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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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ARGENTUM PHARMACEUTICALS LLC

Petitioner

v.

CIPLA LTD.

Patent Owner

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Case IPR2017-0087

Patent 8,168,620

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DEPOSITION OF ROBERT P. SCHLEIMER, Ph.D.

March 30, 2018

Chicago, Illinois

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DIGITAL EVIDENCE GROUP

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1           The deposition of ROBERT P. SCHLEIMER, Ph.D.,  
2   called by the Patent Owner for examination, taken  
3   before Cynthia J. Conforti, CSR, RPR, CRR, at Foley  
4   & Lardner LLP, 321 North Clark Street, Suite 2800,  
5   Chicago, Illinois, commencing at the hour of  
6   9:08 a.m. on the 30th day of March, A.D., 2018.

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1 (Witness sworn.)

2 ROBERT P. SCHLEIMER, Ph.D.,  
3 having been duly sworn, was examined and testified  
4 as follows:

5 DIRECT EXAMINATION

6 BY MR. MILLER:

7 Q. All right, Dr. Schleimer. How are you  
8 doing this morning?

9 A. I am doing all right. How are you?

10 Q. All right. Great. We have had a couple  
11 depositions in related matters, related to the '620  
12 patent. You testified previously in Apotex  
13 litigation between Meta and Cipla against Apotex,  
14 correct?

15 A. Against Apotex?

16 Q. No, I'm sorry. The case was Meta and  
17 Cipla versus Apotex. You testified --

18 A. Yes, I testified in that case.

19 Q. -- on Apotex's behalf.

20 And now we're here. You're testifying on  
21 behalf of Argentum Pharmaceuticals?

22 A. That is correct.

1           Q.     And the '620 patent was involved in both  
2     litigations?

3           A.     Yes.

4           Q.     Okay. I want to start with Exhibit 1144,  
5     which is your second declaration in this IPR.

6           A.     Okay.

7           Q.     One of the things that you talk about here  
8     is the early and late phase, and your view is that  
9     those are relevant to clinical therapy, correct?

10          A.     Yeah, they're often relevant to clinical  
11     therapy. They're more relevant as a way to  
12     understand allergic reactions.

13          Q.     Okay. And so this is -- the phases are  
14     really the mechanism of the disease itself, part of  
15     the mechanism of the disease itself, and not really  
16     the symptom; is that right?

17          A.     Well, the phases are indicators of the  
18     underlying mechanisms, but the mechanisms are what  
19     drive the symptoms, so you can't unlink them.

20          Q.     Okay. Now, I'd like to flip to  
21     paragraph 54 in your declaration if we could. It's  
22     page 37.

1 A. Okay.

2 Q. You talk about Dr. Accetta's records here,  
3 correct?

4 A. Yes.

5 Q. Now, just to be clear, Dr. Accetta was a  
6 physician who testified in the Apotex litigation?

7 A. That's right.

8 Q. And he's a physician, correct?

9 A. Yes.

10 Q. You are not.

11 A. That's correct.

12 Q. So you do not treat patients?

13 A. Correct.

14 Q. Okay. Let me hand you -- this is  
15 Exhibit 1055.

16 MR. HOUSTON: And just to be clear, I think the  
17 original was in color, wasn't it? Or am I  
18 remembering that wrong?

19 MR. MILLER: Yes, it is in color.

20 MR. HOUSTON: I don't know that it matters,  
21 but...

22 MR. MILLER: Fair enough.



1 MR. HOUSTON: Okay.

2 BY MR. MILLER:

3 Q. And this was also used in Dr. Carr's  
4 deposition, which is why you see the exhibit at the  
5 top there. This is one of the exhibits that  
6 Dr. Accetta testified about in trial, correct,  
7 Dr. Schleimer?

8 A. I believe so.

9 Q. And you rely on this in paragraph 54.  
10 This is the prescription that you're talking about?

11 A. I believe that's correct.

12 Q. Okay. Now, to be clear, Dr. Carr is a  
13 clinician. He treats patients, right?

14 A. Yes.

15 Q. Dr. Accetta treats patients?

16 A. Yes.

17 Q. You do not.

18 A. Correct.

19 Q. So when you say that your interpretation  
20 of this -- and let's back up a second.

21 So you can't actually see the complete  
22 record that's buried under this callout, correct?

1 If you look, there's --

2 A. That's correct. It covers the writing  
3 underneath.

4 Q. Okay. Now, the underlying document there,  
5 the document you're referring to in 54, Dr. Carr and  
6 Dr. Accetta actually write these documents  
7 themselves, don't they?

8 A. Yes --

9 Q. And you don't.

10 A. -- usually.

11 That's correct. We've established I am not  
12 a physician.

13 Q. Okay. And I just wanted to clarify that  
14 you don't actually ever write these things?

15 A. Correct.

16 Q. So you wouldn't know what a doctor is  
17 thinking when he puts down, for example, under the  
18 general:

19 Patient's physical exam is normal.

20 A. Well, I can certainly have -- I can read  
21 the English language. I'm very familiar with  
22 medicine and the practice of medicine, and in my

1 recollection Dr. Carr had made a statement in his  
2 declaration or maybe it was his deposition, I don't  
3 remember, that he wouldn't treat a normal patient  
4 with these drugs, and in this case Dr. Accetta said  
5 the patient's physical examination is normal.

6 And my take of Dr. Carr's statements was  
7 that he was suggesting that the patient being normal  
8 doesn't have allergic disease, so that was what the  
9 issue was.

10 MR. MILLER: Okay. And just for the record,  
11 Mr. Marghese just joined us.

12 MR. MARGHESE: Good morning, Dr. Schleimer.

13 BY MR. MILLER:

14 Q. Okay. So we can put that aside for a  
15 moment.

16 I've handed you -- I'm going to hand you  
17 in just a moment an article by Stanley Galant, or is  
18 it Galant? I always mix this up.

19 A. Galant is the way I pronounce it, but it  
20 may be wrong.

21 Q. You're familiar with this?

22 A. I have seen it, yes.

1           Q.    Okay.  Flip in your declaration quickly to  
2   paragraph 7, returning to the early-late phase  
3   concept that we talked about a minute ago.

4           A.    Okay.

5           Q.    You see from the header this is the  
6   section of your declaration that discusses the early  
7   and late phase and how they're clinically relevant  
8   prior to 2002, correct?

9           A.    Yes.

10          Q.    All right.  So looking at paragraph 7  
11   here, you dispute Dr. Carr's view that the early and  
12   late phase are not relevant to clinical treatment of  
13   patients.  Is that essentially an accurate summary  
14   of what you wrote there?

15          A.    I believe that they are relevant to not  
16   only the understanding of allergic disease but also  
17   to the treatment of allergic disease.

18          Q.    Okay.  Now, the Galant reference I just  
19   handed you, Exhibit 1041, you see that, and that's  
20   cited in paragraph 7 of your declaration?

21          A.    Yes.

22          Q.    It's page 455.  Can you flip to page 455

1 for me? Take a moment.

2 I assume that the reference that you're  
3 citing here, the portion of this article that you're  
4 citing in paragraph 7 is Section 3, the pathogenesis  
5 section?

6 A. Well, that section certainly mentions the  
7 early and the late phase and the mediators and  
8 cellular responses that are involved in those two  
9 distinguishable phases, yes.

10 Q. Okay. Now, I just want to explore this  
11 document a little bit because you also talked a good  
12 deal about the context of an article in your  
13 declaration. If you look at Section 2 immediately  
14 preceding the section you just reviewed?

15 A. Reviewed. You mean Section 4?

16 Q. No. Go back to Section 2, the one  
17 immediately preceding, Evaluation and Diagnosis, so  
18 evaluation and diagnosis is what a physician does  
19 when he has a patient, correct?

20 A. Yes.

21 Q. All right. Go ahead and take a look at  
22 that and tell me if you see the word "phase"

1 anywhere.

2 A. I take it by the fact you're asking me that  
3 I won't find it. I skimmed it, I don't see it, but  
4 that doesn't mean that the symptoms or the  
5 manifestations of allergic disease are not mediated  
6 by the pathogenic events that are discussed fairly  
7 well in paragraph 3 or Section 3.

8 Q. But the concept in section 2 is  
9 essentially that when you're evaluating a patient  
10 with allergic rhinitis you look at their history.  
11 You look at their symptoms. Doesn't say anything  
12 about phase. Is that accurate?

13 A. I think it's context dependent. If a  
14 physician has a patient in front of them that  
15 reports that when they go visit a friend who has a  
16 cat and they start sneezing wildly, and then they go  
17 home and in the middle of the night they can't sleep  
18 because they're wheezing or they have complete  
19 blockage, the physician in that case will say, "Oh,  
20 well, that's classic early phase and late phase of  
21 an allergic response," so it's very case dependent.  
22 So I wouldn't agree with what you said. I think

1     that all well-trained allergists understand about  
2     phases and how they contribute to disease.

3           Q.     Okay. And that's a very helpful answer in  
4     terms of understanding, but I just want to be clear  
5     that the evaluation and diagnosis section does not  
6     say anything about phase.

7           A.     This paragraph that you directed me to does  
8     not say anything about phase, but that does not  
9     embrace the totality of evaluation and diagnosis of  
10    allergic disease.

11          Q.     Okay. Now, you mentioned Section 4.  
12    Title is "Treating AR in the Child," correct?

13          A.     I see that, yes.

14          Q.     All right. And that's the one after the  
15    section that you talked about, pathogenesis, in your  
16    paragraph 7?

17          A.     Yes.

18          Q.     I'll represent to you, because this is far  
19    too long to ask you to read, but the only place that  
20    the word "phase" appears in the treatment section is  
21    on page 456 of the article that's stamped 04. You  
22    see "Histamine H1 Receptor Antagonists"?

1           A.    I see that section, yes.

2           Q.    So you'll see -- the easiest way to find  
3   it is "in vivo," there's an "in vivo" in italics.  
4   The sentence after that, can you read that for the  
5   record?

6           A.    The sentence after?

7           Q.    "In vivo, the second generation  
8   antihistamine"?

9           A.    I'm sorry, I still don't know where  
10   you're --

11          Q.    All right. Towards the bottom under the  
12   header 4.1.

13          A.    Okay.

14          Q.    Towards the bottom of the left column  
15   there's a sentence that begins: The  
16   second-generation antihistamine?

17          A.    "The second-generation antihistamine  
18   cetirizine," that one --

19          Q.    Yes.

20          A.    -- that sentence?

21          Q.    Yes, please.

22          A.    -- "inhibits LTC4 and D4 production in



1 nasal secretions and inhibits recruitment of  
2 eosinophils in the cutaneous late-phase model."

3 Q. So I'll represent to you, because I've  
4 read this and searched a couple times, that's the  
5 only place that "phase" appears in the treatment.

6 And I want to be clear about what that is  
7 talking about. Cutaneous models are actually skin  
8 tests, correct?

9 A. Yes.

10 Q. So that's not allergic rhinitis.

11 A. No, but it's a way that an allergist  
12 determines whether a patient is allergic to what's  
13 called an arrow allergen, which is an inhaled  
14 allergen. If you have allergic responses in your  
15 skin, you will also have the same allergic responses  
16 in your nose, so for convenience, since it's very  
17 difficult to test the nose, allergists will test the  
18 skin. If you respond to birch pollen in your skin,  
19 then it informs the allergist that you also will  
20 respond to birch pollen in your nose.

21 Q. Okay. But, again, if you'll accept my  
22 representation that the reference to "late phase" in

1     that sentence you just read is the only one, I want  
2     to talk about a couple of the other --

3           A.     Well, but hang on. You said it's the only  
4     one in diagnosis of disease.

5           Q.     This is treatment.

6           A.     In treatment. You said "diagnosis and  
7     treatment."

8                     And the fact is that this is not some huge  
9     document that describes the totality of diagnosis  
10    and treatment. This is a review that a couple of  
11    guys wrote in a second- or third-string journal and  
12    gave their impression of an overview of a few  
13    topics. So, you know, I think if you look  
14    throughout the documents that are under discussion  
15    in this case, of which there are dozens, a very  
16    large number of them mention the phases, and the  
17    phase is irrelevant not only in pathogenesis, but  
18    irrelevant in symptoms, manifestation of disease,  
19    and sometimes in diagnosis of disease.

20          Q.     Okay. But to be clear, this -- you've  
21    actually cited this article --

22          A.     Yes.

1 Q. -- that's in paragraph 7, correct?

2 A. Yes. The reason that I cited it is because  
3 it has a nice little description of the differences  
4 between the early phase and the late phase, and  
5 those differences bear direct relevance to the  
6 actions of drugs with the antihistamines being very  
7 effective against the early phase, which is a  
8 antihistamine-driven response to great extent, and  
9 the steroids being very effective against the late  
10 phase which is mediated by infiltration of  
11 inflammatory cells and the subsequent release of  
12 mediators by those cells. So that goes straight to  
13 the complementarity argument. It was very well  
14 known before the priority date by people in the  
15 field that the steroids targeted that cellular  
16 inflammation and the release of mediators  
17 secondarily in the late phase, and the  
18 antihistamines were very good at working quickly  
19 against the immediate response to antigen, which is  
20 largely mast cells releasing histamine; so the skin  
21 tests that you were talking about can be blocked  
22 nearly completely with antihistamines. In fact, if

1 a patient has taken oral antihistamines, an  
2 allergist won't even bother to skin test them  
3 because they will have no skin test response.

4 So on the other hand, you can take huge  
5 doses of oral steroids, and it will not inhibit that  
6 immediate skin test response one iota. So that's a  
7 perfect example of what an allergist would know,  
8 which is that antihistamines target the immediate  
9 response, including the skin test, and steroids  
10 inhibit the late-phase response.

11 Q. Now, going back to the sentence you read  
12 in 4.1, that says that an antihistamine works in the  
13 late-phase model; is that right?

14 A. Yes. So as I've mentioned in several of  
15 the documents during this case, there was the  
16 realization that some antihistamines, not all  
17 antihistamines, have some anti-inflammatory effects,  
18 and that includes the things mentioned here and many  
19 other things that are actually summarized in several  
20 of the documents. For example, Berger also  
21 summarizes them. It's less well established whether  
22 the various antihistamines have those profound

1 anti-inflammatory effects in vivo, but there is  
2 reason to believe that topical antihistamines, which  
3 includes azelastine and levocabastine, can exert  
4 some of those particularly well because they can be  
5 given topically to create high concentrations in the  
6 nose. Much of the literature that serves as the  
7 basis for this concept is in vitro, and in vitro a  
8 scientist has no limitation on the amount of drug  
9 they can put in, so very large amounts of drug can  
10 inhibit responses that are known to be important.  
11 But if those concentrations can't be reached in vivo  
12 with either oral or local administration of a drug,  
13 then it's only theoretical but not actual useful  
14 information.

15 Q. Okay. Thank you, Doctor.

16 Next we are going to look at -- if you  
17 flip back to paragraph 7, the next article that you  
18 cite in that string there is Exhibit 1041, which I'm  
19 going to hand you in just a moment.

20 A. Oh, we're still with 1041?

21 Q. Oh, sorry. Did I say 1041? I meant 1035.

22 MR. MILLER: Mike. Ma'am.

1 BY MR. MILLER:

2 Q. All right. So 1035 here, this is a Drouin  
3 article which you're familiar with, I assume?

4 A. Yes.

5 Q. And that's the article cited in  
6 paragraph 7, second paragraph cited in paragraph 7;  
7 is that right?

8 A. Okay.

9 Q. You cite page 341, which is the second  
10 page, first after the cover?

11 A. Uh-huh, yes.

12 Q. Now, looking at this, I'm assuming, take a  
13 moment to read through, but you're probably  
14 referring in paragraph 7 to this third paragraph,  
15 the nasal response to allergen?

16 A. Yes. The third paragraph would be part of  
17 that, I believe.

18 Q. Okay. Read the next paragraph. Begins  
19 "topical steroids" quickly for me, please.

20 A. Topical steroids.

21 Q. Oh, no, you don't have to read it on the  
22 record, sir. Just take a look at it. I'm going to

1 ask you a couple questions.

2 A. Sorry.

3 Q. That's okay.

4 A. Okay.

5 Q. So here, again, we see kind of a dichotomy  
6 where you talk about the phases, they are there, but  
7 the next paragraph is actually talking about how to  
8 treat patients, what symptoms they have and what  
9 drugs to use to treat them.

10 A. Yes.

11 Q. So, again, when actually talking about  
12 treating patients, the word "phase" did not appear  
13 in the paragraph, correct?

14 A. It did not appear in the paragraph, but we  
15 know a lot about the mediators that cause the  
16 various symptoms.

17 For instance, we know very well that  
18 histamine, when released quickly, causes sneezing  
19 and that -- for example.

20 So the underlying allergic response is  
21 complex. It involves not only the immediate  
22 response of mast cells, but then many different cell

1 types come into the tissue, and they each start  
2 singing in a chorus, and that results in symptoms.  
3 And what Drouin is saying is that the congestion  
4 seems to be related to that later response, the  
5 late-phase response with all of those cells coming  
6 in, and steroids are very good at inhibiting that.  
7 The early response is like itching and sneezing  
8 which happen right away. The steroids don't inhibit  
9 those well, at least not quickly, and we know those  
10 to be mediated by histamine because we can  
11 administer a histamine to the nose of even a normal  
12 healthy person, and they'll start sneezing  
13 immediately, and we know that the antihistamines  
14 will block that very well.

15 Q. Okay. If you'll flip to page 344. It's  
16 been stamped at page 5.

17 A. Okay.

18 Q. The table of the actual data that they  
19 were looking at.

20 A. Yes.

21 Q. Does the word "phase" appear anywhere in  
22 there?



1           A.     It does not.

2           Q.     Again, they're looking at symptoms,  
3     correct?

4           A.     It might be helpful if I explain that the  
5     phases originally come out of experimental allergic  
6     reaction studies, so these are studies where someone  
7     with allergy, again, let's say to birch pollen, is  
8     brought into the clinic, and let's say outside of  
9     the birch pollen season, so they have no symptoms.  
10    And then birch pollen is put into their nose to give  
11    them an allergic response, very similar to what  
12    happens if they go outside when the birch trees are  
13    pollenating during the season. And what happens in  
14    that setting, and this has been known for almost a  
15    century, and everyone knows it who studies allergy,  
16    what happens is they have an immediate response or  
17    an early-phase response, and that involves all the  
18    things that we've discussed like itching and  
19    sneezing, some runny nose, and then after 4 to  
20    8 hours, 10 hours and maybe lasting for a day or  
21    two, there's a late response, which may include a  
22    second wave of sneezing but also congestion and

1 other things. So that's how -- and then further  
2 studies have shown what I said before and what  
3 Galant says which is that inflammatory cells come  
4 into the tissue and drive that late phase.

5           So in the clinical setting, in clinical  
6 trials, it depends on the nature of the trial. If  
7 it's a trial that's using normal seasonal exposure  
8 to allergens, and the seasonal exposure lasts for  
9 weeks or months, as is true with these, then the  
10 phases -- the phases are not coming to play in that  
11 situation.

12           If, on the other hand, there are many  
13 studies, none in this case where antigen challenge  
14 is administered and you can study the action of  
15 drugs, in those cases the phases are very much in  
16 play, and in our first meeting in this case we  
17 talked a little bit about antigen challenges but not  
18 in the second declaration.

19           So this is a study where they looked at  
20 symptoms over a week or so, collecting data  
21 critically on Day 3 and Day 7, which is the early,  
22 early part of the treatment response, where I

1 maintain that these two drugs were known to be  
2 highly complementary, but it's not an  
3 antigen-challenge study, so there's no need to  
4 mention the phases. That doesn't mean that the  
5 components of the phases are not driving these  
6 symptoms. Allergists will know that they are.

7 Q. You can put that off to the side, Doctor.

8 A. Sure. I'm sure we'll get back to it.

9 Q. At some point we probably will.

10 I've asked you this before, but just for  
11 the sake of this deposition, you're not a  
12 formulator?

13 A. That is not my job, correct. I am not a  
14 formulator, professional formulator. I've done it  
15 on occasion, but that's not my job.

16 Q. You say you've done it on occasion. Can  
17 you give me a couple examples?

18 A. Well, we did some studies with a drug  
19 decades ago that we administered to people, a simple  
20 formulation.

21 Q. What's the simple formulation?

22 A. It was just saline that was adjusted for

1     pH.

2           Q.     So you're not involved in the selection of  
3     excipients or, for example, particle size or  
4     anything like that?

5           A.     That's correct. I may not -- I have a  
6     minimal working knowledge of it. I understand many  
7     of the concepts and certainly in the court case  
8     heard Maureen Donovan, who is world class, discuss  
9     the issues not only in this case but generally in  
10    formulation for intranasal drugs.

11          Q.     If you'll flip to paragraph 5. It's the  
12    second page of declaration, second declaration,  
13    there's Footnote 1 down there. You see that?

14          A.     Yes, I see that.

15          Q.     Now, here you're responding to Dr. Carr  
16    mentioned in his declaration that you had not said  
17    anything about Claims 4 and 42 through 44.

18          A.     Yes.

19          Q.     And this is your response to his statement  
20    there, correct?

21          A.     Yes.

22          Q.     Now, I wanted to explore this a little

1 bit. The last sentence there, you say:

2 To be clear, I consider the combination of  
3 azelastine and fluticasone in a formulation suitable  
4 for nasal administration to be obvious for Claims 4  
5 and 42 through 44 for the same reasons as all the  
6 claims discussed herein.

7 The "herein," are you referring to this  
8 declaration or is it both -- what do you mean with  
9 "herein"?

10 A. This declaration.

11 Q. Just this declaration? Does this  
12 declaration -- let me simplify this a little bit.  
13 I'll hand you the '620 patent first. That's  
14 Exhibit 1001, '620 patent. That's what this case is  
15 about, correct?

16 A. Yes, I have certainly seen it.

17 Q. If you flip back, you know where the  
18 claims are at the rear of the document. Claim 4 is  
19 in Column 11. It's page 13 as it's been stamped.

20 A. Yes.

21 Q. See Claim 4? The pharmaceutical  
22 formulation of Claim 1, wherein the said formulation

1 has a particle size of less than 10 micrometers,  
2 correct?

3 A. Yes.

4 Q. Now, you just said that you have not  
5 been -- you don't have any experience or expertise  
6 in selecting particle size, correct?

7 A. Well, as I said, I'm aware of issues that  
8 particle size influences. These issues vary  
9 depending on the context, for instance, with inhaled  
10 drugs versus intranasal drugs. I am not a  
11 formulator, and that is correct. We have  
12 established that.

13 Q. In fact, the phrase "particle size"  
14 doesn't appear anywhere in your second declaration,  
15 does it?

16 A. Not that I can recall.

17 Q. Okay. If you'll move to Claim 42 which is  
18 Column 14, the next page over. Actually, we can  
19 group these up, 42, 43 and 44, if you'll take a  
20 quick look at them, by my reading they're the same  
21 list of excipients. They just vary in which  
22 independent claim they depend from?

1           A.     Okay.  I'll accept what you say about that.

2           Q.     I think that's accurate.

3           A.     Yeah, I trust you.

4           Q.     So you don't say anything in your  
5     declaration about edetate disodium, correct?

6           A.     That's correct.

7           Q.     You don't say anything about glycerin?

8           A.     I don't, but I'm familiar with these  
9     compounds.

10          Q.     You don't say anything about thickening  
11     agent comprising microcrystalline cellulose and  
12     sodium carboxymethylcellulose?

13          A.     I've not been asked to opine about  
14     formulation or excipients.  That has been left to  
15     Dr. Donovan, but I could tell you the purpose of  
16     these compounds if you care about my opinion, but  
17     that's not been my mandate.

18          Q.     So I'll just group the rest of them  
19     together.  Polysorbate 80, benzalkonium, chloride,  
20     phenylethyl alcohol, those don't appear in your  
21     second declaration?

22          A.     That's correct.

1           Q.    And I'm excluding water because you do  
2    mention water a couple times, so...

3           A.    I might have challenged you if you said  
4    that wasn't there.  You'd have to do a word search.

5           Q.    It's somewhere in there.

6                    But just to be clear then, you didn't talk  
7    about any of those limitations at all in your first  
8    or second declarations?

9           A.    I did not.

10          Q.    Okay.

11          A.    Well, the first declaration I'm not sure, I  
12    haven't studied as carefully for this deposition  
13    assuming we were going to focus on the second.

14          Q.    Okay.  Now, just remind me.

15                   You said that Footnote 1 is only talking  
16    about your second declaration.  You're not referring  
17    back to the first, correct?

18          A.    Yeah.

19          Q.    Okay.  Okay.  Then we can move on from  
20    that.

21                   I'm going to hand you these two at the  
22    same time.  This first document which has been



1 marked Exhibit 1011 is what we refer to I think as  
2 the Cramer reference, and the second exhibit I'm  
3 handing you is Exhibit 1012, which we have been  
4 referring to as Segal.

5           These are the two documents that we've  
6 been, in this litigation and in others, referring to  
7 as Cramer and Segal, correct?

8           A.    Yes.

9           Q.    All right. Now, before we get to these  
10 documents, you're familiar with Dymista®, the drug  
11 product Dymista®?

12          A.    I'm certainly aware of it.

13          Q.    And it's Effexor's combination of  
14 azelastine and fluticasone for treatment of allergic  
15 rhinitis, right?

16          A.    Yes.

17          Q.    Are you aware that it's a commercial  
18 embodiment of the claims in the '620 patent?

19          A.    I'm aware that the '620 patent, which is  
20 what this whole proceeding is about, is the  
21 underlying intellectual property document that  
22 supports Dymista®.

1 Q. Okay. Are you aware that some physicians  
2 prescribe Dymista® to their patients with allergic  
3 rhinitis?

4 A. Yes, it is prescribed by some physicians in  
5 some situations.

6 Q. Okay. And patients use it to your  
7 knowledge --

8 A. I don't know what the sales numbers are,  
9 but I know that they're selling it and it's being  
10 used.

11 Q. Okay. And so by definition if people are  
12 using it, Dymista® is actually an operable  
13 formulation, a functional formulation?

14 MR. HOUSTON: Objection, form.

15 BY MR. MILLER:

16 Q. I'll withdraw that. We can come back to  
17 it in a little bit. If you flip to paragraph 11 of  
18 your declaration.

19 A. Okay.

20 Q. Take a look at it, read through it real  
21 quickly, and I'll ask you a couple questions about  
22 it.

1           A.     Okay.

2           Q.     Okay.  So here you're essentially pointing  
3     out that Dr. Carr hasn't really disputed the  
4     disclosure of Segal or Cramer, correct?

5           A.     I don't believe he discussed them either  
6     way, yes.

7           Q.     Okay.  And to be clear here, towards the  
8     middle of your paragraph, actually the last sentence  
9     at the bottom of page 5, Cramer contains the same  
10    disclosures, meaning Cramer and Segal have the same  
11    teachings as far as what drugs to apply, et cetera?

12          A.     Well, Cramer and Segal are slightly  
13    different, but if you consider that both of them  
14    mention fluticasone among steroids, and both of them  
15    mention azelastine among alternatives as a second  
16    additional drug, then both of them describe -- among  
17    a different number of combinatorial combinations  
18    both of them describe the combination that dispute  
19    in this.

20          Q.     Okay.  Now, you say they're slightly  
21    different.  I assume the difference you're referring  
22    to is the fact that Segal actually has a lot more

1 drug options than Cramer. Is that what you mean?

2 A. That's one difference.

3 Q. What are the other ones?

4 A. Well, I mean, we could do a word compare.

5 Q. Generally speaking, what differences do  
6 you think are relevant?

7 A. Actually, I think that they're more similar  
8 than they're different. I think that both of them  
9 had the clear intent to build a foundational drug  
10 that is a combination based on glucocorticoids as  
11 the foundation and a second drug that will act  
12 quickly, again, getting back to the phases,  
13 glucocorticoids work against the late phase but they  
14 take time to work. They take days or even a week or  
15 two, whereas antihistamines work immediately, and a  
16 POSA at that time, including Cramer and Segal and  
17 Spector and Berger, and many of the other authors  
18 that we've discussed, realize that it would be  
19 beneficial to combine a rapidly acting drug that  
20 would give instantaneous relief with the superior  
21 drug, which is the intranasal steroid. By that time  
22 it becomes very clear that intranasal steroids are

1 by far the most effective drug for treating allergic  
2 rhinitis.

3           You just have to look at Nielsen which  
4 compares the two main drugs. I think close to 90  
5 percent of the market at that time and maybe today  
6 was intranasal steroids and antihistamines, and they  
7 did -- they summarized it very nicely in Nielsen,  
8 summary of all the studies comparing antihistamines  
9 to steroids, intranasal steroids, and I think in  
10 every occasion either they were not discernible in  
11 terms of superiority or the steroid was better, and  
12 in almost all cases the steroid was better. So it  
13 was well known in the '90s that intranasal steroids  
14 are the best drugs that we have. And so what a POSA  
15 would want to do at that time and what both Segal  
16 and Cramer were proposing was to build on that  
17 knowledge and add a rapidly acting drug that would  
18 in one formulation make for a combination that both  
19 worked quickly and was superior, and that was the  
20 goal.

21           Q. Understood. All right. Now, start with  
22 Segal, which is 1012.

1           You suggest, I think, that this article or  
2   this patent application, the objective was to  
3   capture the benefits of the steroid and find  
4   something that would accelerate it or, you know,  
5   contribute to its efficacy. And I want to explore  
6   that because Segal is, as we mentioned a moment ago,  
7   rather broad. Now, if you could flip to page 3 on  
8   the top, 5 on the bottom, these extra stamps make it  
9   a little bit of a hassle.

10          A.   Strangely I understand you perfectly well.

11          Q.   The first full paragraph, "The  
12   compositions of the invention," et cetera?

13          A.   Yes.

14          Q.   The second sentence there, if you could  
15   read that, "The additional therapeutic agent"?

16          A.   Okay.

17          Q.   Okay. So the additional therapeutic  
18   agents listed are vasoconstrictors -- I think this  
19   is supposed to be flipped because it's supposed to  
20   be neuraminidase. I think you corrected it at some  
21   point.

22          A.   Yes.

1           Q.    Neuraminidase inhibitors, leukotriene  
2   inhibitors, anticholinergic agents, antihistamines,  
3   antiallergic agents, local anesthetics and mucolytic  
4   agents, correct?

5           A.    Yeah.

6           Q.    All right.  What does a vasoconstrictor  
7   treat?

8           A.    Well, so vasoconstrictors cause the blood  
9   vessels to constrict, and by doing so they diminish  
10  the amount of blood and therefore plasma and the  
11  fluids contained into the tissue.

12                   One of the sources or probably the main  
13  source of secretions is from the blood.  So what  
14  a -- by constricting a blood vessel, a  
15  vasoconstrictor will diminish the immediate  
16  secretory response, the running of the nose.  Of  
17  course the problem is, and most of these other drugs  
18  have an issue, and actually Spector goes very well  
19  through these classes and describes the limitations  
20  of all of them, but one of the problems is that the  
21  vasoconstrictor won't diminish the other symptom  
22  categories, and the other immediate responses, like

1 other responses to histamine, for instance,  
2 sneezing, so -- but yes, vasoconstrictor constricts  
3 vessels and diminishes secretions as just a single  
4 symptom that it targets.

5 Q. See, actually, I was going to ask you  
6 about the other ones, but you touched on it with  
7 your discussion of Spector. If you move down to the  
8 next paragraph, "Vasoconstrictors suitable," I'm not  
9 going to ask you to read that, but there's a long  
10 list of specific drugs included in there, right?

11 A. Yeah. I've noticed with patents, including  
12 the first Lulla and Malhotra patent by the way, that  
13 applicants try to put their arms around as much as  
14 they can. But yes, it's true that that was done  
15 here too.

16 Q. All right. Now, at a high level is there  
17 any clinical data in this document?

18 A. Clinical data?

19 Q. Yes.

20 A. I don't know what you mean by "at a high  
21 level," but I don't see any clinical studies with  
22 results, so just some discussion about symptoms



1     which are all clinical phenomena.  So at a high  
2     level there's clinical discussion, but I don't see  
3     any data, clinical data.

4           Q.     Let's swing over to Cramer.

5           A.     Okay.

6           Q.     Which is 1011.  Oh, one last question on  
7     that.  Back to Segal real fast.

8           A.     No problem.

9           Q.     If you look at the top right of the first  
10    page.

11          A.     Okay.

12          Q.     What's the publication date on this  
13    document?

14          A.     November 5th, 1998.

15          Q.     All right.  If you look over to the left,  
16    few lines under "PCT filing date," do you see that?

17          A.     I see priority date.

18          Q.     Right above that.

19          A.     Oh, "filing date, April 2, 1998."

20          Q.     Okay.  That was all I wanted on that one,  
21    so let's swing back to Cramer again.  Apologize for  
22    the shuffling.

1           A.    No problem.

2           Q.    I'm going to warn you that this has  
3   European dating, so I'm going to ask you those same  
4   questions again.  "Date of publication" you'll see  
5   on the left just below that symbol?

6           A.    Yeah, June 25th, 1997.

7           Q.    All right.  And then the date of filing a  
8   couple lines down?

9           A.    December 5th, 1996.

10          Q.    Okay.  Same question as with Segal.  Does  
11   this document contain any clinical data?

12          A.    Again, it talks about clinical symptoms,  
13   treating clinical disease.  It's targeting clinical  
14   problems but I don't see any original clinical data  
15   that were generated by studies unique to this  
16   document.

17          Q.    Okay.  And it's your view that these two  
18   documents are the closest prior art in terms of  
19   objective indicia of nonobviousness, correct?

20          A.    No, that's not correct.  It's -- to me as a  
21   layperson, nonpatent attorney, the most clear prior  
22   art is the fact that doctors and patients were using

1 conjunctive therapy with Flonase and Astelin for  
2 several years before the priority date. It was  
3 already being practiced, so the art was in use by  
4 patients and doctors. And I'm sure we'll talk about  
5 that later, but I understand that to attorneys this  
6 is -- a written document like this is solid evidence  
7 of prior art, so I believe this is also evidence of  
8 prior art, the fact that there was already  
9 disclosure of the invention many years before the  
10 Lulla and Malhotra patent.

11 Q. Can you flip to paragraph 53 of your  
12 report?

13 A. Okay.

14 Q. There you say that Cramer and Segal are  
15 the closest prior art for unexpected results?

16 A. Yes, and this document was a collaborative  
17 effort, and I was convinced that from a legal  
18 perspective that Segal and Cramer are perhaps more  
19 persuasive to a patent board than my view, my lay  
20 view of the prior art, of the fact that this art was  
21 being practiced for many years. It doesn't change  
22 my opinion.

1 Q. Right.

2 A. That my view is correct.

3 Q. Okay.

4 A. So the clinical art was already in  
5 practice, but I guess in the legal proceedings these  
6 documents, which I also fully agree are disclosures  
7 of the invention, if you want to call that, call it  
8 that, is also evidence of prior art.

9 Q. Now, you've gotten close, but the key here  
10 is not prior art. The word is "closest prior art  
11 that has legal meaning." You said that in  
12 paragraph 53.

13 A. Yes.

14 Q. Do you agree that Cramer and Segal are the  
15 closest prior art or are you changing your view now?

16 A. I acceded to that statement because of the  
17 legal explanations that I just described.

18 MR. MILLER: We have been going about an hour.  
19 Do you guys want to take a 5-, 10-minute break?

20 THE WITNESS: That works for me.

21 (Recess taken.)

22 BY MR. MILLER:

1           Q.    All right.  We were just talking about  
2   Cramer and Segal before the break.

3           A.    Yes.

4           Q.    And you said that these were the closest  
5   prior art.

6                   Now, in paragraph 53, we were talking  
7   about paragraph 53 of your declaration.  Continuing  
8   on through that section which is entitled "Dymista®"  
9   shows no unexpected results compared to the closest  
10  prior art.

11                   Down in paragraph 55 you point out that  
12  Dr. Carr avoids all mention of Segal and Cramer in  
13  his discussion of Dymista's® alleged unexpected  
14  efficacy results.  Do you see that?

15           A.    I saw that, but I don't know where --

16           Q.    Paragraph 55?

17           A.    Oh, 55.  Yes.

18           Q.    So this is why we were talking about the  
19  closest prior art question.  Your view is that  
20  Dr. Carr should have compared Dymista® to the  
21  formulations of Cramer and Segal; is that right?

22           A.    No, no.  It's just a statement that he

1     never discusses Segal and Cramer, and that seems to  
2     be ignoring important prior art.

3           Q.     Well, again, in paragraph 53 you said this  
4     is the closest prior art.

5           A.     Yes.

6           Q.     Your view is -- you're stating in  
7     paragraph 55 that Dr. Carr should have compared  
8     Dymista® to Segal and Cramer, the closest prior art;  
9     is that right?

10          A.     Well, no.  It's what I just told you.  He  
11     never mentioned Segal and Cramer -- Dr. Carr's  
12     document, just like this document, is an  
13     amalgamation of scientific, medical and legal  
14     points.  And his document never mentioned those two,  
15     which to me are clear examples that the cat was out  
16     of the bag in the '90s, that this idea was already  
17     very clearly expressed, whether it be in the patent  
18     literature, in the clinic where it was already  
19     practiced or in the medical literature; it was  
20     already discussed.

21          Q.     Okay.  I'm going to hand you what's been  
22     marked as CIP2147.

1           A.     Okay.

2           Q.     Now, recalling our discussion a few  
3 minutes ago about Segal and Cramer, the large -- the  
4 main distinction between the two is that Segal has a  
5 much broader distinction, less specific, correct?

6           A.     That's one, but there's another very  
7 important difference. It's not only that Cramer  
8 limits the second drug possibilities much more, but  
9 may I look at Cramer?

10          Q.     Please do.

11          A.     But Cramer also makes a very important  
12 description of the second drug. I can never find  
13 the names of patentholders on these. They're always  
14 hidden. I think this is Cramer.

15          MR. HOUSTON: It's 1011, Exhibit 1011.

16          THE WITNESS: All right. So Cramer somewhere  
17 talks about a leukotriene-inhibiting antihistamine,  
18 I believe, yeah.

19          BY MR. MILLER:

20          Q.     Where are you looking?

21          A.     Well, there's a section on that. Essential  
22 ingredients are glucocorticoid and a

1 leukotriene-inhibiting antihistamine, so this is  
2 explicit acknowledgment of what I said earlier,  
3 which is that the field had recognized that  
4 antihistamines are not just antihistamines. They  
5 don't just block histamine through the H1 receptor,  
6 although that's probably the most important thing  
7 they do. Some antihistamines, and not all, have  
8 anti-inflammatory effects that are not mediated by  
9 blocking the H1 histamine receptor, and one of those  
10 many effects, and as I mentioned they were outlined  
11 as you pointed out in Galant, a few of them, and  
12 Berger outlines them in others, is blocking the  
13 production of leukotrienes. So leukotrienes are  
14 different from antihistamines. Blocking the H1  
15 receptor won't prevent leukotrienes from causing  
16 inflammation. So they specifically wanted to take a  
17 steroid, which is their anti-inflammatory drug  
18 foundation, and add not only an antihistamine that  
19 will quickly block symptoms driven by histamine, but  
20 also that had some other anti-inflammatory effects,  
21 for instance, inhibiting leukotriene.

22 So Cramer is different from Segal in at



1     least a couple different ways, that the secondary  
2     drug is limited to antihistamines, and, in  
3     particular, those that have topical  
4     anti-inflammatory effects. And, by the way, at the  
5     time there were only two, which are azelastine and  
6     levocabastine, that were already being applied for  
7     that reason.

8           Q.     Okay. So the short of that is Cramer is  
9     more specific to our case than Segal. Is that an  
10    accurate summary of that answer?

11          A.     I think they both describe the invention  
12    within the context of a few other alternatives.  
13    Cramer has a smaller number but also explicitly  
14    states that the antihistamine should be one that has  
15    antileukotriene effects, which narrows the field  
16    dramatically.

17          Q.     Okay. Now at some point in this IPR you  
18    looked at the prosecution history of the '620  
19    patent. Is that accurate?

20          A.     I looked at the prosecution histories  
21    during the court case, the Apotex court case, which  
22    was a year and a half ago.

1           Q.    Right. Look at this way: Are you aware  
2   that formulations -- that people made an effort to  
3   formulate what's disclosed in Cramer?

4           A.    During the Apotex trial there was some  
5   discussion about that, and I was very unimpressed by  
6   the feeble efforts that were made. They almost  
7   seemed to be perfunctory. There were two or three  
8   notebook entries, as I recall, and I don't know  
9   whose -- I don't remember whose notebook it was  
10   where they made these feeble attempts and then threw  
11   up their hands and stopped.

12          Q.    Let me refresh your memory on that. That  
13   was Meta actually trying to make something  
14   different. I'm talking about somebody actually  
15   trying to make the formulations disclosed in Cramer.  
16   Are you aware of anybody trying to do that?

17          A.    I know that somewhere along the line during  
18   the trial they made an attempt for one -- one of the  
19   formulations that were discussed, and that was a  
20   point of discussion. But in that trial, as in this  
21   trial, I was not asked to opine about formulations  
22   and it was outside of my mandate, and so I didn't

1     apply a lot of my efforts to that -- to the details  
2     of that.

3           Q.     Okay.  Now, I've handed you Dr. Carr's  
4     second declaration.

5           A.     Yes.

6           Q.     Flip to page 11.  It's easier than  
7     paragraph.

8           A.     Okay.

9           Q.     You reviewed the entirety of Dr. Carr's  
10    second declaration; is that accurate?

11          A.     I went through it once, when it was first  
12    provided to me a while back.

13          Q.     Okay.  If you read through, this is a  
14    section entitled "Claim Construction."  See that?

15          A.     Yes, um-hmm.

16          Q.     Now, looking down at paragraph 27,  
17    Dr. Carr says:

18                   My interpretation of these claims, et  
19    cetera, et cetera.

20                   You'll see several references to Cramer  
21    Example III, right?

22          A.     I see it mentioned.

1           Q.    You maybe want to have both of them opened  
2           at the same time.  You can see Example III in  
3           Cramer, which is -- yes, it's on page 6.  And just  
4           -- we may as well go through all three real quick.

5                    If you flip back to page 5, you'll see a  
6           beclomethasone loratadine formulation.

7           A.    Okay.  Right.

8           Q.    Neither of those is claimed in any of the  
9           claims in the '620 patent, correct?

10          A.    In the final embodiment?

11          Q.    In the claims, yes.

12          A.    Correct.

13          Q.    All right.  Now, flip to Example II.  
14          That's flunisolide as a steroid and cetirizine  
15          antihistamine, correct?

16          A.    Um-hmm.

17          Q.    Neither of those is claimed in the '620  
18          patent?

19          A.    You mean Example II is not claimed.

20          Q.    Either of the drugs claimed described --

21          A.    Oh, neither of those drugs.  That's  
22          correct.  Although, as I said, the first embodiment

1 of that patent had all of the steroids.

2 Q. Right, understood.

3 A. As I recall.

4 Q. You're right.

5 A. It's one of the few things I recall.

6 Q. Example III we have triamcinolone and  
7 azelastine. Azelastine is claimed; triamcinolone is  
8 not, correct?

9 A. Once again, this exact combination was in  
10 the very original patent, but eventually it's not  
11 claimed in the '620, yes.

12 Q. And then just quickly looking through  
13 Cramer again, do you see any other specific examples  
14 of formulations that we did not just talk about?

15 A. I see only three examples.

16 Q. Okay. Now, go back to Dr. Carr's  
17 paragraph 27. He talks about Cramer Example III,  
18 which is the one that has azelastine. You  
19 understand that?

20 A. I should keep the examples out. That's the  
21 triamcinolone/azelastine one?

22 Q. Correct. And he explained that in his

1 view during testing -- his view was that when Cipla  
2 tested and found several problems with Example III,  
3 those problems are what kind of defined the terms.  
4 Do you see that, paragraph 27, 28 and 29?

5 A. I've skimmed it and I see that that's the  
6 topic.

7 Q. So just quickly looking at paragraph 28,  
8 Dr. Carr said he observed that the testing of Cramer  
9 Example III showed an unacceptably high osmolality  
10 for the product to be used in the treatment of AR,  
11 correct?

12 A. Well, he said that Cipla's testing showed  
13 that.

14 Q. Okay. He also said that it showed  
15 unacceptable spray qualities, jet spray that would  
16 negatively affect the deposition on the nasal  
17 mucosa?

18 A. He said yes, that Cipla's testing showed  
19 that.

20 Q. And he said that there was unacceptable  
21 settling of the active ingredients, which I think we  
22 can all agree would be problematic?

1           A.     Yes.  These are all formulation details  
2     which don't really disturb me at all because I  
3     believe that if one -- if a formulator, such as  
4     Dr. Donovan, spent weeks with those two drugs, they  
5     would be able to successfully formulate a  
6     preparation that contained them both in functional  
7     excipients, but, you know.

8           Q.     Well, certainly --

9           A.     I'm aware that Cipla tested that and stated  
10    that they -- that it had problems.

11          Q.     Okay.  Just so we are clear here then, the  
12    closest prior art is Cramer and Segal according to  
13    your declaration.  Dr. Carr said that the closest  
14    example in the closest prior art did not work and  
15    had several problems.  Is that accurate?

16          A.     He said that, yes.

17          Q.     And so when you say that he did not  
18    mention Cramer or Segal at all, and we've agreed  
19    that Segal is just a broader version of Cramer, he  
20    actually did address Cramer, and he identified  
21    several problems with it.

22          MR. HOUSTON:  Objection, form.

1 BY MR. MILLER:

2 Q. Let me restate it.

3 So Dr. Carr did in fact address Cramer in  
4 his declaration, and he identified several problems  
5 with it.

6 A. Cramer is mentioned; that is correct. He  
7 repeated some problems that were raised by Cipla,  
8 but as a nonformulator, my view is that these are  
9 just examples. There's no -- not only is there no  
10 clinical data, but the formulation I don't believe  
11 they -- they claim that they produced it. It's an  
12 example of a formulation and what formulators do is  
13 they modify these excipients until it works, and  
14 that can take sometimes days, sometimes weeks,  
15 sometimes months, but when I look at all these  
16 formulations, I believe that with a little bit of  
17 work that this disclosure could allow someone else,  
18 if this was an approved patent, could allow someone  
19 else to develop the formulation of the two drugs. I  
20 only care about those two drugs, and I know that  
21 formulating a steroid with an antihistamine is not  
22 an insurmountable problem. So we're talking about



1     some details of formulation which I've not been  
2     asked to testify about, and so literally what you  
3     say is correct; Cramer is mentioned. But in terms  
4     of the actual intent of the Cramer document, I  
5     believe that they fully stated a combination of  
6     anti-inflammatory steroid with azelastine in this  
7     case.

8           Q.     Okay. All right. Now, you can put  
9     Dr. Carr, and, at least for the time being, Segal  
10    and Cramer to the side. I know you're getting quite  
11    a pile of paper there.

12          A.     Pretty pleased about that. Got a little  
13    library going.

14          Q.     Let's flip to page -- well, 6 or 8 of your  
15    declaration, paragraph 13?

16          A.     You said page 6 or 8?

17          Q.     So we have the double. There's a stamp  
18    under the page number.

19          A.     Oh, yeah, okay. Sorry.

20          Q.     I've been giving you both numbers for  
21    everything. I figured I should. So we see  
22    paragraph 13 --

1           A.     Use the big number. My eyesight is not as  
2     good as yours.

3           Q.     Okay. I'll do that then.

4                     We have a header here, Section 8. The  
5     beneficial effect of the combination of  
6     antihistamine and intranasal steroid was known in  
7     the art, right?

8           A.     Yes.

9           Q.     And this section, if you want to quickly  
10    review to refresh your recollection, is about a lot  
11    of what we've called the combination studies over  
12    the course of these litigations; is that accurate?

13          A.     Well, this paragraph is more general than  
14    that.

15          Q.     Okay. Which paragraph is that, 13?

16          A.     Yeah. Is that the one you wanted me to --

17          Q.     Well, just starting with this section.

18                     In general this is about co-administration  
19    of drugs and your argument that there's a benefit to  
20    co-administering, correct?

21          A.     Yes, and that it was known.

22          Q.     All right. While you're flipping through

1 I'm going to hand you guys Exhibit 1038.

2 A. Okay.

3 Q. I think you're familiar with Brooks, we'll  
4 call it?

5 A. Yes.

6 Q. Before we start talking about these  
7 documents, did you grab Drouin a few minutes ago  
8 when I asked?

9 You may know off the top of your head.  
10 Both of these studies looked at the same combination  
11 of drugs?

12 A. Beclomethasone and loratadine, right.

13 Q. Yeah. They're the same dosage.

14 A. If you say so.

15 Q. I believe they are.

16 A. I want to confirm that.

17 Q. If you'd like to, please do.

18 A. Oh, if it matters. Does it matter?

19 One lever of loratadine 10 milligrams, two  
20 sprays of BDP each nostril every morning and  
21 evening, 50 micrograms.

22 Q. So then there's actually more of a steroid

1     than in Brooks if you look at experimental drug  
2     treatment.  It's on page 2, 194.

3             A.     Loratadine, 10 milligrams, beclomethasone  
4     two sprays.  Oh, it's 84.

5             Q.     So Brooks has a little bit more  
6     beclomethasone?

7             A.     They're similar.

8             Q.     All right.

9             A.     We agree on that then.

10            Q.     We'll just quickly kind of walk through  
11     your -- this section of your declaration we talked  
12     about.  If you could jump up to paragraph 15.

13            A.     Okay.

14            Q.     That paragraph is all about the Drouin  
15     article that's in front of you, correct?

16            A.     It appears to be, yes.

17            Q.     And 16 is actually a discussion of  
18     Dr. Carr's analysis of Drouin, a response to that,  
19     correct?

20            A.     Yes.

21            Q.     So we're still generally talking about  
22     Drouin in that paragraph?

1 A. Yes.

2 Q. 17 is a continuation of your discussion of  
3 Drouin as is 18?

4 A. Okay.

5 Q. So we reach Brooks at 19. Brooks is the  
6 reference I just handed you, correct?

7 A. Yes.

8 Q. If you go through here, the next several  
9 paragraphs are directed to Brooks?

10 A. Un-huh.

11 Q. Paragraph 24 you begin a discussion of  
12 Simpson?

13 A. Yes.

14 Q. So you have three articles so far, Drouin,  
15 Brooks and Simpson; 26 you start talking about  
16 Ratner 1998, four articles.

17 A. Okay.

18 Q. And I believe you have one more in here,  
19 don't you?

20 A. Yeah, Juniper.

21 Q. Juniper 1997.

22 A. Um-hmm.

1           Q.     And then, actually, in paragraph 30, you  
2     mention Juniper 1989 article and Benincasa. So we  
3     have Brooks, Drouin, Simpson, Benincasa, Ratner '98,  
4     the second Juniper. And is that everything?

5           A.     Yes.

6           Q.     Okay.

7           A.     Six, there's six.

8           Q.     So there's six.

9                     Now, I'm going to hand you, you talked  
10    briefly about these two references in your  
11    declaration as well.

12                    The first document I'm handing over has  
13    been stamped as CIP2041, and that is Howarth. And  
14    the second one is Nielsen which has been stamped  
15    2042, CIP2042.

16                    Before we dig into these, I'd like to flip  
17    to page 10 of Nielsen. Shows Table III at the top.

18                    So here we have two Junipers, which if  
19    you'd like to cross with the end notes are actually  
20    Juniper 1989 and Juniper 1997. We have Ratner, et  
21    al., which is Ratner '98. We have Simpson. We have  
22    Brooks. We have Backhouse. Backhouse actually is a

1 combination study comparing the combination against  
2 the antihistamine, but the only one we're missing is  
3 Drouin, correct?

4 A. Only one of the ones we just discussed,  
5 yes.

6 Q. Drouin and Benincasa, excuse me.

7 A. Yes.

8 Q. Now we talked about Brooks and Drouin.  
9 Brooks actually had a higher dosage but otherwise --  
10 or dosage of the steroids but was otherwise exactly  
11 the same design as Drouin, correct?

12 A. I wouldn't -- I don't know if it's exactly  
13 the same --

14 Q. Very similar.

15 A. -- I'm sure it's not.

16 Q. Very similar.

17 A. The drugs are the same, the doses are  
18 different, but the studies have some similarities.  
19 That's -- I will agree to that.

20 Q. The endpoints are the same?

21 A. Well, most of these use total nasal symptom  
22 scores and that sort of thing and they tend to be

1 similar, but they're -- as you know, they're not  
2 identical.

3 Q. Right.

4 A. I mean, we are going to do a little math  
5 about that, I'm sure.

6 Q. We might. We might.

7 A. If you insist.

8 Q. We'll see.

9 A. Your funeral.

10 Q. Let's start with -- let's flip back to  
11 Howarth for a moment? You have that?

12 A. I do.

13 Q. That's 2041. It's your position in your  
14 declaration that Howarth is really talking about the  
15 efficacy of an antihistamine in treating  
16 inflammation. Is that essentially what your  
17 argument is?

18 A. That certainly appears to be the goal of  
19 this view. This is sort of an opinion piece, and  
20 he's kicking around the idea for chronic use of  
21 anti-inflammatory antihistamines and considering  
22 whether that's useful prophylactically.



1 Q. Okay. If you could flip to big number 10,  
2 five at the bottom.

3 A. The last page.

4 Q. Yeah.

5 A. Okay.

6 Q. Now, the conclusion here, if you need a  
7 minute to read through that, go ahead, but this is  
8 not about symptoms. This statement says:

9 The lack of additional clinical benefit,  
10 clinical benefit, when antihistamines are used in  
11 combination with corticosteroids, indicates that,  
12 continuing on, the latter -- the action of the  
13 latter, i.e., the antihistamines, is redundant?

14 A. Are you quoting a spot here?

15 Q. If you look at the second sentence in the  
16 paragraph after the conclusions paragraph. It's  
17 "The lack of additional."

18 A. Um-hmm.

19 Q. Go ahead and read that.

20 A. Yes.

21 Q. He's not saying they don't work on these  
22 mechanisms. He's saying there is no clinical

1 benefit, correct?

2 A. Well, that's what he is -- he's saying  
3 that, but he's not providing any evidence to support  
4 it.

5 In fact, the last sentence before that  
6 conclusions paragraph is where he states it more  
7 explicitly:

8 The limited studies available do not  
9 support a superior effect.

10 But he references 52 and 53, which he does  
11 not provide. So as I said, this is an opinion  
12 piece. He's kicking around some viewpoints and  
13 ideas, but he provides no actual support for that  
14 part of it. And I disagree with him. I think that  
15 he's overlooking the clear additivity of these drugs  
16 that was known at that time that was largely  
17 combined -- largely confined to the first two weeks  
18 or so when the drugs are combined after which the  
19 steroid effects continue to get stronger and  
20 stronger and begin to dominate the combination.

21 So when he -- he's talking about chronic  
22 use, and to a certain extent I think he's correct.

1 In fact, I think, these six papers are mostly all  
2 correct. And while Dr. Carr seems to want to  
3 disparage the ones that show some benefit of the  
4 combination over the steroids alone and embrace the  
5 ones that show no advantage over the steroid alone,  
6 my view is that five out of six of these papers  
7 show, in one important context or another, that  
8 there's benefits of the combination compared to the  
9 steroid alone, and that includes two of the three  
10 that Dr. Carr claims show no benefit.

11 So now Howarth has just mentioned  
12 presumably two of the negative ones. If I had to  
13 put in the references which he left out, I would  
14 think Benincasa might be one of them and maybe  
15 Juniper or Ratner is another, because they both  
16 explicitly say, well, you know, the combination is  
17 not that much better than the steroid alone. But  
18 any POSA that would look at the totality of this  
19 literature in the late '90s and really spend some  
20 time with it, which clearly Howarth did not, because  
21 he only referenced two and didn't even give us the  
22 references, would realize that what I said is

1 correct. That early on in the first few days, which  
2 is when the steroids are just starting to work and  
3 the antihistamines will work instantaneously,  
4 there's great additivity and great benefit of  
5 combining them. And that's what Drouin says; that's  
6 what Brooks says. That's what Simpson says. But  
7 once you get to two weeks out or longer, the  
8 combination isn't that much better than the steroid  
9 alone, and so I wouldn't dispute that, that for  
10 chronic treatment it would be hard -- if you did a  
11 study that only read out at four weeks of treatment,  
12 I don't think you'd see much difference. And even  
13 the later studies, the later Ratner conjunctive  
14 therapy study and the Hampel study and the Carr  
15 study, they all show that the steroid is catching up  
16 to the combination, and by day 11 in all those  
17 studies there's no longer a statistically  
18 significant superiority of the combination over the  
19 steroid alone, so I think that an objective POSA  
20 would say these studies are all pretty much correct.  
21 Benincasa, which was an 8-week study,  
22 started with one week of treatment before the season

1 and didn't collect data for three weeks. So by that  
2 time that window of complementarity, as I've called  
3 it throughout my declaration, is gone. It's closed,  
4 completely closed. So it's not at all surprising  
5 that -- wouldn't be surprising in the future. Any  
6 study designed like Benincasa where there's no data  
7 collection in the first week or two is going to  
8 show -- have a hard time showing the difference,  
9 whereas all the studies that looked early on,  
10 including the Ratner study, which is held up as  
11 evidence that there's no improvement. The Ratner  
12 study showed at one week and two weeks that the  
13 patients preferred the combination to the steroid  
14 alone.

15 Now, when he wrote the conclusion of that  
16 paper, he ignored what the patients think, and he  
17 parroted what the doctors thought, which I thought  
18 was par for the course. I mean, patients come in  
19 third in this sort of thing. But you can look at  
20 Ratner Figure 1. It's very clear that the patients  
21 statistically significantly thought that the  
22 combination was better at symptom improvement than

1 the steroid alone. So, you know, I think -- I kind  
2 of summarized what I think is Dr. Carr's pitfall,  
3 but also Howarth pays almost no effort to look at  
4 the combination studies. Doesn't cite any of them.

5           Nielsen, as I mentioned earlier, their goal  
6 was -- and their main purpose of writing that paper  
7 was to show the world that steroids were better than  
8 antihistamines, and they do it just magnificently.  
9 Once they get to the combination, they really don't  
10 want to admit that maybe the combination can be  
11 better, but at the end they say, well, the  
12 combination is probably marginally better but may  
13 not be cost effective. That's the conclusion of  
14 Nielsen. And a couple of those guys are in the  
15 guidelines, and the guidelines say, over and over  
16 and over again, add an antihistamine to a steroid if  
17 you don't have control; or if you have an  
18 antihistamine, add a steroid to it if you don't have  
19 control. And that's still practiced today.

20           So sorry about the soliloquy, but maybe  
21 that helps reduce your number of questions, because  
22 that's my view of the totality of these clinical

1 studies. And I think it's, you know, in science we  
2 have something called Occam's razor. The simplest  
3 explanation should be sought, and to me the simplest  
4 explanation is not for Dr. Carr and I to argue about  
5 the details of every study, because I think all the  
6 studies fit into one simple explanation, which is  
7 that there's additivity and complementarity early  
8 on. Once the steroid has weeks to work and gets to  
9 its full efficacy, then it's harder to show that  
10 benefit of the antihistamine added.

11 Q. That did answer some of my questions. We  
12 can put Haworth away for now.

13 A. My condolences.

14 Q. Go ahead and put Haworth off to the side.  
15 Go ahead and flip back to Nielsen then.

16 A. Yes.

17 Q. All right. So that's Nielsen. Flip to  
18 the front, second page. See the abstract begins and  
19 runs on to the second page?

20 A. Yes.

21 Q. You actually mentioned in your soliloquy,  
22 as you've entitled it, that their conclusion is

1 largely that there may be a little benefit, but it's  
2 not cost effective.

3 A. Right.

4 Q. If you look in the final paragraph of the  
5 abstract, which appears on 1564 in the top left,  
6 page 2 at the stamp, it begins "When the efficacy,"  
7 et cetera. There's a sentence that begins in the  
8 middle, "Combining antihistamines."

9 A. Where in the abstract?

10 Q. The last paragraph.

11 A. Oh, "Combining antihistamines."

12 Q. Yes.

13 A. Out loud or?

14 Q. Yes, please.

15 A. "Combining antihistamines and intranasal  
16 corticosteroids in the treatment of allergic  
17 rhinitis does not provide any additional effect to  
18 intranasal corticosteroids. On the basis of current  
19 data, intranasal corticosteroids seem to offer  
20 superior relief in allergic rhinitis than  
21 antihistamines."

22 Q. That first sentence they're saying no



1 additional benefit. It's not "it may provide a  
2 little bit of a benefit." There's no additional  
3 benefit.

4 A. But, again, as I mentioned their goal --  
5 these are steroid guys. I know some of them.

6 Their goal was to definitively establish  
7 that steroids are superior to antihistamines, but  
8 when it came to discussing the combination, they  
9 kind of gave it short shift. They did not discuss  
10 Drouin. They did not discuss the positive data in  
11 Simpson. They did not discuss some of the other  
12 positive data. So they kind of -- that's why I said  
13 eventually they begrudgingly admit that the  
14 combination has some marginal benefits but the cost  
15 is an issue. So they were less generous in this  
16 sentence than they were later in the paper, but, you  
17 know, these guys are steroid guys. As a steroid guy  
18 myself, or former steroid guy, I know them, and I  
19 know that they believe that steroids are the best  
20 drugs, and they are. They are the best drugs.

21 Q. Okay. So just to be clear, the two  
22 articles that we -- well, I've asked you about, you

1 actually mentioned several others, but Howarth and  
2 Nielsen were both published articles that say that  
3 there's no benefit to a combination.

4 A. Right, but then you have Spector and  
5 Berger, the guidelines, Dykewicz, the Cauwenberge,  
6 they all talk about the necessity to combine these  
7 drugs. So the fact that two guys write a review and  
8 say, "Oh, there's no -- there's nothing here,"  
9 doesn't mean it's so. And, in fact, the  
10 preponderance of the evidence that a POSA would have  
11 had accessible to them in the late ' '90s said very  
12 clearly that when disease is not controlled by  
13 whatever your first-line therapy is, be it steroid  
14 or antihistamine, you add the other one. Those  
15 recommendations, which were unanimous in all the  
16 major organizations, as well as the van Cauwenberge,  
17 which is some kind of a group consensus document,  
18 those were the prevailing practices. And they still  
19 are by the way.

20 So to just say glibly that, oh, there's no  
21 benefit to adding these two drugs, and then ignore  
22 the fact that everyone does it because everyone

1 perceives benefit and they still do it because they  
2 perceive benefit, is very self-serving in my view.  
3 And the same thing with the second Juniper paper.  
4 She did a real-world study. It was a great study  
5 where she said, "Okay. I'm going to give you two  
6 drugs. You take drug A or B, whichever you're  
7 assigned to take, and keep taking that during the  
8 season, but if that's not controlling your symptoms,  
9 add the other drug, and we'll monitor your  
10 quality-of-life assessment, real-world stuff." And  
11 over half of the patients resorted to taking both  
12 drugs. And so, you know, that is the real world,  
13 and it doesn't really pay to ignore the real world  
14 in some kind of statement in a legal document, I  
15 think.

16 Q. Okay. All right. Let me reorganize  
17 myself here after that.

18 You mentioned the Juniper article, the  
19 real world. I'm assuming you're referring to the  
20 Juniper 1997 article as the real-world one. I'll  
21 hand it to you. This is Exhibit 1031.

22 A. Yeah.

1           Q.    Now, you summarized it in there, but it  
2    was buried in a long answer, so I'm going to --

3           A.    I'm sorry.

4           Q.    -- ask just to kind of get it out there  
5    again.

6                   Essentially what Juniper studied was two  
7    patient groups who start on either an antihistamine  
8    or a steroid and are instructed to take the other  
9    one when needed, correct?

10          A.    Yes.

11          Q.    And the drugs involved in this case are  
12    fluticasone and -- or in this study, are fluticasone  
13    and terfenadine, correct?

14          A.    I believe that's right.

15          Q.    Now, if we flip to --

16          A.    Don't ask me to read the French.

17          Q.    I won't. I don't know what it says  
18    either. It's stamped page 7. It's actual  
19    page 1129. Table 3 is what we are looking for here.

20                   So this is a breakdown of how often the  
21    patients use the drug, right? So you have 16  
22    patients who only used fluticasone?

1 A. Yeah.

2 Q. You have four patients who only used  
3 terfenadine?

4 A. Throughout the whole study.

5 Q. Throughout the whole study?

6 A. Yes.

7 Q. And then you have a combination of a  
8 number of patients using 1526, correct?

9 A. Right.

10 Q. All right. Looking down to fluticasone,  
11 so the treatment group says Treatment Group Header  
12 Fluticasone and Terfenadine. Those are the first  
13 drug they were on, correct?

14 A. Yes, I believe so.

15 Q. All right. And so if we look down, it's  
16 broken down essentially with the number we just  
17 talked about. Going down the column, we have  
18 fluticasone and terfenadine. Terfenadine is  
19 actually how many patients took it in both groups,  
20 correct? That quadrant in the table, whatever --

21 A. The bottom --

22 Q. Terfenadine header. Okay.

1                   Now, these patients in the fluticasone  
2   group took on average 0.13 tablets per day; is that  
3   right?

4           A.    In the fluticasone group.

5           Q.    In the fluticasone group, yes, patients  
6   took 0.13 tablets of terfenadine a day.

7           A.    Well, that's an average of all of them, but  
8   not all of them took terfenadine. In fact, as you  
9   can see, 16 of the -- looks like 31 patients that  
10   started with fluticasone never felt a need to take  
11   the terfenadine. And, again, in a way that  
12   indirectly demonstrates what I already said, which  
13   is that it was known by this time that the  
14   intranasal steroids were the superior drug, so if  
15   you then average over the whole group, you get a  
16   small number, but in the fluticasone group the 15  
17   that took terfenadine would have taken a larger  
18   number than .13. So the tablets --

19          Q.    Oh, I see.

20          A.    -- that they took were averaged over the  
21   whole group.

22          Q.    So you're saying that the 13 is really

1 broken down by 15 but the average is for the 31  
2 patients?

3 A. I believe that's how they calculated it.

4 Q. But the point remains that the average was  
5 .13 tablets per day in the fluticasone group?

6 A. Right. Right.

7 But, again, it's consistent with all the  
8 other papers, which is what I was saying, that after  
9 a couple weeks the steroid is nearly fully  
10 effective, and once they got through that window,  
11 and I don't remember if they started the steroid  
12 before the season or on it a little while. What  
13 does it say?

14 During six weeks of the season...

15 Part of the reason that number is small,  
16 I'm sure, is that it's only in that first window  
17 where the steroids are not up to speed where those  
18 pills would be taken. I'm sure that data is not in  
19 the paper but, you know, when along the way they  
20 took those. But it supports both concepts that I  
21 mentioned. One is that the steroid is the superior  
22 drug, and two is that adding an antihistamine to the

1 steroid is something that, well, looks like about  
2 half of those in the fluticasone group did. 26 out  
3 of 30 in the antihistamine group added the steroid,  
4 so they clearly perceived that the antihistamine  
5 wasn't satisfactory.

6 Q. That was a shorter answer but still fairly  
7 long. Do you guys mind if we take a break so I can  
8 just look at the last couple of answers before I ask  
9 questions you've already addressed?

10 A. Sure.

11 (Recess taken from 10:50 a.m. to  
12 11:03 a.m.)

13 (Mr. Marghese no longer present.)

14 BY MR. MILLER:

15 Q. All right. Dr. Schleimer, if you can find  
16 your declaration again, you can put those studies  
17 off to the side for now.

18 A. Second declaration.

19 Q. Second declaration. Yes. Sorry.

20 You mentioned at paragraph 40 -- it's  
21 page 28.

22 A. Okay.



1 Q. You refer to a series of guidelines?

2 A. There's the spelling.

3 Q. Oh, yeah.

4 These guidelines are essentially  
5 instructions on recommended treatment practices for  
6 physicians, correct?

7 A. Yes.

8 Q. And those -- each one of these guidelines,  
9 they talk about how you can step up, step down,  
10 titrate. They describe an iterative treatment  
11 process, right?

12 A. Yes.

13 Q. Okay. So when they say -- you point to a  
14 couple things saying, you know, for example, you  
15 said you can use azelastine and fluticasone. That's  
16 in the context of "Try something, see if it works.  
17 If it does, great. If it doesn't, try something  
18 else"?

19 A. In that spirit, yes.

20 Q. I want to look at paragraph 49, if we  
21 could. Well, starting at 49. This is Section  
22 page 33 and 34, "Side-Effect Analysis."

1           So what is your view -- in your view what  
2   is the basis for the statement that Dr. Carr's  
3   side-effect analysis is scientifically unsound?

4           A.   Well, he's got a couple of different graphs  
5   or charts in his declaration slightly different from  
6   each other, but in each case there are an  
7   amalgamation or mishmosh of data from various  
8   sources, different studies, and so if we're going to  
9   talk about side effects, I think we should start by  
10   looking at the Dymista® label, and that's what I do  
11   somewhere here. If either of you know the  
12   paragraph.

13          Q.   I think -- give me just a second.

14          A.   I think it's later on in the 70s somewhere.

15          Q.   Yeah. It's further. So you're talking  
16   about...

17          A.   Somewhere.

18          Q.   I'm trying to find the graph you wrote.  
19   Here it is. So you're looking at paragraph 74 and  
20   on, page 54?

21          A.   Yeah.

22          Q.   Okay. But it's somewhere --

1           A.     Okay.   So if we start at paragraph 75,  
2     page 55 or stamped 57.

3                     It says explicitly:

4                     Because clinical trials are conducted under  
5     widely varying conditions, adverse reaction rates  
6     observed in clinical trials of a drug cannot be  
7     directly compared to rates in the clinical trials of  
8     another drug and may not reflect rates observed in  
9     practice.

10                    And so I found -- the issue here is by  
11     combining fluticasone, which has its own side  
12     effects profile, and azelastine, which has a  
13     different side effect profile, does the combination  
14     have more, less or about the same level of side  
15     effects?   That's the issue in question.

16                    But there's additional complication which  
17     is that somewhere in his declaration Dr. Carr claims  
18     that there's something special about the formulation  
19     of Dymista® that may help diminish the side effects.

20                    So there's two claims that I find to be  
21     incorrect.   One is that Dymista® is safer than the  
22     individual monotherapies that go into making it, and

1 the other is that in the context of a formulation of  
2 Dymista® the components are somehow safer, the  
3 fluticasone and azelastine.

4 And the best way to test whether his  
5 suggestion is true is to look at the side effect  
6 data from the Hamel study. So there are three  
7 studies that are very similar that we'll be  
8 discussing, I'm sure. They were all, I believe,  
9 supported by Meta or whatever the name of the  
10 company was at the time.

11 One is the original Ratner study. In that  
12 study they took commercial Flonase and commercial  
13 Astelin, and they gave either one or the other, or  
14 they gave both of them conjunctively to patients.

15 Q. Hold on, Dr. Schleimer. Before we go  
16 further down that -- to reign back, because we will  
17 get to this.

18 The question I asked was something along  
19 the lines of: "What is the basis for the science  
20 of --

21 A. And what I'm saying is exactly what the  
22 Dymista® label says, which is that you can't collect

1 data from different sources and compare them.

2 For instance, if you asked about the  
3 frequency of nosebleed or the prevalence of  
4 nosebleed, and you study 20 people, but one study  
5 was for a week and the other study was for a year,  
6 would you expect them to have the same rates?

7 What if they were in different cities,  
8 different places? There's so many variables that  
9 you have to do it in the context of those variables  
10 being controlled, and so the Dymista® label, which  
11 is where I was headed, if you want to go through the  
12 Dymista® label, we certainly can, and then we'll go  
13 to Hampel. I was mentioning those three studies  
14 because it's useful for anyone on the board who is  
15 considering this case to know the differences  
16 between these three studies, but if you don't want  
17 to talk about it, that's okay.

18 Getting back to side effects, let's look at  
19 the Dymista® label. So in paragraph 76 we state:

20 The first study from the label concluded  
21 the, quote, overall adverse reactions were  
22 16 percent in the Dymista® treatment groups,

1 15 percent in the azelastine hydrochloride nasal  
2 spray groups, and 13 percent in the fluticasone  
3 propionate nasal spray groups, and 12 percent in the  
4 placebo groups.

5 So there's a few important things. One is  
6 that these drugs are all very safe. These are low  
7 rates and the events are very mild. Things like bad  
8 taste or headache are the main two ones.

9 The other thing is that the drugs give very  
10 little signal above and beyond placebo. Placebo was  
11 12 percent. Dymista® was 16 percent. That's almost  
12 no incremental increase, reinforcing my statement  
13 these are very safe drugs. But 16 percent in  
14 Dymista® is certainly not less than either  
15 15 percent in azelastine or 13 percent in  
16 fluticasone. So any claim that it is safer than the  
17 monotherapies is incorrect, and it's because  
18 Dr. Carr, as he often is wont to do, took data that  
19 support his contention in this case from different  
20 sources and made those graphs. So if you want to  
21 continue the discussion of side effects, we can do  
22 so. The next thing I would look at is the Hampel

1 study.

2 Q. Before we go there, that was another long  
3 answer, but I think somewhere in there you said --  
4 you mentioned that Dr. Carr had mentioned the  
5 formulation effect, right?

6 A. Somewhere, yeah.

7 Q. The azelastine and fluticasone that you're  
8 pointing to, I think you're pointing to  
9 paragraph 76; is that right?

10 A. Yes.

11 Q. Those are reformulated in the Dymista®  
12 formulation, correct?

13 A. That's correct. In the Carr studies.

14 Q. Okay. And so this isn't actually a  
15 comparison to what was known in the prior art?

16 A. Right. And that's where I was headed  
17 before when you diverted me.

18 Q. Okay.

19 A. The Hampel study is the comparison that  
20 would test that contention of Dr. Carr that there's  
21 a formulation effect. The Hampel study compared  
22 Dymista® to commercial Flonase and commercial

1 Astelin. So if we do the same comparison with  
2 Hampel, now we have the data here somewhere, we can  
3 use this table, although it only talks about the two  
4 top side effects. But if you look at the Hampel  
5 study, you see that for bitter taste Dymista® had  
6 7.2 percent, Astelin had 4.1 percent and Flonase had  
7 zero. So, again, Dymista® is actually -- has the  
8 highest incidence of bitter taste among the three  
9 treatment arms. If you look at headache, Dymista®  
10 had 2.6 percent, Astelin 1.3 percent, Flonase 3.9  
11 percent.

12 Again, these are all very low, and there's  
13 no statistic so I doubt they're different. So both  
14 with bitter taste and headache the combination is  
15 roughly equal to whatever the component it is that  
16 caused that particular side effect. We know that  
17 there's some headache associated with Flonase, and  
18 we know that Astelin tastes bad, so there's no  
19 evidence here that by coformulating them there's  
20 less bitter taste or there's less headache.

21 That's why I think that Dr. Carr's tortuous  
22 treatment of data collected from different sources



1 is not the best way to address the issue of side  
2 effect.

3 Q. Now, you realize that those sources that  
4 you're identifying are all FDA-approved labels?

5 A. I do.

6 Q. You would agree that those are subject to  
7 strict scrutiny as they're getting approved?  
8 Everything that goes into that label, the data is  
9 approved by FDA and approved and rigorously  
10 approved?

11 A. Yes, and I don't want to disparage the FDA,  
12 but I will say when we start talking about rapidity  
13 of onset, you'll see that the FDA, like all  
14 government organizations, is not perfect and does  
15 not pay attention to every detail and sometimes  
16 settles for general data. But by and large, yes, I  
17 agree that the data in those labels is scrutinized  
18 by the FDA.

19 Q. And that's the information the physicians  
20 are going to rely on when they treat a patient,  
21 right?

22 A. Maybe the first time, but the physicians

1     very quickly learn if a drug has undesirable  
2     effects. They prescribe it. Patients complain or  
3     they don't. And these drugs, as I mentioned -- the  
4     most important thing -- we can quibble about the  
5     small differences in numbers here -- is that these  
6     drugs, both the monotherapies and Dymista® are  
7     extraordinarily safe, very safe, minimal side  
8     effects. And the vast majority of the side effects  
9     are also seen in placebo, so the side effects aren't  
10    even drug attributable. So I don't see any evidence  
11    for a magical reduction in side effects by  
12    coformulating them or combining them.

13           Q.    Okay. Now -- strike that.

14                    Let's flip to this section -- well,  
15    actually, there are 52 back -- you flipped ahead.

16           A.    I'm sorry.

17           Q.    Page 52. Paragraph 52, excuse me,  
18    page 36.

19           A.    Oh.

20           Q.    This is the closest prior art. We've  
21    talked about this section a little bit before. I  
22    just want to orient you.

1 A. Yes.

2 Q. If you move forward a couple pages to 40,  
3 this is your first subheader in that section:

4 The efficacy of Dymista® in treating AR is  
5 essentially the same or worse than the active  
6 ingredients co-administered separately.

7 You see that?

8 A. Where is that?

9 Q. The header.

10 A. Oh, yeah.

11 Q. Here you're talking essentially about a  
12 comparison --

13 A. Yes.

14 Q. -- of Hampel, Carr, et cetera, to Ratner  
15 2008 --

16 A. That's correct.

17 Q. -- right?

18 Ratner 2008 is not prior art?

19 A. Yes and no. In my view as a nonattorney,  
20 as I've mentioned before, I believe that -- that the  
21 fact that the combination of Flonase and Astelin was  
22 already being used in the clinic by doctors and

1 patients, and I also mention in the declaration that  
2 at the trial at least four major important doctors,  
3 allergists, said that they prescribed those two  
4 drugs together, including Accetta, Wagner, Kelleher  
5 and Carr.

6 To me that's practice of the prior art in  
7 the sense that those two drugs are being combined in  
8 a nasal formulation. Even though it's not a single  
9 bottle, they're being given at the same period of  
10 time to the same patients.

11 So I'm not a lawyer, and if you tell me  
12 that that's not considered prior art, I'm not going  
13 to have a long legal debate with you, but in my view  
14 of this, it means that the quote/unquote invention  
15 was being practiced already, and so that's why I  
16 view it as prior art.

17 Q. Now, those doctors -- and I don't think  
18 you cited anywhere in your declaration -- those  
19 doctors all testified that their treatment regiments  
20 were inconsistent with ARIA, Dykewicz, et cetera,  
21 correct?

22 A. Did you say "were" or "weren't"?

1 Q. Were.

2 A. Were. That I don't recall specifically.

3 If you've looked at the transcript and say  
4 they did, I'm willing to accept it, because  
5 certainly I recall looking at ARIA and Dykewicz and  
6 they -- and remember them mentioning intranasal  
7 antihistamines, and in one case I think azelastine  
8 specifically.

9 Q. And so, again, if those doctors were  
10 operating consistent with the guidelines, we  
11 discussed earlier the guidelines recommend the  
12 stepwise approach or titration and iterative  
13 process. They're not applying a fixed consistent  
14 dose of the drug to those patients, are they?

15 A. Well, so, yes and no. I think that when  
16 Dr. Accetta prescribed a patient both drugs and said  
17 take these, the patients would be concurrently, as  
18 long as they're compliant, taking both drugs  
19 according to the dosage regimen that was  
20 recommended. So in the real world, of course,  
21 patients have variable compliance and may have gone  
22 off the reservation, but if the patients were

1 compliant they would be taking the prescribed doses  
2 of both medicines for days, weeks or months  
3 continuously.

4 Q. And Dr. Accetta's records actually  
5 frequently said "take as needed." Do you recall  
6 that?

7 A. So, I do recall that.

8 Q. Unfortunately --

9 A. I don't remember all 10 of them.

10 Q. Yeah.

11 A. But that's certainly within the boundaries  
12 of what is common practice then and still now for  
13 individual drugs.

14 Q. So I'm going to hand you Exhibit 1045.  
15 This is Ratner 2008. And we're going to take a look  
16 at -- so it's stamped page 2, print page 75, second  
17 page, towards the right side of the bottom,  
18 "Patients randomized to." You see that paragraph?

19 A. Yes.

20 Q. So here this is the paragraph -- take a  
21 look real quick. Just skim it. You don't have to  
22 read it out loud. This is the paragraph describing

1 the dosing regimen of the study, correct?

2 A. Yeah, I skimmed it.

3 Q. Okay. And so each of these patient  
4 groups, there's multiple patient groups in the  
5 study, and each one is given a specific schedule to  
6 take their drug on, right?

7 A. Yes.

8 Q. That's not "as needed."

9 A. No.

10 Q. Okay. So that's actually different than  
11 several of the records and the instructions in ARIA?

12 A. Well, I don't think you can argue that ARIA  
13 and the guidelines are saying "as needed." They're  
14 saying if there's not adequate control with one  
15 drug, whatever your drug of first choice was, add  
16 the second drug. But once you've added it then it  
17 would be according to whatever the dosage regimen  
18 that both drugs are used unless a physician made the  
19 effort to say, "Oh, you know, just take it when you  
20 feel bad," which does happen, but -- and I can't say  
21 if the majority of cases would be according to a  
22 fixed-dose regimen, but a certain significant number

1 would be. Doctors would prescribe it and say take  
2 it and maybe give no instructions about deviating  
3 from the prescribed regimen, which is on the bottle.

4 Q. While we're in Ratner, let's flip to the  
5 seventh stamped page. It's the last text page  
6 before the reference list. Let me know when you get  
7 there.

8 So you see there's the reference list.  
9 Right above that is acknowledgment?

10 A. Yes.

11 Q. And then a paragraph right before that.

12 A. Okay.

13 Q. The first sentence of that paragraph, if  
14 you could, could you read that for the record?

15 A. "The use of intranasal azelastine in  
16 combination with intranasal fluticasone produced an  
17 unanticipated magnitude of improvement in rhinitis  
18 symptoms amongst patients with allergy to Texas  
19 mountain cedar pollen."

20 Q. So these authors, who as an aside are the  
21 same authors as -- generally the same author group  
22 as Ratner '98, correct?



1           A.     Yeah, and I think it's virtually identical.

2           Q.     I think there's one or two changes, either  
3     way.

4                     So these guys and gals had done that  
5     study, a similar study a decade before, and they  
6     concluded no benefit in Ratner '98, right?

7           A.     No, they had not done the study.

8           Q.     No, a similar study, so they did  
9     fluticasone and loratadine.

10          A.     It was not similar.

11          Q.     It's not?

12          A.     No.

13          Q.     How is it dissimilar?

14          A.     You want to talk about that paper?

15          Q.     We'll get to it.

16          A.     Very different.

17          Q.     So let's stick with this for a second.  
18     This is the Ratner team, same team as Ratner '98  
19     essentially.

20          A.     And this is a  
21     pharmaceutical-company-sponsored study, MedPoint,  
22     which became Meta or owned by Meta as the sponsor,

1 and that should be kept in mind.

2 Q. Okay. So even if we were to accept the  
3 position that the dosing regimen in this study  
4 actually reflects what was happening before the date  
5 of invention, doesn't this statement imply that six  
6 years later the authors were surprised by the  
7 efficacy of their regimen?

8 A. To me, as I've testified, a POSA would have  
9 anticipated an additivity, and a POSA would have  
10 looked at these results and thought, yeah, that  
11 makes sense, because basically in that window,  
12 especially the first in this case, 11 days, the  
13 first 11 days, the combination is better than the  
14 steroid. After that the combination is no better  
15 than the steroid alone. And in the context of the  
16 totality of the clinical studies that I've talked  
17 about, that is the pattern that someone who hadn't  
18 studied this literature would expect. Why they  
19 wrote it's unanticipated and to what extent it truly  
20 reflects the views of all the authors, I cannot  
21 comment.

22 Q. Okay. While we're on it, I'm going to

1 hand you...

2 If you flip back to -- at some point in  
3 our discussion we were at paragraph 61 of your --

4 A. Oh, yeah, it's still there.

5 Q. Okay. Good. I wasn't sure if we had  
6 skipped out of it or anything like that.

7 So this Carr paper you're referencing is  
8 by Dr. Carr --

9 A. Yes.

10 Q. -- your opposition in this case shall we  
11 call him?

12 A. If you must.

13 Q. Opposing expert.

14 A. Your expert, yes.

15 Q. So the efficacy data that you've pulled  
16 for Figure -- I don't know if you have the number  
17 for it but the chart on page 42, that entire right  
18 column relies on Dr. Carr's paper; is that correct?

19 A. Yes.

20 Q. Okay. And we'll keep going through here.  
21 So I think that this chart between paragraph 62 and  
22 64 also relies on Dr. Carr's paper?

1           A.     It does.

2           Q.     Continuing on the chart that appears on 46  
3     between paragraphs 63 and 64 also relies on  
4     Dr. Carr's paper?

5           A.     Yeah, in both cases the right-hand panel is  
6     Dr. Carr's study. The middle one is the Hampel  
7     study, and the left-hand one is the Ratner study,  
8     and both of these illustrations show that the  
9     results are virtually identical in these three  
10    studies, which is quite remarkable in and of itself,  
11    but maybe not so much since these are the same group  
12    doing three different studies to a large extent.

13          Q.     Continuing on, so Figure C, this one's  
14    actually labeled. I think this was one of your  
15    rebuttal slides at trial from the Apotex litigation?

16          A.     Yeah.

17          Q.     This is the Carr paper relied on in this  
18    figure or is this all about Hampel?

19          A.     Yeah, as you said, this was -- what did you  
20    call it, a screen grab from the --

21          Q.     From the trial --

22          A.     -- trial demonstrative. It says it's

1       recreated from Hampel, so that's probably the case.

2           Q.     Okay. I mean, the point of that one is  
3       less important than the pre -- than A and B.

4           Continuing a page or two on, you'll see  
5       page 50, paragraph 70, we talk about -- I'm going to  
6       ask you again for the pronunciation. Is this Grife  
7       or Grief?

8           A.     I don't know. I don't know the person.  
9       I've called them Grief but I'll probably say Grife  
10      because I just revert to that.

11          Q.     But so we understand we're referring to  
12      the article referenced here?

13          A.     Yes.

14          Q.     So Greiff was published in 1997, right?

15          A.     That's correct.

16          Q.     You didn't cite it in your opening report  
17      at all; is that correct?

18          A.     I accept that that's probably true. I  
19      don't recall citing it, yeah.

20          Q.     Okay. But you talked about it quite a lot  
21      in the Apotex litigation?

22          A.     Yes, for legal reasons lawyers in the two

1 different cases decide what to ask me my opinion  
2 about and when, and in the trial, although I had  
3 opinions about lots of the secondary indicia, they  
4 only asked me about a couple of them, and in this  
5 case, in this proceeding, I don't think we dealt  
6 with those much at all in the first declaration,  
7 but, I mean, I'm an adviser and expert. I don't  
8 drive the legal parts of this.

9 Q. Right. If you could search through your  
10 library for the first declaration, your first  
11 declaration, give me just a moment to find this, you  
12 actually talk about the 15-minute onset of  
13 azelastine in your first declaration, don't you?

14 A. I don't know. I may well.

15 MR. MILLER: Why don't we take a break.

16 (Recess taken 11:34 a.m. to  
17 11:36 a.m.)

18 BY MR. MILLER:

19 Q. All right. Dr. Schleimer, if you could  
20 flip to paragraph 55 of your original declaration?

21 A. Okay.

22 Q. See towards the end, first full sentence

1 on page 23, you say:

2 Notably...histamine quickest onset of  
3 action which can improve nasal symptoms in as  
4 quickly as 15 minutes, is that accurate?

5 A. Yes.

6 Q. So you do talk about onset there. That's  
7 a little bit broader. We can also look at  
8 paragraph 64 if you move forward a couple pages.

9 Patients found that symptom relief  
10 occurred as fast as 15 minutes after taking  
11 azelastine.

12 A. Yes.

13 Q. So Greiff is essentially just a new  
14 reference to say the same thing.

15 A. Not really. This is one of those cases  
16 where there was a fact that was widely known which  
17 is that azelastine, in topical antihistamines in  
18 general, worked in 15 to 30 minutes. It's talked  
19 about in the ARIA guidelines, in the Dykewicz  
20 article, it's talked about in Berger, McNeal --  
21 everyone talks about it. Meltzer, who we're not  
22 talk -- it's everywhere. Everyone says works within

1 15 to 30 minutes, but go and try to find an original  
2 source document for a rigorous study where they  
3 measured it like every five minutes, the efficacy.  
4 You can't find it. So it's like everyone knows it  
5 so why study it to prove it because everyone knows  
6 it.

7 Q. Right.

8 A. And Greiff, I think your pronunciation is  
9 probably right because they don't want to be called  
10 Grief, Greiff is the one study that I can find that  
11 definitively actually shows it. And it didn't even  
12 parse it by minutes. It just -- it was at one hour,  
13 and by one hour, when using the moderate dose of  
14 histamine to challenge, they showed that azelastine  
15 100 percent completely inhibited the  
16 histamine-reduced secretion, so that would mean it's  
17 working within an hour, but the onset curve whether  
18 it maxed -- reaches a maximum at 30 minutes or  
19 45 minutes or 20 minutes can't tell. Now, there are  
20 some studies after the fact, after the priority  
21 date, which are totally legitimate to look at if  
22 there's a claim by Dr. Carr that in the context of



1 Dymista® that azelastine works faster or that  
2 Dymista® works faster than azelastine. And, in  
3 fact, he attempts that risky and dangerous  
4 statement, but if you look at studies that were done  
5 afterwards where people actually went to the trouble  
6 to measure its effect over minutes, there are some  
7 subsequent studies, and I think we show those also,  
8 showing that it -- about 40 percent respond by  
9 15 minutes and 60 some-odd percent by 30 minutes.  
10 So the source of all the contention in this is  
11 simply that the FDA, getting back to the FDA and  
12 their rigor, they decided to say that Astelin works  
13 within three hours, and then Dr. Carr I believe  
14 misinterpreted that to mean that it only works at  
15 three hours. It takes three hours to work, despite  
16 the fact that everyone knew it worked at 15 and  
17 30 minutes, and everyone said it in guidelines and  
18 in papers, et cetera. So just since Dr. Carr is  
19 taking that position I thought it was necessary to  
20 demonstrate with data that both before and after the  
21 priority date very clear studies show that  
22 azelastine by itself works just as fast as Dymista®.

1 Q. Okay. But, again, just to be clear then,  
2 Greiff, saying it the right way.

3 A. Let's go with Greiff.

4 Q. You got me confused.

5 A. No, I'm agreeing with you. I think that's  
6 right.

7 Q. All right. So Greiff is being cited for  
8 the proposition of the 15-minute onset.

9 A. Onset -- complete onset by an hour, so less  
10 than an hour.

11 Q. Right.

12 A. Meaning in minutes.

13 Q. Okay. It was available when you filed --

14 A. Before the priority date, right.

15 Q. No, no, no. It was available when you  
16 filed your first declaration in this case?

17 A. What do you mean by "available"?

18 Q. You could have cited Greiff in your first  
19 declaration but you didn't.

20 A. I could have. I could have.

21 But, again, as I mentioned, I wasn't asked  
22 to opine to any extent about the secondary indicia,

1     so I didn't. I'm not going to -- other than in this  
2     proceeding maybe, I'm not going to give unasked for  
3     opinions.

4             Q.     Okay. Now, you mentioned these post  
5     invention studies that are mentioned on the very  
6     next page after Greiff.

7             A.     Yes.

8             Q.     This is Corren and Han are the two you're  
9     referring to?

10            A.     Yes.

11            Q.     This has been marked already as  
12     Exhibit 1160, and it is the -- this is the Corren  
13     article, 1160. And here comes 1148, which is the  
14     Han reference. There you are.

15                   And these are the two articles cited in  
16     paragraph 72 of your second declaration; is that  
17     right?

18            A.     Yes.

19            Q.     If you look top right of the Han article,  
20     1148, it wasn't even received by whoever published  
21     this until April 5, 2011, correct?

22            A.     That's right.

1           Q.    Nearly a decade after the date of  
2   invention.

3           A.    Yeah, but I think for this issue that's not  
4   important.  Because if there's a claim that the  
5   fundamental pharmacology is different for the  
6   combination in Dymista® than for the monotherapy,  
7   that should be -- should transcend a point in time.  
8   And so you all can argue about whether it's  
9   admissible, but I don't think azelastine has changed  
10   its rate of onset in monotherapy since 2002.  So in  
11   my view, since we're talking about a concrete fact  
12   that Dr. Carr I think is misstating, I should have  
13   the ability to correct that misstatement.

14          Q.    Go to the other article, Corren?

15          A.    Yes.

16          Q.    I'm going to ask you the same thing.  The  
17   date's actually on the second page.

18          A.    Same answer.

19          Q.    But the date is what?

20          A.    You said it's on the second page?  The date  
21   is accepted for publication April 8th, 2005, and  
22   publication date is November 5th, 2005.

1           Q.    So this is several years after the date it  
2   was mentioned?

3           A.    That's right.

4           Q.    So the simple thing I'm going to ask you  
5   is not whether or not you disagree with Dr. Carr.

6                   A person of ordinary skill in 2002 could  
7   not have known of these references, right?

8           A.    That is correct, unless they had a time  
9   machine.

10          Q.    And I don't think any POSA does.

11          A.    No. All you have to do is read the  
12   guidelines and all those other articles to know that  
13   it works in 15 minutes.

14          MR. MILLER: I'm thinking that I don't really  
15   have any more questions. Take like a five-minute  
16   break just to make sure I don't have anything else.  
17   Go back off the record.

18                   I don't have anything.

19          MR. HOUSTON: Yeah, let me take a minute and  
20   chat with Dr. Schleimer here.

21          MR. MILLER: I have no further questions at  
22   this time.

1 MR. HOUSTON: We'll take a short break to see  
2 if we need any redirect.

3 (Recess taken from 11:48 a.m. to  
4 11:56 a.m.)

5 CROSS-EXAMINATION

6 BY MR. HOUSTON:

7 Q. Dr. Schleimer, earlier this morning when  
8 you were being question, do you recall counsel  
9 asking you questions about whether or not the Segal  
10 and Cramer references -- those are Exhibits 1011 and  
11 1012 -- whether or not those references contain any  
12 clinical data?

13 A. I do.

14 Q. Do you have a copy of the '620 patent in  
15 front of you, Exhibit 1001?

16 A. Yes.

17 Q. Can you review the '620 patent and let me  
18 know whether or not the '620 patent contains any  
19 clinical data?

20 A. Sure.

21 So just like Segal and Cramer, they very  
22 generally talk about allergic disease and some of

1 the symptoms, et cetera, but I do not see any, as I  
2 said with Cramer and Segal, I do not see any  
3 original clinical data in this patent.

4 Q. In the '620 patent?

5 A. In the '620 patent, yes.

6 Q. Okay. Thank you. You can set that aside.

7 Could you find Exhibit 1031 in front of  
8 you, which should be I believe what we referred to  
9 as the Juniper article or maybe we call it Juniper  
10 '97?

11 A. Yes.

12 Q. You have that?

13 A. I do.

14 Q. If you flip to stamped page 7, you see  
15 Table 3 there?

16 A. Yes.

17 Q. And you recall being asked questions about  
18 at least one of the data points in that table that  
19 indicates that .13 tablets daily per patient --

20 A. Yes.

21 Q. -- of terfenadine --

22 A. Yes.

1 Q. -- were taken by the patients there?

2 Now keeping that in mind, I'd ask you to  
3 turn to stamped page 3?

4 A. Okay.

5 Q. And I point your attention to the  
6 right-hand column at the very top that has the  
7 heading Nasal Steroid Group. Do you see that?

8 A. Yes.

9 Q. Can you review that paragraph and  
10 determine when the patients in this study started  
11 taking a nasal steroid relative to the pollen  
12 season?

13 A. Yeah. This is what I was speculating at  
14 the time when I was talking about it, I thought I  
15 had remembered that this was a study that had a  
16 run-in period. And indeed it does. On the fourth  
17 line under the Nasal Steroid Group paragraph it says  
18 that one week before the start of ragweed season  
19 they had begun their fluticasone nasal spray, and  
20 based on my testimony throughout this, that about  
21 that window of time of a week or two at the most  
22 where the steroid is not acting at full strength, I



1 would expect -- I'm not surprised by the relative  
2 modest use of the addition of the antihistamine in  
3 the fluticasone group. And although they don't  
4 provide the data, as I mentioned in my answer to  
5 Mr. Miller, I would speculate that mostly they were  
6 adding antihistamine to the steroid only in the very  
7 beginning of the study. Once the steroid is working  
8 very well, they -- many of them may have seen less  
9 need.

10 So the fluticasone group only half of them  
11 use the terfenadine, whereas the terfenadine group,  
12 nearly all of them took the steroid. And that's  
13 because the steroid is so much more effective, but  
14 the additivity, as I've mentioned throughout this  
15 case, it's lost in a couple weeks, so I'm just  
16 guessing that those tablets that were taken would  
17 have been taken in the first week or two of the  
18 study.

19 Q. Dr. Schleimer, the fact that the -- as I  
20 think you reported the nasal steroid was started  
21 about a week before the start of the pollen season,  
22 is that meaningful one way or the other in terms of

1 the number of tablets that you would have expected  
2 to see reported, number of antihistamine tablets  
3 taken?

4 A. Well, yeah, it would mean before there was  
5 any allergen to drive symptoms the steroid had  
6 already had a week to gain nearly full effect. So  
7 since -- once the steroids are at full effect after  
8 two or three weeks the addition of the antihistamine  
9 is, as Nielsen said, marginal. There would have  
10 been less of a period of time when that was true in  
11 this study because they -- even before the pollen  
12 started coming into the air, they would have already  
13 had the steroid working quite well.

14 Q. Well, okay. Maybe I can ask you two  
15 hypotheticals just to make sure I'm clear what  
16 you're saying.

17 Let's just hypothetically say that the  
18 steroid had been started two weeks before the start  
19 of the pollen season.

20 Would you expect that to have led to more  
21 pills taken by the patients or less pills --  
22 antihistamine pills taken by the patient if they

1     started two weeks in advance?

2             A.     It's hard to speculate, but possibly  
3     slightly less.

4             Q.     Okay.  What about if the steroid treatment  
5     had been started just commensurate with the start of  
6     allergy season.  Do you have an expectation of  
7     whether that would have led to more or fewer pills?

8             A.     My expectation is it would have led to  
9     more, because as we've seen in the Drouin paper and  
10    the Simpson paper and some of the others, that first  
11    period of three or four days, and then later in the  
12    Ratner, Hampel and Carr study, that first period of  
13    a few days is when the steroid is working least well  
14    and the need for additional therapeutic intervention  
15    would have been most intense.

16            MR. HOUSTON:  Thank you, Dr. Schleimer.  No  
17    more questions for me.

18            MR. MILLER:  I have just one on cross.

19                               REDIRECT EXAMINATION

20    BY MR. MILLER;

21            Q.     So these hypotheticals, Dr. Schleimer --  
22    let's back up.

1                   Did you talk about the substance of your  
2   testimony with counsel before you came back in for  
3   redirect?

4           A.    He briefly asked me that question.

5           Q.    Did he give you any input into your  
6   answer?

7           A.    No.

8           Q.    Okay.

9           A.    He didn't.

10          Q.    Now you're talking about Juniper 1997, and  
11   it's your hypothetical or hypothesis rather --  
12   strike that.   Start that over.

13                   Talking about Juniper 1997, it's your  
14   hypothesis that if the antihistamine was affected by  
15   the timing of the steroid, the start of the steroid  
16   treatment and also your hypothesis that the  
17   antihistamine would have been used within the two  
18   week window you've talked about today, correct?

19          A.    Yeah, the latter part is speculation on my  
20   part.

21          Q.    Right.   And so there's nothing to say that  
22   that's actually true in this reference.

1           A.     Well, my guess is that Elizabeth still has  
2     the data, and it could actually possibly be tested  
3     to go back to Juniper who's in Canada now. I don't  
4     know if this was in Canada. Yeah, the French.

5                 But the data were not reported in the  
6     paper. So it is a -- thank you for calling it  
7     hypothesis as opposed to speculation.

8           Q.     I didn't want to accuse you. But yes,  
9     exactly, okay. That's all I have.

10                         (Ending time noted: 12:05 p.m.)

11                         (Signature reserved.)

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STATE OF ILLINOIS )  
 ) SS:

2 COUNTY OF COOK )

I, Cynthia J. Conforti, a notary public within and for the County of Cook and State of Illinois, do hereby certify that heretofore, to-wit, on the 30th day of March, 2018, personally appeared before me at Foley & Lardner LLP, 321 North Clark Street, Suite 2800, Chicago, Illinois, ROBERT P. SCHLEIMER, Ph.D., in a cause now pending and undetermined before the United States Patent and Trademark Office, Before the Patent Trial and Appeal Board, wherein Argentum Pharmaceuticals, LLC is the Petitioner, and Cipla, Ltd. is the Patent Owner.

I further certify that the said witness was first duly sworn to testify the truth, the whole truth and nothing but the truth in the cause aforesaid; that the testimony then given by said witness was reported stenographically by me in the presence of the said witness, and afterwards reduced to typewriting by Computer-Aided Transcription, and the foregoing is a true and correct transcript of the testimony so given by said witness as aforesaid.

13 I further certify that the signature to the  
foregoing deposition was not waived by counsel for  
14 the respective parties.

15 I further certify that I am not counsel for nor  
in any way related to the parties to this suit, nor  
am I in any way interested in the outcome thereof.

16           IN TESTIMONY WHEREOF:    I have hereunto set my  
hand and affixed my notarial seal this 3rd day of  
17   April, 2018.

18  
19 Cynthia J. Conforti  
20  
21

CSR License No. 084-003064

Cynthia J. Conforti, CSR, CRR

1 Robert P. Schleimer c/o

2 FOLEY & LARDNER LLP

3 321 North Clark Street, Suite 2800

4 Chicago, Illinois 60654-5313

5

6 Case: Argentum Pharmaceuticals LLC, v. Cipla, Ltd.

7 Date of deposition: March 30, 2018

8 Deponent: Robert P. Schleimer

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