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

ARGENTUM PHARMACEUTICALS, LLC,	)	
	)	
Petitioner,	)	
	)	
vs.	)	Patent No.
	)	8,168,620
CIPLA LTD.,	)	
	)	
Patent Owner.	)	
	)	

DEPOSITION OF HUGH DAVID CHARLES SMYTH, Ph. D. ,  
Washington, D. C.  
January 31, 2018

REPORTED BY: Tina Alfaro, RPR, CRR, RMR

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Deposition of HUGH DAVID CHARLES SMYTH,  
Ph.D., held at the offices of:

Sterne Kessler Goldstein Fox  
1100 New York Avenue, NW  
Washington, D.C. 20005

Taken pursuant to notice before Tina M.  
Alfaro, a Notary Public within and for the District  
of Columbia.

1                   A P P E A R A N C E S:

2

3                   ON BEHALF OF THE PETITIONER:

4                   FOLEY & LARDNER, LLP

5                   BY: ANDREW CHESLOCK, ESQ.

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7                   Washington, D.C. 20007

8                   (202) 945-6009

9

10                  ON BEHALF OF THE PATENT OWNER:

11                  STERNE KESSLER GOLDSTEIN FOX

12                  BY: UMA EVERETT, ESQ.

13                  ADAM LaROCK, ESQ.

14                  1100 New York Avenue, NW

15                  Washington, D.C. 20005

16                  (202) 371-2600

17

18                  ALSO PRESENT: Tyler Liu (Argentum)

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I N D E X

EXAMINATION

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1 (Witness sworn.)

2 WHEREUPON:

3 HUGH DAVID CHARLES SMYTH, Ph.D.,  
4 called as a witness herein, having been first duly  
5 sworn, was examined and testified as follows:

6 EXAMINATION

7 BY MR. CHESLOCK:

8 Q. Good morning, Dr. Smyth. If you could  
9 please state your full name for the record.

10 A. Hugh David Charles Smyth.

11 Q. Have you been deposed before?

12 A. Yes.

13 Q. Okay. How many times have you been  
14 deposed before?

15 A. Maybe six, seven, eight, something like  
16 that.

17 Q. And have those depositions all been for  
18 patent matters?

19 A. Yes.

20 Q. And all those patent matters, were those  
21 all relating to pharmaceutical formulation  
22 technologies?

1           A.   Yes.

2           Q.   So you're familiar with the general ground  
3           rules of a deposition, right?

4           A.   I think so, yes.

5           Q.   So just to reiterate, as you can see, we  
6           have a court reporter. I'm going to pose questions  
7           to you, you're going to answer. Your counsel may  
8           interject an objection to form. So what I'd like  
9           to ask you to do is make sure that you allow all of  
10          those sequences to happen, give time so those  
11          questions can be asked, your answers can be given,  
12          and your counsel's objections may be given.

13          Also throughout the day I may ask  
14          questions that call for a yes or no answer. So I'd  
15          like you to enunciate your answer instead of simply  
16          nodding your head so the court reporter can take  
17          that down.

18          A.   Yes.

19          Q.   Is there any reason why you can't provide  
20          truthful testimony today, no medical conditions or  
21          any medicines that you're taking that would prevent  
22          that from happening?

1           A.   No.

2           Q.   And you understand you're here today to  
3   give truthful testimony?

4           A.   That's right.

5           Q.   I'm going to provide to you, Dr. Smyth,  
6   Petitioner's notice of deposition. Have you seen  
7   this document before?

8           A.   I don't think so.

9           Q.   Okay. But as I asked you before, you  
10   understand that you're here in connection with  
11   certain declarations that you've submitted in the  
12   proceeding here and that you're here to offer  
13   testimony in connection with those submissions,  
14   right?

15          A.   Yes.

16          Q.   What did you do to prepare for the  
17   deposition today?

18          A.   I read through my declarations, looked  
19   through some of the prior art references. That's  
20   pretty much it.

21          Q.   Did you have any meetings in connection  
22   with your preparation efforts?



1           A. I had a meeting with -- with the Sterne  
2           Kessler attorneys yesterday.

3           Q. Any other meetings besides that meeting  
4           yesterday?

5           A. No.

6           Q. So earlier you testified that you've given  
7           approximately six depositions in connection with  
8           patent matters; is that right?

9           A. Yeah. I can't remember the exact number,  
10          but somewhere around there.

11          Q. Approximately six is a fair number, right?

12          A. Sure.

13          Q. So what is your familiarity with patents  
14          in general?

15                 MS. EVERETT: Objection, form.

16          BY THE WITNESS:

17          A. I'm an inventor on patents, I've read  
18          patents, and I've been involved in patent  
19          litigation. So some understanding of patents I  
20          guess.

21          Q. Okay. So you mentioned you've been an  
22          inventor on patents. How many patents on which --

1       sorry. Let me try that again.

2               You mentioned that you're an inventor  
3       that's listed on patents. How many patents are you  
4       listed as an inventor on?

5               A. On issued patents probably 12 to 15.

6               Q. And have you been responsible for drafting  
7       any portion of those 12 to 15 patents?

8               A. In some cases, you know, we provide the  
9       law firm, you know, sort of a writeup of  
10      experimental work and findings and they sort of  
11      convert that into patent form.

12              Q. And so in connection with the 12 to 15  
13      patents on which you're listed as an inventor do  
14      you have an understanding of independent claims?

15              A. Yes.

16              Q. And do you also have an understanding of  
17      dependent claims?

18              A. I think I do.

19              Q. And would it be fair to say that your  
20      understanding is that a dependent claim contains  
21      all the limitations of the claim from which it  
22      depends?

1           A. A dependent claim would be narrower than  
2           the independent claim.

3           Q. And the dependent claim would be within  
4           the scope of the independent claim, correct?

5           MS. EVERETT: Objection, form.

6           BY MR. CHESLOCK:

7           Q. Let me try that differently. And so what  
8           would be stated in a dependent claim would come  
9           within the scope of an independent claim?

10          MS. EVERETT: Objection, form.

11          BY THE WITNESS:

12          A. A dependent claim would have the elements  
13          of the independent claim in addition to other  
14          requirements, if that's kind of what you're saying,  
15          within the scope.

16          Q. Dr. Smyth, I will now hand to you what has  
17          previously been marked as Petitioner's  
18          Exhibit 1001. Do you recognize Petitioner's  
19          Exhibit 1001?

20          A. I recognize this as the '620 Patent, yes.

21          Q. Okay. And you've mentioned that you  
22          recognize Exhibit — Petitioner's Exhibit 1001 as

1 the '620 Patent. So are you comfortable throughout  
2 the deposition today if we refer to it as such?

3 A. As the '620, yes, that sounds good.

4 Q. Sounds good.

5 If you would, please, Dr. Smyth, in the  
6 '620 Patent can you advance to column 11 and let me  
7 know when you're there.

8 A. Okay. I'm there.

9 Q. So we had a discussion just now about the  
10 understanding you have of independent and dependent  
11 claims; do you remember that?

12 A. Yes.

13 Q. So looking in column 11, claim 1, that  
14 would be an independent claim, right?

15 A. That is right.

16 Q. And claim 2 would be a dependent claim,  
17 right?

18 A. Claim 2 is dependent on claim 1.

19 Q. Right. And your understanding is that a  
20 dependent claim contains all the limitations of the  
21 claim from which it depends. In this case claim 2  
22 contains all the limitations of claim 1?

1           A. Claim 2 contains all the limitations of  
2 claim 1, yes.

3           Q. And claim 2 as a dependent claim can't be  
4 broader than its independent claim 1, right?

5           A. That's at least my understanding.

6           Q. In addition to -- there will be a few  
7 times during the deposition today where I will  
8 clarify the language that we're going to use, but  
9 one of the things I'll say is "person of ordinary  
10 skill." My understanding is you have an  
11 understanding of what that term means. So you're  
12 comfortable with us using that term today, right?

13          A. Sure.

14          Q. I will now provide to you, Dr. Smyth,  
15 what's been previously labeled as Patent Owner's  
16 Exhibit 2150. Do you recognize Patent Owner's  
17 Exhibit 2150?

18          A. Yes.

19          Q. And what is Patent Owner's Exhibit 2150?

20          A. The second declaration of myself.

21          Q. And, again, another terminology item. You  
22 mentioned earlier that you in preparation for your

1 deposition reviewed your declarations, plural,  
2 right?

3 A. Yes.

4 Q. So there's a first Dr. Smyth declaration  
5 and there's a second Dr. Smyth declaration in this  
6 proceeding, right?

7 A. That's my understanding, yes.

8 Q. So for purposes of clarity today, are you  
9 comfortable if I refer to Patent Owner's  
10 Exhibit 2150 as your declaration?

11 A. Sure. I'll try and keep that in mind.

12 Q. Would it be simpler if I refer to it as  
13 the second declaration?

14 A. That would be good.

15 Q. That would be better?

16 A. Yeah.

17 Q. Okay.

18 If you could please look again at the  
19 '620 Patent and in particular claim 1. You would  
20 agree with me that claim 1 generally claims a  
21 combination of azelastine and fluticasone, right?

22 MS. EVERETT: Objection to form.

1 BY THE WITNESS:

2 A. It claims azelastine, its pharmaceutically  
3 acceptable salt fluticasone, a pharmaceutically  
4 acceptable ester of that, where in the  
5 formulation -- pharmaceutical formulation suitable  
6 for nasal administration.

7 Q. Okay. So just generally, I'm just asking  
8 generally, would you understand claim 1 in addition  
9 to its particular claim language to be a  
10 combination of azelastine and fluticasone?

11 A. It has those two elements in it, yes, in  
12 addition to others.

13 Q. Okay. Let's look, please, at column 13 of  
14 the '620 Patent, please. You see claim 24 there?  
15 That's an independent claim at issue in this  
16 proceeding, right?

17 A. Yes, that looks like an independent claim.

18 Q. And similar to claim 1, appreciating the  
19 claim language itself, it's also generally a  
20 combination of azelastine and fluticasone, right?

21 A. It contains an element of azelastine  
22 hydrochloride and fluticasone propionate in

1 addition to other language.

2 Q. And here in claim 24 the azelastine is  
3 claimed as an azelastine hydrochloride, correct?

4 A. Yes.

5 Q. So azelastine in the context of  
6 independent claims 24 and 1 is a hydrochloride  
7 salt, correct?

8 A. For azelastine it's a hydrochloride form  
9 of that drug, yes.

10 Q. For purposes of both independent claim 24  
11 and independent claim 1, right?

12 A. So claim 1 does not specify whether it's a  
13 hydrochloride salt.

14 Q. But claim 1 does specify that it's a  
15 pharmaceutically acceptable salt?

16 A. It does say that, yes.

17 Q. Of the azelastine, right?

18 A. Yes.

19 Q. I'd now like you to look at your second  
20 declaration while you also have the '620 Patent  
21 out, if you could, please, and in particular I'd  
22 like you to look at paragraph 47 that starts on



1 page 29. Here in paragraph 27 you explain that  
2 azelastine as a hydrochloride salt will  
3 disassociate into its cationic and anionic portions  
4 when dissolved in an aqueous solution, right?

5 A. So in 47 I say that a POSA would have  
6 understood that azelastine was a cationic drug; in  
7 a pharmaceutical aqueous solution the tertiary  
8 amine of azelastine will get a positive charge;  
9 azelastine salt will disassociate into cationic and  
10 anionic portions when dissolved; a POSA would have  
11 known that azelastine would have behaved like a  
12 cationic drug.

13 Q. So what you're saying here in that portion  
14 of paragraph 47 that you read starting with "In a  
15 pharmaceutical aqueous solution" is that azelastine  
16 as a hydrochloride salt will disassociate into its  
17 cationic and anionic portions when dissolved in an  
18 aqueous solution, right, when dissolved in water?

19 A. In a pharmaceutical aqueous solution.

20 Q. And that basically means dissolving into  
21 water, right?

22 A. It would be a situation where the pH would

1 be, you know, pharmaceutically relevant.

2 Q. So as you state here in paragraph 47, a  
3 portion of which you read, that azelastine as a  
4 hydrochloride salt will behave as a cationic drug  
5 and produce electrolytes, right, when dissolved?

6 A. Yes, in a pharmaceutical aqueous solution.

7 Q. And that's typical of hydrochloride salts,  
8 right?

9 A. It can be.

10 Q. And when you say "can be," is it typical  
11 of pharmaceutical hydrochloride salts?

12 A. If they're soluble.

13 Q. There are many such hydrochloride salts  
14 that are used in pharmaceuticals, right?

15 A. Can you clarify the question?

16 Q. So hydrochloride salts are used in  
17 pharmaceutical aqueous solutions in a variety of  
18 different products, right?

19 A. Yes. So you would have many different  
20 types of active pharmaceutical ingredients that may  
21 be synthesized as a hydrochloride salt.

22 Q. So an example of that would be like

1       tetracycline hydrochloride?

2           A.   I'm not sure about tetracycline, but maybe  
3       there's a hydrochloride salt.

4           Q.   And with respect to those hydrochloride  
5       salts, are pharmaceutical compounds intentionally  
6       designed to be salts so they will dissolve and  
7       disassociate into water?

8           MS. EVERETT:  Objection to form.

9       BY THE WITNESS:

10          A.   They're designed for many aspects.  Could  
11       be stability, solubility, bioavailability,  
12       depending on the physicochemical characteristics of  
13       the drug different salt forms will be synthesized  
14       or made into a free base form.  Depends, you know,  
15       essentially on the desired outcome.

16          Q.   But with respect to at least hydrochloride  
17       salts that are used in pharmaceuticals, they're  
18       intentionally designed that way to be salts at  
19       least in one respect so that they will dissolve and  
20       disassociate into water?

21          MS. EVERETT:  Objection to form.

22       BY THE WITNESS:

1           A. That may be the case for some  
2       hydrochloride salts. It could be the case that  
3       it's not for other hydrochloride salts.

4           Q. So there's at least a class of  
5       pharmaceutical hydrochloride salts that are  
6       designed specifically to be salts so they'll  
7       dissolve and disassociate into water?

8           A. That's probably a fair statement. Some  
9       hydrochloride salts are designed for solubility.

10          Q. So for that grouping of hydrochloride  
11       salts that are designed for solubility as you just  
12       testified the general expectation of a person of  
13       ordinary skill in the art is that when such a  
14       hydrochloride salt version of a given  
15       pharmaceutical compound is dissolved into water it  
16       will disassociate into its cationic and anionic  
17       portions, right?

18               MS. EVERETT: Objection, form.

19       BY THE WITNESS:

20           A. One aspect of solubility is disassociation  
21       of salts. So if it was designed so that you had a  
22       salt form that had suitable solubility in an

1       aqueous environment, then you would expect it to be  
2       disassociating into ionic forms.

3           Q.   Are you familiar with pseudoephedrine  
4       hydrochloride?

5           A.   I've heard of pseudoephedrine  
6       hydrochloride.

7           Q.   And you're aware that pseudoephedrine is  
8       at times formulated as a hydrochloride salt for  
9       solubility, right?

10          MS. EVERETT:  Objection to form.

11       BY THE WITNESS:

12          A.   I haven't really looked into that, but  
13       that's a potential.

14          Q.   So as an expert in pharmaceutical  
15       formulations you're saying that you do not have any  
16       knowledge of whether or not pseudoephedrine is  
17       formulated at times as a hydrochloride salt?

18          A.   Yeah.  I would need to look that up.  I  
19       can't remember if pseudoephedrine is predominantly  
20       a hydrochloride salt.  It's not one that I've  
21       studied in my lab.

22          Q.   How about tetracycline hydrochloride, are

1       you familiar with that?

2           A. Same thing. It's not something that I  
3       have looked into recently or can really remember to  
4       give you accurate testimony on.

5           Q. But you are aware that there are other  
6       active ingredients -- sorry. Let me try that  
7       again.

8           As you testified earlier, you're aware  
9       that there are other drug active ingredients that  
10      are formulated as hydrochloride salts for  
11      solubility, right?

12          A. Yes. There will be a number of active  
13      pharmaceutical ingredients with hydrochloride  
14      salts.

15          Q. Can you give me an example besides  
16      azelastine hydrochloride?

17           MS. EVERETT: Objection, form.

18      BY THE WITNESS:

19          A. I think one is cyprofloxacin  
20      hydrochloride.

21          Q. So cyprofloxacin hydrochloride?

22          A. cyprofloxacin.

1 Q. Oh, cyprofloxacin hydrochloride?

2 A. Yes.

3 Q. And similar to azelastine hydrochloride,  
4 you would expect cyprofloxacin hydrochloride to  
5 disassociate into its cationic and anionic portions  
6 when dissolved in water right?

7 MS. EVERETT: Objection to form.

8 BY THE WITNESS:

9 A. Cyprofloxacin does have aqueous solubility  
10 and disassociate into different ionic forms.

11 Q. And will likewise produce electrolytes  
12 when dissolved?

13 A. It will produce an electrolyte  
14 concentration in a solution when dissolved, yes.

15 Q. And with respect to that dissolving  
16 process, hydrochloride salts lead to what would be  
17 referred to as monovalent anions and cations,  
18 correct?

19 A. It can't be monovalent. It may be  
20 bivalent, trivalent. I actually don't know the  
21 valency of those cations.

22 Q. What about with respect to azelastine

1 hydrochloride specifically, are you aware that when  
2 it's dissolved in water that it gives a monovalent  
3 cation?

4 A. I haven't studied the valency of  
5 azelastine, but it could be monovalent, bivalent,  
6 maybe even trivalent.

7 Q. Dr. Smyth, I'll now hand you what was  
8 previously designated Patent Owner's  
9 Exhibit 2113. I will also hand to you what was  
10 previously labeled Patent Owner's Exhibit 2104.

11 So focusing first on Patent Owner's  
12 Exhibit 2113, what is that exhibit?

13 A. The front page indicates that it's the  
14 Lieberman textbook "Pharmaceutical Dosage Forms:  
15 Disperse Systems, Volume 2," and it is chapter 5,  
16 "Topical Suspensions."

17 Q. And this Exhibit 2113 is a document that  
18 you rely upon in your second declaration and  
19 references; is that right?

20 A. I think it is, yes.

21 Q. The exhibit copy that I gave you, that's a  
22 full copy of what Patent Owner's have submitted in



1       this proceeding?

2           A.   I presume so.

3           Q.   Do you have any reason to doubt that's not  
4       the case?

5           A.   No, I don't suppose I do, but you never  
6       know.

7           Q.   Let's look at Patent Owner's Exhibit 2104,  
8       which is the other one I gave you. Do you  
9       recognize that exhibit?

10          A.   Yes. This is the same textbook by  
11       Lieberman as the other exhibit, and this is chapter  
12       4, "Oral Aqueous Suspensions."

13          Q.   And similar to the other exhibit, you  
14       don't have any reason to believe that this isn't a  
15       complete copy of the exhibit that was submitted by  
16       Patent Owner?

17          A.   Sure.

18          Q.   And similar to Patent Owner's  
19       Exhibit 2113, you rely on Patent Owner's  
20       Exhibit 2104 and reference it in your second  
21       declaration?

22          A.   Yeah, I think I do.

1           Q. And your testimony was that Patent Owner's  
2 Exhibit 2104 is chapter 4 of a reference edited by  
3 or authored by Lieberman and Exhibit 2113 is  
4 chapter 5 of the same reference; isn't that right?

5           MS. EVERETT: Objection, form.

6 BY THE WITNESS:

7           A. I think these are two chapters out of the  
8 same textbook, yes.

9           Q. So similar to some of the other wording  
10 issues that we discussed before, are you  
11 comfortable if we refer to, as a whole, these two  
12 together as the Lieberman reference?

13          A. That's fair.

14          Q. And I'll direct you to any particular  
15 pages in each of the two respective exhibits.  
16 Okay?

17          A. Sure.

18          Q. So just now I asked you whether or not  
19 azelastine as a hydrochloride salt when dissolved  
20 into water gives a monovalent cation and you said  
21 you don't know?

22          A. I would suspect that it would have some

1       monovalence, maybe some bivalence, some trivalence.

2           Q.   I believe what you testified to was "I  
3       haven't studied the valency of azelastine, but it  
4       could be monovalent or it could be trivalent" isn't  
5       that right? So you haven't studied it, correct?

6           A.   I have looked at the structure of  
7       azelastine. I haven't experimentally determined  
8       its valency.

9           Q.   So it's fair to say you don't know the  
10      answer to that question?

11          A.   I can't speculate on that.

12          Q.   So any information you would have with  
13      respect to whether or not azelastine as  
14      a hydrochloride -- so it would be fair to say that  
15      any information you have sitting here in your  
16      deposition today and also in connection with when  
17      you prepared your second declaration about whether  
18      or not azelastine as a hydrochloride salt would  
19      give a monovalent anion when dissolved in water is  
20      based on speculation?

21           MS. EVERETT: Objection to form.

22      BY THE WITNESS:

1           A. It would be my expert opinion based on the  
2 chemical structure that azelastine has several  
3 tertiary amines, which I talk about in my report,  
4 which would give rise to the cationic nature of the  
5 drug molecule in solution.

6           Q. But based on the fact that you haven't  
7 studied, as you previously testified, with respect  
8 to the valency of cations that azelastine  
9 hydrochloride would give during dissolving in  
10 water, that would be based on speculation, right?

11           MS. EVERETT: Objection to form.

12 BY THE WITNESS:

13           A. No. It would be based on my understanding  
14 of disassociation and protonation of amines in  
15 solution.

16           Q. But even based on that general  
17 understanding, you don't know for sure what type of  
18 cations azelastine hydrochloride gives when  
19 dissolved in water, right?

20           MS. EVERETT: Objection to form.

21 BY THE WITNESS:

22           A. To definitively know what valency of the

1 cations or distribution of the valency one would  
2 need to actually experimentally do a titration to  
3 determine that.

4 Q. And you've never done that?

5 A. I have not done a titration on azelastine  
6 hydrochloride in solution.

7 Q. If you could take the 2113 exhibit from  
8 the Lieberman reference and go to page -- Bates-  
9 labeled page at the bottom 24.

10 A. 24.

11 Q. And just in general before we get into the  
12 reference and your declaration, microcrystalline  
13 cellulose is commonly referred to as MCC, right?

14 A. Yes.

15 Q. And similar to some of the other areas  
16 that we've been through today, would you be  
17 comfortable referring to microcrystalline cellulose  
18 as MCC during the deposition?

19 A. That's fine.

20 Q. And similarly, sodium carboxymethyl  
21 cellulose is commonly referred to as CMCC, right?

22 A. CMC, yes.

1           Q. And you're comfortable if we use that term  
2 during the deposition today?

3           A. That's fine.

4           Q. And if you could while you have the 2113  
5 Lieberman exhibit in front of you also take out  
6 your declaration and in particular go to paragraph  
7 45. Do you have those in front of you now?

8           A. Yes.

9           Q. So it's your understanding that Petitioner  
10 in this proceeding advances that a person of  
11 ordinary skill would have used MCC and CMCC as the  
12 thickening agent for an azelastine fluticasone  
13 combination formulation, right?

14          A. Can you say that again? Sorry.

15          Q. Sure. So it's your understanding, which  
16 is also stated in paragraph 45, that Petitioner in  
17 this proceeding is advancing that a person of  
18 ordinary skill would have used MCC and CMC as the  
19 thickening agent for an azelastine fluticasone  
20 combination formulation, right?

21          A. So some of that language I'm not clear on.  
22 So the Petitioner, who is that?

1 Q. That's Argentum Pharmaceuticals.

2 A. Okay. And then "advancing"?

3 Q. Okay. I'll change it a little bit. Just  
4 to be clear, Petitioner, Argentum, is arguing that  
5 one of skill in the art would have used MCC and CMC  
6 as the thickening agent for an azelastine  
7 fluticasone combination, right?

8 A. My opinion was -- in 45 I think you're  
9 referring to that where Argentum asserts a POSA  
10 would have used MCC and CMC as a thickening agent  
11 for an azelastine fluticasone combination  
12 formulation.

13 Q. And it's your opinion, again, stated there  
14 in paragraph 45, that certain references in the art  
15 would have discouraged a person of ordinary skill  
16 from using MCC and CMC with the azelastine portion  
17 of that combination, right?

18 A. Yes.

19 Q. And in order to support that opinion you  
20 refer to the Lieberman reference, right?

21 A. Yes.

22 Q. And in particular you refer to a statement

1       which is more fully reproduced not in your opinion,  
2       but in the Lieberman Exhibit 2133 reference that  
3       states "Carboxymeth" -- and this is -- to direct  
4       your attention to where I'm reading, firstly, the  
5       statement from the 2133 -- 2113 Lieberman reference  
6       is halfway down paragraph 46. Do you see where it  
7       starts with "Carboxymethyl cellulose solutions"?

8           A. Yes.

9           Q. Now, if you could look to the Lieberman  
10       2113 reference and do you see in the fourth  
11       paragraph down the same sentence starts with  
12       "Carboxymethyl cellulose solutions"?

13          A. I see that paragraph.

14          Q. And that paragraph is present under a  
15       subsection A that's entitled "Sodium carboxymethyl  
16       cellulose," right?

17          A. That is correct.

18          Q. And that's the same CMCC that we've been  
19       talking about, right?

20          A. Yes. CMC.

21          Q. CMC. You would agree with me that the  
22       sentence from Lieberman Exhibit 2113 is not fully



1 reproduced in your opinion, paragraph 46, correct?

2 A. In 46 I have pulled out the elements that  
3 "Carboxymethyl cellulose solutions have poor  
4 tolerance for electrolytes as they precipitate the  
5 polymer," and "CMC is compatible with other  
6 nonionic cellulose derivatives, clays, and commonly  
7 into preservatives but is incompatible with  
8 cationic drugs." It doesn't state this whole  
9 paragraph 4 from Lieberman.

10 Q. Right. So you would agree with me that  
11 the portion that's missing is the part that states  
12 "Especially di- and trivalent cations," correct?

13 A. That's not in my report, "Especially  
14 divalent -- di- and trivalent cations as they  
15 precipitate the polymer."

16 Q. And the incompatibility of CMC with  
17 electrolytes of the type especially di- and  
18 trivalent cations would be important in terms of  
19 the understanding of what one of skill in the art  
20 would take away from this sentence, right?

21 MS. EVERETT: Objection to form.

22 BY THE WITNESS:

1           A. So that's electrolytes, but further down  
2           in that paragraph it explicitly says "But is  
3           incompatible with cationic drugs," which is in my  
4           report which is really the key thing here with  
5           azelastine.

6           Q. You would agree with me that azelastine is  
7           not explicitly stated in Lieberman Exhibit 2113,  
8           correct?

9           A. Lieberman does not make mention of any  
10          specific drugs or azelastine in that paragraph.

11          Q. And then focusing in again on the first  
12          sentence of paragraph 4 under subsection A on page  
13          24 of Lieberman 2113, its highlighting of the di-  
14          and trivalent electrons would suggest to a person  
15          of ordinary skill that the main problems with CMC  
16          involve multivalent cations, right?

17               MS. EVERETT: Objection to form.

18          BY THE WITNESS:

19          A. I don't read it that way. It says  
20          especially divalent, trivalent cations, the polymer  
21          is going to have poor tolerance for them  
22          especially, but it also says it's incompatible with

1 cationic drugs.

2 Q. If you could please take out the other  
3 Lieberman reference, which is Exhibit 2104, and let  
4 me know when you have it.

5 A. I'm there.

6 Q. Okay. Can you advance to the Bates label  
7 at the bottom to page 19.

8 A. Okay.

9 Q. And if you look at paragraph 46 of your  
10 declaration, you would agree with me that you cite  
11 this page 19 of the Lieberman 2104 reference in the  
12 third-to-last sentence, correct?

13 MS. EVERETT: Objection, form.

14 BY THE WITNESS:

15 A. In the third-to-last sentence? At the end  
16 of paragraph 46 --

17 Q. The second-to-last sentence.

18 A. Yes.

19 Q. This Exhibit 2104, specifically page 19 is  
20 cited there?

21 A. Yes.

22 Q. But there's no quotation from Lieberman --

1       there's no quotation in your paragraph 46 in your  
2       second declaration to any text from Lieberman  
3       Exhibit 2104 at page 19, right?

4           A.   Essentially it says the same thing in  
5       Lieberman on that page 19 where it says "Because it  
6       is anionic it is usually incompatible with cationic  
7       drugs," which is essentially what is the same  
8       statement in the quote above.

9           Q.   Well, is it true that the statement we  
10      just focused on on page 19 of Exhibit 2104 uses the  
11      term "usually," correct?

12          A.   It does use that word, yes.

13          Q.   And the plain language meaning of  
14      "usually" means not always, right?

15           MS. EVERETT:  Objection to form.

16      BY THE WITNESS:

17          A.   Or most often.

18          Q.   Or in another manner of speaking, not  
19      always?

20           MS. EVERETT:  Objection to form.

21      BY THE WITNESS:

22          A.   There are always exceptions to certain

1 things in pharmaceutical formulations.

2 Q. And this sentence is speaking by using the  
3 word "usually" to those potential exceptions,  
4 correct?

5 MS. EVERETT: Objection to form.

6 BY THE WITNESS:

7 A. I think it's warning the reader that this  
8 polymer, it's anionic. So it's going to be  
9 incompatible with cationic drugs.

10 Q. But as you just testified, there are  
11 always exceptions, right?

12 A. There are often exceptions to those, yes.

13 Q. So a person of ordinary skill focusing on  
14 the statement that we've been focused on in  
15 Lieberman 2104 at page 19 wouldn't understand  
16 Lieberman to say that CMC will never work with  
17 cationic drugs, right?

18 A. They would understand it's usually  
19 incompatible with cationic drugs. Actually in the  
20 same reference on page 11, for example, where it  
21 talks about chemical incompatibilities, you know,  
22 it says with similar language sodium carboxymethyl

1 cellulose will usually precipitate with cationic  
2 molecules. So it's just something that would have  
3 been expected to happen.

4 Q. And can you help me out on page 11 where  
5 you're referring to, Dr. Smyth?

6 A. Down at the bottom there it says "F,  
7 Chemical incompatibilities" and it would be the  
8 second sentence.

9 Q. That sentence uses "usually" as well,  
10 doesn't it?

11 A. "Usually" precipitates with cationic  
12 molecules.

13 Q. And that doesn't mean always?

14 A. Usually does not mean always.

15 Q. Right. So including this statement that  
16 you've additionally identified on page 11 of  
17 Lieberman 2104, a person of ordinary skill reading  
18 either of the statements on page 11 or 19 wouldn't  
19 understand Lieberman to be saying that CMC will  
20 never work with cationic drugs, right?

21 MS. EVERETT: Objection to form.

22 BY THE WITNESS:

1           A. What it's saying is that, you know, the  
2       reader should use caution that this is an anionic  
3       polymer and it's usually incompatible with cationic  
4       drugs.

5           Q. Right. And as you've testified, I have it  
6       here in front of me, usually does not mean always?

7           A. It does not mean always, but it means most  
8       often.

9           Q. But there are exceptions, right?

10          A. There could be exceptions.

11          Q. And the two sentences that you've  
12       identified in Exhibit 2104, Lieberman chapter 4 on  
13       both 11 and 19, they use the word "usually,"  
14       correct?

15          A. They do.

16          Q. So if there are exceptions and it doesn't  
17       always mean always, meaning the word "usually," the  
18       person of ordinary skill wouldn't understand  
19       Lieberman to be saying that CMC will never work  
20       with cationic drugs, right? That's a fair  
21       understanding of what's being said there?

22               MS. EVERETT: Objection to form.

1 BY THE WITNESS:

2 A. I think a person reading this document  
3 would understand that in most cases -- not always,  
4 but in most cases carboxymethyl cellulose is  
5 incompatible with cationic drugs and electrolytes.

6 Q. Okay. So there are potentially  
7 exceptions, not always?

8 A. I agree with that.

9 Q. Beyond the Lieberman reference that we've  
10 been treating together in terms of Patent Owner's  
11 Exhibit 2113 and Patent Owner's Exhibit 2104, did  
12 you consider any other references besides the  
13 Lieberman reference for your opinion in paragraph  
14 45 of your second declaration that a person of  
15 ordinary skill would have been discouraged from  
16 using MCC and CMC with azelastine?

17 A. You know, Lieberman is one of these  
18 authoritative textbooks that's sort of well known  
19 in the field and people rely upon it. I think  
20 that's the only one that I've cited here. So it's  
21 the only one that I've turned to.

22 Q. Okay. So your analysis of the



1 incompatibility of azelastine with CMC started with  
2 and ended with the Lieberman text; is that fair?

3 MS. EVERETT: Objection to form.

4 BY THE WITNESS:

5 A. Well, my own knowledge of formulating with  
6 CMC, obviously experience with that as well.

7 Q. But you didn't look to any other  
8 references, correct?

9 A. Not that I can recall. Essentially all  
10 I'm citing here is Lieberman as far as these  
11 numbers indicate.

12 Q. Well, just to confirm, you can actually  
13 take your time and look at paragraphs 45 through 49  
14 to see if you find any other references that you  
15 may have looked to besides the Lieberman text.

16 (Witness reviewing document.)

17 BY THE WITNESS:

18 A. I guess in CIP-2061.

19 Q. Just for clarity of the record, CIP-2061  
20 is the -- is a lab notebook, right?

21 A. That is correct.

22 Q. And that's not a well understood and used

1 text as you characterize Lieberman, right?

2 A. It's not a textbook, no, but it does  
3 provide sort of additional evidence of potential  
4 incompatibility.

5 Q. But it's not a reference in the sense that  
6 it's a peer reviewed reference such as Lieberman,  
7 right?

8 A. No. The notebook is not publicly  
9 available. It could be peer reviewed.

10 Q. But you don't have any information that  
11 that 2061 lab notebook was peer reviewed, correct?

12 A. Generally lab notebooks are countersigned  
13 so they have to be reviewed by another scientist,  
14 but I can't remember if that one was countersigned.

15 Q. In looking through the balance of those  
16 paragraphs, Lieberman is the only publicly  
17 available peer reviewed reference that you relied  
18 upon to form your opinions about the  
19 incompatibility of azelastine with CMC, right?

20 A. That's the only reference that was  
21 publicly available that I have cited there, yes.

22 Q. And you didn't look for anything beyond

1       Lieberman of that form in order to formulate your  
2       opinion as to the incompatibility of CMC with  
3       azelastine, right?

4               MS. EVERETT: Objection to form.

5       BY THE WITNESS:

6               A. As I said before, Lieberman is, you know,  
7       one of these sort of well-known, well-accepted  
8       textbooks that in multiple places in Lieberman  
9       states essentially, you know, that CMC is  
10      incompatible with electrolytes and cationic drugs.  
11      That was a known fact, it still is today. There  
12      was no need to provide many additional references.

13              Q. If you could, I think you have one of the  
14      Lieberman references in front of you, would you  
15      look at Lieberman -- which one is in front of you?

16              A. The 2104.

17              Q. Okay. If you look at Bates-numbered page  
18      3, you would agree with me that Lieberman was  
19      published in 1996, correct?

20              A. Yes. It has a copyright 1996.

21              Q. And the time frame for addressing  
22      patentability of the claims in the '620 Patent

1 includes up to 2002 generally, right?

2 A. The prior date is somewhere around June of  
3 2002 I think.

4 Q. So in view of the fact that you didn't  
5 look for any of these other references, if there  
6 are any other references that contradict what  
7 Lieberman says about compatibility of MCC and CMC  
8 with cationic drugs, would you be willing to  
9 revisit your opinion about that compatibility  
10 between azelastine as a cationic drug and CMC and  
11 MCC?

12 A. What I think a person of ordinary skill  
13 would have known is what is -- would have read is  
14 what's known and described in Lieberman. That's a  
15 very well-known interaction between these anionic  
16 polymers that you should avoid cationic drugs and  
17 usually they precipitate. There may be other  
18 reports of specific individual drugs that may have  
19 been successfully formulated in different types of  
20 formulations, maybe for different therapeutic  
21 purposes, but that wouldn't change my opinion that  
22 a person of ordinary skill would have been

1 discouraged from using a thickening agent like CMC  
2 because of this interaction with cationic drugs.

3 Q. So as you just testified, there may be  
4 reports of other specific individual drugs that may  
5 have been successfully formulated in different  
6 types of formulations for different therapeutic  
7 purposes, right? That's your testimony?

8 A. That's what I said, yes.

9 Q. So in your expert opinion it doesn't  
10 matter what other teachings are out there in the  
11 prior art, including those that you've just  
12 indicated may exist, you're just going to stick  
13 with your opinion that a person of ordinary skill  
14 would have been discouraged from using MCC and CMC  
15 with azelastine focusing on Lieberman?

16 MS. EVERETT: Objection to form.

17 BY THE WITNESS:

18 A. So in some cases a gel -- rigid gel may be  
19 sought where cross-linking of the polymer is  
20 actually a positive thing because you don't want  
21 this -- you know, this gel that may be orally taken  
22 to disintegrate because it would encapsulate the

1 drug. So in some cases you need a cationic  
2 cross-linker for an anionic polymer. That would be  
3 one example where CMC could be used with a cationic  
4 cross-linking agent. So that's a very different  
5 case to a nasal spray that's suitably -- you know,  
6 for suitable administration to the nasal passages,  
7 the viscosity and osmolarity, and the like. So  
8 there might be cases where you can find a cationic  
9 drug with an anionic polymer, but that's different  
10 to what I'm saying here.

11 Q. Okay. So let's just take the case that  
12 we're talking about a situation where the cationic  
13 drug is being dissolved as a hydrochloride salt and  
14 there's another active ingredient that's being  
15 suspended with the assistance of CMC and MCC in  
16 that case. If there's a reference that shows that  
17 that combination is not incompatible, would you  
18 consider that germane to your opinion that CMC and  
19 MCC are not compatible with cationic drugs across  
20 the board?

21 MS. EVERETT: Objection, form.

22 BY THE WITNESS:

1           A. That's kind of a long question and I  
2 forget what you said at the start.

3           Q. So the example you were giving in response  
4 to my prior question related to a gel. Do you  
5 agree with that?

6           A. Yes.

7           Q. So let's just assume that there's an  
8 example where we have a situation where there's a  
9 cationic drug being dissolved as a hydrochloride  
10 salt and there's another second active component  
11 ingredient that's being suspended with the  
12 assistance of MCC and CMC. Do you understand that  
13 hypothetical?

14          A. So there's a cationic drug and you've got  
15 MCC and CMC?

16          Q. Yes. And it's not a gel.

17          A. It's not a gel.

18          Q. Do you understand that?

19          A. I understand that preface.

20          Q. And there's another active ingredient  
21 that's being suspended with the use of MCC or CMC.

22          A. Depending on the application, if it was a

1 nasal spray that would be very relevant. If it was  
2 a situation where you needed a high viscosity it  
3 wouldn't be so relevant to nasal sprays because  
4 obviously you can't have very high viscosity for a  
5 nasal spray.

6 Q. But if that example formulation existed  
7 where we had a cationic drug, MCC, CMC, and another  
8 active ingredient that was being suspended,  
9 wouldn't you agree that that would be something  
10 that a person of ordinary skill would take into  
11 account when considering whether or not azelastine  
12 was fundamentally incompatible with CMC?

13 A. They would likely take those sort of  
14 observations into account, but I think they would  
15 take into account in the context of Lieberman which  
16 says, you know, usually there is an incompatibility  
17 between those two types of polymers and drugs.

18 Q. So they would at least take it into  
19 account?

20 A. If it was relevant to an intranasal nasal  
21 spray formulation.

22 Q. And, again, if it was relevant, as you



1       said, those formulations that demonstrated that CMC  
2       is not fundamentally incompatible with cationic  
3       drugs would inform one of skill in the art to  
4       potentially experiment with CMC and the cationic  
5       drug?

6           A.   Sorry.  Can you say that again, just  
7       repeat it.

8           Q.   Sure.

9                So earlier I asked you if there was an  
10       example formulation that existed where we had a  
11       cationic drug, MCC, CMC, and another active  
12       ingredient that was suspended, you would agree that  
13       one of ordinary skill would take that into account  
14       as part of the teachings of the prior art, correct?

15          A.   If it was relevant to the formulation of a  
16       nasal spray combining an antihistamine and a  
17       steroid.

18          Q.   So let's just set aside the specific  
19       azelastine portion of what we're discussing.  Okay.  
20       If it was relevant generally to whatever  
21       formulation somebody of skill in the art is working  
22       on --

1           A.   Why would we set aside the azelastine?

2           Q.   So let's start again with the example  
3           formulation that we've been working with.   So we  
4           have an example formulation that exists in the  
5           prior art with a cationic drug, MCC, CMC, and  
6           another ingredient that's suspended, and you agree  
7           that one of ordinary skill would take that into  
8           account as part of the teachings of the prior art  
9           if it's relevant, right?

10          A.   Yeah, if it's relevant, you know,  
11          depending on the concentrations of those  
12          ingredients, depending on the types of formulation  
13          that it represents, depending on, you know, what  
14          site of administration it was being administered  
15          to, you know, many other factors would play into  
16          what a POSA would look to as they were looking to  
17          develop an intranasal formulation.

18                MS. EVERETT:   Andrew, we've been going for  
19                over an hour.   Would this be a good time to take a  
20                break.

21                MR. CHESLOCK:   Yeah, we can take a break.  
22                Let's go off the record.

1 (A short break was had.)

2 BY MR. CHESLOCK:

3 Q. Dr. Smyth, did you discuss the substance  
4 of your testimony during the break we just had with  
5 your counsel?

6 A. No.

7 Q. You're generally familiar with the concept  
8 of nasal sprays, right?

9 A. Sure.

10 Q. And you're similarly generally  
11 knowledgeable with the concept of nasal drops?

12 A. I'm familiar with nasal drops, yes.

13 Q. They're both useful ways of administering  
14 drugs to the nose, right?

15 A. In general nasal sprays are a preferred  
16 administration because of the deposition on the  
17 nasal cavity, inside the nasal cavity is much  
18 better than nasal drops.

19 Q. But they're both useful for administration  
20 purposes even though one's more preferable than the  
21 other?

22 A. Sure. Nasal drops have been used in the

1 past. They have sort of gone out of favor and  
2 nasal sprays have really taken the predominant  
3 focus of nasal administration.

4 Q. So you wouldn't consider the two to be  
5 synonymous, right?

6 A. Nasal drops and nasal sprays are very  
7 different types of dosage forms.

8 Q. And when you say they're very different  
9 types of dosage forms, that means that they're  
10 different methods of actually administering the  
11 drug, right?

12 A. Different methods of administration and  
13 where they deposit in the nasal cavity and their  
14 absorption profiles, things like that.

15 Q. So besides some of the differences you've  
16 already highlighted, what would be another  
17 difference between a nasal spray versus a nasal  
18 drop form of administration?

19 A. For example, a nasal spray has a sort of  
20 narrower design requirement for viscosity. A nasal  
21 drop could be more viscous, for example. A nasal  
22 spray needs to be in a specialized type of

1 container for administration.

2 Q. Okay. So viscosity would be an example of  
3 a difference between a nasal spray formulation and  
4 a nasal drop formulation, right?

5 A. It could be.

6 Q. And I believe you just testified that a  
7 nasal spray has a narrower design requirement for  
8 viscosity, right, as compared to a nasal drop?

9 A. Right.

10 Q. So to close that out, depending on which  
11 nasal drop and which nasal spray you're comparing  
12 between, viscosity could be a difference between  
13 the two?

14 A. That's a possibility, yes.

15 Q. Okay. Focusing in on viscosity and what  
16 you have testified to as the narrower design  
17 requirement for viscosity, what would be an  
18 acceptable range of viscosities for a formulation  
19 to act as a suitable nasal spray, in your opinion?

20 A. It would be a range that could be used  
21 effectively to produce a nasal spray through a  
22 nasal spray device. So one with low enough

1 viscosity such that a spray is formed, taking into  
2 account other formulation considerations as well.

3 Q. Okay. So it would depend on the type of  
4 spray and the container would be one thing that  
5 would affect the range of suitability viscosities;  
6 is that what your testimony is?

7 A. It would take into account that it needs  
8 to be sprayed through a nasal spray device.

9 Q. And what about temperature, would that  
10 affect the suitable viscosity range for a  
11 formulation to act as a suitable nasal spray?

12 MS. EVERETT: Objection, outside the scope  
13 of Dr. Smyth's declaration.

14 BY THE WITNESS:

15 A. Viscosity changes with temperature, that's  
16 well known. However, most formulations have to  
17 operate at ambient temperature. So that's where  
18 they're tested.

19 Q. So in terms of a viscosity, you would  
20 agree with me that characterizing viscosity  
21 relative to water is a common way of understanding  
22 viscosity; would you agree with that?

1           A. Can you say that again.

2           Q. The understanding of viscosity relative to  
3 water is one way that we can understand what the  
4 viscosity requirements would be for a suitable  
5 nasal spray; would you agree with that?

6           A. It's certainly possible you can compare  
7 the viscosity of a formulation to the viscosity of  
8 water.

9           Q. So with that in mind, would water at  
10 10 degrees Celsius have an acceptable viscosity to  
11 be a suitable nasal spray?

12           MS. EVERETT: Objection, outside the scope  
13 of Dr. Smyth's declaration.

14           MR. CHESLOCK: And I'd caution counsel  
15 that I have the Trial Practice Guide and I believe  
16 that to be an inappropriate objection. You're more  
17 than welcome to interject objections to form, and  
18 if you want we can have a separate discussion  
19 without the witness here and I can explain to you  
20 why that question is not outside the scope if you  
21 want to do that.

22           MS. EVERETT: I'll keep my objection on

1 the record. You can continue.

2 BY THE WITNESS:

3 A. So I'm not sure why we would be  
4 considering a 10-degree Celsius water viscosity for  
5 nasal sprays.

6 Q. How about -- instead of 10 degrees how  
7 about at room temperature. Would you agree that  
8 water at room temperature would have a suitable  
9 viscosity for a nasal spray?

10 A. There are formulations that don't contain  
11 any viscosity-modifying agents that I've tested  
12 that predominantly are water and are suitably  
13 sprayed from a nasal spray applicator, yes.

14 Q. At room temperature?

15 A. At room temperature.

16 Q. So just to clarify that, based on your  
17 experience considering what a suitable viscosity  
18 would be, water at room temperature would have a  
19 viscosity that would be suitable for a nasal spray,  
20 right?

21 A. Most likely, yes, to form an aerosol  
22 plume. There's other aspects to viscosity in nasal



1 sprays such as residence time in the nasal cavity.

2 Q. And so, again, trying to understand what a  
3 suitable range would be, as the temperature of  
4 water is lowered is there a point at which it would  
5 exhibit a viscosity that would render it not  
6 suitable as a nasal spray?

7 A. I would need to look at -- I mean,  
8 certainly if the product was frozen it could not be  
9 sprayed and I think at 4 degrees Celsius water has  
10 its highest viscosity, but I cannot remember what  
11 viscosity that is or if anyone's actually ever  
12 tested that in a nasal spray device.

13 Q. So to quantify maybe some limitations for  
14 what the viscosity should be for a suitable nasal  
15 spray, can you say one way or another whether a  
16 viscosity between 1 and 1.3 millipascals would be  
17 sufficient for a nasal spray in your view?

18 MS. EVERETT: Objection to form.

19 BY THE WITNESS:

20 A. You know, I would need to look that up.

21 Q. But certainly a person of ordinary skill  
22 at the time of the '620 Patent would have known

1       that solution viscosity has an effect on the  
2       suitability of the formulation as a nasal spray,  
3       right?

4           A.   Yes.   They would consider, you know,  
5       viscosity as a formulation parameter to look at --

6           Q.   And they would know -- sorry.

7           A.   -- when developing a nasal spray.

8           Q.   And that person of ordinary skill before  
9       the time of the '620 Patent would have known how to  
10      vary viscosity and test for a formulation that  
11      would have been suitable for a nasal spray in your  
12      opinion, correct?

13          A.   Viscosity is something that can be  
14      modified by using formulation approaches such as  
15      changing the type of -- or concentration of the  
16      viscosity-modifying agent, but that has to be  
17      balanced with the other functions of the  
18      viscosity-modifying agents such as, you know,  
19      residence time in the nasal cavity, providing  
20      physical stability for suspensions.

21          Q.   All right.   So just to be clear, a person  
22      of ordinary skill before the '620 Patent would have

1 known that solution viscosity has an effect on the  
2 suitability of a formulation as a nasal spray and  
3 they would have the knowledge to vary that  
4 viscosity and perform tests to determine if it was  
5 suitable, correct, in general?

6 A. In general formulators, persons of  
7 ordinary skill would look to study viscosity and  
8 the effects on the formulation.

9 Q. Before the '620 Patent, right?

10 A. Sure. Yes.

11 Q. All right. If you could, please, take  
12 your second declaration out again and in particular  
13 I'd like you to go to paragraph 23. It starts on  
14 page 10. Are you there?

15 A. Yes.

16 Q. Okay. I'd like you to now go to the next  
17 page because paragraph 23 continues onto the next  
18 page. Do you see there at paragraph 23 you make  
19 the statement that "Cipla also told the patent  
20 examiner that the term 'suitable for nasal  
21 administration' was synonymous with the term 'nasal  
22 spray' as used in the '620 Patent"; do you see

1       that?

2           A.   I see that, yes.

3           Q.   And you recall that the term "suitable for  
4       nasal administration" is present in claim 1, right,  
5       of the '620 Patent, which you can refer to to  
6       confirm that if you'd like?

7           A.   "Suitable for nasal administration" is in  
8       claim 1, yes.

9           Q.   Okay.  So it's your understanding that  
10       claim 1 because it cites "suitable for nasal  
11       administration" that the formulation that's  
12       actually claimed by claim 1 must be suitable as a  
13       nasal spray; that's your opinion, right?

14          A.   Cipla during the prosecution of the patent  
15       told the examiner that those two terms were  
16       synonymous.

17          Q.   Right.  So claim 1 has to be a nasal  
18       spray?

19          A.   Claim 1 is a nasal spray, yes.

20          Q.   If you could in the '620 Patent in column  
21       12 look at claim 14.

22          A.   Yes.

1 Q. Do you see that claim 14?

2 A. Yes.

3 Q. And that claim 14 depends from claim 1,  
4 right?

5 A. Yes.

6 Q. And claim 14 reads "The pharmaceutical  
7 formulation of claim 1, wherein said dosage form  
8 suitable for nasal administration comprises nasal  
9 drops"; do you see that?

10 A. Yes.

11 Q. And as we discussed earlier, nasal drops  
12 and nasal sprays are different in your opinion?

13 A. Yes.

14 Q. And in addition as we've discussed a  
15 couple of times today, dependent claims contain all  
16 the limitations of the independent claim from which  
17 they depend; do you agree with that?

18 A. Yes.

19 Q. And the dependent claim can't be broader  
20 than its independent claim, right?

21 A. That's right.

22 Q. So claim 14 cannot be broader than

1 independent claim 1, right?

2 A. Right.

3 Q. And claim 14 includes all the limitations  
4 of independent claim 1?

5 A. Yes.

6 Q. So you would agree that based on that  
7 logic claim 1 must be broad enough to capture the  
8 nasal drops of claim 14, right?

9 A. Or claim 14 is narrower than the nasal  
10 spray formulation in claim 1.

11 Q. Okay. So your testimony before was nasal  
12 sprays and nasal drops are different; do you agree  
13 with that?

14 A. They're different ways of administering to  
15 the nasal cavity, yes.

16 Q. And your opinion based on, in part, the  
17 language in claim 1 and what Cipla said to the  
18 examiner is that claim 1 is limited to a nasal  
19 spray; do you agree with that?

20 A. I say that a pharmaceutical -- sorry --  
21 the term "suitable for nasal administration" is  
22 synonymous with the term "nasal spray."

1           Q. So if nasal sprays and nasal drops are  
2       different, it's logically not possible for claim 14  
3       to be narrower than claim 1? Let me state it a  
4       different way. It's not possible for what's  
5       claimed in dependent claim 14 to be a subset of  
6       what's claimed in claim 1 because nasal drops and  
7       nasal sprays are different?

8           A. Yeah. I think claim 14 -- nasal drops  
9       cannot be a subset of nasal sprays, I'm just  
10      thinking about that.

11          Q. Let me try it a different way. You would  
12      agree based on your understanding of the way patent  
13      claims work, dependent and independent claims, that  
14      independent claim 1 cannot be limited to nasal  
15      sprays if there's a dependent claim that separately  
16      claims nasal drops because the two are different?

17          A. Yeah. I think that claim 14 is -- because  
18      it comprises nasal drops is in a different  
19      category, it's not a nasal spray as we've  
20      discussed, but I think in the file history it's  
21      clear that claim -- what Cipla is defining as  
22      "suitable for nasal administration" was synonymous

1 with the term "nasal spray." So yeah, I'm not sure  
2 how to -- you know, in terms of legal claims how 14  
3 fits under 1.

4 Q. Okay. But you can agree with me that  
5 there's at least an inconsistency with an  
6 understanding that claim 1 is limited to nasal  
7 sprays when claim 14 as a dependent claim claims  
8 nasal drops? You would agree with at least that  
9 much logically, correct?

10 MS. EVERETT: Objection, form.

11 BY THE WITNESS:

12 A. I understand claim 14 to be a separate  
13 sort of -- I'm not sure how to I guess reconcile 14  
14 nasal drops with the nasal spray definition, but in  
15 the file history, you know, what they explicitly  
16 state is, you know, "suitable for administration"  
17 is synonymous with the term "nasal spray."

18 Q. So sitting here right now by your  
19 testimony you just gave, you're just not able to  
20 reconcile the inconsistency between dependent claim  
21 14 that's specific to nasal drops and your  
22 understanding of independent claim 1 that it's



1 limited to nasal sprays, right?

2 A. Drops are different formulations from  
3 nasal sprays and maybe during the amendments they  
4 just didn't consider 14 -- amending 14. It's hard  
5 to say why it would be this inconsistency.

6 Q. And you sitting here right now can't  
7 reconcile that, correct?

8 A. I don't know what they were thinking when  
9 they kept claim 14 as a nasal drop.

10 Q. You're familiar with osmolality, correct?

11 A. Yes.

12 Q. And osmolality relates to physiological  
13 osmotic pressure, right?

14 A. It relates to the osmotic pressure across  
15 membranes.

16 Q. For example, in a nasally-administered  
17 drug there would be a osmolality parameter?

18 A. It would be a parameter -- a formulation  
19 characteristic.

20 Q. A formulation characteristic, let's use  
21 that. So as a formulation characteristic as you  
22 just testified osmolality would be something a

1 person of ordinary skill would consider when  
2 formulating a nasally-administered drug before the  
3 '620 Patent, right?

4 A. Osmolality is considered important for  
5 nasal formulations before the '620 Patent.

6 Q. And adjustment of osmolality would have  
7 been made by using tonicity adjustors before the  
8 '620 Patent, right, in general?

9 A. In general there are certain agents called  
10 tonicity-adjusting agents that can be used to  
11 increase the tonicity of a formulation, not  
12 decrease.

13 Q. So tonicity-adjusting agents or tonicity  
14 agents or isotonization agents as the '620 Patent  
15 refers to would have been things that were used  
16 prior to the '620 Patent to adjust osmolality,  
17 correct?

18 A. Those agents would be used to adjust  
19 tonicity or to increase tonicity or osmolarity.

20 Q. And osmolarity and osmolality are  
21 interchangeable, right?

22 A. Not quite. Osmolality is an

1 experimentally determined value, whereas osmolarity  
2 is a theoretical calculation of the -- so there are  
3 slight differences.

4 Q. Let's maybe focus on osmolality, then,  
5 just to make sure we're being clear because it's  
6 what we were talking about before.

7 A. Sure.

8 Q. So based on all that testimony, use of the  
9 tonicity agents and the isotonicity agents, those  
10 were all well known in the prior art before the  
11 '620 Patent, right?

12 A. A formulator would have known there were  
13 certain agents, tonicity-adjusting agents or other  
14 terms that one could use to increase the tonicity  
15 of a formulation.

16 Q. So in formulating a nasally-administered  
17 drug before the '620 Patent what I believe you're  
18 testifying to is it was well within the knowledge  
19 of a person of ordinary skill to use these tonicity  
20 adjustors or isotonation agents to adjust  
21 osmolality, right, well within the ability of a  
22 person of skill in the art before the '620 Patent?

1           A. You can adjust tonicity and isotonicity  
2           agents. Again, these are only substances when you  
3           add them you increase the tonicity. So they can't  
4           be used to adjust it downwards.

5           Q. But with that clarification, well within  
6           the skill of a person of ordinary skill before the  
7           '620 Patent for formulating nasally-administered  
8           drug?

9           MS. EVERETT: Objection, form.

10          BY THE WITNESS:

11          A. Depending on the type of formulation and  
12          the requirements, the other components, the  
13          interactions, compatibilities, osmolarity agents  
14          could be used to adjust.

15          Q. It certainly was in the formulator's tool  
16          kit, so to speak, before the '620 Patent?

17          A. Certainly people had been adjusting  
18          formulations before the '620 Patent.

19          Q. And the '620 Patent certainly wasn't the  
20          first example of a nasally-administered drug with  
21          an osmolality that didn't irritate patients when in  
22          use, right?

1           A. Can you say that again.

2           Q. Sure. The '620 Patent certainly wasn't  
3 the first example of a nasally-administered drug  
4 with an osmolality that didn't irritate patients  
5 when in use, correct?

6           A. That is correct. There were several  
7 nasal -- intranasal formulations that had been  
8 marketed and shown to be nonirritating.

9           Q. And you're also familiar with pH, right?

10          A. Sure.

11          Q. And similar to osmolality that too would  
12 be a parameter a person of ordinary skill would  
13 consider would formulating a nasally-administered  
14 drug?

15          A. PH is an important characteristic of a  
16 formulation for a number of different reasons. The  
17 stability of the drug, the tolerability of the  
18 formulation, interactions between components within  
19 the formulation would be an important parameter to  
20 characterize for any formulation.

21          Q. And adjustment of pH is done generally  
22 through the addition of acids, bases, and buffering

1 substances, right?

2 A. You can adjust pH using acids and bases.

3 Buffers are used to help maintain the pH at a  
4 particular value.

5 Q. Okay. So in this circumstance we can have  
6 adjustment up or down in terms of pH, and with  
7 respect to the buffer substances as you've just  
8 testified, those can be used to maintain the  
9 existing pH level of a formulation; is that  
10 accurate?

11 A. For the most part.

12 Q. And use of acids, bases, and buffering  
13 substances for purposes of adjustment in pH was  
14 well known in the prior art before the '620 Patent,  
15 right?

16 A. Adjusting pH is, you know, a very common  
17 formulation requirement, but, again, like the other  
18 factors, osmolarity and viscosity, they must be  
19 considered in the totality of the formulation. So  
20 you can adjust a pH to a lower value to increase  
21 solubility, for example, but you may increase  
22 instability of the drug molecule or formulation

1       excipients.

2           Q.   Setting aside any of the other factors, I  
3       just want to know it's true that uses of acids,  
4       bases, and buffering substances was for -- for the  
5       purpose of adjusting of pH was well known within  
6       the prior art before the '620 Patent and within the  
7       formulator's tool kit as we said before, right?

8           A.   So adjusting pH, you can't just adjust pH  
9       for one reason without considering the other  
10      effects that it's going to have on your  
11      formulation.

12          Q.   And I appreciate that, but my question was  
13      really simple. Use of bases, acids, and buffering  
14      substances for the purpose of adjusting pH was well  
15      known by a person of ordinary skill in the prior  
16      art and was well within their tool kit before the  
17      '620 Patent, right?

18          A.   It's known you can adjust pH using acids  
19      and bases and maintain pH using buffers, but a  
20      formulator adjusts pH to optimize the balance  
21      between the formulation and those characteristics  
22      that are required for a pharmaceutical product.

1           Q. You would agree with me that the  
2       '620 Patent wasn't the first example of a nasally-  
3       administered drug with a pH that didn't irritate  
4       patients, right? You'd agree with that?

5           A. There were other formulations, products  
6       that had been tested in clinical trials and had  
7       been shown they could be formulated at pH with  
8       other characteristics obviously that contribute to  
9       nasal irritation, such as osmolarity, that have  
10      been successfully developed.

11          Q. So that necessarily follows that use of at  
12      least bases, acids, or buffer substances to adjust  
13      pH would have been used by the formulators of the  
14      drugs that you mentioned well before the  
15      '620 Patent, right?

16          A. For example, in the azelastine product  
17      which came before the '620 Patent they used a  
18      buffering system, a citric acid buffering system to  
19      formulate the pH within required limits for  
20      azelastine in that particular product.

21          Q. And I think you mentioned before that pH  
22      is an important characteristic for nasally-



1 administered drugs, right?

2 A. It is. Well, for many pharmaceutical  
3 products, but in particular nasal because of the --  
4 you know, the site of administration of the drug  
5 being into a mucosal surface, but also because of  
6 the influence that it has on solubility, stability,  
7 and, you know, other aspects of the formulation.

8 Q. And so in your opinion is there a high and  
9 low end range for pH that is appropriate for a  
10 nasally-administered drug?

11 A. There have been reported ranges for pH.  
12 Obviously it's best to be close to the  
13 physiological pH of the nasal cavity if possible  
14 for the tolerability. However, you've got to take  
15 into account, you know, solubility, stability,  
16 other effects that your pH is going to have in your  
17 formulation. So it's kind of a balance.

18 Q. What's the physiological pH of the average  
19 human nasal cavity?

20 A. There's a variety of values that have been  
21 reported, but generally it's around 6.5 to 6.8,  
22 slightly acidic.

1           Q. I'd like to go back to your second  
2       declaration again if we could. I think you still  
3       have that in front of you.

4           A. Yes.

5           Q. If you could go to paragraph 40 which  
6       starts on page 25. Are you there?

7           A. Yes.

8           Q. Okay. Do you see in the second sentence  
9       where you mention that in Dr. Herpin's reproduction  
10      of Cramer formula 3 the pH was approximately 3 or  
11      below; do you see that?

12          A. I see that.

13          Q. And then in that same paragraph, which I  
14      think is consistent with the average pH you just  
15      gave me for a human nasal cavity, you say that  
16      approximately 3 or below as found by Dr. Herpin are  
17      well below the acceptable pH of a nasal  
18      formulation. "Such formulations would not be  
19      tolerable to patients and therefore would not be  
20      suitable for nasal administration." Do you see  
21      that?

22          A. Yes.

1           Q. And you would agree, as we've already  
2           discussed, that suitable for nasal administration  
3           is a requirement of at least claim 1 of the  
4           '620 Patent, right?

5           A. That's right.

6           Q. So I'd like to direct you to a different  
7           claim of the '620 Patent which is in column 14,  
8           claim 45. The first question I have is you'd agree  
9           with me that claim 45 depends from independent  
10          claim 1, right?

11          A. That's right.

12          Q. And would you also agree with me that  
13          because claim 1 recites that the formulation is  
14          suitable for nasal administration and claim 45  
15          recites that the formulation includes a pH ranging  
16          from 3 to 7, doesn't that indicate a pH of a  
17          minimum 3 that's not suitable for nasal  
18          administration?

19          A. So in claim 45 it would indicate that  
20          anything less than 3 would be not suitable.

21          Q. Let me try that again. In your -- looking  
22          at your declaration, your declaration indicates

1       that the Dr. Herpin results which identified a pH  
2       that was approximately 3 or below, that formulation  
3       would not be suitable for nasal administration,  
4       right? That's what your declaration says, the  
5       second one?

6           A. Right.

7           Q. Right there in paragraph 40?

8           A. That's right.

9           Q. And you would also agree with me that  
10       claim 45 claims that the formulation of claim 1  
11       that in your opinion must be suitable for nasal  
12       administration comprises a pH ranging from 3 to 7,  
13       right?

14          A. I see that.

15               MS. EVERETT: Objection, form.

16       BY MR. CHESLOCK:

17          Q. So by the claims of the '620 Patent  
18       doesn't claim 45 indicate that a pH of, for  
19       example, 3.00 is suitable for nasal administration?

20          A. That's what claim 45 of the '620 indicates  
21       that this formulation should be between 3.00 to 7.

22          Q. And likewise as another example, a pH of

1        3.04, which was one of the other values that came  
2        up, that too by the claims themselves would be a pH  
3        of a formulation that would be suitable for nasal  
4        administration, right?

5                MS. EVERETT: Objection to form.

6        BY THE WITNESS:

7                A. According to claim 45. I personally  
8        wouldn't formulate anything near pH 3 at all for  
9        nasal administration.

10              Q. But the '620 Patent certainly claims a  
11        formulation as low as 3, with a pH as low as 3?

12              A. In claim 45 it does, yes.

13              Q. So by including in claim 45 the range --  
14        the pH range of between 3 to 7 and making it depend  
15        from claim 1, it's at least the case that the  
16        inventors of the '620 Patent thought that was an  
17        acceptable pH range for a suitable nasal spray,  
18        right?

19              A. In 45 they say that pH from 3 to 7 would  
20        be a suitable formulation.

21              Q. So setting aside what you would do, the  
22        inventors at least believe that range to be

1       suitable for a nasal spray, right?

2           A.   It appears so.   In 46 they narrow that  
3       range to 4.5 to 6.5, which would be more  
4       acceptable, but as --

5           Q.   But both 45 and 46, both claims are  
6       present in the '620 Patent, right?

7           A.   They both are, yes.

8           Q.   And so a person of ordinary skill looking  
9       at the '620 Patent consistent with the inventors  
10      would have felt looking at claim 45 that a range  
11      that included as low as a pH of 3 would be suitable  
12      as a formulation for nasal use?

13           MS. EVERETT:  Objection to form.

14       BY THE WITNESS:

15           A.   I think a person of ordinary skill would  
16      be more in the mind of thinking that a pH range of  
17      what was more commonly cited in the textbooks and  
18      other resources, publications that show a pH in the  
19      range of around 4 to 8 would be suitable.  I'm not  
20      aware of any products that are formulated at pH 3  
21      or ever been approved.  A person of ordinary skill  
22      would consider that, in my opinion, to be

1 unacceptable.

2 Q. But at least the inventors believed that  
3 range to be suitable, including the lower bound of  
4 3 for the pH such that the formulation would be  
5 suitable for nasal administration based on claim  
6 45, right?

7 MS. EVERETT: Objection to form.

8 BY THE WITNESS:

9 A. On 45 they certainly claim pH 3 to 7. So  
10 they must have had some reason to include that  
11 range.

12 Q. And at least one of those reasons would be  
13 that it would be acceptable and suitable for nasal  
14 administration at a pH of 3, correct?

15 A. Since it depends on claim 1, you know, it  
16 would have to be suitable. You know, there may be  
17 other reasons, you know, the chemical stability or  
18 solubility may have been enhanced, but in my  
19 opinion something formulated at pH 3 is  
20 unacceptable for nasal administration.

21 Q. I'd like to talk to you a little bit about  
22 solutions and suspensions and, again, we can

1 continue our focus on the '620 Patent which I  
2 believe you still have in front of you.

3 Earlier we had a brief discussion that in  
4 a general sense both claims -- independent claims 1  
5 and 24, which are the challenged independent claims  
6 in this proceeding, are directed to a combination  
7 of azelastine with fluticasone, right, in the  
8 general sense?

9 A. Generally speaking, with other limitations  
10 for sure.

11 Q. And again, generally speaking, in that  
12 combination you would expect the azelastine to be  
13 dissolved to form a solution, correct?

14 A. If it was in an aqueous environment you  
15 would anticipate the azelastine hydrochloride to be  
16 predominantly in solution.

17 Q. Just so we're clear on solution versus  
18 suspension, a solution is a formulation where the  
19 ingredients are fully dissolved or at least mostly  
20 dissolved, correct?

21 A. Yeah. An acceptable pharmaceutical  
22 solution would be one where the drug product is



1 dissolved in a solvent.

2 Q. Into like an aqueous solution, water?

3 A. That would be one example, yes.

4 Q. So with that understanding, the azelastine  
5 would be the solution formulation of the  
6 combination for what's claimed in claims 1 and 24,  
7 right, in a general sense?

8 A. Yeah. In an aqueous solution azelastine  
9 hydrochloride would be the drug which would be in  
10 solution.

11 Q. And then moving on to the fluticasone, in  
12 the combination of the independent claims 1 and 24  
13 it mostly would not be dissolved such that it forms  
14 a suspension, right?

15 MS. EVERETT: Objection to form.

16 BY THE WITNESS:

17 A. An example of an aqueous pharmaceutical  
18 formulation, fluticasone propionate without the  
19 use of, you know, solubilizers or other cosolvents  
20 would most likely be in a suspension form.

21 Q. And "in suspension form" means a  
22 formulation with particular ingredients that aren't

1 fully dissolved; is that a fair characterization?

2 A. A suspension would be -- a pharmaceutical  
3 suspension would be one where the drug particles  
4 are in solid form dispersed within a liquid medium  
5 and not dissolved.

6 Q. So in the case of the combination that's  
7 claimed in independent claims 1 and 24, the  
8 fluticasone would be the suspension formulation or  
9 the suspension portion of the formulation, right?

10 A. In an aqueous formulation it's highly  
11 likely that the fluticasone proprionate is going to  
12 be a solid particle in that environment creating a  
13 suspension or at least being a solid particle in a  
14 liquid.

15 Q. So with that understanding of the  
16 discussion we've had about the azelastine and  
17 fluticasone components of what's claimed in claims  
18 1 and 24, would it be correct to refer to either of  
19 those formulations as a solution-suspension?

20 A. So the question said either of those  
21 formulations?

22 Q. I'm sorry. So we've been discussing the

1 combination that's claimed by both independent  
2 claims 1 and 24 which is generally a combination of  
3 azelastine and fluticasone, right?

4 A. Those two drugs are listed in those  
5 claims, yes.

6 Q. Right. And then in an aqueous formulation  
7 the azelastine, as we discussed, would generally be  
8 in solution form, correct?

9 A. Most likely, yes.

10 Q. And then correspondingly the fluticasone  
11 aspect of the formulation would generally be in  
12 suspension form?

13 A. Okay. Yes.

14 Q. In the aqueous pharmaceutical formulation,  
15 right?

16 A. Correct.

17 Q. Okay. With that understanding, would it  
18 be appropriate to refer to the azelastine and  
19 fluticasone formulation in aqueous pharmaceutical  
20 formulation as a solution-suspension?

21 A. It would be a solution of azelastine and a  
22 suspension of fluticasone most likely in that case.

1           Q. So what's claimed in claims 1 and 24 would  
2       be considered an aqueous solution-suspension,  
3       right, with those two different active ingredient  
4       components; is that a fair characterization?

5           A. I like the term a solution-suspension  
6       because that accurately determines what it is.  
7       There's other ways of characterizing it. It may be  
8       that somebody just characterizes it as a  
9       suspension.

10          Q. Because of the suspension part?

11          A. Just because that's the obvious visual --  
12       you know, visually apparent nature of that  
13       formulation.

14          Q. But you're comfortable with solution-  
15       suspension as you just testified?

16          A. Sure.

17          Q. Okay. So the combination that's claimed  
18       in claims 1 and 24, it's not just a solution,  
19       right?

20          A. Well, really all that claim 1 indicates is  
21       it's a pharmaceutical formulation that contains  
22       azelastine, a pharmaceutically acceptable salt,

1 or -- and, sorry, a pharmaceutically acceptable  
2 ester of fluticasone wherein the pharmaceutical  
3 formulation is in a dosage form suitable for  
4 administration. It doesn't make any mention of,  
5 you know, aqueous environment, solution,  
6 suspension.

7 Q. It also doesn't say nasal spray, right?

8 A. Not in -- not explicitly in the claim, but  
9 in the file history those two terms, "suitable for  
10 nasal administration" and "nasal spray," are  
11 equivalent.

12 Q. Right, but as we've already discussed and  
13 you testified, you would understand in an aqueous  
14 pharmaceutical formulation that the azelastine  
15 would be in solution and the fluticasone would be  
16 in suspension, right?

17 A. Yes, in an aqueous environment.

18 Q. And then you said also that you're  
19 comfortable saying that that would be a solution-  
20 suspension formulation, right?

21 A. That's right.

22 Q. Okay. And such a solution-suspension

1 formulation wouldn't be considered just a solution,  
2 right?

3 A. A solution formulation that also had a  
4 drug suspended would not be appropriately  
5 characterized as just a solution.

6 Q. Thank you for clarifying. I just wanted  
7 to make sure that was clear.

8 MR. CHESLOCK: I think I've been going  
9 about an hour again. Do you want to take a break?

10 MS. EVERETT: Sure.

11 (A short break was had.)

12 BY MR. CHESLOCK:

13 Q. Welcome back, Dr. Smyth. During the break  
14 that we just had did you discuss the substance of  
15 your deposition testimony with your counsel?

16 A. No.

17 Q. As we were just discussing, you would not  
18 consider the combination of azelastine and  
19 fluticasone as just a solution, right?

20 A. If one of those ingredients was in there  
21 as a solid particulate form, then it would be not  
22 just a solution.

1           Q. Do you have your second declaration there  
2           in front of you?

3           A. Yes, I do.

4           Q. Can you go to page 35. Are you there?

5           A. Yes.

6           Q. Then I'd actually like to -- that's where  
7           paragraph 56 begins. I'd like to go to the next  
8           page where paragraph 56 continues.

9           A. Okay.

10          Q. And do you see the third sentence on that  
11          page that starts with "Beyond"; do you see that?  
12          It would be the second full sentence on that page.

13          A. Sure. "Beyond their use," that sentence?

14          Q. Yeah. Do you see where in your  
15          declaration it says "Allen discloses a preference  
16          in the art for using dextrose and sodium chloride  
17          as isotonic agents in nasal spray formulations"?

18          A. I see that.

19          Q. And Allen is a reference to one of the  
20          references that you relied upon in forming your  
21          opinion, right?

22          A. That's right. It's Exhibit 2112, "The

1 Art, Science, and Technology of Pharmaceutical  
2 Compounding."

3 Q. Dr. Smyth, I will now hand to you what was  
4 previously designated as Patent Owner's  
5 Exhibit 2112. Do you recognize Patent Owner's  
6 Exhibit 2112?

7 A. Yes.

8 Q. And is that the same exhibit that's  
9 referenced in the portion of paragraph 56 of your  
10 second declaration that we read earlier?

11 A. I believe it is, yes.

12 Q. If you could, please, in Patent Owner's  
13 Exhibit 2112 go to page 19. Do you see the label  
14 "Tonicity Adjustment"?

15 A. I see that.

16 Q. And before we get there can you look back  
17 again at your declaration, please. So just to  
18 clarify, what you're saying in this portion of  
19 paragraph 56 that we looked at, it's your opinion  
20 that dextrose and sodium chloride are the preferred  
21 isotonic agents for nasal formulations generally,  
22 right?



1           A. So Allen discloses in that first sentence  
2 after the label "Tonicity adjustment," "The  
3 preferred agents for adjusting the tonicity of  
4 nasal solutions are sodium chloride and dextrose."

5           Q. Right. But your opinion as stated in  
6 paragraph 56 focuses on nasal spray formulations  
7 generally, correct?

8           A. It does, yeah, nasal spray formulations.

9           Q. And you would agree with me that there's a  
10 distinction between nasal spray formulations that  
11 are just solutions and nasal spray formulations  
12 that are suspensions? You would agree they're  
13 different things?

14          A. A solution is a different type of  
15 formulation than a suspension.

16          Q. So the corollary to that would be the  
17 statement that you highlighted from Patent Owner's  
18 Exhibit 2112 that's specific to nasal solutions and  
19 in particular that sodium chloride and dextrose are  
20 preferred agents for such solutions can't support a  
21 broader understanding of them being preferred for  
22 nasal spray formulations generally, right?

1           A. No, I disagree with that. I think  
2           basically under the broader title "Physicochemical  
3           Considerations," those characteristics that are  
4           listed under that, pH and buffering, tonicity,  
5           sterility, antioxidants, for example, those apply  
6           for nasal preparations in general.

7           Q. But you would agree with me that the  
8           statement on page 19 of Patent Owner's Exhibit 2112  
9           is specific to nasal solutions, right?

10          A. It would be specific to nasal preparations  
11          that contain a solution component or would be  
12          applying an aqueous liquid to the nasal passages.

13          Q. But there's no mention in this statement  
14          that we see here on page 19 that you've identified  
15          regarding suspensions, correct?

16          A. A person of ordinary skill would read this  
17          as the general physicochemical considerations that  
18          would apply both to solutions and suspensions being  
19          applied to the nasal cavity. I don't see the word  
20          suspension in there, but a person of ordinary skill  
21          would obviously know that tonicity adjustment is  
22          important in both.

1           It goes on to say "Nasal fluid has a  
2           isotonicity value similar to a .9 percent sodium  
3           chloride." Then it says "If the isotonicity is  
4           beyond the proper range" and it talks about "nasal  
5           ciliary movement." That would apply equally to  
6           solutions and suspensions.

7           Q. I appreciate those additional statements,  
8           but suffice it to say -- and this is a yes-or-no  
9           question -- in that sentence that you've identified  
10          in Patent Owner's Exhibit 2112 there's no mention  
11          of suspension, it only uses the word solution,  
12          correct?

13          A. That first sentence says "tonicity of  
14          nasal solutions" and in a suspension you would have  
15          a solution component. So, you know, that would  
16          equally apply to suspensions and solutions.

17          Q. Again, this is a yes-or-no question and  
18          I've given you a lot of opportunities to give long  
19          narrative answers. With respect to this specific  
20          sentence on page 19, it uses the word solutions and  
21          the word suspension or suspensions is not used,  
22          correct? Yes or no.

1           A. I used this reference because it talks  
2           about solutions and suspensions in this chapter and  
3           then it talks about physicochemical considerations  
4           of both of those in this list here on page 19.

5           Q. So yes or no, it uses the word solutions  
6           and not suspension or suspensions in that sentence?  
7           Yes or no.

8           MS. EVERETT: Objection to form.

9           MR. CHESLOCK: It's a yes-or-no question.

10          BY THE WITNESS:

11          A. The word suspension is not in there, but,  
12          you know, a POSA would know that it applies to  
13          suspensions as well.

14          Q. And it's certainly accurate based on some  
15          of the preceding pages that the author of Patent  
16          Owner's Exhibit 2112 used the words solution and  
17          suspension separately, correct?

18          MS. EVERETT: Objection to form.

19          BY MR. CHESLOCK:

20          Q. I'll draw your attention -- it's a very  
21          simple question. So page 17 says "Preparation of  
22          Nasal Products, Solutions," right, at the bottom?

1           A. I'm sorry. Where?

2           Q. So page 17 says "Preparation of Nasal  
3 Products"?

4           A. Yes.

5           Q. And then it says "Solutions." You agree  
6 with me on that, right?

7           A. It has a list of steps for solutions.

8           Q. Right. And then on page 18 it separately  
9 lists a set of two different methods for the  
10 formulations of suspensions, right?

11           MS. EVERETT: Objection to form.

12           MR. CHESLOCK: That's a yes-or-no  
13 question.

14 BY THE WITNESS:

15           A. So it says "Suspensions" -- "Preparation  
16 of Nasal Products," continues "Suspensions (Method  
17 1), "Suspensions (Method 2)" on page 18.

18           Q. So it's clear that the authors of Patent  
19 Owner's Exhibit 2112 knew and understood there's a  
20 difference between solutions and suspensions and  
21 they used those words differently in the text?  
22 That's either true or false, right?

1 MS. EVERETT: Objection, form.

2 BY THE WITNESS:

3 A. Certainly the authors would have known  
4 that solutions and suspensions are different types  
5 of formulations.

6 Q. I'd like to draw your attention to Bates-  
7 labeled page 3 of Patent Owner's Exhibit 2112,  
8 please. Do you see the heading "Definitions/  
9 Types"?

10 A. Yes.

11 Q. Do you see there's a definition for  
12 "Ophthalmic solutions"?

13 A. I see "Ophthalmic solutions are sterile,  
14 free from foreign particles, and prepared  
15 especially for installation into the eye."

16 Q. Do you see also see there's a separate  
17 definition for ophthalmic suspensions in the same  
18 paragraph, right?

19 A. I see that, yes.

20 Q. And so, again, doesn't the fact that  
21 Patent Owner's Exhibit 2112 provides two different  
22 definitions of suspensions and solutions indicate

1       that a person of ordinary skill when reading Patent  
2       Owner's Exhibit 2112 would consider those two to be  
3       different?

4           A.   I don't think so because essentially if  
5       you look at, for example, on page 18 of that  
6       reference where it talks about the preparation of  
7       nasal products, suspensions, in both of those  
8       examples they say "Take a sample of the suspension  
9       and determine the pH and other quality control  
10      factors," which would be those physicochemical  
11      considerations that are listed on page 19.

12          Q.   Okay.   So let's look back at page 17 of  
13      Patent Owner's Exhibit 2112.   Do you see at the top  
14      underneath "Nasal Preparations" there's a section  
15      called "Definitions"?

16          A.   Yes.

17          Q.   Okay.   And do you see that there's a nasal  
18      solutions definition of "Nasal solutions are  
19      solutions prepared for nasal administration either  
20      as drops or as sprays"?

21          A.   I see that.

22          Q.   And then similarly there's a separate and

1 distinct definition of "Nasal suspensions are  
2 liquid preparations containing insoluble materials  
3 for nasal administration"; do you see that?

4 A. Yes.

5 Q. And you would agree with me that in this  
6 Patent Owner's Exhibit 2112 there are two separate  
7 definitions that are satisfied separately for  
8 solutions and suspensions, yes or no?

9 MS. EVERETT: Objection to form.

10 BY THE WITNESS:

11 A. They define nasal solutions and nasal  
12 suspensions separately, yes.

13 Q. So a corollary to that would be in the  
14 text of Patent Owner's Exhibit 2112 when they meant  
15 to emote that something was applicable to solutions  
16 or suspensions they actually used those terms, yes  
17 or no?

18 A. A person of ordinary skill would know that  
19 tonicity adjustment is important for anything  
20 that's applied to the nose whether it's a solution  
21 or suspension. So the fact that they put nasal  
22 solutions in there, a person of ordinary skill



1 would also know that that also applies to nasal  
2 suspensions and would be important.

3 Q. You didn't consider the fact that Patent  
4 Owner's Exhibit 2112 included these separate  
5 definitions for nasal solutions and nasal  
6 suspensions when you formed your conclusion as to  
7 what's stated on paragraph 19, right?

8 MS. EVERETT: Objection to form.

9 BY THE WITNESS:

10 A. I understand there's a difference between  
11 nasal solutions and suspensions and that one  
12 contains solid particles, the other one doesn't,  
13 but I also understand that if you're formulating  
14 something for nasal delivery you have to take into  
15 account the osmolarity, the tonicity.

16 Q. To answer my question -- and it's a yes or  
17 no answer -- you didn't consider the fact that as  
18 shown here on page 17 Patent Owner's Exhibit 2112  
19 explicitly has two separate definitions for  
20 solutions and suspensions when you formed your  
21 opinions as to what is stated with respect to  
22 tonicity agents on page 19? You did not consider

1       what's on 17, right?

2             A.   Oh, no.

3             MS. EVERETT:  Objection to form.

4       BY THE WITNESS:

5             A.   I considered the whole reference.

6             Q.   Do you recall earlier we were talking  
7       about some general parameters of nasally-  
8       administered drugs like osmolarity and pH; do you  
9       remember that?

10            A.   Sure.

11            Q.   Is physical stability another parameter  
12       that a person of ordinary skill would consider when  
13       formulating a nasally-administered drug?

14            A.   Stability including physical stability is  
15       a really important characteristic of a formulation.

16            Q.   And that would be true of a solution-  
17       suspension nasally-administered drug such as the  
18       azelastine-fluticasone combination that we've been  
19       discussing earlier?

20            A.   Physical stability is particularly  
21       important in suspension-based formulations.  So if  
22       you have a suspended particle, then physical

1 stability would definitely need to be considered.

2 Q. And one of the ways that a person of  
3 ordinary skill can make adjustments to physical  
4 stability is with thickening agents, right?

5 A. Potentially they can use thickening  
6 agents, suspending agents.

7 Q. Just to clarify, do you consider the terms  
8 "thickening agents" and "suspending agents" to be  
9 mostly interchangeable?

10 MS. EVERETT: Objection to form.

11 BY THE WITNESS:

12 A. Not exactly. Suspending could also  
13 include agents used to change the sort of  
14 electrical properties of the -- of the suspension  
15 such that there's no aggregation or agglomeration.  
16 Suspending agents may be a little bit broader.

17 Q. Okay. Let's just for now stick with  
18 thickening agents for now. So I think consistent  
19 with what you've just explained in terms of the  
20 importance with respect to the suspension piece of  
21 a formulation, would it be accurate to say that  
22 thickening agents in general help with the

1 dispersion of ingredients that are not fully  
2 dissolved; would that be correct?

3 A. It helps maintain -- a thickening agent  
4 may slow the sedimentation rate of particles that  
5 are dispersed in a liquid medium.

6 Q. Okay. So another way of stating that is  
7 they help prevent certain undissolved ingredients  
8 from settling to the bottom of a container, for  
9 example?

10 A. They can reduce the time --

11 Q. Reduce the time.

12 A. -- Sorry, increase the time for those  
13 particles to stay suspended.

14 Q. So if you take a container that is a  
15 suspension, the thickening agents increase the time  
16 at which the nondissolved ingredients would settle  
17 to the bottom of a container, for example?

18 A. That's one essentially way of increasing  
19 the time for settling is to increase the viscosity  
20 by using thickening agents.

21 Q. And those thickening agents also assist in  
22 allowing the nondissolved ingredients to be

1       redispersed upon shaking a container with that  
2       particular suspension formulation in the container,  
3       right?

4           A.   No.   They actually work in the opposite.  
5       They often prevent the redispersion of those  
6       agents.   So it's kind of a balance between  
7       sedimentation rate and the ability to impart enough  
8       sheer forces within the suspension to disperse --  
9       redisperse the particles.

10          Q.   So it's a balance between those two  
11       different characteristics, that the thickening  
12       agents can balance the ability or limit the ability  
13       over time for the ingredients to settle and also  
14       allow those ingredients to be redispersed by  
15       applying sheer force; is that accurate.

16          A.   If you're just using a thickening agent to  
17       provide physical stability it's a very fine balance  
18       between being too viscous so that you can't  
19       redisperse any sediment particles and being not  
20       viscous enough such that particles sediment too  
21       quickly.

22          Q.   I understand.   In general use of

1 thickening agents to control -- let me ask you this  
2 first. Viscosity is a parameter that a thickening  
3 agent affects, right?

4 A. A thickening agent changes viscosity or --  
5 and rheology.

6 Q. And when you say "rheology," I think  
7 you're referring to a fluid's general reaction to  
8 application of sheer; is that a fair  
9 characterization?

10 A. Right. Viscosity is just one element of  
11 the rheology of a formulation.

12 Q. And so use of thickening agents to control  
13 viscosity was well known in the prior art before  
14 the '620 Patent for pharmaceutical formulations,  
15 right?

16 A. Certainly there's a number of thickening  
17 agents, polymers that had been used to change  
18 viscosity in a variety of different dosage forms in  
19 the prior art.

20 Q. So in formulating a nasally-administered  
21 drug before the '620 Patent, including any  
22 solution-suspension formulations, it was well

1       within the knowledge of a person of ordinary skill  
2       to use thickening agents to arrive at a formulation  
3       with a suitable physical stability as we've been  
4       discussing, right?

5           A. First of all, I'm not aware of any  
6       solution-suspension nasal sprays prior to the '620,  
7       and then, you know, as we talked about earlier, the  
8       viscosity and the rheological properties are sort of  
9       a fine balance. One can adjust it, but one may not  
10      find an optimal value or viscosity or rheology for  
11      a particular formulation.

12          Q. So let's set aside the solution-suspension  
13      formulations and let's just ask this. The  
14      '620 Patent certainly wasn't the first time that  
15      somebody disclosed a physically stable homogeneous  
16      drug suspension, right? That's a yes or no answer.

17          A. So physical stability you're always --  
18      nothing is always completely physically stable,  
19      you'll always have some degree of sedimentation,  
20      but for a particular -- for a pharmaceutical use  
21      there have been formulations formulated that had  
22      appropriate physical stability for suspensions.

1           Q. As an example, Flonase itself was a drug  
2           that came before the '620 Patent that was a  
3           physically stable nasal drug suspension, right?

4           A. Flonase had adequate physical stability to  
5           suspend fluticasone particles in that formulation.

6           Q. And certain thickening agents were used to  
7           effect that physical stability in Flonase, right?

8           A. Yeah. I would call them suspending agents  
9           in that case.

10          Q. The broader category?

11          A. Yes.

12          Q. Than we talked about before?

13          A. Yes.

14          Q. Now, you mentioned that you're unaware of  
15          any solution-suspension formulations in your  
16          understanding that are nasally-administered drugs  
17          that existed before the '620 Patent; is that your  
18          testimony?

19          A. That were pharmaceutically acceptable and  
20          suitable for administration to the nasal passages.

21          Q. We also just talked about Flonase; do you  
22          remember that?



1           A. Yes.

2           Q. Isn't it true that even in Flonase there  
3 must have been something dissolved into solution,  
4 right?

5           A. There could be some excipients, inactive  
6 ingredients that were dissolved in that  
7 formulation.

8           Q. And in that circumstance it could be  
9 considered a solution-suspension if you're focused  
10 on excipients other than active ingredients for  
11 Flonase?

12          A. Not by my definition. So the excipients  
13 are selected around a active pharmaceutical  
14 ingredient. So when we talked earlier about  
15 solution-suspension systems, we were talking about  
16 the active ingredients being in solution and  
17 suspension. So, you know, the difficulty there is  
18 where you have excipients that are required for a  
19 suspension and then you have to have certain other  
20 excipients required for a solution. So that's, you  
21 know, what we were talking about earlier.

22          Q. So setting aside your definition, if we

1       just focus on the excipients and those being in  
2       solution in the Flonase product, one could consider  
3       that to be a solution-suspension in the broadest  
4       sense, correct?

5               MS. EVERETT: Objection to form.

6       BY MR. CHESLOCK:

7               Q. Focusing only, again, on the excipient and  
8       the active ingredient, one in solution, one in  
9       suspension.

10              MS. EVERETT: Objection to form.

11       BY THE WITNESS:

12              A. If you wanted to consider just Flonase by  
13       itself, right, with no other active ingredients in  
14       there, you would have fluticasone in suspension and  
15       then some other components like carboxymethyl  
16       cellulose, for example, would be considered, you  
17       know, partially solubilized in that formulation.

18              Q. Okay. Thank you.

19              As kind of a follow-on to that, setting  
20       aside your understanding of nasally-administered  
21       drugs, the '620 Patent was not the first time  
22       anyone had ever developed a solution-suspension

1 drug combination, right? Those had been in  
2 existence well before the '620 Patent?

3 A. Setting aside nasal sprays, did you say?

4 Q. Yeah. So the question is the '620 Patent  
5 wasn't the first time that anyone had ever  
6 developed a solution-suspension drug with active  
7 ingredients, right? Not the first time?

8 A. Right. I'm aware of certain oral syrups,  
9 for example, available over-the-counter that  
10 contained an active in a solution, maybe an active  
11 in a suspension.

12 Q. In the most general sense with respect to  
13 the examples you just gave, the concepts are  
14 similar between the examples that you gave and a  
15 nasally-administered drug because what one of skill  
16 in the art wants to do is develop a formulation  
17 where the suspension stays relatively homogeneous  
18 over time; isn't that right?

19 MS. EVERETT: Objection to form.

20 BY THE WITNESS:

21 A. No. They're quite different types of  
22 dosage forms. So the formulation requirements for

1       those are very, very different. Nasal sprays have  
2       a much narrower sort of design requirements as we  
3       talked about earlier. So the types of excipients,  
4       the types of viscosity that you can use for a nasal  
5       spray are going to be very different than those you  
6       can use for an oral syrup, for example.

7           Q. But the use of the thickening agents to  
8       achieve an appropriate viscosity and the general  
9       goal of trying to make the pharmaceutical  
10      formulation homogeneous, setting aside all the  
11      other factors, that was a similar concept, right?

12        A. You can't really set aside the other  
13      factors. Like for sprayability that we talked  
14      about earlier there's a certain viscosity that you  
15      need to be able to spray a formulation. So, you  
16      know, you can't really set that aside and just  
17      focus in on viscosity. Some of that was  
18      illustrated in the testing that was done in the  
19      Apotex case.

20        Q. But the desire to have homogeneous  
21      pharmaceutical formulations in the examples that  
22      you gave for cough syrup and the desire for having

1 homogeneous formulations for a nasal spray, that  
2 desire is the same?

3 A. Right. A pharmaceutical product has to be  
4 uniform. Otherwise the dose administered is not  
5 going to be accurate. So you have to ensure  
6 homogeneity.

7 Q. So the homogeneity is important because,  
8 as you just testified, it will accurately measure  
9 over time the dose that's actually administered  
10 when someone's using the product?

11 A. Those are slightly different words, but  
12 the concept is that you need a homogeneous product  
13 to dispense a known and reproducible dose.

14 Q. So the need for a homogeneous product that  
15 will dispense, in your words, a known and  
16 reproducible dose, that's not unique to nasal  
17 sprays, correct? That's unique -- that's not  
18 unique to nasal sprays. That's true of other  
19 pharmaceutical drug formulations, right?

20 A. Most formulations are a unit dose where a  
21 certain specific dose is required to be  
22 administered for safety and efficacy.

1           Q. And by controlling for that homogeneity  
2 each time you take a dose the patient will be  
3 getting an accurate administration of an active  
4 ingredient?

5           A. As much as possible the doses should be  
6 homogeneous.

7           Q. Do you have your -- you still have your  
8 second declaration. If you could please go to  
9 paragraph 32 that starts on page 16. Then for this  
10 I'd also like if you could have access to the  
11 '620 Patent which I can see there on your left.

12           So do you see in paragraph 32 where you  
13 have a quotation that comes from the patent that  
14 starts with "In examples where only the ingredients  
15 of formulations according to the present invention  
16 are listed, these formulations are prepared by  
17 techniques well known in the art"? And the  
18 citation to that quote from the '620 Patent is on  
19 the next page to column 7, line 67 through column  
20 8, line 2; do you see that?

21           A. I see that.

22           Q. And do you see that corresponding quote in

1 the '620 Patent?

2 A. Yes, I see that.

3 Q. Okay. Then looking further in your  
4 paragraph 32, you explain what a person of ordinary  
5 skill would have understood from that sentence,  
6 correct?

7 A. Yes. I said "A POSA would have viewed  
8 this sentence to be limited to the examples listed  
9 in the '620 Patent which set out the specific  
10 formulation ingredients and concentrations."

11 Q. And following that statement you have a  
12 citation to the '620 Patent, column 8, line 1  
13 through column 11, line 43 in that paragraph 32,  
14 right?

15 A. Column 8, line 1 to column 11, line 43,  
16 yes.

17 Q. And if you look at the '620 Patent in  
18 those locations, there's a number of examples that  
19 are listed there with particular ingredients in  
20 each example, right?

21 A. Yes.

22 Q. So based on the statements that you

1       have -- and there's another statement in your  
2       declaration in the next line in paragraph 32 that  
3       reads "In that context the fact that these formulas  
4       are prepared by techniques well known in the art  
5       makes sense because the examples already identify  
6       what and how much formulation ingredients to use";  
7       do you see that?

8           A.   Yes.

9           Q.   So what you're stating as your opinion in  
10       paragraph 32 is that the statement in the  
11       '620 Patent that these formulations are prepared by  
12       techniques known in the art is limited only to the  
13       examples that are actually provided in the  
14       '620 Patent at the locations in column 8 through 11  
15       that you've cited in your declaration, right?

16          A.   So what I'm saying there is that the  
17       statement of -- you know, examples where only the  
18       ingredients of formulations according to the  
19       present invention are listed, these formulations  
20       are prepared by techniques well known in the art.  
21       So looking through column 8, line 3 through column  
22       11, line 43, those are all the examples in the



1 '620 Patent. Some of those examples do not give  
2 instructions for the process of putting those  
3 ingredients together. So that's what that  
4 statement means, "prepared by techniques well known  
5 in the art."

6 Q. So just to clarify, what you're saying is  
7 the examples that are provided in the '620 Patent  
8 in column 8 through 11 that have particular  
9 ingredients but don't provide the techniques for  
10 actually formulating that formulation of those  
11 examples would be done by techniques well known in  
12 the art; is that correct?

13 A. Not formulating them, but I guess  
14 processing them.

15 Q. Okay. So in order -- so your opinion is  
16 that the examples that are listed in column 8  
17 through 11, those specific examples would be  
18 processed and prepared by techniques that are well  
19 known in the art?

20 A. Where the ingredients are given and the  
21 amounts are given, yes.

22 Q. So as a corollary to that, I just want to

1       make sure I understand your opinion, if there are  
2       any other formulations that include ingredients  
3       that differ from those examples specifically listed  
4       in the '620 Patent, those must be formulated by  
5       techniques not known by a person skilled in the art  
6       at the time?

7               MS. EVERETT: Objection to form.

8       BY THE WITNESS:

9               A. I think within the invention these  
10       compositions that have been identified can be  
11       prepared using techniques well known.

12              Q. And so in your answer that you just gave  
13       where you refer to "these compositions," are you  
14       referring to the compositions that are specifically  
15       listed in column 8 through column 11 of the  
16       '620 Patent?

17              A. So these compositions can be prepared --  
18       you know, where they haven't given you the process  
19       of putting, you know, the steps of how to add the  
20       ingredients together, they would be prepared by  
21       commonly known methods of adding and mixing those.

22              Q. So my question is -- the corollary to that

1 is -- the corollary to that opinion is if there are  
2 other compositions or formulations that include  
3 ingredients different from those in the examples  
4 that are specifically listed in the '620 Patent at  
5 column 8 through 11, must those be formulated by  
6 techniques that are not known by those skilled in  
7 the art at the time?

8 A. So I think we're using "formulated"  
9 slightly different. Here we're talking about in  
10 these statements the process -- the preparation  
11 techniques.

12 Q. Okay, preparation techniques.

13 A. The mixing, the water addition, that kind  
14 of thing. Formulating is different. That's where  
15 you have to actually figure out the ingredients and  
16 the amount, right.

17 Q. Okay. We can use preparation technique.  
18 Is that better?

19 A. Right. So within the scope of the  
20 examples and within the scope of the claims those  
21 formulations can be prepared, mixed, processed  
22 using techniques known in the art.

1           Q. Okay. So to clarify what you're saying,  
2           the examples that are given in column 8 through 11,  
3           those can be prepared using preparation techniques  
4           that are well known in the art because it lists the  
5           actual compositions of each example; is that right?

6           A. It lists the ingredients, yes.

7           Q. So my question is this. As a corollary to  
8           that opinion that the statement in column 7 and 8  
9           that references well-known techniques in the art is  
10          if there are any other compositions or formulations  
11          that use ingredients different from those of the  
12          specific examples in column 8 through 11, must  
13          those be prepared with preparation techniques that  
14          are not or were not generally known by persons of  
15          skill in the art?

16               MS. EVERETT: Objection to form.

17          BY THE WITNESS:

18               A. Depends on those other excipients that are  
19               not disclosed. It could be that, you know, you're  
20               making an emulsion, then you'd have to use a  
21               different type of processing method, for example.

22               Q. Well, maybe let me ask it this way.

1           A. Depends on the circumstance. That's a  
2           pretty general question.

3           Q. Sure. Let me ask you this way. I just  
4           want to confirm that your opinion is that the  
5           preparation techniques that would be used that were  
6           well known in the art as stated in the '620 Patent,  
7           the ability to prepare using those well-known  
8           techniques is limited to the examples that are  
9           specifically listed in columns 8 through 11, right?

10           MS. EVERETT: Objection to form.

11           BY THE WITNESS:

12           A. I guess in the bottom of column 7 it says,  
13           you know, "The present invention is now illustrated  
14           by the following examples which do not limit the  
15           scope of the invention," and then the second part  
16           is what we're talking about here, "In examples  
17           where only the ingredients of formulations  
18           according to the present invention are listed,  
19           these formulations are prepared by techniques well  
20           known in the art."

21           So putting together these formulations,  
22           once you have the list of ingredients, the

1 composition, you can use techniques well known in  
2 the art. That doesn't mean if you have slight  
3 changes to these ingredients you wouldn't be able  
4 to still use those same techniques well known in  
5 the art. Now, if you use completely different, you  
6 know, formulations, then, you know, that would be a  
7 different question.

8 Q. Okay. So if you could please take the  
9 '620 Patent out and look at claim 11.

10 A. Claim 11.

11 Q. Do you see that claim 11 depends from  
12 claim 7?

13 A. Claim 11 says "A pharmaceutical  
14 formulation of claim 7 wherein."

15 Q. So it depends from claim 7, right?

16 A. That's right.

17 Q. And 7 depends from claim 1?

18 A. That's right.

19 Q. And so based on what you've told me is  
20 your opinion about the ability to actually process  
21 a formulation, would a person of ordinary skill  
22 know or not know using techniques known in the

1 prior art how to formulate a pharmaceutical using  
2 some of the additional excipients claimed in, for  
3 example, claim 11 that would be added to any one of  
4 these other specific examples?

5 A. Just to make sure I understand your  
6 question, so looking at claim 11, which gives  
7 suspending agent or thickening agent examples with  
8 respect to claim 7 which talks about other  
9 excipient classes, buffers, preservatives, which  
10 depends on claim 1 which is the dosage form  
11 suitable for nasal administration, your question is  
12 would a person of ordinary skill be able to mix  
13 those excipients together?

14 Q. Or use those excipients in combination  
15 with one of the specific examples that you said  
16 could be slightly altered and still -- the person  
17 of ordinary skill would know how to process the  
18 formulation according to well-known techniques.

19 A. Yeah. I think being able to choose like  
20 alginic acid, for example, they could -- they would  
21 know how to add process mix, hydrate that polymer  
22 if it was added to, you know, one of those

1       examples.

2               MR. CHESLOCK: I think we can take a break  
3       here and I can look over my notes and sort of see  
4       where I'm at, and then we can decide if we want to  
5       go through lunch or have lunch or whatever. Is  
6       that okay?

7               MS. EVERETT: Okay.

8                               (Whereupon, at 12:00 p.m., the  
9                               deposition was recessed, to  
10                              reconvene at 12:45 p.m., this  
11                              same day.)

12  
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1           A. I see that.

2           Q. And would you agree with me that HPMC by  
3 its full name is hydroxypropyl methylcellulose?

4           A. That's one of its names, yes.

5           Q. And would you also agree with me that HPMC  
6 is considered a cellulose derivative?

7           A. It is -- has a fundamental cellulose basis  
8 and it's derived from cellulose, yes.

9           Q. So if we continue on in paragraph 42 onto  
10 the next page, 27, the first two bullet points  
11 mention the general fact that HPMC is available in  
12 different viscosities, right?

13          A. Bullet points or --

14          Q. Bullet points.

15          A. "Dr. Govindarajan selected to use a low  
16 viscosity HPMC." "Dr. Herpin used a medium  
17 viscosity HPMC."

18          Q. And HPMC would be considered a thickening  
19 agent, right?

20          A. A thickening agent, a suspending agent.

21          Q. And do you recall earlier you testified  
22 that viscosity for such thickening agents or

1 suspension agents is important, right?

2 A. Right. Viscosity of a formulation depends  
3 upon the type of thickening agent, the  
4 characteristics of that thickening agent.

5 Q. And one of those characteristics would be  
6 the viscosity, right?

7 A. Its molecular weight of the polymer can  
8 give rise to different viscosities.

9 Q. And in selection of a thickening agent or  
10 suspension agent viscosity would be part of an  
11 ultimate formulation process as well for a  
12 pharmaceutical drug, for example, right?

13 MS. EVERETT: Objection to form.

14 BY THE WITNESS:

15 A. Certain formulations that require  
16 increased viscosity you would look at viscosity in  
17 those formulations, sure.

18 Q. If you could bring out again the  
19 '620 Patent. Before we went to lunch we were  
20 focused on claim 11; do you remember that?

21 A. Yes.

22 Q. Claim 11 lists a variety of suspending

1 agents and thickening agents that were known in the  
2 prior art before the '620 Patent, right?

3 A. Claim 11 talks about different thickening  
4 agents that would have been previously used in a  
5 variety of different formulations.

6 Q. Before the '620 Patent?

7 A. Before the '620 Patent.

8 Q. And then with respect to the HPMC  
9 thickening or suspending agent that we've been  
10 discussing, I'd like to direct your attention to  
11 column 3 of the '620 Patent and in particular lines  
12 40 through 45. Do you see --

13 A. Sorry. Which lines?

14 Q. Lines 40 through 45.

15 A. Okay. Got it.

16 Q. Do you see there in that section of the  
17 '620 Patent it mentions thickening agents may be,  
18 for example, cellulose derivatives and one of the  
19 cellulose derivatives that's mentioned is HPMC  
20 where there seems to be a typo in the long form  
21 name at line 45; do you see that?

22 A. Yes.

1 Q. Would you agree that's a typo?

2 A. Yes.

3 Q. So that references in line 45 is the same  
4 HPMC that we were discussing earlier where  
5 viscosity would be important, right?

6 MS. EVERETT: Objection to form.

7 BY THE WITNESS:

8 A. What they have made is an error, a  
9 typographical error in line 45. It should read  
10 hydroxypropyl methylcellulose.

11 Q. That's HPMC, right?

12 A. Yes.

13 Q. It's a cellulose derivative according to  
14 the '620 Patent?

15 A. Yes.

16 Q. So if you wouldn't mind, let's go back to  
17 claim 11 and you would agree with me that claim 11  
18 claims use of a suspending agent or thickening  
19 agent that comprises cellulose derivatives, right?

20 MS. EVERETT: Objection to form and as to  
21 scope.

22 BY THE WITNESS:



1 solution from flowing out of the nose too quickly  
2 and to give the solution a viscosity of about 1.5  
3 to 3, preferably 2 millipascals.

4 Q. So that --

5 A. This is some kind of general guidance in  
6 terms of viscosity ranges to prevent the solution  
7 from flowing out of the nose, for example.

8 Q. But that passage is with respect to the  
9 entire solution formulation and not guidance as to  
10 HPMC itself or any other cellulose derivative,  
11 right?

12 MS. EVERETT: Objection to form.

13 BY THE WITNESS:

14 A. I think a person reading this patent would  
15 understand that this is a certain preferred  
16 viscosity to prevent, you know, a solution from  
17 flowing out of the nose when you're adding a  
18 thickening agent. So it would include those  
19 thickening agents that they talk about in the next  
20 paragraph.

21 Q. Right, but the guidance that's provided  
22 here is for the ultimate result and not for the

1 intermediate addition of, for example, HPMC,  
2 correct? Let me rephrase.

3 The guidance that's provided here in  
4 column 3 at 36 through 39, that is the guidance for  
5 the viscosity of the solution itself and not any  
6 individual components of that solution which could,  
7 for example, include HPMC, correct?

8 MS. EVERETT: Objection to form.

9 BY THE WITNESS:

10 A. I don't think so, no. I read that  
11 differently.

12 Q. Well, is there any other -- is there any  
13 guidance in the '620 Patent, for example, regarding  
14 the weight-to-weight percentage that should be used  
15 for HPMC?

16 A. Well, I guess because HPMC comes in, you  
17 can't just give a weight-to-weight percentage  
18 because that's not going to tell you exactly what  
19 the viscosity is because different grades of HPMC  
20 are available with different molecular weights. So  
21 a weight-to-weight percentage for one HPMC is going  
22 to give a different viscosity than the same weight-



1 to-weight percentage for a different HPMC grade.

2 So you would not provide it in weight-to-weight  
3 percentages, but more something along the lines of  
4 what you see on line 39 in column 3 where you'd  
5 give a range of viscosities.

6 Q. But, again, the range of viscosities that  
7 are given in column 39 is for the entire solution  
8 itself and not any individual components, correct?

9 A. The most important thing is the  
10 composition viscosity, right. What you end up  
11 formulating your product to, that's the important  
12 resultant viscosity. Individual viscosities, you  
13 know, of different excipients and components are  
14 going to add to that overall viscosity and that's  
15 what you're formulating it to.

16 Q. So I think what you're telling me is that  
17 one of skill in the art would know by prior  
18 techniques how to use HPMC to achieve a particular  
19 viscosity result; is that correct?

20 A. One could -- if you knew the viscosity  
21 that you were looking for you could select a  
22 particular grade of HPMC, select a concentration of

1       that HPMC that's going to give you approximately  
2       that viscosity that you were looking for.

3           Q.   And that would all be known to one of  
4       skill in the art before the '620 Patent, correct?

5           A.   Selecting just one ingredient by itself  
6       and its concentration, there would be guidance  
7       along what viscosities those concentrations give  
8       for that particular ingredient, but you would have  
9       to -- if you were making a formulation you have to  
10      consider not HPMC by itself, but in the total  
11      composition.

12          Q.   Right.  And since there isn't any specific  
13      guidance as to those factors for HPMC in the  
14      '620 Patent, that would necessarily have to be  
15      known in the prior art, correct?

16           MS. EVERETT:  Objection to form.

17      BY THE WITNESS:

18          A.   Well, no.  I think that guidance is  
19      provided here in column 3, for example.

20          Q.   I just want to be clear what we're talking  
21      about here.  You stated that if you knew the  
22      viscosity that you were looking for you could

1 select a particular grade of HPMC, select a  
2 concentration of that HPMC that's going to give you  
3 approximately the viscosity that you're looking  
4 for. Do you remember that testimony?

5 A. Yes. You're just making up a solution of  
6 HPMC.

7 Q. And so what I'm asking is that would have  
8 been within the skill and understanding of one of  
9 skill in the art before the '620 Patent, right?

10 A. Somebody could make a solution of HPMC  
11 before the '620 Patent for sure.

12 Q. So to clarify, if somebody could make a  
13 solution with a particular range of viscosity using  
14 HPMC, not by itself, that would have been within  
15 the knowledge of a person of ordinary skill before  
16 the '620 Patent, right?

17 A. One would have to consider what other  
18 ingredients were in that composition in addition to  
19 HPMC, but adding in HPMC to a formulation would  
20 have been known to increase the viscosity, for  
21 example.

22 Q. I'd like to go back to claim 11 again. So

1       there's some additional excipients recited in claim  
2       11 besides cellulose derivatives; do you agree with  
3       that?

4               MS. EVERETT: Objection, outside the  
5       scope.

6       BY THE WITNESS:

7               A.   There's other thickening agents listed in  
8       claim 11 in addition to cellulose derivatives, yes.

9               Q.   So some of the examples of those are  
10       polyvinylpyrrolidone, polyvinyl alcohol, polyacrylic  
11       acid, and pectin?

12              MS. EVERETT: Objection, outside the  
13       scope.

14       BY THE WITNESS:

15              A.   I see those listed there, yes.

16              Q.   I have a similar question with respect to  
17       those excipients. Those were known in the prior  
18       art to one of skill in the art before the  
19       '620 Patent, right?

20              MS. EVERETT: Objection, outside the  
21       scope.

22       BY THE WITNESS:

1           A. These excipients would be listed in, you  
2 know, reference books like the Handbook of  
3 Pharmaceutical Excipients. These would have been  
4 known as potential thickening agents for generally  
5 pharmaceutical formulations.

6           Q. And similar to some of the questions I had  
7 about HPMC, is there any particular guidance about  
8 the use of any of those additional excipients that  
9 are claimed in claim 11 in the '620 Patent?

10           MS. EVERETT: Objection, outside the  
11 scope.

12           MR. CHESLOCK: On that I'll reiterate I  
13 think that's an objection that goes outside the  
14 permissible bounds. If you want to have a  
15 conversation about why this is relevant we can do  
16 that, but I'd appreciate not asserting that  
17 objection.

18           MS. EVERETT: Andrew, we've had a couple  
19 depositions already go forward in this case and  
20 your co-counsel, Mike Houston, certainly used that  
21 objection. So to the extent you have an issue with  
22 that, I suggest you take it up with him. It's

1 outside the scope, you didn't challenge those  
2 (inaudible). It's not in Dr. Smyth's report. My  
3 objection stands.

4 BY MR. CHESLOCK:

5 Q. Same question. I'll repeat it.

6 With respect to those well-known  
7 excipients that are additionally claimed in claim  
8 11, there isn't anything specific about their use  
9 in the '620 Patent in terms of being able to  
10 process them for a formulation in the context that  
11 you mentioned, correct?

12 MS. EVERETT: Objection, outside the  
13 scope.

14 BY THE WITNESS:

15 A. Processing polymers and thickening agents,  
16 mixing those types of techniques are known, if  
17 that's what your question is asking.

18 MR. CHESLOCK: Okay. With that I don't  
19 have anything further.

20 MS. EVERETT: I think we're going to take  
21 a break and I'll talk to Dr. Smyth and see if we  
22 have anything for redirect.

1 MR. CHESLOCK: And of course --

2 MS. EVERETT: Then you'll go again if you  
3 feel it's necessary.

4 MR. CHESLOCK: That's exactly right.  
5 Thank you.

6 (A short break was had.)

7 EXAMINATION

8 BY MS. EVERETT:

9 Q. Dr. Smyth, I'd like to direct you to your  
10 second declaration, which is CIP-2150.

11 A. Okay.

12 Q. And specifically to paragraph 23.

13 A. Yes.

14 Q. Do you recall giving testimony about this  
15 paragraph earlier today?

16 A. Yes. I recall talking about the claim  
17 construction terms.

18 Q. I'd just like to clarify a few points. On  
19 page 11 in the middle of that paragraph you wrote  
20 in your second declaration "Cipla also told the  
21 patent examiner that the term 'suitable for nasal  
22 administration' was synonymous with the term 'nasal

1        spray' as used in the '620 Patent"; do you see  
2        that?

3            A.    Yes.

4            Q.    What do you mean by that?

5            A.    So I think if you look back on to page 10  
6        it helps sort of clarify this. In paragraph 21 I  
7        think it is that the terms -- the phrases "dosage  
8        forms suitable for nasal administration" and "nasal  
9        spray" both require pharmaceutical formulations  
10       that are tolerable to patients, that are  
11       homogeneous, and that can be suitably deposited in  
12       the nasal mucosa. So on page 11 where Cipla told  
13       the patent examiner the term "suitable for nasal  
14       administration" was synonymous with the term "nasal  
15       spray," what I mean by that is those both -- both  
16       of those terms must meet those requirements of  
17       being formulations that are tolerable to patients,  
18       homogeneous, and could be suitably deposited on the  
19       nasal mucosa.

20           Q.    Now I'd like to have you turn to the  
21       patent and look at claim 1.

22           A.    Yes.



1           Q. And I direct you to the part of the claim  
2           that says "Pharmaceutical formulation is in a  
3           dosage form suitable for nasal administration"; do  
4           you see that?

5           A. Yes.

6           Q. Can you give us examples of dosage forms  
7           that are suitable for nasal administration?

8           A. So an example would be a nasal spray  
9           formulation. Another suitable for nasal  
10          administration could be nasal drops as we talked  
11          about earlier today in claim 13, I think it is, or  
12          14.

13          Q. So I'll direct you to claim 14. Do you  
14          recall testifying about that earlier today?

15          A. I do.

16          Q. And earlier I believe you had some --  
17          there was some confusion in the testimony on claim  
18          1 versus claim 14; do you recall that?

19          A. Yes.

20          Q. Are you able to reconcile that now?

21          A. So having refreshed my memory on the claim  
22          construction, a dosage form suitable for

1 administration would be a broader term that  
2 includes different formulations like nasal sprays  
3 and nasal drops. So even though that nasal spray  
4 and dosage forms suitable for nasal administration  
5 must meet the same -- these limitations of being  
6 tolerable, homogeneous, and suitably deposited, the  
7 dosage form suitable for nasal administration would  
8 be more general than that of a nasal spray.

9 MS. EVERETT: I have no further questions.

10 MR. CHESLOCK: I have a couple questions.

11 FURTHER EXAMINATION

12 BY MR. CHESLOCK:

13 Q. Dr. Smyth, did you after the termination  
14 of my questioning have a discussion about the  
15 substance of your deposition testimony, including  
16 the testimony that you've given just now?

17 A. I asked my attorneys whether or not I  
18 could look at my report because I thought I wasn't  
19 very clear on the point on the claim construction.

20 Q. So when you say you've asked your  
21 attorneys if you could look at your report, did you  
22 have any discussions about the substance of what

1       you had already testified and how you would change  
2       that testimony, including anything that you said  
3       just now?

4               MS. EVERETT: Objection to form,  
5       mischaracterizes testimony.

6       BY THE WITNESS:

7               A. I was pretty sure I hadn't been very clear  
8       earlier today. So I wanted to look at my report  
9       and read through the claim construction. So I  
10      asked if I could see that, but I didn't have any  
11      discussions on what I should say or, you know, how  
12      I could change my testimony. I just wanted to look  
13      at my report.

14              MR. CHESLOCK: Okay. I don't have any  
15      other questions.

16                               (Whereupon, at 1:33 p.m. the  
17                               taking of the instant  
18                               deposition ceased.)

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CERTIFICATE OF DEPONENT

I hereby certify that I have read the foregoing pages of my deposition testimony in this proceeding, and with the exception of changes and/or corrections, if any, find them to be a true and correct transcription thereof.

\_\_\_\_\_

Deponent

\_\_\_\_\_

Date

NOTARY PUBLIC

Subscribed and sworn to before me this \_\_\_\_\_ day of \_\_\_\_\_, 20\_\_.

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Notary Republic

My Commission Expires: \_\_\_\_\_

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1 CERTIFICATE OF SHORTHAND REPORTER – NOTARY PUBLIC

2

3 I, TINA M. ALFARO, Certified Reporter and  
4 Notary Public within and for the District of  
5 Columbia do hereby certify:

6

7 That HUGH DAVID CHARLES SMYTH, Ph.D., the  
8 witness whose deposition is hereinbefore set forth  
9 was duly sworn by me before the commencement of  
10 such deposition and that such deposition was taken  
11 before me and is a true record of the testimony  
12 given by such witness.

13

14 I further certify that the adverse party,  
15 Cipla Limited, was represented by counsel at the  
16 deposition.

17

18 I further certify that the deposition of  
19 HUGH DAVID CHARLES SMYTH, Ph.D., occurred at the  
20 offices of Sterne Kessler Goldstein Fox, 1100 New  
21 York Avenue, NW, Washington, D.C. on the 31st day  
22 of January, 2018.

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I further certify that I am not related to  
any of the parties to this action by blood or  
marriage, I am not employed by or an attorney to  
any of the parties to this action, and that I am in  
no way interested, financially or otherwise, in the  
outcome of this matter.

IN WITNESS WHEREOF, I have hereunto set my  
hand this 31ST day of JANUARY, 2018.  
My Commission expires October 31, 2020.

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NOTARY PUBLIC IN AND FOR THE  
DISTRICT OF COLUMBIA