustness of data is always
14 much more robust in the presence of placebo, so you can
15 what the placebo effect is. Earlier I talked about
16 study that I will imprint in my mind and ones that I
17 won't. I believe I identified this study as the first
18 study I imprinted in my mind because of the study
19 design. So yes, you always want to compare the active
20 to the placebo.

21 Q BY MR. HOUSTON: Okay. So just again, using
22 hypothetical numbers, but if you in your fluticasone

1 arm, if you saw an improvement in the TNSS score of,
2 say, 25 percent, but your placebo arm showed an
3 improvement of 23 percent, you would say, okay,
4 fluticasone isn't showing much of an improvement over
5 placebo. Maybe a little bit, but in other words, it
6 would be sort of relative to placebo; right?

7 A It's more complicated than that.

8 Q You would agree, though, that you at least, if
9 you're going to compare among the three, you would want
10 to know what the placebo level is?

11 A I would definitely want to know what the
12 placebo response rate was.

13 Q Now, let me ask the same question but as to
14 side effects. So if you want to compare the side
15 effects among these three, would you want to know what
16 the placebo response rate was, as you put it, or the
17 placebo side effect rate?

18 A These are safety and efficacy studies, so I
19 would want to know all four treatment arms what was the
20 efficacy and what was the safety, realizing that placebo
21 is the vehicle for Dymista. It's basically Dymista
22 minus azelastine and fluticasone.

1 What if this is really acidic? What if has an
2 excipient that causes a problem? Definitely I'd want to
3 know what the adverse event profile would be.

4 Q Okay. I go back to your graph here in
5 paragraph 123 of your declaration. Did you consider the
6 rate of the placebo effect for any of these side effects
7 in reporting this data?

8 A As I said before, I basically cut and pasted
9 the data and put it in a different format directly from
10 the label. That's what I did.

11 Q But the labels also report placebo percentages;
12 right?

13 A Typically.

14 Q And so for a given side effect reported in your
15 table, if the placebo percentage were also quite high,
16 similar to what you've reported here for the actual
17 drugs, that might influence your perception of how
18 severe that side effect really is for that drug; right?

19 A Well, it wouldn't have been approved, and they
20 wouldn't have a label. There would be a problem with
21 that drug product. If you're having a lot of adverse
22 events with your placebo, you've got serious problems.

1 The FDA is not going to approve that product.

2 Q What level do you think the placebo reports
3 would have to rise to to be, as you say, a problem, a
4 serious problem?

5 A That's a review issue for each individual
6 clinical development program.

7 Q Well, let's use a hypothetical. If Astelin has
8 a -- I'll just make one up. Has a dry mouth response
9 rate of 10 percent, but the placebo that was conducted
10 at the same time says it's 8 percent. So 10 versus 8,
11 Astelin, placebo.

12 And now, in Dymista -- again, I'm making this
13 up -- but Dymista, let's say you have a dry mouth rate
14 of 4 percent, but the placebo says 2 percent. Is it
15 fair for me to just compare the 4 percent for Dymista
16 and the 10 percent of Astelin, or should I factor in
17 somehow the different relative placebo rates in each of
18 those studies?

19 MR. LaROCK: Object to the form of the
20 question.

21 THE WITNESS: There are so many different
22 variables present in your question that I simply can't

1 answer it. If you have such a high placebo rate to
2 start with, you may not even get approved, and then
3 there would be no label comparison.

4 It's a review issue. They would have to
5 review. Placebos should have some degree of benefit,
6 but it shouldn't be that much more unsafe. So there's
7 an issue with this development program that the reviewer
8 would have to review and try to figure out. And it may
9 mean that the drug is not approved, and then there would
10 be no label.

11 Q BY MR. HOUSTON: But in this case, we're
12 talking about ones that were approved. This is from the
13 FDA label. So we don't have that -- we know we've
14 already passed that hurdle, whatever it is. Do you have
15 any sense of what percentage for a placebo side effect
16 would start to raise those alarms?

17 A The placebo rates, since -- so we're no longer
18 talking about your hypothetical example. We are now
19 talking about drugs that are approved and have a label.
20 So presumption is those placebo response rates are very
21 low.

22 Q Give me some idea of what you're talking about

1 when you say "very low." 1 percent? 2 percent? Is
2 that the sort of very low number you're talking about?

3 MR. LaROCK: Object to the form of the
4 question.

5 THE WITNESS: Again, it's all about comparison,
6 active versus the placebo, and what the individual
7 adverse event is and how frequently it occurs normally
8 in a normal general population. So as long as the
9 adverse event profile isn't significantly accentuated
10 with the placebo, and you see a typical placebo
11 response, I mean, most people know that a placebo is not
12 dangerous. It doesn't have a lot of bad side effects.
13 It's a placebo.

14 Q BY MR. HOUSTON: Let's look at table 2 of
15 Exhibit 1043, the Hampel article. What's being reported
16 in table 2? Do you have an understanding of that?

17 A The header on table 2 is "Commonly Reported
18 Adverse Events (Safety Population)." And it has a super
19 script "a." You go down below, "a" says:

20 "A patient with multiple adverse
21 events is counted only once in any row.

22 Adverse events were coded using the

1 Medical Dictionary for Regulatory
2 Activities."

3 That's what it's reporting.

4 Q So does that go to, just to use an example, if
5 the same patient reported a headache at two different
6 times during the study, it's only going to be counted
7 once, it's only going to be counted as one person having
8 a headache for that given treatment arm? Is that what
9 that footnote means that you just read?

10 A My interpretation of that footnote is if a
11 patient has multiple headaches, it will only be counted
12 once per adverse event. So if it's headache, they'll be
13 counted once. But the same patient could have headache,
14 dysgeusia, epistaxis, and then each of those are
15 different adverse events, so they would be counted
16 separately.

17 Q The way that footnote "a" says it treats
18 patients with multiple adverse events, is that standard?
19 Is that the way the FDA data does it?

20 A That's what I said earlier. That's in
21 conjunction with my understanding of how it's reported.

22 Q I don't know, so I'm just asking. Thank you.

1 And I think you did say that earlier, and I forgot.

2 Okay. So this table's reporting the commonly
3 reported adverse events for Dymista, azelastine, the
4 generic version of Flonase, and a placebo; right?

5 A Correct.

6 Q Would you agree with me that the reporting for
7 Dymista, the adverse events reported for Dymista are
8 generally higher for almost all of these side effects
9 shown here in the table as compared to Astelin or the
10 Flonase arms?

11 MR. LaROCK: Objection. Mischaracterizes the
12 document.

13 THE WITNESS: Some of these are confusing to
14 me. I think that the problem here is that it's such a
15 small number. If you look at the header, it says "N"
16 equals how many number of patients there are. And
17 inside the parentheses is how many patients. So I don't
18 know how they got 0.7, 1.3, 2.6 number of patients.

19 Q BY MR. HOUSTON: No, that's the percentage,
20 isn't it?

21 A Is that the percentage?

22 Q I mean, you can tell me, you can correct me if

1 I'm wrong --

2 A Maybe that's the percentage.

3 Q -- but I believe it's reporting the number of
4 patients, that's the number outside the parentheses, and
5 then the number inside the parentheses is percentage.
6 That seems to be what is indicated right here.

7 A Okay, thank you.

8 Q Is that fair?

9 A No, it is fair. So in this small proof of
10 concept study, whose primary purpose was to look at
11 efficacy and exploring safety, then I would say yes.
12 But this is not a, quote-unquote, pivotal, to use that
13 term I used before, pivotal safety and efficacy study.
14 So the robustness of the data is not the same as the
15 FDA-approved protocols.

16 Q Are you aware of any studies that tested
17 Dymista against -- that compared Dymista to Flonase or
18 generic equivalent of Flonase for a study period of
19 longer than 14 days?

20 A To clarify the question, am I aware of a
21 Dymista study that compares itself against Flonase or
22 generic form of Flonase for greater than 14 days?

1 Q Maybe I'll broaden it and say a fluticasone
2 treatment arm. Because I know there's sort of this
3 comparative fluticasone formulation.

4 MR. LaROCK: Object to the form of the
5 question.

6 THE WITNESS: I think so. I think so, yes.

7 Q BY MR. HOUSTON: What study would that be?

8 A I could be wrong, so please forgive me. I
9 believe a component of the long-term safety study that
10 is in the label for Dymista had a fluticasone arm that
11 lasted longer than two weeks. So yes. I could be
12 wrong, though. And I will stand corrected if you can
13 produce that and let me review it.

14 Q This is one of those questions where I'm just
15 asking because I don't know. But I will hand you, and
16 we'll see if this helps, I will hand you what's been
17 marked Exhibit 2066. I don't know if you would call
18 this the label. This is I think what you would refer to
19 as the package insert for Dymista. But you can correct
20 me there as well.

21 A Yes.

22 Q Yes, what?

1 A My answer was correct. Page 7.

2 Q Okay. Can you point me to where on page 7
3 you're referring to?

4 A If you go to the top of page 7, it says
5 long-term 12 month safety trial in adults and
6 adolescents. Go to the second paragraph:

7 "Any 12-month open label active
8 controlled long-term safety trial in
9 these patients, Dymista was given one
10 spray per nostril twice daily, 207
11 patients, with fluticasone two sprays
12 per nostril once daily for 12 months."
13 Primary outcome here is safety.

14 Q Okay. And then to further clarify, that
15 fluticasone propionate nasal spray there, would that
16 have been the fluticasone comparative formulation as
17 opposed to a Flonase formulation?

18 A My goodness. I honestly don't know. I
19 honestly cannot recall. This is a long-term safety
20 study. I could see it either way.

21 Q I suppose they don't provide an experimental
22 section that would describe that anywhere in here.

1 A You can see another study that was three months
2 right below that too.

3 Q That also contains a fluticasone arm?

4 A Yeah. That was the pediatric safety trial.

5 Q How should I be referring to this? Is this the
6 package insert?

7 A Yeah, or label.

8 Q Or label? Fine. Does the Dymista label
9 instruct the patients to shake the Dymista bottle gently
10 before use?

11 A The label includes this section that looks like
12 the page numbers are the same. That includes -- starts
13 on page 20. That includes some patient counseling in
14 then it should have some information on use. And if you
15 go down to the very bottom of page 20, you'll see where
16 it says "Priming":

17 "Instruct patients to shake the
18 bottle gently before each use and prime
19 the pump before initial use and when
20 Dymista has not been used for 14 or more
21 days. "

22 Q In your experience, is having to shake the

1 bottle before each use a hindrance to patient compliance
2 or patient usage of Dymista?

3 MR. LaROCK: Objection. Outside the scope of
4 his declaration.

5 THE WITNESS: I believe when you look at
6 various devices and methods of delivery, there are
7 different patient preferences for different deliveries.
8 So it's individualized per patient.

9 Q BY MR. HOUSTON: Do you have any evidence that
10 suggests that needing to shake the bottle of a nasal
11 spray medication is a particular issue in terms of
12 patient, what did you call it, patient preference?

13 MR. LaROCK: Objection.

14 Q BY MR. HOUSTON: Whether it's Dymista or any of
15 the other, or Flonase, for example?

16 MR. LaROCK: Object to the form of the
17 question. Outside the scope of his declaration.

18 THE WITNESS: I didn't really comment on this
19 in my declaration, so -- and I do not have any of the
20 patient preference studies available in front of me.
21 But I do believe this issue has been looked at, because
22 there are some nasal sprays that are solutions rather

1 than suspensions, and that perhaps it would be a patient
2 preference to have the solution over the suspension, and
3 one of the things could be shaking.

4 I don't have the reference in front of me.
5 These are patient preference studies, and it's
6 individualized with each patient. So that's the best
7 answer I could give.

8 MR. HOUSTON: I want to take a short break so I
9 can calculate my time. Could we go off the record?

10 (Recess 4:01 to 4:09 p.m.)

11 Q BY MR. HOUSTON: Let's for the moment turn to
12 paragraph 81 of your declaration first.

13 A Page 39.

14 Q Page 39, crossing over into 40. You can go
15 ahead and read that if you like.

16 A (Examining document) Starting on page 39:

17 "Dr. Schleimer opines that a POSA
18 would have been motivated to arrive at
19 claims 1, 5 through 6, 24 through 26,
20 and 29. Notably he says nothing
21 whatsoever about a POSA's motivation to
22 arrive at claims 4 and 42 through 44.

1 It, therefore, appears that
2 Dr. Schleimer and I agree: a POSA would
3 not have been motivated to develop the
4 pharmaceutical formulations covered by
5 claims 4 and 42 through 44. "

6 Q So, Dr. Carr, am I understanding your testimony
7 correctly that you think that Dr. Schleimer's silence as
8 to claims 4 and 42 through 44 makes it reasonable for
9 you to conclude that he must agree with you,
10 specifically, that a POSA would not have been motivated
11 to develop the pharmaceutical formulations in claims 4
12 and 42 through 44? Is that right?

13 MR. LaROCK: Objection. Mischaracterizes
14 Dr. Carr's testimony and his declaration.

15 THE WITNESS: So Dr. Schleimer gives his
16 opinion on this case, and he discusses motivation of a
17 POSA, and he explicitly talks about the claims in the
18 first sentence, but he says nothing about a POSA's
19 motivation to arrive at claims 4 and 42 through 44. So
20 therefore it appears that Dr. Schleimer and I would
21 agree. It appears that we would. Perhaps he, I don't
22 know, maybe on his -- when he gave his deposition, maybe

1 he said something different. But it appears as if
2 Dr. Schleimer and I agree.

3 Q BY MR. HOUSTON: Well, so my question is, so
4 it's his silence, the fact that he didn't address those
5 claims, is what leads you to conclude that it appears
6 that you agree? In other words, he didn't say anything
7 on it, so he must agree with you. Is that your logic?

8 A Well, he opined extensively on all of the
9 others, but left these out. So if he felt differently,
10 he would have said something about it. So it appears
11 that Dr. Schleimer and I agree, a POSA would not have
12 been motivated to develop the formulation covered under
13 those claims.

14 Q Okay. Did you review Dr. Schleimer's
15 declaration in this proceeding?

16 A Yes. I don't have it in front of me.

17 Q Did you review the decision from the Patent
18 Office in which they instituted this proceeding?

19 A So earlier you had expressed that you didn't
20 quite speak the same lingo sometimes as the doctors do.
21 And so I may not speak the same lingo as you do. Could
22 you clarify for me?

1 Q So to have this proceeding go forward, the
2 board issues what they call an "institution decision," a
3 decision that reviews the parties' submissions to date
4 and decides whether to proceed or not. And I'm asking
5 if you reviewed that decision from the board in
6 preparing your declaration.

7 A I don't believe it appears in the list of
8 items -- let me look and see. So the basis for my
9 opinions are listed on page 4 of my declaration,
10 paragraph 14. I've considered the following documents.
11 I don't believe that decision is listed here. So these
12 are the documents.

13 Q Just to be clear --

14 A -- that I reviewed.

15 Q Is that every piece of paper you reviewed in
16 connection with this proceeding, or are those the ones
17 that you reviewed that had some impact on your opinions
18 or testimony?

19 A These are the documents that I've listed that
20 are the basis for my opinions for my declaration.

21 Q So I suppose that leaves open the possibility
22 that you reviewed the institution decision, but it's

1 just not forming the basis for any of your opinions.

2 I'm just asking. I don't know the answer. I'm
3 asking you whether or not you recall reviewing the
4 institution decision.

5 A I can't recall.

6 Q But you did review Dr. Schleimer's declaration;
7 correct?

8 A Yes.

9 Q Do you recall that one of the primary
10 references that Dr. Schleimer relies on for arguing that
11 the challenge claims here should be held invalid was a
12 reference that he refers to as Segal, Exhibit 1012? Do
13 you recall that?

14 A I'd have to look at it. Do I have it?

15 Q I can tell you it's not in your declaration.
16 I'm just asking you if you recall any discussion of that
17 reference, if you recall that reference.

18 A Who was the author? Chuck Segal?

19 Q Let me look up the first name.

20 A I've seen a lot of Chuck Segal's work. Is he
21 an allergist?

22 Q Catherine Segal, Warner-Lambert Company.

1 A This is a manuscript that is reviewing a
2 clinical trial?

3 Q It's a patent application.

4 A Oh, patent application. I'm sorry. I thought
5 you were talking about a manuscript from Chuck Segal,
6 who's an allergist. I didn't know where you were going
7 with it. I thought you were going to whip out another
8 paper for me.

9 Q It's just a reference. In this proceeding we
10 refer to it as Segal, because that's the --

11 A I can't recall. I'm sorry.

12 Q Now, I've done a search on your declaration for
13 both that name and the exhibit number for Segal, and I
14 can't find it mentioned anywhere in your declaration.
15 Do you have any reason to think that it is mentioned in
16 there somewhere?

17 A I don't have any reason to believe it would be
18 mentioned in there without me recalling it. I suppose
19 it would be possible. But if you're telling me you
20 searched my declaration and you didn't see it in there,
21 then I probably didn't use it as a reference in the
22 basis of forming my opinions.

1 Q So is it reasonable, then, for Dr. Schleimer to
2 assume that you agree with his opinions that were in his
3 declaration as to Segal, since you stayed silent on it
4 in your declaration the way you did with his?

5 MR. LaROCK: Hold on. Object to the form of
6 the question. Calls for speculation.

7 THE WITNESS: I can't speak for Dr. Schleimer.

8 Q BY MR. HOUSTON: Would it be reasonable for
9 anyone in this proceeding to assume that you agree with
10 Dr. Schleimer's testimony regarding Segal, since you
11 were silent on it in your declaration?

12 A I would need to look at it.

13 Q Need to look at what?

14 A Segal.

15 Q Just Segal?

16 A Whatever the context of your specific question
17 is. Let me see the document.

18 Q I'll let you see it. Although I'm not asking
19 you about Segal. I'm asking about Dr. Schleimer's
20 testimony regarding Segal in his declaration.

21 There's Exhibit 1012.

22 A This is the international application from

1 1998, Warner-Lambert.

2 Q So just to be clear, Dr. Carr, I'm simply
3 asking, the fact that you stayed silent on this in your
4 declaration, isn't it reasonable to assume that you
5 agree with Dr. Schleimer and what he said about Segal in
6 his declaration, based on your silence?

7 A I believe this was all on the same patent, in
8 item -- page 39 and 40, that was all on the same patent;
9 right?

10 Q Those claims are all from the same patent;
11 right.

12 A So he gave an opinion about the patent. In my
13 declaration, I don't talk about this patent. I don't
14 partially talk about this patent. I don't completely
15 talk about this patent.

16 Q Oh, that we agree on.

17 A Schleimer talked about this patent. It's the
18 same patent. So you cannot make the same assumption or
19 you cannot infer the same appearance, because I didn't
20 opine on this. I didn't say anything about this.

21 Q My point is, it's in Dr. Schleimer's
22 declaration, and you are opining about Dr. Schleimer's

1 declaration. You're just opining selectively about
2 certain things in his declaration; right?

3 MR. LaROCK: Objection. Mischaracterizes his
4 declaration. Asked and answered.

5 THE WITNESS: So I'm discussing a very specific
6 component in page 39 over to page 40, which is paragraph
7 81 on those two pages. I'm making a comment about a
8 very specific component of his declaration.

9 Q BY MR. HOUSTON: Well, you're making a comment
10 about something that is not in his declaration, right?
11 Specifically, claims 4 and 42 through 44. You said
12 "he's silent on those, so he must agree with me."

13 MR. LaROCK: Objection. Mischaracterizes
14 Dr. Carr's declaration.

15 THE WITNESS: Well, he is discussing this
16 patent, and he goes through a variety of different items
17 in the patent. He doesn't cover the entire patent in
18 his objections.

19 In the example you're giving, I don't opine
20 about any of this. So how could he presume I agree with
21 him, when I don't opine about even one sentence of this
22 document? I haven't even discussed this document.

1 Q BY MR. HOUSTON: You opine throughout your
2 declaration about Dr. Schleimer's declaration, don't
3 you? If I did a word search for "Schleimer" in your
4 declaration, I bet it would show up a hundred times.

5 A Perhaps.

6 Q So you don't get the analogy I'm making here at
7 all? It's going over your head?

8 MR. LaROCK: Whoa.

9 Q BY MR. HOUSTON: I'm just asking. I think it's
10 pretty simple what I'm asking, and if you don't
11 understand, that's fine. You can say that.

12 MR. LaROCK: Objection. Harassing the witness.
13 You can answer.

14 THE WITNESS: So I may not be saying what you
15 want me to say. I may not be giving you the answer that
16 you want to hear, which is why you think this is going
17 over my head.

18 But no, that is not the case. I do not believe
19 that this is going over my head. I fundamentally am
20 saying, in my declaration, I'm talking about what
21 Schleimer says about this patent. He has a lot to say
22 about this patent. There's a section that he doesn't

1 criticize, so to speak. So it would appear that
2 Schleimer and I would he agree on that particular
3 section. We may not agree on all of it.

4 Now, to stretch that, which I believe is what
5 you're trying to do, to say, since I didn't bring up
6 this entire patent, then the presumption would be I
7 agree with Schleimer, no, that's a total
8 mischaracterization.

9 Q BY MR. HOUSTON: I think the point I'm trying
10 to make is you respond to various portions of
11 Dr. Schleimer's declaration, but not the portion that
12 addresses Segal. That much we can agree on. Right?
13 That much is true.

14 MR. LaROCK: Objection. Asked and answered.
15 Mischaracterizes Dr. Carr's declaration. Form.

16 THE WITNESS: I do not opine in my declaration
17 on Segal or on Schleimer's interpretation and opinions
18 of Segal.

19 Q BY MR. HOUSTON: Right. So you opine on a lot
20 of Dr. Schleimer's declaration, but not the portion
21 addressing Segal. We can agree on that; right?

22 A I believe I've answered that already.

1 Q Well, just to be clear, the answer is yes.

2 Correct?

3 MR. LaROCK: Objection. Mischaracterizes his
4 testimony.

5 THE WITNESS: So again, I don't opine on this
6 document, nor do I opine on Schleimer's opinions of this
7 document.

8 Q BY MR. HOUSTON: Could I ask you to turn to
9 paragraph 59 of your declaration.

10 A Page 24? Are we in the same place?

11 Q 24 and 25. While I'm getting a document, you
12 can review that to yourself. I'm going to hand you an
13 exhibit that I believe you're talking about the
14 Drouin -- am I pronouncing that correctly?
15 Exhibit 1035.

16 A (Examining document) Okay.

17 Q On page 25 of your declaration -- can you turn
18 to page 25 of your declaration? Okay. There you're
19 talking about Drouin; correct?

20 A Yes, this upper section is about Drouin.

21 Q You say:

22 "The study data, summarized in Table

1 2 of the publication, shows the
2 percentages of improvement in the
3 study. "

4 You go on to say:

5 "The TNSS numbers reported for the
6 combination and the steroid-only groups
7 differ by 7 percent...."

8 You see that?

9 A I see that sentence.

10 Q I'd like to try to understand -- I want to
11 understand where that 7 percent comes from, what you
12 mean by the groups differed by 7 percent. And I presume
13 this comes out of table 2. But can you walk me through
14 or explain where that 7 percent number comes from?

15 A Well, what that means, if you read the rest of
16 the sentence, just right after the 7 percent:

17 "...meaning that the total
18 difference between the combination group
19 and the steroid-only group was about .4
20 points -- a meaningless difference. "

21 That's what that means.

22 Q I understand that you're saying that's what

1 that means. Where does the 7 percent number come from?
2 You say, "The TNSS numbers reported for the combination
3 differ by 7 percent." Where did that come from?

4 A I may have to read the text. So the study
5 data -- I'm recapping the sentence on the top of page
6 25:

7 "The study data, summarized in table
8 2 of the publication, shows the
9 percentages of improvement in the
10 study."

11 So if we go to table 2, it's showing the
12 evaluation day, the total symptom score, the total nasal
13 score, the individual nasal symptoms, and then the
14 ocular scores, and then the nonocular component of the,
15 quote-unquote, total symptom score, which is either ear
16 or palate itching. So there's the day, there's the
17 percent and the combination, and here's the percent in
18 the monotherapy.

19 And obviously, you notice a huge flaw in this
20 study, the huge bias in this study, the fact that there
21 is no placebo. So we don't know what the placebo effect
22 is in this study.

1 So if you go to the total nasal score and you
2 look at day 3 and day 7, you see that for the
3 combination of loratadine and BDP, the percentage is 55,
4 but for the BDP plus placebo group, it's 48. That's a 7
5 percent difference, 48 plus 7 is 55.

6 And then if you look at day 7, 59 percent in
7 the BDP only as compared to 66 percent in the loratadine
8 plus BDP, that is 7.

9 So the big problem here is, we don't know what
10 the placebo effect is. And placebo effect in these
11 clinical studies for allergic rhinitis is usually
12 somewhere around 30 to 40 percent.

13 Q Now, you say that the difference of 7 percent
14 means that the total difference between the combination
15 group and the steroid-only group was probably 0.4
16 points. Do you see that?

17 A Yes, I do.

18 Q How did you arrive at your testimony that this
19 equates to approximately 0.4 points?

20 A Well, you have to do math and look at the
21 symptom scores. Because this is expressed in a
22 percentage. And so percentages of what? You have to

1 look at the -- you're trying to find out, how many
2 points improvement in your total nasal score is that?
3 There's generally what's considered a clinically
4 meaningful improvement.

5 So the total nasal score -- and this is an
6 older study. In the studies we've talked about, like I
7 conducted, it was called the total nasal symptom score.
8 So TNS is the TNSS. It's for symptoms -- nasal
9 discharge, nasal stuffiness, nasal itch, and sneezing.

10 And in fact, if you go right down to this
11 footnote, I kind of talk about this rating system, the
12 footnote on 25, I kind of talk about this rating system
13 a little bit. So you can have a zero to a 3 for each
14 individual symptom.

15 Q So Dr. Carr, I think I understand basically
16 what the TNSS --

17 MR. LaROCK: He's explaining where that came
18 from. You're cutting him off now.

19 MR. HOUSTON: We have a limited amount of time.
20 I get it. Total nasal symptom score can add up to 12.

21 Q Can you help me understand how you got to the
22 0.4 without giving me so much of the background? That's

1 all I'm asking.

2 A Well, if you just do some math.

3 Q What math? I've done the math as far as I
4 understand it, and I don't come up with that number. So
5 that's why I'm -- can you walk me through what the math
6 would be?

7 A Let's see your math.

8 Q I'm not going to show you my math. I want to
9 know where you came up with that number that's in your
10 testimony.

11 A Well, that's what it equates to. It's a
12 difference of less than a half a point. Clinically
13 insignificant. Meaningless.

14 Q How did you arrive at 0.4? Describe it to me.

15 A Well, I was trying to do that, but you said I
16 didn't have time to explain to you what the total nasal
17 symptom score was and to do percentages of improvement.
18 So you figured out what a 7 percent improvement is when
19 those are your total nasal symptom scores. And that
20 will equal roughly about .4 points.

21 Q I'd like to understand what calculations you
22 did to arrive at that. So --

1 A You want me to take the rest of our time and
2 try to sit -- on a piece of paper and draw math
3 equations for you?

4 Q Well, if it's that complicated, start to walk
5 me through it. That's what want to understand. I can't
6 come up with that 0.4 number. I'm trying to understand
7 it.

8 A So I'll give you an example. Back to our
9 example of 100 patients and 10 sites. 100 patients and
10 10 sites. That's 10 percent. If you have a thousand
11 patients and 100 sites, that's 10 percent.

12 But there's a difference in the numerical
13 values of those percentages. The difference between 1
14 and 2 and the difference between 2 and 4, yeah, they're
15 both doubled, but one is 1 point difference and one is 2
16 points difference. The difference between 0.25 and 0.5,
17 it's sill a doubling, it's still a percentage increase
18 equal to all the other percentages in my example. But
19 it's only a difference of 0.25. So that's how you get
20 to these absolute differences, doing those fractions.

21 Q So we will have to do it in more detail,
22 because I'm not following you. I'd like to understand

1 how you got to 0.4. Please explain it to me. With
2 paper, with pens --

3 A I just did.

4 Q Show me what math you did using the data out of
5 Drouin. Is it just 7 percent times something? I want
6 to do a series of calculations where I end up with 0.4.
7 I'd like to understand what those should be.

8 A Why don't we put it this way. If you go on and
9 you read the rest of my declaration:

10 "This improvement is less than
11 typically obtained from placebo."

12 Q I don't care about that. I want to know how
13 you got to 0.4.

14 MR. LaROCK: Objection. He's answering the
15 question. You keep cutting him off.

16 Q BY MR. HOUSTON: Are we going to end up with a
17 series of calculation that show me how you got to 0.4?
18 Let me ask that.

19 A You've asked me so many questions. You keep
20 cutting me off. You're not giving me an opportunity.
21 You are saying you don't have enough time, but you're
22 not giving me a chance to answer the questions.

1 I'm trying to make it, as an expert in treating
2 allergic rhinitis and looking at these studies, I'm
3 trying to explain to you in a different way that perhaps
4 maybe we could save some of your time and I would be
5 able to answer your question.

6 So to continue on with what I was trying to
7 say. In clinical studies such as this in general for
8 allergic rhinitis, a placebo response, if you go on, you
9 say, "this improvement is less," in my declaration,
10 "this improvement is less than that typically obtained
11 from placebo."

12 We can look at multiple studies. Placebo
13 response rates is around 30 to 40 percent. We've
14 already discussed that in more than one study. So I
15 think we can all agree that 7 percent is less than a 30
16 to 40 percent response, and that is what I am saying:

17 "This 'improvement' is less than
18 typically obtained from placebo. A POSA
19 would have seen no meaningful
20 improvement in the symptoms."

21 So I don't believe it's within the scope of my
22 declaration to sit here and do math.

1 Q It's within the scope of your declaration, the
2 .4 is, and I'd like to know where it came from. How did
3 you arrive at a number of 0.4?

4 A By doing the calculations like I described.

5 Q Please explain them. You have an obligation,
6 if you're going to testify as an expert and provide
7 calculations, you have an obligation to explain them.

8 A If you look at the percentage of improvement --

9 Q So the ones we just talked about in table 2?

10 A If you look at the percentage of improvement in
11 each treatment arm, and you compare that to what the
12 patient's total nasal symptom scores are, you're trying
13 to figure out how many points improvement is that.

14 Q So would I start from the nasal symptom score
15 that's reported on the previous page in table 1 of
16 Drouin?

17 A That would be a good place to start.

18 Q You tell me. I'm not trying to tell you how to
19 do it. I'd like to know how you did it.

20 A Well, this is where the patient's baseline
21 demographic data is, and it lists their baseline symptom
22 scores.

1 Q So walk me through it. How do you get to 0.4?

2 A So if you look on table 1, you'll see that the
3 baseline scores, the total symptom scores of loratadine
4 plus budesonide is 14.9. Placebo plus budesonide.
5 Again, huge flaw to this study. Huge flaw. There was
6 no placebo arm. So this data is flawed from its very,
7 very, very beginning. Okay?

8 And then you look at the percentage of
9 improvement. So how much percentage of improvement did
10 we get for the loratadine to budesonide? You got a 55
11 percent improvement at day 3. So take the baseline
12 value for loratadine for budesonide, 14.9, times 55
13 percent.

14 Q 14.9 times .55. Is two significant digits
15 sufficient? 8.20.

16 A So that's a 55 percent improvement from
17 baseline.

18 Patient after 3 days of treatment went from,
19 let's say, roughly 15 to roughly 8. They had a 55
20 percent improvement. Now do it, the same calculation
21 for day 7. 66 percent times 14.9.

22 Q One second. Day 7, you said. So 14.9 times

1 .66? Is that right, Dr. Carr?

2 A Yeah. What did you get for that?

3 Q 9.83.

4 A So that is a 9.83 percent -- I'm sorry, point
5 improvement. So 14.9 minus 8.2 is what? 6.7. So
6 that's your patient symptom score, 6.7. That's your
7 delta.

8 Q After day 3.

9 A 55 percent improvement, so 55 percent is 8.2.
10 Right?

11 Q Yes.

12 A So if at baseline they were 14.9, and they had
13 a 55 percent improvement, that's 8.2. 8.2 from 14.9, if
14 your calculations are correct, are 6.7.

15 Now do the same thing for the other one.

16 Q So I'm going to do 14.9 minus 9.83. 5.07.

17 A So those are the patients' total nasal score at
18 day 3, and day 7 for loratadine plus BDP. You got to do
19 the same thing for placebo plus BDP.

20 Q So it would be 15.1 times the 55 --

21 A No, it's 48 percent improvement. 48 percent.

22 Q Thank you. So times 48 and times 59?

1 A 59.

2 Q Okay. 15.1 times .48, 7.25. 15.1 times .59,
3 8.91. So now we'll do that subtraction again. 7.85,
4 6.19.

5 A So that is their day 3 and day 7. Right?

6 Q 3, 7, 3, 7. So I believe this is -- just to be
7 clear, the loratadine plus BDP is the steroid plus
8 antihistamine. The placebo plus BDP is just the placebo
9 plus the steroid.

10 A Say again?

11 Q BDP is the steroid?

12 A That's the steroid. Beclomethasone
13 dipropionate.

14 Okay, so let's check our math and make sure
15 that the difference between that is 7 percent real
16 quick. So the difference between --

17 Q What would you like me to compare?

18 A We added up these numbers and it was 7 percent
19 difference, so we want to make sure that we -- so .4
20 would be --

21 Q Well, actually --

22 A -- so if you add .4 to this, what do you get?

1 Q Add .4 to what?

2 A If you add .4 to this, what do you get?

3 Q 7.1.

4 A 7.1?

5 Q Yeah.

6 A And if you add .4 to this, you get 5.57. So
7 those don't add up 100 percent.

8 Okay. I can't give you the .4 right now. If
9 you have got a lot of time, I'd have to sit down and do
10 some statistic evaluation. That simple math that we've
11 done upside down, I can't get to it.

12 But I think I will stand firm on the 7 percent
13 and the comparison to placebo. That statement stands.
14 This is clearly a 7 percent difference, and you
15 typically see a difference in placebo, a placebo effect
16 in a clinical trial for allergic rhinitis is about a 30
17 to 40 percent improvement.

18 Q 30 to 40 percent, whereas here --

19 A There is no placebo arm.

20 Q Right. You're just saying it's typically 30 to
21 40 percent, and here the effect of the drugs is in the
22 48 to 66 percent range; right?

1 A We're talking the delta versus placebo. So
2 let's say it's 40 percent. You'll see maybe 8
3 percent -- and by the way, that's at two weeks, you'd
4 see 8 percent and 15 percent. Very small numbers, in a
5 biased study.

6 Q That's assuming your placebo's at 40. If it's
7 at 30, all of a sudden that number goes up pretty fast;
8 right?

9 A No, they should have done a better study.

10 Q Going back to the numbers I have on my sheet
11 here, can you at least suggest to me where you would
12 have expected to see this 0.4 number come out?

13 A I would have done something along these lines
14 and seen a comparison of this group and this group that
15 was around .4. That's what I was trying to get to, and
16 I apologize, we didn't get there.

17 Q Well, I would like to know where it came from.
18 So if you want to take a break and think about it, if
19 you want to talk about it with your counsel after I'm
20 done and come back, please do. I'm not going to accept
21 your 0.4 if you can't show me how you got there, but
22 that's fine.

1 Let's move on, unless there's anything else you
2 want to add on that issue.

3 Why do you say that the difference being 0.4
4 points is a clinically meaningless difference? What is
5 that based on?

6 A Experience with clinical trials, and drugs that
7 work usually have about a 1 point improvement.

8 Q Well, I believe you defined "clinically
9 meaningful," I think you reversed -- you changed the
10 wording slightly earlier in your declaration, but you
11 said that's a result that patients can actually notice.

12 A I think it's at about 1 point. I think
13 somebody looked at that, and I can't give you the
14 reference off the top of my head, but that's kind of
15 like a dogma that we use.

16 Q So you have to have a difference in TNSS scores
17 of about one point before patients can actually notice
18 it?

19 A In general with a nasal spray, that is a
20 general guideline that we look at. So if you pull out
21 the label for Flonase and you compare it to placebo, I'm
22 sure it will be around 1 point.

1 Q I'll hand you what I think is the label for
2 Flonase. These don't have the exhibit labels. Excuse
3 me, Dr. Carr, while I just confirm that that's the right
4 exhibit, since it doesn't seem to have the label on it.

5 I'll represent to you that I think this is
6 Exhibit 1010, and you can write that on there if you
7 like. I think it's just missing its exhibit label.
8 Does this look like the Flonase label?

9 A It does look like the Flonase label. Some of
10 the newer medications have it in a table so you can
11 easily do the math. What is the date on this label?
12 This must be an older label. Do you see a date on it?

13 Q The very last page says December 1998.

14 A December 1998, so that's kind of a 20-year-old
15 label. They've changed how they put this stuff in here.

16 So let's go to the clinical trials section. 13
17 randomized double-blind and parallel multicenter
18 studies, seasonal allergic --

19 (Reporter interruption)

20 Q BY MR. HOUSTON: Maybe you could start by
21 reading it silently, Dr. Carr, and if there's something
22 you want to put on the record explicitly, you can.

1 A I'll start by reading page 3, "Clinical
2 Trials."

3 So this label is so old, in the clinical trials
4 section, it doesn't actually even give the results. So
5 I've got to keep searching. Unless you see it somewhere
6 else. This label is so old, it doesn't even list the
7 absolute values.

8 Q I haven't located any TNS scores.

9 A So like I said before, it's dogma that we use
10 that for these nasal spray products. Typically a score
11 of about 1 is what we consider meaningful.

12 Q A difference of about 1; right?

13 A The delta compared to placebo.

14 Q And that's on a scale of 0 to 12?

15 A Correct. So we can keep searching if you want,
16 we can start picking off other nasal sprays that were
17 approved since that time.

18 Q Let's look at Drouin a little bit more before
19 we move on. You would at least agree with me that the
20 difference between the steroid plus placebo and steroid
21 plus antihistamine, the percentage difference reported
22 in table 2 is more than 7 percent for the nasal score

1 symptom of sneezing; right? At the three-day mark in
2 particular.

3 A Just for clarification, are you referring to
4 loratadine plus BDP being 57, and placebo plus BDP being
5 46?

6 Q Actually, that was what I was referring to, and
7 now I realize I need to direct you to a slightly
8 different place.

9 I meant to ask you about nasal itching, so
10 loratadine plus BDP 61, and placebo plus BDP being 48.

11 A Okay, I see where you're at.

12 Q So that's a difference of 13 percent; correct?

13 A In a subset of what we would consider the
14 metric we use to determine effectiveness for allergic
15 rhinitis. So what we really look at is the total nasal
16 symptom score. Perhaps as a secondary evaluation we're
17 curious about each individual nasal symptom, but that's
18 not how we determine the efficacy of these nasal sprays.

19 Q Okay, but just as to that issue, the way you
20 get the total nasal score is you look at all four of
21 these symptoms listed here combined, right? You just
22 add them up? There's four symptoms listed there, and

1 you add the four up to get your total nasal score;
2 correct?

3 A That is correct. And then you look at changes
4 in the total nasal symptom score over a time period.
5 And typically for allergic rhinitis medicines it's two
6 weeks, and you compare that to placebo.

7 So there's huge flaws in this study that
8 invalidate the study, in my view --

9 Q I understand.

10 A -- the fact that there's no placebo. To me,
11 like I said, I imprint studies that are clinically
12 meaningful. This is so biased that -- and I believe, if
13 I go back to my declaration, Neilsen, who published a
14 review of all of the body of literature, also included
15 Drouin, and Neilsen said that there was no difference,
16 essentially there was no benefit of this combination.

17 Q If we look at the four symptoms that are listed
18 here on table 2 on Drouin for the total nasal score --
19 discharge, stuffiness, itching, and sneezing -- was it
20 known in the art that antihistamine drugs tended to act
21 faster on some of those symptoms as compared to others?

22 A Well, I believe it depends on the antihistamine

1 that you're talking about. They have different onset of
2 actions.

3 And we have to be very careful about how you
4 define "onset of action." Onset of action is defined by
5 an improvement in the total nasal symptom score on at
6 least two different time points as compared to placebo.
7 That's how you define onset of action.

8 So when you pull up a label for Dymista, and
9 you look at the onset of action of Dymista, that's how
10 onset of action is defined. We don't look at individual
11 symptoms. You may be chipping around the edges, but if
12 you're not going to get the full improvement, then we
13 don't call it changes -- that that's actual onset of
14 action.

15 That being said, azelastine is one of numerous
16 antihistamines that was currently available on the
17 market at that time, and loratadine was another
18 antihistamine that was available. These medicines were
19 generally felt to work faster than a drug like BDP or
20 fluticasone, which took several hours to start working.
21 In fact, I don't recall BDP showing onset in the first
22 day in its label. I'd have to pull the label.

1 I believe the fluticasone label showed some
2 onset in the first day, to the best of my recollection.
3 I'd have to read it. I believe it's somewhere around 9
4 to 12 hours. And I believe azelastine is around 3
5 hours. So 3 hours would be faster than 9 or 12 hours.
6 Sorry about the difference between the 9 and the 12.
7 I'd have to look at it.

8 Q Okay. What I had asked you was, was it
9 understood or known that antihistamines were generally
10 thought to act faster on some of these symptoms than
11 others? So of the four that are listed here, were
12 antihistamines such as, you mentioned azelastine, this
13 study uses loratadine. Were these antihistamines
14 thought to act faster on some of these four nasal
15 symptoms than others?

16 MR. LaROCK: Objection. Form. Asked and
17 answered.

18 THE WITNESS: Perhaps it's semantics, but I
19 think I've defined what I consider as onset of action.
20 It's not a change in one symptom at one time point. You
21 have to affect all four.

22 Q BY MR. HOUSTON: I understand that. That's why

1 I'm specifically not asking you about onset of action.

2 I'm trying to not ask you that, because I understand the
3 distinction.

4 So I'm asking, were the antihistamines such as
5 azelastine, loratadine thought to have -- thought to
6 affect any of these four symptoms under the nasal score
7 faster than it might have affect some of the other
8 symptoms?

9 A Yes.

10 Q Which ones was it generally thought that the
11 antihistamines would act faster on? Which one or ones,
12 of the four nasal score symptoms?

13 MR. LaROCK: Objection to form.

14 THE WITNESS: I would say in general
15 antihistamines are least effective at affecting the
16 nasal stuffiness or congestion. While they do have
17 effect, I believe it is least effective. So the other
18 three, I would have to say I'm not sure which ones --
19 how to categorize 1, 2, 3, 4.

20 Q BY MR. HOUSTON: Understood. I do want to just
21 clarify, though. You said least effective as to nasal
22 stuffiness. And I just want to make sure that we're not

1 confusing overall effectiveness in some way with the
2 quickness, the quickness with which you start to see an
3 improvement. I was specifically asking about the
4 quickness.

5 I just want to clarify, is it the case that the
6 nasal stuffiness would generally be the symptom that
7 would take the longest to be affected by those
8 antihistamines, of these four?

9 MR. LaROCK: Objection. Compound.

10 THE WITNESS: I believe it would be the least
11 effective and the longest.

12 Q BY MR. HOUSTON: Among the other three, do you
13 have any sense of which one would be the fastest, the
14 quickest to be affected, or does one not stand out from
15 the other?

16 MR. LaROCK: Objection, form.

17 THE WITNESS: I think on any given day you
18 could, in any given patient, you could change the order
19 of those three. So it's very difficult for me to make a
20 general statement and categorize them as a 1, 2, 3. By
21 the way, which is why drugs like Zyrtec-D and Allegra-D
22 were approved, because of the effect of the

1 pseudoephedrine, the Sudafed, on the nasal congestion.

2 Q BY MR. HOUSTON: How about I ask the same
3 question as to steroids. And I really want to ask about
4 fluticasone. But we could do fluticasone and BDP, since
5 that's in this table sitting here in front of you, if
6 you like. Was there any understanding that those
7 steroids tended to act faster or slower on any of these
8 four symptoms compared to the others?

9 A I think it's pretty well described that
10 steroids act on all four symptoms. And it would be hard
11 for me to categorize them 1, 2, 3, 4.

12 Q Okay, so they act on them. Fine. What about
13 the speed with which they begin to act on them? How
14 quickly? Is there any difference among the four
15 symptoms, when we're talking about the steroids?

16 A This is a very difficult thing to speculate on.
17 I would say, since -- I would say no. Probably you're
18 not going to see any difference in any of the individual
19 symptoms.

20 Q Now, let's go back, then. You clarified that
21 onset of action is only going to be viewed when you see
22 an impact on all four symptoms; right? If we're going

1 to talk about onset, it has to be all four symptoms.

2 A As compared to placebo.

3 Q Okay. So if one were looking at the onset of
4 action for an antihistamine, that onset is really going
5 to be driven by whichever of these symptoms is the
6 slowest to be acted upon. Is that fair?

7 A I don't know what you mean by "driven by."

8 Q Well, if we ask ourselves, what's the onset of
9 action of a given antihistamine, because onset of action
10 is, I guess I'll call it a term of art, seems like a
11 term that you have a specific definition for, you say it
12 considers all four symptoms. You have to see
13 improvement in all four symptoms. So you're never going
14 to see onset of action until you have improved all four
15 symptoms. And if there's one that's slow, slow to be
16 acted upon, well, that's going to tend to dictate when
17 you're going to see onset of action for a given drug or
18 given antihistamine; right?

19 MR. LaROCK: Object to the form of the
20 question.

21 THE WITNESS: No, I don't believe that's what I
22 said, or what the implication of my statement is.

1 Q BY MR. HOUSTON: Okay, maybe I could ask it
2 this way. If you'll indulge me, let's just assume for
3 the moment that we want to define onset of action
4 differently, and we want to just define it as
5 encompassing three of these symptoms -- nasal discharge,
6 itching, and sneezing. Just hypothetically. If now I
7 want to look at my onset of action for an antihistamine,
8 aren't I likely to see a faster onset of action under
9 that hypothetical scenario than if I include nasal
10 stuffiness as one of my symptoms, where we know that
11 antihistamines act more slowly?

12 MR. LaROCK: Objection. Compound, calls for
13 speculation.

14 THE WITNESS: I don't think you can say that,
15 no.

16 Q BY MR. HOUSTON: Can you help me understand why
17 not? Is there something I'm missing? I didn't think it
18 was so complicated. I thought I understood it, but
19 apparently I don't. Can you shed any light on that?

20 A Sure. So the total nasal symptom score has all
21 four symptoms, as you have identified. The magnitude of
22 improvement as compared to placebo, let's use your

1 hypothetical situation, okay? And let's use my dogma of
2 1 point. Is that fair for the sake of our conversation
3 and my explanation to elucidate this to you?

4 Q I think so.

5 A So let's say that you have a placebo drug that
6 has no improvement in stuffiness, but it has a 1 point
7 improvement in discharge, itching, and sneezing. So
8 that's a delta from baseline of 3.

9 Now let's say you have your antihistamine, and
10 it has an improvement in the nasal discharge of 2, nasal
11 stuffiness of 1, nasal itching of 2 and nasal sneezing
12 of 2. So that's a 7-point difference from baseline.

13 The delta versus placebo, then, is 3 points. 7
14 minus 4, or 3, maybe it's 4 points. So it's a big
15 difference, okay? It's more than the one point. And
16 let's say that you first see that delta at three hours.

17 Q When you say "that delta," you mean the delta
18 of the 3 to 5 points?

19 A The delta compared to placebo.

20 Q But does it have to reach 3 or 4, or are you
21 just talking about it reaches 1, because that's dogma
22 number?

1 A Well, maybe they didn't record it until three
2 hours. So the first time point.

3 Q The first time point that we see at least a
4 delta of 1.

5 A Yes. For the purpose of this example, so when
6 you see that first time point, then you have to -- the
7 second half is, you have to maintain it. You have to
8 maintain that difference. So if you get it at one but
9 then it goes away and doesn't come back until three
10 hours later and then it's there at four hours and five
11 hours and six hours, then your onset is the second one,
12 because you have to have it at two time points.

13 So this is an example where it could take
14 longer for stuffiness to have as big an effect as the
15 other ones, but the other ones have such a robust effect
16 that you see a change in the total nasal symptom score
17 as compared to placebo that is sustained over multiple
18 time points. Thus the drug gets its onset of action.

19 Q So -- okay, I see what you're saying. So an
20 onset might be controlled, might be triggered by a quick
21 and significant change in one's symptom that is then
22 sustained as compared to placebo, or it could be a

1 smaller change as to all four symptoms that at least add
2 up to more than one, again, as compared to placebo.

3 Okay, thank you, that helps.

4 If I go back to antihistamines, if I ask the
5 question, were antihistamines known to act relatively
6 fast or slow as compared to placebo, for each of these
7 four symptoms, do any symptoms stand out as faster or
8 slower, if we're looking at the delta as compared to
9 placebo?

10 A Wow.

11 MR. LaROCK: Object to the form of the
12 question.

13 THE WITNESS: Okay, so this is a complicated
14 question. So -- and you're saying onset.

15 Q BY MR. HOUSTON: Well, except I'm hesitating to
16 say onset, because I know onset has to group all four
17 together. I want to break it into each of the four
18 symptoms, or just ask if there's a difference among
19 them. But yeah, start to see an effect.

20 A So let me build this answer in reverse. I said
21 before placebo effect, ballpark it, 30 to 40 percent at
22 the end of two weeks as compared to the active therapy.

1 Your question then is looking at that 30 to 40
2 percent improvement, when did you start seeing that
3 happen in the total nasal symptom score. And then yet
4 another subset of that is, is there a difference in each
5 individual symptom that drives that improvement.

6 That's tough. It's really hard for me to
7 answer that question. I mean, the whole reason you get
8 an onset of action is because you have separation from
9 placebo. So I guess the only way we could say there's
10 an improvement in placebo is just comparing it to
11 baseline.

12 So let's say your baseline total nasal symptom
13 score was 6, and at the end of two weeks, the -- I'm
14 going to make it up. It's 4, just for the sake of
15 conversation. You had a 2-point improvement in your
16 total nasal symptom score.

17 Which symptom drove that and when? I think
18 that would be hard to say, depending on the study. So
19 if it's a pill, that's probably all placebo effect, and
20 it's individualized per patient. If it's a nasal spray,
21 there is effect. We have a nasal sinus rinse that we
22 give to people, because they get benefit. And you'll

1 typically see those patients in clinical studies improve
2 the first day.

3 So I think the answer depends on method of
4 delivery of the medication, I'm sorry, the placebo, and
5 it's a toss-up for the symptoms. It's a placebo effect.
6 It's very hard to characterize it, other than to say
7 it's a placebo effect.

8 MR. HOUSTON: Let's go off the record for just
9 a second.

10 (Off record 5:19 to 5:21 p.m.)

11 Q BY MR. HOUSTON: Dr. Carr, you have a section
12 in your declaration right at the very end, near the end,
13 page 67. Starting on page 67. You make reference to,
14 in the heading "F" that's on that page, you make
15 reference to several Indian copycat products. Do you
16 see that?

17 A Yes.

18 Q I'd like to ask you about your knowledge about
19 the pharmaceutical industry in India, if you have any.
20 Do you know how common it is or whether it's common for
21 products that get approved by the equivalent of the
22 Indian FDA, how common it is that copycat products then

1 come onto the market?

2 MR. LaROCK: Objection. Outside the scope of
3 his declaration.

4 THE WITNESS: My understanding is for
5 successful therapies, it's quite common for copycats to
6 be produced.

7 Q BY MR. HOUSTON: Once they've been approved by
8 the equivalent of the Indian FDA? Maybe I should ask it
9 this way. Is it the approval by the equivalent of the
10 Indian FDA that marks a successful product, designates a
11 product as successful in the statement you just gave?

12 MR. LaROCK: Object to the form of the
13 question. Outside the scope of his declaration.

14 THE WITNESS: Not in totality.

15 Q BY MR. HOUSTON: So when you say "my
16 understanding is for successful therapies," what makes
17 something a successful therapy in India?

18 A There's multiple things that go into these
19 products being successful. I would say having an
20 approved product and then it becomes rapidly, or at some
21 point adopted by the prescribers. And it is commonly
22 used for the indication. And there's a monetary aspect

1 of it. When the company that's the innovator is making
2 a profit, I think that would be another step that would
3 motivate somebody to try to copy that. So there's
4 multiple reasons. I don't believe if they approve
5 something, but within the marketplace it's a
6 catastrophic failure, nobody uses it, I don't believe
7 there would be the same degree of motivation to copy it.

8 Q For a product to be considered successful in
9 India and therefore susceptible to copycatting, is it
10 your opinion that that product would have to represent a
11 novel improvement over the prior art, a patentable
12 improvement over the prior art? Is that a prerequisite
13 to being successful?

14 MR. LaROCK: Object to the form of the
15 question. Outside the scope of his declaration.

16 THE WITNESS: I guess it depends on the disease
17 and the product.

18 Q BY MR. HOUSTON: So for some diseases or
19 products, it would be a prerequisite that it be novel,
20 but for others, it wouldn't an prerequisite?

21 MR. LaROCK: Objection. Form. Outside the
22 scope. Calls for a legal conclusion.

1 THE WITNESS: I don't believe that's what I
2 said.

3 Q BY MR. HOUSTON: Well, you said, "I guess it
4 depends on the disease and product." What do you mean
5 by that?

6 A What was the question to that answer?

7 Q For a product to be considered successful in
8 India and therefore susceptible to copycatting, is it
9 your opinion that that product would have to represent a
10 novel improvement over the prior art? A patentable
11 improvement over the prior art? Is that a prerequisite
12 to being successful?

13 MR. LaROCK: Object to the form of the
14 question. Outside the scope of his declaration, calls
15 for a legal conclusion.

16 THE WITNESS: Again, so the conclusion is here
17 is it patentable, and I'm not familiar with the patent
18 laws in India and all the nuances, perhaps. So it's
19 very difficult for me to answer that question. So I'm
20 going to answer based on my knowledge sitting here today
21 as an expert in allergic rhinitis for the case of this
22 deposition, and for this disease state, allergic

1 rhinitis. And in this case, there was a novel,
2 patentable invention that eventually became approved in
3 the U.S., Dymista, and in that case, it was novel and
4 patentable.

5 Q BY MR. HOUSTON: Well, that's what we're here
6 to dispute; correct?

7 A Well, they have a patent.

8 Q And we're here to dispute the validity of that
9 patent. You understand that; right? That's what this
10 dispute is all there?

11 A You asked me my opinion. I gave you my
12 opinion.

13 Q And I'm asking you a follow-up question. Do
14 you understand that this whole proceeding is focused on
15 whether or not that patent is valid?

16 A I understand.

17 Q If this proceeding were to result in the patent
18 being invalidated -- if this proceeding were to result
19 in the '620 patent being invalidated, would that lead to
20 more or less copycatting in India?

21 MR. LaROCK: Object to the form of the
22 question. Outside the scope of his declaration. Calls

1 for speculation.

2 THE WITNESS: Gosh, I don't know. I don't know
3 how India would respond.

4 MR. HOUSTON: Okay. No further questions.
5 I'll pass the witness.

6 MR. LaROCK: Okay. Let's take a break.

7 (Recess 5:29 to 5:40 p.m.)

8 / / /

9 EXAMINATION

10 BY MR. LaROCK:

11 Q Dr. Carr, I'd like to turn your attention to
12 paragraph 59 of your declaration. Are you there?

13 A Yes.

14 Q In particular, on page 25. Do you recall being
15 asked by Mr. Houston about how you came up with the .4
16 points that's referenced in paragraph 59?

17 A Yes, I do recall.

18 Q How did you come up with that number?

19 A If you look at the baseline total symptom
20 scores for nasal symptoms -- nasal symptoms -- it's 8.4,
21 for nasal. 8.4. There's a -- so to be fair, nasal
22 steroids really reach their maximum benefit, I think, at

1 about one week. And then they can get better and better
2 over time. But that's really researching the
3 separation.

4 So if you take that one-week time point, it's a
5 66 percent improvement, .66, times 8.4. Can I get my
6 calculator out?

7 Q Yes.

8 A So 8.4 times .66 is 5.544. And then if you
9 look at the nasal symptoms -- nasal symptoms for the BDP
10 only, it's 8.6. And you have a 59 percent improvement.
11 So 8.6 times .59 is 5.074. If you do 5.544 minus 5.074,
12 that gives you 0.47.

13 Q And that's how you arrived at the approximately
14 0.4 points that's referenced in paragraph 59?

15 A Yes.

16 MR. LaROCK: No further questions.

17 (Off record 5:44 to 5:48 p.m.)

18

19 FURTHER EXAMINATION

20 BY MR. HOUSTON:

21 Q Dr. Carr, with respect to the calculations you
22 just did, let's consider a scenario where the first

1 group had a beginning nasal symptom score of 10 and saw
2 an 80 percent improvement after treatment in group 1.
3 So the calculation you just did, you would multiply 10
4 by .8 and come up with 8. Correct? That would be the
5 analogous calculation to what you just did; correct?

6 A This is a hypothetical situation, and if you
7 can show me a drug that gives you an improvement of 10,
8 we need to get a patent on that sucker. Because that's
9 a very remarkable improvement, to get that big of an
10 improvement, or have that severe and have an 80 percent
11 improvement. That's really good. But this is
12 hypothesis generating. So that's a hypothetical
13 situation. I understand what you're doing, yes.

14 Q 80 percent improvement for group 1, so 10 times
15 .8 gives you 8.

16 Now let's consider group 2, that these are
17 really severe patients, and so they start at a total
18 nasal score of 12. And for the treatment group 2, they
19 saw a 66 percent improvement. 12 times 66 percent,
20 maybe it's better if I call it 67 percent, you again end
21 up at 8. Right?

22 A Based on your math, looking across the table,

1 that's what you have written down, yes.

2 Q And the difference between those two, 8 and 8,
3 would be zero.

4 A These are two totally unrelated hypothetical
5 scenarios, and it's not actual data.

6 Q No, but I'm trying to highlight what I think is
7 a fallacy in your calculation here, or your analysis
8 here.

9 If you had this situation, as you just said,
10 wow, you had a pretty amazing treatment here. But
11 according to you, because 8 and 8 come out identical and
12 there's no difference between them, suddenly that
13 renders it a clinically meaningless difference.

14 A No, that's not what I'm saying. You're
15 mischaracterizing me. You're comparing apples and
16 oranges. You're comparing two different populations.
17 One population has a 10, one population has a 12. Those
18 are two different populations. One population here is
19 14.9, essentially 15, and the other population -- or I'm
20 sorry, has 8.4 nasal, pardon me, 8.4, and the other one
21 has an 8.6. They're essentially at the same starting
22 point.

1 You're talking about patients that are starting
2 at different locations. That's totally a different
3 comparison. So you cannot use that analogy, no.

4 Q In the actual data here, they're not starting
5 at the same starting point. Right? One's at 8.4, one's
6 at 8.6. Correct?

7 A Very close to the same.

8 Q They're not the same starting points; right?

9 A I would have to look at the confidence
10 intervals, because that's a mean number.

11 Q The numbers you're using as the starting point
12 in your calculation are not the same. Right?

13 A This is a mean value. I would have to look at
14 the confidence intervals and see if the confidence
15 intervals are overlapping. I will tell you, if the
16 confidence intervals are not overlapping, that would be
17 another flaw to this study. They have to be basically
18 the same patient population that you're studying to make
19 a comparison. You can't compare people that have
20 headache from migraines to people that have headache
21 from blunt-force trauma to the head and make a
22 comparison. It's two different groups of people.

1 Q Okay. I disagree with you, but that's fine.

2 That's your testimony.

3 Let's try a different scenario. Let's say that
4 these two patient populations had mean -- had the nasal
5 symptom score of 8.5 identically. That's plausible,
6 isn't it? So if you're telling me I'm not really seeing
7 a difference between 8.4 and 8.6, let's make the numbers
8 the same. We'll call them both 8.5.

9 Now if we see a 66 percent reduction in one and
10 a 59 percent reduction in the other, the difference is
11 .6, isn't it?

12 A Well, I don't believe it's fair to artificially
13 manipulate data as you're trying to do. But based on my
14 calculation, I get a difference of 0.59. But that's an
15 unfair manipulation of data, and that would be seriously
16 frowned upon.

17 Q Well, it's just to illustrate the point of the
18 calculation. You appreciate that; right, Dr. Carr? And
19 the point being that the way you've calculated it, the
20 group that has the bigger percent change starts from a
21 lower nasal score, whereas the group that has the higher
22 nasal score and has the lower percent change tends to

1 make these numbers even out, because they don't start at
2 the same place. That's all I'm trying to illustrate.
3 I'm trying to use some examples to illustrate my point.

4 But you're not going to agree with any of that.
5 You're going to stick by your number of .4. Is that
6 right?

7 A I'm sticking with the facts and not artificial
8 manipulation of the data. This is the data reported by
9 the authors. Your question was to me how I got to it.
10 This is how I got to it. You're artificially
11 manipulating data, and you can't do that.

12 Q And I also asked you to confirm or agree with
13 me that 8.4 was different from 8.6, and you refused to
14 do that as well; right?

15 A I did not refuse. I said I need to see the
16 confidence intervals.

17 Q If we're just talking about absolute numbers,
18 8.4 and 8.6, are those numbers the names?

19 A This is not an absolute number. It's a mean.

20 Q Why did you round .47 down to .4?

21 A No particular reason. Ease of reading the
22 data.

1 MR. HOUSTON: No further questions.

2 MR. LaROCK: Not for me.

3 (Discussion off the record)

4 (Deposition Exhibit 1010 was marked
5 for identification.)

6 (At 5:56 p.m. the deposition of
7 WARNER WESTOVER CARR, M.D., was
8 concluded.)

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CERTIFICATE OF DEPONENT

I hereby certify that I have read the foregoing pages of my deposition testimony in this proceeding, and with the exception of changes and/or corrections, if any, find them to be a true and correct transcription thereof.

Deponent

Date

NOTARY PUBLIC

Subscribed and sworn to before me this

_____ day of _____, 20__.

Notary Republic

My Commission Expires:_____

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REPORTER'S CERTIFICATE

I, Lindsay Pinkham, CSR No. 3716, a Certified
Shorthand Reporter in and for the State of California,
do hereby certify:

That the witness named in the foregoing
deposition, prior to being examined, was by me first
duly sworn;

That said deposition was taken before me at the
time and place therein set forth and was taken down by
me in shorthand and thereafter transcribed into
typewriting under my direction and supervision;

That said deposition is a true record of the
testimony given by the witness and of all objections
made at the time of the examination;

I further certify that I am neither counsel for
nor related to any party to said action, nor in anywise
interested in the outcome thereof.

Before completion of the deposition, review of
the transcript [X] was [] was not requested.

Dated this 13th day of February, 2018.

Lindsay Pinkham, CSR 3716