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UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION
OFFICE OF ADMINISTRATIVE LAW JUDGES

In the Matter of:)
IMPAX LABORATORIES, INC,)
a corporation,) Docket No. 9373
Respondent.)
-----)

1 APPEARANCES:

2

3 ON BEHALF OF THE FEDERAL TRADE COMMISSION:

4 CHARLES A. LOUGHLIN, ESQ.

5 J. MAREN SCHMIDT, ESQ.

6 NICHOLAS A. LEEFER, ESQ.

7 Federal Trade Commission

8 Bureau of Competition

9 Constitution Center

10 400 7th Street, S.W.

11 Washington, D.C. 20024

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1 P R O C E E D I N G S

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3 JUDGE CHAPPELL: Okay. Let me call to order
4 Docket 9373.

5 Next witness.

6 MR. LOUGHLIN: Good morning, Your Honor.

7 Before we call our next witness, could I raise
8 a scheduling issue?

9 JUDGE CHAPPELL: I was wondering when that
10 would happen.

11 Go ahead.

12 MR. LOUGHLIN: Your Honor, unfortunately, we
13 found out that one of our witnesses for tomorrow,
14 Mr. Bryan Reasons, has had a family issue come up and
15 he won't be here tomorrow.

16 In light of that, we tried to rearrange some
17 witnesses, but we've been unsuccessful in finding
18 anyone who can come tomorrow, and so I think we're
19 going to be done probably my guess is midafternoon with
20 our final witness, unfortunately.

21 JUDGE CHAPPELL: You mean today or tomorrow?

22 MR. LOUGHLIN: Tomorrow, Your Honor. Today
23 we're fine. Tomorrow, Mr. Reasons, who was supposed to
24 attend, cannot make it.

25 JUDGE CHAPPELL: Have you and respondent's

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1 witness, that witness is finished.

2 MR. HASSI: Yes, Your Honor.

3 MR. LOUGHLIN: Yes, Your Honor.

4 JUDGE CHAPPELL: I don't know what's going on
5 with Mr. Reasons, but perhaps is he available Monday?

6 MR. LOUGHLIN: He is available -- no,
7 Your Honor. He's available next Friday. We intend to
8 call him then.

9 JUDGE CHAPPELL: So tomorrow we would go -- so
10 you've got -- you're expecting Cuca to go a day and a
11 half or do you have someone after Cuca?

12 MR. LOUGHLIN: We have Mr. Cuca this morning,
13 and we have Dr. Seddon Savage after Mr. Cuca, and then
14 we have Professor Bazerman.

15 JUDGE CHAPPELL: So you do have those people
16 lined up this week.

17 MR. LOUGHLIN: Yes.

18 JUDGE CHAPPELL: So we'll play out the string
19 and see where we end up. All right. Thanks for
20 letting me know.

21 MR. LOUGHLIN: Thank you, Your Honor.

22 At this time, Your Honor--

23 JUDGE CHAPPELL: Wait a minute. I thought that
24 there was more than one. I thought you said a few
25 matters.

1 MR. LOUGHLIN: No. That was the only issue I
2 wanted to raise.

3 JUDGE CHAPPELL: Okay. Good. I don't want to
4 encourage them.

5 MR. LOUGHLIN: Understood, Your Honor.

6 At this time complaint counsel calls
7 Mr. Roberto Cuca.

8 And Your Honor, my colleague Maren Schmidt will
9 conduct the examination.

10 JUDGE CHAPPELL: Okay.

11 - - - - -

12 Whereupon --

13 ROBERTO CUCA

14 a witness, called for examination, having been first
15 duly sworn, was examined and testified as follows:

16 MS. SCHMIDT: Good morning, Your Honor, and may
17 it please the court.

18 My name is Maren Schmidt on behalf of complaint
19 counsel.

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21 DIRECT EXAMINATION

22 BY MS. SCHMIDT:

23 Q. Good morning, Mr. Cuca.

24 Would you please introduce yourself to the
25 court by stating your full name.

1 A. Roberto Cuca.

2 Q. Mr. Cuca --

3 JUDGE CHAPPELL: Could I ask you to slow down
4 and speak up.

5 MS. SCHMIDT: Yes, sir. Yes, Your Honor.

6 BY MS. SCHMIDT:

7 Q. Mr. Cuca, we met in Philadelphia back in August
8 of this year when I took your deposition.

9 How are you doing today, Mr. Cuca?

10 A. Good.

11 Q. Great.

12 Is there anything that may affect your ability
13 to give truthful, complete testimony today?

14 A. No.

15 Q. And I will just let you know, if we look at any
16 documents this morning, we will publish them on the
17 screen before you, but there are also paper copies in
18 the binder placed on the table next to you that I may
19 direct you to.

20 Just to briefly go over your background,
21 Mr. Cuca, I believe you have a master's in business
22 administration?

23 A. Yes.

24 Q. And where did you earn your M.B.A.?

25 A. The University of Pennsylvania.

1 Q. And when did you graduate?

2 A. 2004.

3 Q. And do you hold any financial certifications?

4 A. Yes.

5 Q. And what financial certifications do you hold?

6 A. The chartered financial analyst designation.

7 Q. And what is a designation as a chartered
8 financial analyst?

9 A. It's a nonacademic but chartered designation
10 that is granted after a series of three tests
11 establishing competence in financial matters.

12 JUDGE CHAPPELL: How does that vary from a
13 CPA?

14 THE WITNESS: A CPA is for auditing, whereas a
15 financial analyst is for analysis of financial
16 statements and companies.

17 JUDGE CHAPPELL: Is one about as tough as the
18 other to pass?

19 THE WITNESS: CFAs typically claim that the CFA
20 is harder.

21 JUDGE CHAPPELL: I would go with that.

22 BY MS. SCHMIDT:

23 Q. And Mr. Cuca, when did you obtain your CFA
24 designation?

25 A. 2010 I believe.

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1 Q. And how long did you hold that position?

2 A. For most of the time I was there until the last
3 five or six months.

4 Q. And in those last few months what was your new
5 position at Endo?

6 A. I was treasurer and head of business
7 development, finance and tax.

8 Q. And when you joined -- pardon me.

9 When you joined Endo as vice president of
10 financial planning and analysis, who did you report
11 to?

12 A. Alan Levin, the CFO.

13 Q. And how long did you report to Mr. Levin?

14 A. The entire time I was there.

15 Q. And just throughout the day, is financial
16 planning and analysis also referred to or shortened as
17 FP&A?

18 A. Yes.

19 Q. And while you were at Endo, what was the
20 function of the financial planning and analysis
21 division?

22 A. FP&A was in charge of budgeting and forecasting
23 and analyzing the variances between actual results and
24 forecasted results.

25 Q. And what did budgeting involve at Endo?

1 A. Setting out the resources that each function in
2 the company would be targeted to spend in a certain
3 period.

4 Q. And how would you determine what resources were
5 available?

6 A. We sized the amounts of spend based in part on
7 prior year spends and then forecasted expectations for
8 effort to support new products.

9 Q. And is there any component of forecasted
10 revenues in your budgeting process?

11 A. Part of the budget would include an expectation
12 or a forecast of revenues.

13 Q. And was there a regular timeline for the
14 budgeting process at Endo?

15 A. Yes.

16 Q. And what was that?

17 A. The budgeting process began in the fall of one
18 year and concluded with the presentation of the budget
19 to the board of directors at a January board of
20 directors meeting.

21 Q. And what would occur when -- after the budget
22 was presented to the board of directors?

23 A. If the board of directors approved it, that
24 became the budget for that year.

25 Q. Would the budget be subject to change or was

1 that firm once approved by the board?

2 A. The budget wasn't changed once it was set, but
3 new numbers were forecast, and those forecasts were
4 used as new targets for operating goals.

5 Q. Okay. And I think you also mentioned
6 forecasting.

7 What is involved -- or what was involved in
8 forecasting at Endo?

9 A. Forecasting meant that the revenues and spends
10 were updated for actual period spends and revenues and
11 the remaining periods were -- were reforecast.

12 Q. And did the FP&A group at Endo work with any
13 other divisions to accomplish its forecasting work?

14 A. Yes. The FP&A group worked with all the
15 divisions to forecast their expenses and then with
16 commercial to forecast revenues.

17 Q. And what is commercial?

18 A. Commercial is the part of the company that was
19 responsible for marketing and sales of approved
20 products.

21 Q. And what kind of assumptions go into
22 forecasting your product sales?

23 A. I'm sorry. Can you repeat?

24 Q. Certainly.

25 What are some of the major assumptions that you

1 need to make in order to forecast your product sales
2 area at -- Endo's product sales?

3 A. The two components are price and volume, so
4 you forecast what the demand is for volumes of
5 products and then what the achieved price would be
6 given certain assumptions around rebates and
7 discounts.

8 Q. And what are some of the primary events that
9 could cause your assumptions to change?

10 A. If actuals had come in lower suggesting that
11 trends had changed. If the mix of payers had shifted
12 such that more heavily discounted purchasers were
13 purchasing. Anything that would affect price or
14 volume.

15 Q. And how would the -- your expectations of
16 competition affect your expectations of price or
17 volume?

18 A. If there was an expectation for increased
19 competition, that could affect certainly volume and
20 potentially price as well.

21 Q. And in your forecasting I think -- I'm sorry.
22 I believe you just went over price and volume.

23 Is that what would result in a forecast of
24 revenue?

25 A. Yes.

1 Q. And for what purpose would you forecast
2 revenues?

3 A. To understand what the achieved revenues were
4 likely to be and consequently what the earnings of the
5 company would be.

6 Q. And then how in turn did that go into your
7 budgeting?

8 A. In the forecasting, as we got actuals for
9 individual periods and updated the forecasts for the
10 year, we would reforecast the revenues and then
11 potentially adjust spending if needed to achieve a
12 certain bottom-line result.

13 Q. And for accounting purposes, when are revenues
14 recognized?

15 A. Pharmaceutical product revenues are recognized
16 when the company sells to the next user, which in the
17 pharmaceutical supply chain for retail products is a
18 wholesale distributor.

19 Q. So even though you might forecast your revenues
20 for upcoming years, you wouldn't recognize those sales
21 until they had actually been realized?

22 A. Correct.

23 Q. Mr. Cuca, do you recall Endo engaging in
24 settlement negotiations with Impax in the spring to
25 early summer of 2010?

1 JUDGE CHAPPELL: Before you do that, I have a
2 couple questions for the witness.

3 This process you just described, the job you
4 did at Endo, were you the only person doing that or
5 were there others doing the same job?

6 THE WITNESS: There were others doing
7 components of the same job.

8 JUDGE CHAPPELL: How many?

9 THE WITNESS: In the finance organization and
10 FP&A it was probably ten people, and then revenue
11 forecasting, which was done separately in commercial,
12 probably had six people.

13 JUDGE CHAPPELL: And all of these people, did
14 they all report to Mr. Levin?

15 THE WITNESS: The commercial team in commercial
16 did not.

17 JUDGE CHAPPELL: These processes you just
18 described, did you actually crunch numbers or did
19 someone who reported to you crunch numbers?

20 THE WITNESS: Both.

21 JUDGE CHAPPELL: Go ahead.

22 MS. SCHMIDT: Okay.

23 BY MS. SCHMIDT:

24 Q. And just to follow up on Your Honor's
25 questions, Mr. Cuca, out of those number of people

1 involved in the financial planning and analysis
2 division, how many of those reported to you?

3 A. Several of them reported directly to me. All
4 of them reported indirectly to me.

5 JUDGE CHAPPELL: That would be of the ten?

6 THE WITNESS: Yes.

7 BY MS. SCHMIDT:

8 Q. Mr. Cuca, do you recall Endo engaging in
9 settlement negotiations with Impax in the spring to
10 early summer of 2010?

11 A. Yes.

12 Q. And did you have a role in those settlement
13 negotiations between Endo and Impax?

14 A. Yes.

15 Q. And what was that role?

16 A. I supported Alan Levin in his discussions with
17 Impax and attended some of the phone calls and
18 meetings.

19 Q. And Mr. Levin was the CFO?

20 A. Correct.

21 Q. And what was Mr. Levin's role in the settlement
22 negotiations with Impax?

23 A. He would have discussions directly with the
24 counterparty and would advise the rest of the

25

1 settlement.

2 Q. So was he the primary negotiator?

3 A. He was one of them.

4 Q. One of them. Okay.

5 And what kind of help did Mr. Levin seek from
6 you?

7 A. Analysis of proposed settlement terms.

8 Q. Any particular kind of analysis?

9 A. Financial analysis.

10 Q. Okay. And what type of financial analysis did
11 you do for Mr. Levin of the settlement agreement?

12 A. Analyzing the effect of different proposed
13 settlement packages on the financial performance of the
14 company.

15 Q. And how could the potential settlement with
16 Impax impact the performance of Endo, the financial
17 performance of Endo?

18 A. Depending on, for example, when Impax might
19 enter the market and any other provisions around any
20 other terms, the sales of Endo's products could be
21 affected by competition.

22 Q. And how could the timing of Impax' entry into
23 the market financially affect Endo?

24 A. When a generic enters a market when there's
25 generic competition, usually the innovator product's

1 sales decline in volume because of competition.

2 Q. And does the timing of that entrance have any
3 impact on that analysis?

4 A. It determines the beginning of the -- the
5 beginning of that effect occurring.

6 Q. And were there any particular provisions
7 regarding timing of that effect performed this type of analysis? for)

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1 Q. Did that date vary between any of the
2 settlements?

3 A. Let me rephrase to be more clear.

4 Q. Did the entry date that was being discussed in
5 any of the settlement drafts exchanged between the
6 parties-- did that generic entry date differ at all?

7 A. I don't recall if it did.

8 Q. Beyond the generic entry date, were there any
9 other provisions being or potential provisions being
10 discussed between Endo and Impax that you performed
11 financial analysis of?

12 A. I performed financial analysis of how the
13 whole -- all the provisions of the agreement would
14 affect Endo.

15 Q. And beyond analysis of provisions being
16 discussed, did you have any other role in the
17 settlement negotiations with Impax?

18 A. I think I prepared a draft of one of the
19 provisions.

20 Q. And which provision was that?

21 A. That was the -- I think what ended up being
22 named the Endo credit provision.

23 Q. And what is the Endo credit?

24 A. The Endo credit, and there was a royalty
25 provision as well, were provisions to reduce the

1 uncertainty around likely cash flows between the
2 companies.

3 Q. What do you mean by "cash flows between the
4 companies"?

5 A. Well, actually, let me correct that. Cash
6 flows to each of the companies.

7 Q. And how did the Endo credit seek to achieve
8 that objective?

9 A. The Endo credit established terms based on
10 expectations of Endo product sales and Impax product
11 sales under which there could be a payment from Endo to
12 Impax if those expectations weren't met.

13 Q. And what were those expectations?

14 A. They were expectations of growth from the time
15 of the signing of the agreement or the absence of a
16 decline from the signing of the agreement.

17 JUDGE CHAPPELL: You said you drafted the
18 agreement. Did you call it the Endo agreement yourself
19 from the beginning -- I mean, the Endo credit?

20 THE WITNESS: Internally we referred to it as a
21 make-whole payment. I think the defined term became
22 the Endo credit at some point.

23 JUDGE CHAPPELL: Because I think you just said
24 earlier it also could have required a royalty from
25 Impax to Endo; correct?

1 THE WITNESS: Correct. There was a second
2 provision that was a royalty provision that I -- I
3 don't think I drafted but that worked as kind of the
4 mirror image of the Endo credit.

5 JUDGE CHAPPELL: And had that happened, it
6 would have been an Impax credit?

7 THE WITNESS: Essentially.

8 BY MS. SCHMIDT:

9 Q. And prior to your work on the --

10 JUDGE CHAPPELL: Hold on a second.

11 Did I hear you say you -- when you said you
12 drafted this, you're not talking about the royalty
13 prong, you're talking about the credit based on Endo's
14 sales --

15 THE WITNESS: Yes, Your Honor.

16 JUDGE CHAPPELL: -- that may bring a credit
17 back to your company. That's the portion you drafted?

18 THE WITNESS: I drafted what was called the
19 Endo credit, which would have required a payment from
20 Endo to Impax.

21 The royalty provision was drafted I think by
22 somebody else, and that would have required a payment
23 from Impax to Endo.

24 JUDGE CHAPPELL: Well, you think it was
25 someone else. If you didn't draft it, someone did;

1 right?

2 THE WITNESS: Yes, sir.

3 JUDGE CHAPPELL: Okay. In the final form
4 that's in the -- are you familiar with the actual
5 settlement agreement that was signed by the parties?

6 THE WITNESS: I've seen it. Yes.

7 JUDGE CHAPPELL: Do you know if your draft is
8 exactly how it occurs, or was it changed after you
9 drafted it?

10 THE WITNESS: It was definitely changed after
11 the first draft that I prepared, but I was involved in
12 some of the changes, and some of them were proposed by
13 Impax.

14 JUDGE CHAPPELL: Had you -- did you have
15 experience with other agreements in drafting a term
16 like this one? Had you done this before?

17 THE WITNESS: Not -- not like this one.

18 JUDGE CHAPPELL: Did you go to someone for
19 advice or counsel on how to word this thing?

20 THE WITNESS: No.

21 JUDGE CHAPPELL: You created it out of whole
22 cloth yourself.

23 THE WITNESS: Yes, sir.

24 JUDGE CHAPPELL: Any legal training?

25 THE WITNESS: Yes.

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1 this provision, what was your starting point?

2 A. Can you clarify?

3 Q. Sure.

4 What instructions were you given in terms of
5 what you were trying to achieve in drafting this
6 provision?

7 A. I don't recall the exact instructions.

8 Q. Did you have any objectives in drafting the
9 provision?

10 A. So the goal was to reduce the uncertainty
11 around what each of the parties would experience from
12 cash flows, so the goal was to -- if the market changed
13 substantially before the date that the parties agreed
14 that Impax could launch, there would be a way of making
15 Impax whole.

16 Q. And what do you mean by "making Impax whole"?

17 A. Helping them achieve cash flows that would have
18 been similar to what they would have achieved had the
19 change in the marketplace not occurred.

20 Q. And what sort of change in the marketplace were
21 the parties anticipating?

22 A. I don't know that anyone was anticipating a
23 change in the marketplace, but the provision was
24 designed to insulate against a substantial decrease in
25 sales of the innovator product.

1 Q. If the parties weren't anticipating any sort of
2 substantial change, why were they bothering to create
3 this provision?

4 A. In case such a change took place.

5 Q. Is that a standard practice in patent
6 settlement agreements between brands and generics?

7 A. I don't know.

8 Q. But nobody gave you a prior version to look at
9 to include?

10 A. Correct.

11 Q. Have you ever heard of one in another brand
12 patent settlement in any other context?

13 A. I have not.

14 Q. And -- I'm sorry. I think -- when you're using
15 the term "market," what do you mean by "market"? How
16 are you defining that?

17 A. The sales for the innovator product.

18 Q. And that would be Opana ER?

19 A. Correct.

20 Q. And what could potentially cause the sales of
21 Opana ER to decrease in a substantial fashion?

22 A. A supply disruption.

23 Q. Anything else?

24 A. A change in the strategy of the company.

25 Q. And at that time when you were negotiating with

1 Impax, was Endo considering a change in strategy
2 regarding Opana ER?

3 A. Endo was working on a different formulation
4 that could have affected the sales of ER.

5 Q. How so?

6 A. There was -- Endo was working on what was
7 called CRF, a crush-resistant formulation of Opana, and
8 depending on when that came to market, that could have
9 affected the sales of the non-crush-resistant
10 formulation.

11 Q. And was that a particular concern that Impax
12 raised?

13 A. I don't recall if they raised that.

14 Q. Is there -- did you have any other
15 understanding of why Impax was seeking this provision?

16 A. I didn't.

17 Q. And just to make sure I'm clear, Endo was the
18 plaintiff in the action, in the patent action with
19 Impax?

20 A. Correct.

21 Q. And Impax was the defendant?

22 A. Yes.

23 Q. And why was Endo working with Impax to create a
24 provision in which the plaintiff would be paying the
25 defendant?

1 JUDGE CHAPPELL: I'm not sure we've heard a
2 foundation for him to tell us about any litigation.

3 MS. SCHMIDT: Sure. I appreciate the comment,
4 Your Honor. I'll back up.

5 BY MS. SCHMIDT:

6 Q. Let me actually go back a little further.

7 I think you mentioned CRF, crush-resistant
8 formula?

9 A. Formulation. Yes.

10 Q. Formulation. Sorry.

11 And how could the reformulation to a
12 crush-resistant formulation affect the sales of the
13 Opana ER that was on the market when Impax and Endo
14 were negotiating a settlement?

15 JUDGE CHAPPELL: Excuse me. You're asking him
16 a scientifically based question, aren't you?

17 I mean, I don't have any -- I haven't heard
18 anything that tells me he knows tamper-resistant from
19 water-resistant or anything else.

20 MS. SCHMIDT: I'm sorry. I was -- thank you,
21 Your Honor.

22 JUDGE CHAPPELL: Let's just say that's an
23 improper hypothetical, in my opinion. You know, I want
24 the answers to be something we can all use.

25 MS. SCHMIDT: Thank you, Your Honor. Let me

1 definitely strive to be more clear.

2 BY MS. SCHMIDT:

3 Q. Mr. Cuca, earlier you mentioned a
4 crush-resistant formulation?

5 A. Yes.

6 Q. In your work in financial planning and
7 analysis, did you incorporate -- did you have any
8 reason to analyze Endo's potential introduction of a
9 crush-resistant formulation?

10 A. There were forecasts, yes, of the sales of a
11 crush-resistant formulation.

12 Q. And how far in advance would you start making
13 those forecasts?

14 A. Typically as soon as a development project
15 began.

16 Q. And was that underway when you joined in the
17 spring of 2010?

18 A. Yes.

19 Q. And did Endo anticipate that the introduction
20 of a crush-resistant formulation would have some sort
21 of impact on its current Opana ER formulation sales?

22 A. I don't recall specifically.

23 Q. What would Endo's introduction of a
24 crush-resistant formulation -- would that have any
25 impact on the expected sales of Impax' generic

1 product?

2 A. I don't know.

3 Q. At your deposition in August, do you recall
4 testifying that, quote, "If we discontinued selling
5 Opana ER, then their replacement of the market would be
6 less valuable"?

7 A. That sounds familiar.

8 Q. Do you agree with that statement still?

9 A. Yes.

10 Q. Thank you.

11 JUDGE CHAPPELL: You realize that was a
12 different question than you asked the man.

13 MS. SCHMIDT: I'm sorry.

14 JUDGE CHAPPELL: The one you asked him here
15 is different than the one you asked him in a
16 deposition.

17 MS. SCHMIDT: Yes, Your Honor. I apologize. I
18 wasn't trying to impeach Mr. Cuca.

19 JUDGE CHAPPELL: I understand that. I'm just
20 letting you know. To be fair to a witness -- this
21 happens far too often in front of me -- if you're
22 going to bring something out of a deposition, make
23 sure it's the same question you just asked the
24 witness.

25 MS. SCHMIDT: Thank you, Your Honor.

1 BY MS. SCHMIDT:

2 Q. So how --

3 JUDGE CHAPPELL: You know, in other words,
4 think about yourself sitting in that chair. I don't
5 know if any of you have ever done that, but it's a
6 whole new world. Every trial lawyer should have to be
7 a witness in a case at some point; it will change the
8 way you examine a witness.

9 MS. SCHMIDT: I believe you. Thank you,
10 Your Honor.

11 JUDGE CHAPPELL: Go ahead.

12 MS. SCHMIDT: Thank you.

13 BY MS. SCHMIDT:

14 Q. Mr. Cuca, going back to your work on drafting
15 the make-whole provision, what was your starting basis
16 for coming up with a mechanism for the payment?

17 A. It would have been an expectation -- it would
18 have been a guess or some understanding of what the
19 parties thought would happen if nothing disrupted the
20 ordinary course.

21 Q. If nothing would happen to what?

22 A. If nothing would happen to disrupt the -- the
23 ordinary progress of branded Opana sales and the entry
24 of a generic.

25 Q. And with that as your starting point, what did

1 you next look at?

2 A. What would happen when that disruption occurred
3 or if a disruption occurred.

4 Q. And how -- what did you include into the
5 provision to address that?

6 A. An expectation about the relative sales
7 immediately before Impax entered the market and sales
8 earlier in the trajectory of Opana ER's sales.

9 JUDGE CHAPPELL: When you were working on this
10 provision, sir, did you have any knowledge of your
11 company's plans to introduce a tamper-resistant or
12 crushproof product to compete with Opana ER or replace
13 it?

14 THE WITNESS: I knew that CRF was under
15 development.

16 JUDGE CHAPPELL: And were you told in any way,
17 shape, or form to keep that in the back of your mind
18 when you worked on this provision?

19 THE WITNESS: No. I don't think so.

20 JUDGE CHAPPELL: Did the knowledge of that,
21 what little you did have, did that affect the way you
22 drafted the provision?

23 THE WITNESS: No. No. Because it didn't
24 matter what disrupted the revenues, you would draft it
25 the same way.

1 JUDGE CHAPPELL: Let's try to move this along.
2 What assumptions did you start with when you
3 drafted this?

4 THE WITNESS: So the provision was intended to
5 capture a loss of value to Impax' launch and its six
6 months of exclusivity post that launch, so I started
7 with what the Opana ER sales could be expected to look
8 like if nothing changed the trajectory of its growth
9 and then tried to understand what the negative impact
10 to Impax would be from a profit perspective if
11 something did disrupt that growth.

12 JUDGE CHAPPELL: And those were your concerns
13 and assumptions.

14 THE WITNESS: Correct.

15 JUDGE CHAPPELL: And you told me earlier that
16 the version you drafted differs from the final version;
17 correct?

18 THE WITNESS: The first version I drafted
19 differs from the final version. Yes.

20 JUDGE CHAPPELL: Can you tell me whether or
21 not the final version, the signed agreement,
22 incorporated and covered all of your concerns and
23 assumptions?

24 THE WITNESS: Yes, it did.

25 JUDGE CHAPPELL: Did you make any assumption

1 one way or the other of whether the payment may end up
2 being zero?

3 THE WITNESS: I didn't make any assumption. I
4 knew that the payment could be zero.

5 JUDGE CHAPPELL: And that was inartfully
6 worded.

7 Did you assume there would be a payment when
8 you drafted it?

9 THE WITNESS: I did not.

10 JUDGE CHAPPELL: Go ahead.

11 BY MS. SCHMIDT:

12 Q. Pardon me. I'm just going to skip here.

13 Mr. Cuca, what did you mean by Impax' six
14 months of exclusivity?

15 A. Under the Hatch-Waxman provisions of the
16 Federal Food, Drug and Cosmetic Act, when a
17 Paragraph IV -- so when a generic competitor asserts
18 that patents are -- of the innovator are invalid or
19 inapplicable to their drug product and wins in
20 litigation and becomes the first to enter the market,
21 the FDA is precluded for six months from approving
22 another generic version of the innovator drug, so
23 that's referred to as six months of exclusivity.

24 Q. And did you include specific metrics or did
25 Endo and Impax ultimately include specific metrics to

1 capture their expectations of earnings during those six
2 months of exclusivity?

3 A. In the Endo credit provision?

4 Q. Yes.

5 A. Components of the Endo credit provision were
6 intended to reflect that. Yes.

7 Q. And what were those components?

8 A. A generic erosion assumption.

9 A profitability assumption.

10 A volume assumption preceding the Impax
11 launch.

12 Q. And would volume be based on a substitution
13 rate?

14 A. Sorry. I should have been clearer.

15 Well, a price and volume, so a revenue
16 assumption of the innovator product before the Impax
17 launch.

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1 the final version?

2 A. At least one change had to do with measuring
3 revenues before genericization versus measuring units
4 of different strengths of Opana ER before
5 genericization.

6 Q. And what was the purpose of that change?

7 A. A version of the provision that was a
8 counterproposal from Impax combined different strengths
9 of Opana ER in a way that didn't allow for the
10 calculation of dollars from that.

11 Q. And how would that -- how would the inability
12 to calculate the dollars from that have an effect on
13 the payment?

14 A. You wouldn't be able to use the provision to
15 calculate the payment.

16 Q. Okay. Earlier Your Honor -- strike that. Let
17 me rephrase.

18 Earlier you stated that you knew that the
19 potential payment could be zero; is that correct?

20 A. Correct.

21 Q. Did you do any analyses to determine what the
22 payment could be?

23 A. I tested the provision to make sure that it was
24 producing outputs that I thought it was supposed to be
25 producing, and one of them, one of the potential

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1 substitution rate. It was a question I considered
2 leading because it was suggesting an answer. To your
3 credit, you didn't just say yes.

4 Have you ever heard of the phrase
5 "substitution rate"?

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1 worked, and once I was satisfied with that, that would
2 have been the end of it.

3 (Pause in the proceedings.)

4 JUDGE CHAPPELL: Anything further?

5 MS. SCHMIDT: Yes, Your Honor.

6 JUDGE CHAPPELL: Do you need a moment to
7 consult with co-counsel?

8 MS. SCHMIDT: Yes. I would appreciate --

9 JUDGE CHAPPELL: I would rather have you do
10 that than waste our time. Go ahead.

11 MS. SCHMIDT: Thank you, Judge.

12 (Pause in the proceedings.)

13 JUDGE CHAPPELL: Go ahead.

14 MS. SCHMIDT: Thank you, Your Honor.

15 BY MS. SCHMIDT:

16 Q. And who did you share this analysis with?

17 A. No one.

18 Q. Mr. Cuca, do you recall testifying at your
19 deposition in August, quote, "I would have talked about
20 it with Alan, reviewed it with Alan"?

21 A. I would have told him that I confirmed that the
22 provision worked, but I wouldn't have brought any
23 results with me or analysis.

24 Q. Okay. Thank you.

25 At this point -- and Mr. Cuca, did you continue

1 to work on the -- on this provision through execution
2 of the agreement with Impax?

3 A. Yes.

4 MS. SCHMIDT: At this point I would like to
5 show Mr. Cuca RX 364.

6 And Ms. Allen, if you would put it up at 001.

7 Your Honor, this document is admitted as part
8 of JX 002, and it is not subject to Your Honor's
9 in camera ruling.

10 JUDGE CHAPPELL: Thank you.

11 MS. SCHMIDT: And Ms. Allen, if you could
12 highlight the top portion prior to Recitals, including
13 the corner. Yes. Thank you.

14 BY MS. SCHMIDT:

15 Q. Mr. Cuca, do you recognize this as the
16 settlement and license agreement between Endo and
17 Impax?

18 A. Yes.

19 Q. And do you see in the corner that it's marked
20 Execution Version?

21 A. Yes.

22 Q. Thank you.

23 And if I could turn your attention to
24 RX-364.0003.

25 And if you -- although we will publish this on

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1 would be replaced by generic demand.

2 Q. Thank you.

3 And what is the WAC price as -- pardon me. Let
4 me restate -- the WAC price of unit as measured by FDB
5 data?

6 A. So WAC is wholesale acquisition cost, so that
7 is the published, call it, list price for each one of
8 the individual strengths that was being measured there,
9 individual strengths of Opana.

10 Q. And what is Impax net profit margin?

11 A. That is an attempt to measure the net profit
12 that would be achieved by Impax, so including things
13 like their cost to manufacture the generic product and
14 their distribution costs and any G&A or R&D costs.

15 Q. Okay. And what was the purpose of including
16 the generic substitution rate in the market share
17 profit factor?

18 A. That was to capture an expectation about the
19 amount of demand, the amount of preexisting demand for
20 the branded product that would be replaced by demand
21 for the generic product.

22 Q. And what was the purpose of including the WAC
23 price of unit as measured by FDB data?

24 A. That was intended to capture the typical
25 discount that a generic entrant in the six-month

1 exclusivity period reduces the price by compared to the
2 branded product.

3 Q. And what was the purpose of including Impax net
4 profit margin?

5 A. To calculate the net profit effect rather than
6 the effect on revenues that the -- that this provision
7 was trying to capture.

8 Q. And what is the overall purpose of the market
9 share profit factor?

10 A. It is -- it serves as an input into the Endo
11 credit that replicates some expectation of the
12 economics to Impax during the six-month exclusivity
13 period.

14 Q. Thank you.

15 And I'm sorry. I forgot to ask about one more
16 of those components.

17 What was the purpose of including half a year
18 or 180 days?

19 A. That's to capture the six-month exclusivity
20 period.

21 Q. Thank you.

22 JUDGE CHAPPELL: Sir, these definitional terms
23 of the agreement you just discussed, did you have
24 anything to do with drafting these?

25 THE WITNESS: Yes.

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1 A. Because to make Impax whole for what they --
2 what could occur if there was disruption to the
3 supply, we were trying to make them whole at the
4 bottom line, so at their profit line, whereas the
5 prior provision would have made them whole at the
6 revenue line and actually would have advantaged them
7 as compared to what was trying to be achieved.

8 Q. And how did the switch from revenues to
9 profits impact any potential payment to Impax?

10 A. All else being equal, it would have reduced the
11 payment.

12 Q. Thank you.

13 JUDGE CHAPPELL: Did you say it would have
14 reduced the payment?

15 THE WITNESS: Yes, Your Honor.

16 JUDGE CHAPPELL: The payment Impax would have
17 paid you.

18 THE WITNESS: We would have paid them.

19 JUDGE CHAPPELL: I'm sorry. Going the other
20 way.

21 So the amount you pay Impax would have reduced
22 based on this change.

23 THE WITNESS: Correct. The prior version of
24 the provision captured revenues, and this version of
25 the provision is attempting to capture profit, which

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1 Q. And what relationship does generic competition
2 have to loss of exclusivity?

3 A. So generic competition would be the -- what
4 actually happens when you lose the exclusivity.

5 Q. So that would be the market results of the
6 legal loss of --

7 JUDGE CHAPPELL: Leading. Rephrase.

8 MS. SCHMIDT: Thank you, Your Honor.

9 BY MS. SCHMIDT:

10 Q. What typically happens once exclusivity is
11 lost?

12 A. So by definition, when you lose exclusivity,
13 there's nobody else on the market, you're exclusively
14 on the market even if there's -- you know, even if your
15 patent has expired and nobody has entered, and that
16 does happen for small products sometimes.

17 So when you've lost exclusivity, there's
18 another entrant in the market, and so there's increased
19 competition.

20 Q. And is loss of exclusivity something that the
21 financial planning and analysis group would account for
22 or prepare for?

23 A. We would prepare scenarios, model scenarios,
24 that would include loss of exclusivity.

25 Q. Model scenarios of what?

1 A. Of the financial results of the company.

2 Q. And what impact does generic competition
3 typically have on a brand's sales from a financial
4 planning and analysis perspective?

5 A. It typically negatively affects volume.

6 Q. Does the number of generic competitors have any
7 impact on that?

8 A. So when there are more generic competitors,
9 there's more competition, and that often more adversely
10 affects volume.

11 Q. And when you joined Endo in the spring of 2010,
12 do you recall whether Endo was facing potential generic
13 competition for Opana ER?

14 A. At that time you mean?

15 Q. Yes.

16 A. There -- well, there had been ANDAs filed for
17 generic versions of Opana ER, but there was not
18 imminently at that point going to be a generic.

19 Q. Did your group do any work to analyze a
20 potential impact of any generic entry in 2010?

21 A. One of the scenarios that was included in the
22 analysis included what -- examined what would be the
23 effect of a generic entry after the expiration of the
24 30-month stay during the patent litigation that was
25 ongoing between Endo and Impax.

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1 and loss statement or did you have profit and loss
2 statements for different products?

3 A. We -- we analyzed profit and loss statements
4 for different products and across the company as a
5 whole.

6 Q. And how often would you create profit and loss
7 statements for the individual products?

8 A. Typically monthly.

9 Q. Monthly.

10 A. And more frequently depending on what the
11 demands were for analysis.

12 Q. And what could cause a more frequent demand
13 than monthly for a profit and loss analysis?

14 A. Any request from senior management to
15 understand different scenarios or...

16 MS. SCHMIDT: I'd like to show Mr. Cuca what
17 has been marked as CX 3017. And this document has been
18 admitted as part of JX 002 and is not subject to
19 Your Honor's in camera ruling.

20 I'd actually like to start at CX 3017-002.

21 And Ms. Allen, if you could call up the
22 beginning of the e-mail starting in the middle of the
23 page from Hogan, Brian.

24 BY MS. SCHMIDT:

25 Q. And Mr. Cuca, do you see where it says from

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1 JUDGE CHAPPELL: You understand you're leading
2 the witness now, don't you? You need to correct that.

3 MS. SCHMIDT: I'm sorry, Your Honor. Let me
4 fix that.

5 BY MS. SCHMIDT:

6 Q.

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1 A. Traditional erosion as determined by
2 forecasting.

3 Q. Does "traditional erosion" mean anything to
4 you?

5 A. That it would look like some precedence of
6 generic entry.

7 Q. Okay. And what is the second traditional -- or
8 I'm sorry.

9 What is the second erosion possibility?

10 A. The second erosion scenario is traditional
11 erosion for most segments but that 25 percent access
12 would be maintained at no additional cost.

13 Q. And does that say "25 percent access through
14 contracts at no additional cost"?

15 A. Yes.

16 Q. And what does that mean?

17 A. That for most of the segments, it looks like
18 probably 75 percent of the segments, that the erosion
19 would be traditional, for the remaining 25 percent of
20 the segments via some aspect of contracting there would
21 be -- there would not be that erosion and there would
22 not be cost for that erosion, for maintaining -- for
23 preventing that erosion.

24 Q. And what is the third erosion scenario?

25 A. Traditional erosion for most segments --

1 sorry -- but maintain 50 percent access through
2 contracts.

3 Q. And what would be the difference between the
4 first and second scenario that would account for the
5 retention of 50 percent rather than 25 percent of
6 sales?

7 A. Between the second and third scenarios?

8 Q. Yes.

9 A. The difference between them seems to be that
10 there would be a change in the pricing of Opana, so
11 some cost to retain access to the greater portion of
12 contracts.

13 JUDGE CHAPPELL: I'm looking at this e-mail and
14 I see Scenario 1 and Scenario 2. Where's this third
15 scenario you're talking about? I don't see it on the
16 e-mail.

17 THE WITNESS: I was similarly confused at
18 first, too.

19 Under "Opana ER - generic 7/1" you see there's
20 three subbullets?

21 So those are sub-scenarios within the major
22 scenario.

23 MS. SCHMIDT: Thank you, Mr. Cuca. You
24 explained it better than I did.

25 JUDGE CHAPPELL: So Scenario 1 we're told has

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1 A. That there would be no generic for IR in the
2 second scenario.

3 Q. Are there any other differences between
4 Scenario 1 and Scenario 2?

5 A. That looks like the only difference.

6 Q. Thank you, Mr. Cuca.

7 I'd like to turn to CX 3017-001.

8 And Ms. Allen, if you could highlight the top
9 e-mail, actually just the e-mail portion and the
10 address and top line of the e-mail. Oh, I'm sorry.
11 You can actually go ahead and include the first
12 paragraph.

13 JUDGE CHAPPELL: Tell us again, who is
14 Brian Hogan?

15 THE WITNESS: He was a member --

16 JUDGE CHAPPELL: Maybe not again. Just tell us
17 who is Brian Hogan.

18 THE WITNESS: He was a member of the FP&A team
19 who worked with the commercial contracting group on
20 issues of uptake via the contracting process.

21 JUDGE CHAPPELL: Was he on something that might
22 have been called the settlement team regarding this
23 patent litigation?

24 THE WITNESS: I don't think so.

25 JUDGE CHAPPELL: Was he a bean counter?

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1 What is Opana ER demand sales?

2 A. That is the actual end user demand not at the
3 wholesaler or distributor level but at the retail
4 pharmacy level for the product.

5 Q. So at the actual patient level?

6 A. Correct.

7 Q. And what is Opana ER burndown?

8 A. That would be the amount by which wholesalers
9 and other pipeline participants, distributors, are
10 reducing their holdings in order to offset in this case
11 the expected decrease in demand for the product.

12 Q. How would they reduce their holdings?

13 A. By buying less from us -- Endo.

14 Q. And I'm sorry. I'm not trying to be
15 repetitive, but just to be clear, why would they be
16 buying less from Endo?

17 A. In expectation of decreased future demand.

18 Q. What would be driving the expectation of
19 decreased future demand?

20 A. The erosion in the -- in the ongoing sales for
21 Opana.

22 JUDGE CHAPPELL: You said, "What would be
23 driving the expectation of decreased future demand?"
24 Just so I'm clear, and I want to make sure the witness
25 is clear, were you actually asking him what would cause

1 decreased future demand?

2 MS. SCHMIDT: Yes, Your Honor.

3 JUDGE CHAPPELL: Is that the way you understood
4 it?

5 THE WITNESS: Yes.

6 BY MS. SCHMIDT:

7 Q. And I'm sorry. I'm not sure if I -- I
8 apologize if I missed it, but I'm not sure if I quite
9 heard.

10 What would be the driver of the decreased
11 future demand?

12 A. It would be the -- so with the erosion and the
13 two -- retention scenarios, it would be the entry of a
14 generic version of ER.

15 Q. Thank you.

16 And looking at this Scenario 1, is this a
17 typical approach to a profit and loss scenario for a
18 branded drug?

19 A. It's an approach. Yes.

20 Q. An approach. Okay.

21 And is -- under Scenario 1, are there any
22 differences between -- and feel free to look at your
23 paper copy, to flip back and forth, but are there any
24 differences between the assumptions set out here and
25 the assumptions we reviewed in that initial e-mail from

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1 Q. Oh, I'm sorry.

2 A. Can you clarify?

3 Q. You can tell I'm not -- I'm not a financial
4 analyst.

5 What would be the Opana ER net sales under
6 steep erosion?

7 A. The Opana ER net sales under steep erosion net
8 of the burndown would be 110,841,133.

9 Q. And what about under 25 percent retention?

10 A. 122,000,291.

11 Q. And under 50 percent retention?

12 A. 127,929,044.

13 Q. And looking between 25 percent retention and
14 50 percent retention, by my math there's only about a
15 five to six-million-dollar difference between Opana ER
16 net sales; is that correct?

17 A. Yes.

18 Q. And if you were doubling the amount of your
19 retention, why wouldn't you also be doubling the amount
20 of your Opana ER net sales?

21 A. Because you were doing it at increased cost.

22 Q. What's the increased cost?

23 A. Increased rebates or discounts via
24 contracting.

25 Q. So that would -- you would be charging a

1 different price?

2 A. Correct.

3 Q. Thank you.

4 And I just want to look at one more page. The
5 next page of that same spreadsheet is at CX 3017-006.

6 And actually, Ms. Allen, could you cut the --
7 cut off the box at the bottom of Scenario 1c.

8 And do you see at the top of this box it says
9 "Key Assumptions"?

10 A. Yes.

11 Q. And the first entry is baseline? Do you see
12 that?

13 A. Yes.

14 Q. And what is a baseline?

15 A. It's the scenario against which the other
16 scenarios are being compared.

17 Q. Okay. And what are the key assumptions for
18 Opana ER under the baseline scenario?

19 A. It says "No generic entries until 7-1-11."

20 Q. And for Scenario 1a, Scenario 1b and
21 Scenario 1c, what is the assumption date for generic
22 entry for Opana ER?

23 A. It says, "Opana ER has generic entry (at-risk)
24 on 7-1-10."

25 Q. Okay. You can actually set that aside.

1 Earlier I think you mentioned management
2 requests for additional analyses?

3 A. Yes.

4 Q. What would some of those requests be?

5 A. For requests -- for analyses of scenarios
6 including different assumptions.

7 Q. Okay. And who from senior management most
8 frequently made those requests to you?

9 A. Alan Levin.

10 Q. And if I could direct your attention to
11 CX 1314.

12 And again, this is admitted as part of
13 JX 002 and is not subject to Your Honor's in camera
14 ruling.

15 And this is a single-page document.

16 Ms. Allen, if you could start by emphasizing the bottom
17 e-mail.

18 And just to be clear, you see from the top
19 where this is from Alan Levin, sent June 1, 2010, to
20 Roberto Cuca, no subject, but importance high? Do you
21 see that?

22 A. Yes.

23 Q. And Mr. Levin writes to you: Roberto, can you
24 please -- let me rephrase that -- "Can you tell me
25 please: 1. If we were to assume that Impax launches

1 Opana ER at risk on July 1, how much would we lose in
2 forgone sales of the branded drug this year?"

3 Do you see that?

4 A. Yes.

5 Q. Would this be a request of the type you were
6 mentioning earlier from senior management for modeling
7 new assumptions?

8 A. Yes.

9 Q. Okay. And in number 2, he writes, "What would
10 be the offset at revenues for our authorized generic of
11 Opana ER, assuming we also launched at July 1."

12 Do you see that?

13 A. Yes.

14 Q. And Ms. Allen, if we could now switch to the
15 top e-mail.

16 And do you see this is a reply from you to
17 Mr. Levin on the same day, June 1, 2010?

18 A. Yes.

19 Q. And on Mr. Levin's first question regarding
20 "how much we would lose in forgone sales of the branded
21 drug this year," what was your response?

22 A. I said, "We would lose \$71.2 million in branded
23 ER sales assuming a generic launch on July 1 (using our
24 erosion assumptions)."

25 Q. And what was your response to Mr. Levin for his

1 second question of "What would be the offset at
2 revenues for our authorized generic of Opana ER,
3 assuming we also launched at July 1"?

4 A. "We would gain \$25 million in authorized
5 generic sales."

6 Q. And I don't think we've talked about
7 authorized generic -- what are authorized generic
8 sales?

9 A. An NDA holder can sell product under its NDA as
10 a generic, and that's sometimes called authorized
11 generic sales.

12 Q. Is that a practice that Endo used?

13 A. I don't recall if Endo had sold authorized
14 generics previously.

15 Q. In order to gain 25 million in authorized
16 generic sales, how would Endo need -- what would Endo
17 need to do to achieve that?

18 A. To sell an authorized generic.

19 MS. SCHMIDT: Okay. Thank you, Cuca.

20 Your Honor, at this time I have no further
21 questions.

22 JUDGE CHAPPELL: Any cross?

23 MR. ANTALICS: Yes, Your Honor. Not too
24 lengthy.

25 (Pause in the proceedings.)

1 Good morning, Your Honor.

2 JUDGE CHAPPELL: Go ahead.

3 - - - - -

4 CROSS-EXAMINATION

5 BY MR. ANTALICS:

6 Q. Good morning, Mr. Cuca.

7 A. Good morning.

8 Q. Michael Antalics with O'Melveny & Myers. We
9 met once before at your deposition. Do you recall
10 that?

11 A. Yes.

12 Q. Okay. Mr. Cuca, on direct examination you
13 talked a little bit about forecasts and assumptions and
14 things.

15 When you create a forecast, does that mean that
16 the forecast will come true?

17 A. No.

18 Q. Okay. Are there assumptions that are built
19 into that forecast?

20 A. Yes. Many.

21 Q. Okay. And when you put assumptions into a
22 forecast, does that mean that the assumptions will come
23 true?

24 A. No.

25 Q. Okay. How many different assumptions do you

1 put into a forecast?

2 A. It depends on the forecast, but it can be lots
3 of different ones.

4 Q. Okay. I think you said that the timing of
5 generic entry was one of the assumptions that you
6 built in some of the forecasts surrounding Impax
7 entry?

8 A. Correct.

9 Q. Okay. And did you include an assumption of
10 entry that Impax would enter at the first moment after
11 the statutory 30-month stay?

12 A. Yes.

13 Q. Okay. Did you include other assumptions as to
14 other dates when Impax might enter?

15 A. Yes. In different scenarios, yes.

16 Q. Okay. Did you -- how many scenarios did you
17 do, if you can recall?

18 A. I don't, but multiple scenarios.

19 Q. Okay. So when you were creating these
20 scenarios with different assumptions, did you have any
21 idea at what date Impax would actually enter?

22 A. No.

23 Q. Okay. So why would you then create scenarios
24 with varying assumptions?

25 A. To analyze the full range of potential

1 outcomes.

2 Q. During your direct examination, you were shown
3 a number of different forecasts and scenarios. Do you
4 recall that?

5 A. Yes.

6 Q. Okay. Were those the only forecasts and
7 scenarios that you created during the time leading up
8 to the signing of the deal with Impax?

9 A. No.

10 Q. Okay. There were many others?

11 A. Yes.

12 Q. Okay. At the time the settlement agreement
13 with Impax was concluded, did the company book a
14 reserve of any sort for payment under the Endo credit?

15 A. No.

16 JUDGE CHAPPELL: Would you be aware -- if the
17 company booked a reserve, is that something you would
18 be aware of?

19 THE WITNESS: Yes.

20 JUDGE CHAPPELL: Thank you.

21 BY MR. ANTALICS:

22 Q. Why did you not book a reserve at the time the
23 settlement agreement was signed?

24 A. Under generally accepted accounting
25 principles, which is what would have governed the

1 booking of that reserve, you wouldn't book that
2 reserve unless the event was probable and the amount
3 of the reserve was estimable, and so we would not have
4 concluded that it was both probable and estimable at
5 that point.

6 Q. So first it would have to be probable?

7 A. Correct.

8 Q. And you would also have to estimate it.

9 A. Correct.

10 Q. And did you ever conclude that a payment was
11 required under the Endo credit?

12 A. Yes.

13 Q. When was that?

14 A. After the supply disruption of Opana after
15 which we launched a CRF version and completely pulled
16 the original ER version off the market.

17 Q. Was that the supply disruption involving
18 Novartis?

19 A. Correct.

20 Q. And that was in 2012?

21 A. Correct.

22 Q. Okay. Prior to the conclusion and signing of
23 the settlement agreement, did you ever hear anyone at
24 Endo express any view about the likelihood of a payment
25 under the Endo credit?

1 A. No.

2 Q. Okay. And did you hear anyone at the time of
3 the settlement agreement, when it was being negotiated,
4 express any view about the potential size of a payment
5 under the Endo credit?

6 A. No.

7 Q. Was there any plan, to your knowledge, to pay
8 Impax a large sum of money and in return Impax would
9 delay its intended entry?

10 A. No.

11 JUDGE CHAPPELL: Would you be aware of such a
12 plan if there was one at the time?

13 THE WITNESS: Probably.

14 MR. ANTALICS: I have nothing further,
15 Your Honor.

16 JUDGE CHAPPELL: Any redirect based on the
17 cross?

18 MS. SCHMIDT: Yes, Your Honor.

19 (Pause in the proceedings.)

20 May I proceed?

21 JUDGE CHAPPELL: Go ahead.

22 - - - - -

23 REDIRECT EXAMINATION

24 BY MS. SCHMIDT:

25 Q. Mr. Cuca, I think during Mr. Antalics'

1 examination you mentioned GAAP principles?

2 A. Yes.

3 Q. What are GAAP principles?

4 A. Generally accepted accounting principles.

5 Q. And what significance do they hold for your
6 work in financial planning and analysis?

7 A. They govern the standards for presenting and
8 submitting to the SEC actual results on Forms 10-Q and
9 10-K, and financial planning and analysis, the forecast
10 component of that, attempts to capture what will be
11 actually booked.

12 Q. How strict are the rules of when things are
13 booked under GAAP principles?

14 A. Strict.

15 Q. How so?

16 A. For example, a liability, you wouldn't book it
17 unless it was both probable and estimable.

18 Q. And does GAAP have defined meanings for
19 "probable"?

20 A. I believe it does.

21 Q. Do you know the definition off the top of your
22 head?

23 A. I -- I'm not sure of the exact definition, but
24 I think it specifies a probability.

25 Q. And what about estimable? What does that mean

1 under GAAP principles?

2 A. That you can produce an estimate with
3 substantiation that's appropriate for SEC filings.

4 Q. And when you are going to -- when something is
5 both probable and estimable, what does that mean for
6 the company?

7 A. So when a liability is probable and estimable,
8 you would book it and publish it in your financials.

9 Q. What does that mean, to book it?

10 A. Put it into the accounting system.

11 Q. Now, when you book it and put it into your
12 financials, can you put a range in there or does it
13 have to be a precise number?

14 A. It has to be a precise number.

15 Q. So how precise does it have to be in order to
16 be estimable?

17 A. You have to be able to create a dollar figure
18 for it.

19 Q. Okay. And under the Endo credit, what was the
20 triggering event for payment from Endo to Impax?

21 A. The -- the triggering event was the expiration
22 of the period immediately before Impax' generic
23 launch.

24 Q. Would the Endo credit payment be both probable
25 and estimable prior to the triggering event?

1 A. Yes.

2 Q. How so?

3 A. When the Novartis supply disruption occurred
4 and we knew that we wouldn't be selling any more
5 Opana ER, we were able to -- we knew what the peak
6 period sales were and were consequently able to
7 estimate -- we also knew that we probably would be
8 selling almost nothing in the final period, so we were
9 able to estimate the difference between the two.

10 Q. But my question was actually could you have
11 been able to estimate -- would the amount have been
12 estimable prior to that triggering event of knowing
13 when the quarterly peak was?

14 A. Not prior to knowing when the quarterly peak
15 was but prior to the triggering event to actually pay
16 the credit, so we booked the credit before we were
17 actually obliged to pay it.

18 Q. So let me back up and be clear because we're
19 using a number of terms here that I think we may not
20 have already gone over today.

21 And I actually think it might be helpful to
22 turn back to RX-364.

23 And Ms. Allen, if you could turn to
24 RX-364.0012 and highlight section 4.4.

25 And if I could just read this, it says,

1 "Section 4.4. Endo Credit. If the Pre-Impax Amount is
2 less than the Trigger Threshold, then Endo shall pay to
3 Impax the Endo Credit."

4 Do you recognize this as the Endo credit
5 provision of the settlement and license agreement with
6 Impax?

7 A. Yes.

8 Q. Okay. And just to go over those two more terms
9 here, Ms. Allen, if you could turn to --

10 JUDGE CHAPPELL: Before you do that, I have a
11 question.

12 You were asked whether the Endo credit payment
13 was both probable and estimable prior to the triggering
14 event and you said yes. You were asked, "How so?" And
15 you referred to the Novartis supply disruption
16 occurring.

17 That was still prior to a triggering event?

18 THE WITNESS: So the -- so the Endo credit --
19 maybe I misunderstood the original question.

20 I understood that what triggered our
21 obligation to pay the Endo credit is that Impax
22 delivers to us a documentation of all of the inputs
23 into the formula.

24 JUDGE CHAPPELL: So now you're telling me how
25 you define the triggering event.

1 THE WITNESS: Yes.

2 JUDGE CHAPPELL: Would the triggering event
3 also be the status of the market at a point in time
4 specified in the agreement?

5 THE WITNESS: That would be a component of it.
6 Yes.

7 JUDGE CHAPPELL: All right.

8 THE WITNESS: One of the components of the
9 formula is the sales of Opana in the last quarter
10 immediately before Impax' launch. When the Novartis
11 supply disruption took place, we knew that sales in
12 that quarter were likely to be close to zero.

13 JUDGE CHAPPELL: Once the disruption occurred.

14 THE WITNESS: Correct.

15 JUDGE CHAPPELL: Did anyone discuss a possible
16 supply disruption before the agreement was signed,
17 when you were negotiating and talking about this term?

18 THE WITNESS: Not that I recall.

19 JUDGE CHAPPELL: And go ahead. What were you
20 telling me about this supply disruption?

21 THE WITNESS: So Endo would have known that
22 the sales in that final quarter before the Impax
23 launch were likely to be zero or were close enough to
24 zero to estimate the payment, but Impax would not have
25 been able to provide us documentation of what those

1 sales were in that quarter, so could not have from a
2 legal perspective triggered our obligation to pay yet.

3 JUDGE CHAPPELL: And if I follow what you just
4 told me, you said Endo would have known the sales in
5 the final quarter were likely to be zero.

6 And if that were true, there would be zero
7 payment either way; correct?

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1 JUDGE CHAPPELL: And I think you told us
2 earlier in response to some questioning that you did
3 sit around and brainstorm or talk about possible
4 scenarios that would affect what's called the Endo
5 credit.

6 THE WITNESS: We didn't talk about what would
7 have prompted our obligation to pay it. We talked
8 about how it was supposed to work and what it was
9 supposed to do.

10 JUDGE CHAPPELL: All right. Thank you.

11 Go ahead.

12 BY MS. SCHMIDT:

13 Q. Mr. Cuca, when you say "we" talked about it,
14 who are you referring to?

15 A. The Endo settlement team and specifically
16 probably me and Alan.

17 Q. So that's an internal discussion?

18 A. Correct.

19 Q. So that's not a discussion with Impax.

20 A. Correct.

21 Q. If I could turn your direction -- attention
22 to RX-364-005 and actually continuing over to .006,
23 there's a term called Quarterly Peak, and if I
24 could -- Ms. Allen could somehow bring attention to
25 the -- to the definition even though it's over two

1 pages.

2 Thank you.

3 It reads, "'Quarterly Peak' means the highest
4 Prescription Sales of the Endo Product during any
5 calendar quarter period from July 1, 2010 through
6 September 30, 2012, or the last day of the full
7 calendar quarter described in clause (ii) of the
8 defined term Pre-Impax Amount."

9 Do you see that?

10 A. Yes.

11 Q. Do you recall what role the quarterly peak
12 played in the Endo credit?

13 JUDGE CHAPPELL: Are you asking him about what
14 actually happened?

15 MS. SCHMIDT: No. I'm actually not --

16 JUDGE CHAPPELL: Let's be clear if you're
17 asking what they anticipated, what they planned for or
18 what actually happened.

19 MS. SCHMIDT: Actually a fourth option, which
20 is what role this definition played in the Endo credit
21 provision that was encapsulated in the agreement
22 between Endo and Impax.

23 THE WITNESS: So it's a component of the
24 defined term "Pre-Impax Amount," which is itself a
25 component of the defined term "Endo Credit."

1 BY MS. SCHMIDT:

2 Q. And does "Quarterly Peak" also appear in the
3 market share profit value definition on RX-364-004?

4 A. Yes.

5 Q. And what is the quarterly peak capturing?

6 A. The highest calendar quarter's sales of
7 Opana ER.

8 Q. And that's between the third quarter of
9 2010 and the third quarter of 2012?

10 A. Yes. Including the third quarter of 2010.

11 Q. And if the payment was triggered, was that in
12 fact based on the difference between the quarterly peak
13 of the highest sales of Opana ER and the Opana ER sales
14 in the fourth quarter of 2012?

15 A. Yes.

16 Q. Would it be -- under GAAP standards, would any
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1 I have no further questions.

2 JUDGE CHAPPELL: Anything further?

3 MR. ANTALICS: I just have one question,
4 Your Honor.

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6 RE-CROSS-EXAMINATION

7 BY MR. ANTALICS:

8 Q. Just to clarify, Mr. Cuca, one point, the point
9 in time when Endo first knew that Endo's sales would be
10 zero in the quarter immediately prior to Impax' entry,
11 was that after the Novartis disruption?

12 A. Correct.

13 MR. ANTALICS: Okay. Thank you.

14 JUDGE CHAPPELL: Anything further?

15 MR. ANTALICS: No, Your Honor.

16 MS. SCHMIDT: No, Your Honor.

17 JUDGE CHAPPELL: Thank you. You may stand
18 down.

19 We're going to take a short break, and when we
20 come back I expect the next witness to be standing by.
21 We'll reconvene at 12:00 noon.

22 We're in recess.

23 (Recess)

24 JUDGE CHAPPELL: Okay. We're back on the
25 record.

1 Call your next witness.

2 MR. LOUGHLIN: Thank you, Your Honor.

3 Complaint counsel calls Dr. Seddon Savage.

4 And Your Honor, my colleague,

5 Mr. Nicholas Leefer, will conduct the examination.

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7 Whereupon --

8 SEDDON SAVAGE, M.D.

9 a witness, called for examination, having been first
10 duly sworn, was examined and testified as follows:

11 MR. LEEFER: Good afternoon, Your Honor.

12 Nicholas Leefer here on behalf of the

13 Federal Trade Commission.

14 - - - - -

15 DIRECT EXAMINATION

16 BY MR. LEEFER:

17 Q. Dr. Savage, thank you for being here.

18 Could you please introduce yourself to the
19 court.

20 A. Yes. My name is Seddon Savage. I am a
21 physician in pain medicine and addiction medicine.

22 Q. Without getting into the details of your
23 opinion, can you please briefly tell us what you're
24 here to testify about today.

25 A. I have been asked to testify most specifically

1 on differences between Opana ER and other long-acting
2 opioids and more generally my understandings about the
3 treatment of pain and the diversity of options
4 available for the treatment of pain, both pharmacologic
5 and nonpharmacologic.

6 Q. Now, I'd like to ask you a little bit about
7 your professional experiences and education that
8 qualifies you to offer these opinions.

9 To begin with, could you please describe your
10 current professional positions.

11 A. I currently am medical director of the
12 Chronic Pain Recovery Center at Silver Hill Hospital in
13 New Canaan, Connecticut.

14 I'm also an adviser to the Dartmouth Hitchcock
15 Medical Center in New Hampshire on issues of pain and
16 addiction. My advisory role is particularly around
17 developing education for clinicians and the general
18 public as well. It's a fairly broad educational role.

19 I have a number of professional volunteer roles
20 as well.

21 Q. Okay. We'll get to those in just a minute.

22 First, I want to go over your education a
23 little bit.

24 A. Okay.

25 Q. Where did you receive your medical degree?

1 pharmacology?

2 THE WITNESS: I took courses in pharmacology as
3 a medical student.

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1 Dartmouth called the Dartmouth Center on Addiction
2 Recovery and Education, DCARE, which specifically was
3 aimed at mentoring and developing student interest and
4 skills and knowledge in that field.

5 Q. Over the course of your career, have you held
6 any leadership positions in organizations related to
7 pain management?

8 A. In organizations and also some in relation to
9 agencies as well.

10 I for the past two years have been cochair of a
11 National Institutes of Health work group aimed at
12 developing research priorities for or around chronic

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1 years of experience you have with the use of medication
2 to treat pain?

3 A. Certainly over thirty years.

4 Q. Within those thirty years, can you break that
5 down a little bit and explain what you did over the
6 course of that time?

7 A. Early in my career I directly practiced pain

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1 A. All of them have involved it --

2 JUDGE CHAPPELL: Do you mean -- do you mean the
3 use of or prescription of?

4 MR. LEEFER: Thank you, Your Honor. I should
5 be much more specific. That's an excellent point. I
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1 who come into the program have not had adequate or
2 successful management of their pain as outpatients and
3 are struggling in some way either with pain, with
4 co-occurring psychiatric disorders and/or addictive
5 disorders.

6 Our goal is really to engage them in a
7 recovery plan for both pain and any co-occurring
8 disorders, and to that end, we engage them in a focus
9 on self-management, so an emphasis on nonpharmacologic
10 therapies, noninterventionalist therapies, on exercise
11 physical therapy, medication and use of physical --

12 (Admonition to slow down.)

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1 antidepressants that are used for pain, and to opioids,
2 which are clearly used for treatment of pain.

3 JUDGE CHAPPELL: You wouldn't include muscle
4 relaxants?

5 THE WITNESS: I'm sorry?

6 JUDGE CHAPPELL: You wouldn't include muscle
7 relaxants?

8 THE WITNESS: Muscle relaxants are interesting
9 medications. We do not generally recommend them for
10 the treatment of chronic pain. They are sometimes
11 helpful in the treatment of acute musculoskeletal
12 pain.

13 Muscle relaxants are more -- could -- most of
14 them could be classified as -- muscle relaxants some
15 people would like to classify as sedative-hypnotic
16 medications in that many of them act to relax the
17 individual, to relieve stress and anxiety, and
18 therefore allow them to relax their muscles.

19 There are some subcategories of muscle
20 relaxants that actually do act on the nervous system
21 to cause some muscular relaxation. And then there are
22 certainly potent ones that are used in anesthesia that
23 actually paralyze patients and relax their muscles in
24 that way.

25 But in general, muscle relaxants are not direct

1 relievers of pain. If somebody has --

2 (Admonition to slow down.)

3 JUDGE CHAPPELL: If somebody has pain?

4 Continue after you said "If somebody has pain."

5 THE WITNESS: If somebody has pain?

6 JUDGE CHAPPELL: It was your sentence. "But in
7 general, muscle relaxants are not direct relievers of
8 pain."

9 THE WITNESS: That is correct.

10 JUDGE CHAPPELL: "If somebody has pain" -- it
11 was your statement. That's where she -- she couldn't
12 understand you after that.

13 THE WITNESS: I'm sorry.

14 MR. LEEFER: Well, let me --

15 JUDGE CHAPPELL: Hold on a second.

16 MR. LEEFER: Sorry.

17 JUDGE CHAPPELL: If I'm coming to you and I'm
18 in pain, I don't care how it's categorized, I just want
19 the pain to end; correct?

20 THE WITNESS: That is correct.

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1 A. We are all biologically and genetically
2 somewhat different. It depends upon the class of
3 drugs that you're talking about.

4 With respect to opioids, there are differences
5 in the way different opioids bind to different opioid
6 receptors, and we all express opioid receptors
7 somewhat -- there's variability in the way human beings
8 express opioid receptors, so we may or may not respond
9 the same to a different opioid, so somebody may respond
10 better to oxycodone than to hydromorphone than to
11 morphine.

12 They may not only experience different levels
13 of analgesia in response to the drug but different
14 side effects. Most people who have taken opioids have
15 experienced different effects with different opioids.

16 Q. We'll come back to discussing --

17 A. Okay.

18 Q. -- these differences in a little bit more
19 detail, but --

20 JUDGE CHAPPELL: Did this witness submit an
21 expert report in this case?

22 MR. LEEFER: Yes, she did, Your Honor.

23 JUDGE CHAPPELL: Are we to the point yet where
24 she's telling us the opinions she formulated in this
25 case?

1 possible to switch a patient from one long-acting
2 opioid to another?

3 A. It's both possible and it's frequently
4 necessary or advisable to switch patients. But we
5 can't do so with a priori predictable effects of what
6 the outcome of the switch will be. Often it requires
7 trial of a number of medications.

8 JUDGE CHAPPELL: There's an example, Doctor, of
9 a question that required a yes or no answer, yet you
10 went beyond yes or no and gave us a narrative. Please
11 pay attention to the question.

12 THE WITNESS: I will try to answer yes or no
13 going forward. I'm...

14 BY MR. LEEFER:

15 Q. Now, I think that your answer to the last
16 question was that it may be possible to switch a
17 patient from one opioid to another but that you can't
18 do that with a priori knowledge of whether that will
19 work; is that -- am I understanding that correctly?

20 A. That is correct.

21 Q. Can you explain what you mean by not having
22 a priori knowledge that the new opioid will work for
23 the patient?

24 A. Well, as I began to explain earlier, our --
25 individuals respond differently to different opioids

1 based on a number of physiologic and pharmacologic
2 processes.

3 Q. Other than opioids, what are some of the
4 available treatments for pain?

5 A. Pharmacologic treatments for pain include a
6 number of classes of medications, nonsteroidal
7 anti-inflammatories, acetaminophen, which is a
8 different class of its own, anticonvulsant/anti-seizure
9 medications are often used, antidepressant medications,
10 certain antidepressant medications, tricyclics and
11 certain adrenergic and noradrenergic reuptake
12 inhibitors.

13 Q. So other than pharmacologic treatments, what
14 are the nonpharmacologic treatments available for
15 pain?

16 A. Let me mention there are also a number of
17 topical agents that act by different mechanisms
18 pharmacologically.

19 Other than pharmacologic mechanisms, there are
20 a number of psychobehavioral approaches.

21 It may be surprising to some people, but
22 meditation is actually turning out to be a
23 neurobiologically active treatment that actually
24 changes conduction of pain and experience of pain.

25 Cognitive behavioral therapy can be very

1 And then finally, we've talked about
2 pharmacologic, psychobehavioral, interventionalist and
3 physical therapeutics, so those are the four classes,
4 large classes that I would name.

5 Q. Okay. Thank you, Dr. Savage.

6 Understanding that there are these four
7 different classes of pain treatments, when are opioids
8 generally indicated in the treatment of pain?

9 A. Opioids are generally indicated when other
10 interventions are not effective in treating pain or
11 when opioids present less risk to an individual patient
12 than other therapeutic interventions.

13 Q. Do you have an opinion on whether or not
14 Opana ER is interchangeable with other treatments for
15 pain?

16 A. Yes.

17 Q. Okay. What is that opinion?

18 A. I believe that Opana ER is not certainly
19 interchangeable with the classes -- with non-opioid
20 interventions. Opioids are not interchangeable with
21 other interventions.

22 Opana ER as a specific opioid is not reliably
23 interchangeable with other long-acting opioids.

24 Q. What do you mean when you say that it's not --
25 that Opana ER is not reliably interchangeable with

1 other long-acting opioids?

2 A. That means that while it may provide analgesia
3 to patients who are using another opioid, the level of
4 analgesia that patients experience may be variable and
5 different from that that they experience even when the
6 doses are adjusted to that of other opioids, and the
7 side effect profile that they experience may be
8 different.

9 Q. Can you predict in advance whether a patient
10 using Opana ER will achieve equivalent results if you
11 switch to another opioid?

12 A. No.

13 Q. Now, I'd like to return to the broader category
14 of pharmaceutical treatments for pain, and you
15 mentioned a number of those.

16 To start with, one of the first ones I believe
17 was nonsteroidal anti-inflammatory drugs; is that
18 right?

19 A. That's correct.

20 Q. And for that category of drugs can you just
21 give us one or two examples so we would know what we're
22 talking about?

23 A. Yes. Those would be drugs such as Naprosyn or
24 ibuprofen.

25 Q. And for these anti-inflammatory drugs, can you

1 explain just a couple of the key differences that you
2 see between those drugs and opioids?

3 A. Nonsteroidal anti-inflammatories are generally
4 indicated for mild to moderate pain. They have some
5 use in severe pain when there's inflammation present,
6 it may be helpful in that category, whereas opioids and
7 Opana are indicated for moderate to severe pain, so
8 greater pain severity.

9 Nonsteroidal anti-inflammatories, one of the
10 primary mechanisms is a peripheral mechanism
11 interfering with the inflammatory cascade.

12 Q. So is it fair to say that anti-inflammatory
13 drugs have a different mechanism of action from
14 opioids?

15 A. That is correct.

16 Q. I believe another category or another example
17 of a non-opioid medication you provided was
18 acetaminophen.

19 Again, can you just provide some of the key
20 differences you see between acetaminophen and opioids.

21 A. Acetaminophen is indicated again for mild to
22 moderate pain. It has a different mechanism of action
23 than opioids. Its mechanism of action is not entirely
24 understood. It appears to have a central mechanism of
25 action, which may relate in part to cannabinoid

1 receptors.

2 Q. And you also mentioned antidepressants and
3 anticonvulsants.

4 How do these drugs differ in important respects
5 from opioids?

6 A. Anticonvulsants are more often indicated for
7 the treatment of pain that has a neuropathic component
8 that is abnormal conduction of pain signals along
9 either peripheral or central neural pathways. Its
10 mechanism of action is related to changes in ion
11 fluctuations that change transmission of the pain
12 signal along neural pathways, which is different than
13 binding to opioid receptors.

14 Q. That's helpful. I think we might be venturing
15 a little deeply into the underlying science, which is
16 certainly confusing to me. But generally speaking, you
17 mentioned anticonvulsants were helpful -- more helpful
18 for neuropathic pain.

19 How does that compare to an opioid, for
20 example?

21 A. Opioids are the most potent pain-relieving
22 medications we have available. They are effective both
23 for tissue-based pain called nociceptive pain related
24 to injury or inflammation or tissue disruption.
25 They're also effective for neuropathic pain, though

1 they may need a higher dosing for their efficacy. And
2 they, as I said, are our most potent medications, so
3 they're used for moderate to severe pain.

4 Anticonvulsants are not as potent (Bl're nun1Ienx1cy.)weT

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1 used in the context of opioids?

2 A. I am familiar with the term "half-life."

3 Q. And what does "half-life" mean?

4 A. Half-life is the amount of time that's required
5 for the plasma level of a drug to be reduced by
6 about -- by 50 percent.

7 Q. And what will typically have a longer
8 half-life, a short-acting opioid or a long-acting
9 opioid?

10 A. Typically, a long-acting opioid has a longer
11 half-life.

12 Q. And generally speaking, how is a longer
13 half-life related to the duration of action for an
14 opioid?

15 A. Generally, the duration of action is longer
16 with a longer half-life.

17 May I correct something that I said
18 previously?

19 Q. Yes. Please.

20 A. I'd just clarify. It's not really a
21 correction.

22 But the molecule in a long-acting --
23 extended-release opioid is not changed, and the
24 half-life of the molecule itself is not changed. The
25 half-life -- the effective half-life is changed

1 because medication is continuing to go into the body as
2 it is slowly released by the extended-release
3 medication at the same time that the molecule is being
4 cleared, so the effective half-life is longer. The
5 molecule's half-life is unchanged.

6 Q. I'm sorry. I just want to make sure that I
7 understand this.

8 Are you saying that the active ingredient
9 doesn't change between a short-acting and a long-acting
10 formulation?

11 A. That's correct.

12 I should mention, however, there are two
13 naturally -- three that come to mind, longer-acting
14 opioids with longer half-lives naturally, methadone,
15 Levo-Dromoran and buprenorphine.

16 Q. Thank you, Dr. Savage.

17 Now, even though the -- let me start that
18 question over.

19 Despite the fact that the opioid molecule is
20 not changed when it's incorporated into an
21 extended-release formulation, how does the
22 extended-release formulation provide more lasting pain
23 relief?

24 A. Well, I can't speak to the physical chemical
25 properties of all the various formulations that are on

1 Q. Okay. Let's take a look at that figure. I'd
2 like to show you figure 3 from your report, Dr. Savage.
3 This is CX 5002-35.

4 And Your Honor, for the record, CX 5002 has
5 been admitted as part of JX 2 and is not subject to an
6 in camera order.

7 JUDGE CHAPPELL: Okay.

8 BY MR. LEEFER:

9 Q. And can you explain to us what this figure is
10 designed to show?

11 A. Yes. This is designed to show the clinical --
12 when -- the clinical effects of short versus
13 long-acting opioids.

14 In addition, there's patient-controlled
15 analgesia as shown on there.

16 I want to point out that I noted that the
17 colors -- the color coding is wrong. The
18 sustained-release, controlled-release formulation is in
19 yellow; it's not in red. Patient-controlled analgesia
20 is in red.

21 So I'm not going to talk about
22 patient-controlled analgesia. I don't think it's
23 relevant here.

24 But if we look at sustained-release
25 medication, if we are trying to relieve pain, we would

1 like optimally to be between those two parallel black
2 lines, which represent steady-state -- steady blood
3 levels of the medication.

4 If we go above those blood levels of the
5 medication, the patient is more at risk for side
6 effects, particularly cognitive side effects, sedation,
7 reward, other cognitive side effects.

8 If we go below, the patient will dip into
9 unrelieved pain, so we'd like ideally to relieve pain
10 to stay at a steady blood level.

11 Q. And which class of drugs is more likely to
12 achieve that steady blood level, long-acting or
13 short-acting opioids?

14 A. Well, in clinical settings, long-acting
15 medications are more likely to achieve that.

16 Theoretically, it is possible to overlap doses
17 of short-acting medications in a way that provides a
18 steady state, but many of them are quicker in onset and
19 fall off, so you're -- you more -- you risk more often
20 having unmasked pain as a result of fallen blood levels
21 or having to have side effects in order to sustain
22 analgesia for a prolonged period of time.

23 So, generally speaking, for patients with
24 sustained pain, long-acting or extended-release opioids
25 will provide more stable analgesia.

1 Q. Thank you, Doctor.

2 Now, we spent some time talking about
3 differences with non-opioid medication and we've talked
4 a little bit about differences with short-acting
5 opioids.

6 I'd like to now spend some time focusing on
7 differences between long-acting opioids. Okay?

8 A. Okay.

9 Q. At a high level, how does Opana ER differ from
10 other long-acting opioids?

11 A. Well, first, it's a different opioid molecule
12 from other long-acting opioids, most other long-acting
13 opioids. There are generic Opana ERs -- I'm sorry --
14 oxymorphone, sustained-release oxymorphone.

15 But it's a different molecule from many of the
16 other long-acting opioids; therefore, we can expect
17 that individuals may experience different levels of
18 analgesia, adjusted for dose, different side effect
19 profiles, and different tolerance depending upon what
20 they've been using and different potential for
21 interactions with other medications.

22 Q. Sorry, Doctor. What are the practical
23 implications of these differences between Opana ER and
24 other long-acting opioids?

25 A. Well, that's just one difference, so there are

1 many differences, but as I said, it means that people
2 may respond differently to Opana ER than they do to
3 oxy- -- sustained-release oxycodone or morphine or
4 hydromorphone.

5 JUDGE CHAPPELL: Excuse me. I think I've heard
6 you say twice "may respond differently."

7 It's not your opinion that they will respond
8 differently; is that correct? But that they may
9 respond differently?

10 THE WITNESS: I can't predict that
11 prospectively whether they will or they may.

12 JUDGE CHAPPELL: Well, I've heard you say "may"
13 more than once.

14 THE WITNESS: They may. I can't predict how
15 any particular patient will respond to an opioid that
16 I'm going to prescribe them. They may respond very
17 similarly to oxycodone as they do to oxymorphone as
18 they do to hydromorphone, or they may experience them
19 very differently.

20 We can get some information on that based on
21 their history of past responses, so we'll always take a
22 history and ask, you know, did you tolerate this
23 particular medication, did you have nausea or vomiting
24 or itching or other side effects, in particular,
25 sedation, or other side effects with different opioids,

1 so it's important to take a history of what people have
2 used in the past in order to begin to predict what
3 they're going to tolerate best.

4 But as I said in my report and as the
5 literature supports, many patients need to try two,
6 three or four different opioids before they arrive at
7 one that's both effective for them with minimal side
8 effects.

9 JUDGE CHAPPELL: And since your opinion --
10 you're an expert, you're limited to an opinion, which
11 is speculation, you're going to say may respond rather
12 than will respond differently because your testimony is
13 not based -- is not to be here as a fact witness.

14 THE WITNESS: I'm sorry. Say that again,
15 please.

16 JUDGE CHAPPELL: You're an expert witness; am I
17 correct?

18 THE WITNESS: I am an expert witness.

19 JUDGE CHAPPELL: You understand that's not the
20 same as a fact witness. I saw something, I did
21 something, you understand the difference.

22 THE WITNESS: I do not understand the
23 difference between an expert and a fact witness. I'm
24 sorry.

25 JUDGE CHAPPELL: Interesting. Okay. A fact

1 witness is someone who observed an event. I saw the
2 collision at the intersection.

3 THE WITNESS: Uh-huh.

4 JUDGE CHAPPELL: An expert is someone who comes
5 in later and says, I'm calculating that this occurred
6 because of, fill in the blank, weren't there, didn't
7 see it.

8 Do you understand the difference?

9 THE WITNESS: I do.

10 JUDGE CHAPPELL: Thank you.

11 Go ahead.

12 MR. LEEFER: Thank you, Your Honor.

13 THE WITNESS: Thank you.

14 BY MR. LEEFER:

15 Q. In your view, Dr. Savage, is it important to
16 have a variety of opioids as options for treatment of
17 pain?

18 A. It's very useful to have a variety of opioids
19 for the treatment of pain.

20 Q. Why --

21 A. It's --

22 Q. -- why is that?

23 A. Because, as I've said, people respond very
24 differently to different opioids. And it's not only
25 because -- I mentioned the differences in the

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1 you identified was the fact that Opana ER incorporates
2 the molecule oxymorphone. Is that right?

3 A. That is correct.

4 Q. And generally speaking, is it easier to switch
5 a patient that is doing well on Opana ER to a different
6 opioid molecule, for example, oxycodone, or to switch
7 them to a generic version of oxymorphone?

8 A. The outcomes of switching a patient to a
9 generic version of oxymorphone would be more
10 predictable than switching them to oxycodone.

11 Q.

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1 metabolized, which -- what's called glucuronidated.
2 It's -- it does not require a system that many drugs
3 require, which is called the cytochrome P450 system,
4 which is a system that many opioids, not all, but many
5 of them do require, and it's known to have variability
6 so that people may have even more unpredictable effects
7 from use of those opioids if they have a -- either a
8 deficit or an increase of certain enzymes, whether if
9 they are rapid metabolizers or slow metabolizers of
10 drugs that use that system.

11 Oxymorphone doesn't require that system.

12 Q. Let's go into in just a little bit more detail
13 about what you called the CYP450 system. Can you
14 explain what that is?

15 A. It is a system of enzymes that -- there are
16 multiple different CYP450 enzymes that break down
17 molecules, drug molecules, into metabolites.

18 Q. Do most opioids use the CYP450 metabolic
19 pathway?

20 A. Many of them do. Probably most of them do. I
21 can think of three that do not.

22 Q. Are there other drugs other than opioids that
23 use the same metabolic pathway?

24 A. Yes. Many drugs use those metabolic pathways.

25 Q. What are the possible complications that exist

1 if a patient taking an opioid that uses this metabolic
2 pathway is also on another drug using the same
3 pathway?

4 A. You may need to adjust the dose of the opioid
5 that you're using. And particularly, if a drug is
6 introduced that inhibits an enzyme that is metabolizing
7 a drug, you might find a patient with a higher level of
8 the opioid in their body because it's not being broken
9 down as rapidly.

10 Q. What's the practical implication of a patient
11 having a higher blood level of the opioid?

12 A. They may develop more side effects,
13 particularly sedation. It's conceivable that they
14 could have an overdose as a result of that.

15 Q. And conversely, is it possible that this sort
16 of interaction between drugs could result in lower
17 blood levels of an opioid?

18 A. Yes. And that does occur as well.

19 Q. And what are the practical implications of
20 experiencing a lower blood level of an opioid?

21 A. They may experience a recrudescence of pain.
22 If they're physiologically dependent, they can
23 experience withdrawal.

24 Q. Can you give us any real-world examples from
25 your experience in which you've seen these sorts of

1 effects with the CYP450 metabolic pathway?

2 A. I can.

3 I would say that we are only in the last two to
4 three years becoming more aware in medicine of these
5 types of interactions. We've known about them for many
6 years, but now that we're beginning to be able to test
7 people for certain drug interactions and/or for the
8 propensity -- for metabolic differences, I think our
9 awareness of them is being heightened.

10 So looking back on my career, I know that many
11 patients I've followed on opioids have occasionally
12 had unexpected changes. Their pain suddenly is much
13 worse with no change in medication. Tolerance
14 sometimes occurs over time, but a sudden change is
15 unusual.

16 Some people have suddenly had increased opioid
17 effects for reasons that are unclear. Looking back, I
18 wonder whether some of those may have been due to our
19 introducing other drugs.

20 More recently, we had a patient, who was
21 followed by our team, who had been on methadone for a
22 period of time and out of the blue, on a stable dose of
23 methadone, became very sedated and sleepy on the
24 medication. We looked at many of the different
25 variables, what could have been associated with that,

1 and it was our conclusion that it was likely an
2 antidepressant that inhibited one of the important
3 methadone breakdown enzymes that caused an increase in
4 the methadone level.

5 Q. So was it the medical judgment of your team
6 that the unexpected sedation of this patient resulted
7 from an interaction with the CYP450 pathway?

8 A. That is correct.

9 Q. And are there examples of these sorts of
10 CYP450 interactions in the medical literature as well?

11 A. Yes, there are. I cited some in my rebuttal
12 report I believe.

13 Q. Could you just provide one example that you're
14 familiar with.

15 A. One of the articles talked about an individual
16 who had been on oxycodone and was then put on a -- I
17 believe it was an antifungal agent and had -- which it
18 can inhibit breakdown of oxycodone, and it had an
19 increased medication effect as a result.

20 Q. What do you mean by "increased medication
21 effect"?

22 A. Became sedated on the medication.

23 Q. And just to make sure I'm clear on this, this
24 sort of sedation is undesirable for a patient?

25 A. Yes. In most circumstances. If you're trying

1 to nap, it may not be, but I'm trying to --

2 Q. So now, going back to differences between --
3 other differences between Opana ER and other opioids,
4 generally speaking, how does the half-life of the
5 molecule oxymorphone compare to other opioids?

6 A. The half-life of the molecule is somewhat
7 longer for even for the immediate -- well, the molecule
8 itself is somewhat longer than typical
9 immediate-release opioids. I believe it's about seven
10 hours as opposed to three --

11 THE REPORTER: I'm sorry. Can you say that
12 again, please.

13 THE WITNESS: It is approximately seven hours,
14 my understanding is, as compared to three to four hours
15 for oxycodone, hydrocodone, morphine and others.

16 BY MR. LEEFER:

17 Q. And what is the practical significance of the
18 relatively long half-life of oxymorphone compared to
19 other opioids?

20 A. We would expect it to have a longer duration of
21 action.

22 Q. In preparing your report, Dr. Savage, did you
23 review any documents from Endo Pharmaceuticals that
24 described the significance of oxymorphone's relatively
25 long half-life?

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1 longer half-life?

2 A. I'm looking at it.

3 (Document review.)

4 Q. Can you identify the portion of this document
5 that identifies the advantages of Opana ER's longer
6 half-life?

7 A. Oh, I'm sorry. That was a question.

8 Yes. I'm -- I'm -- can I identify it?

9 Q. Please do, Dr. Savage.

10 A. Yes.

11 I believe under Clinical Evidence Endo has
12 listed at least two qualities that it believed were
13 clinical benefits.

14 Q. And what is the first of those qualities that
15 it believed was a clinical benefit?

16 A. It states "True 12 hour dosing."

17 Q. Now, here --

18 A. And --

19 Q. Sorry.

20 (Counsel and witness speaking at the same time
21 and cautioned by court reporter.)

22 MR. LEEFER: My apologies.

23 BY MR. LEEFER:

24 Q. In about the middle of this page here, this
25 says: Lower daily average consumption with Opana ER as

1 compared with -- to OxyContin.

2 What does "lower daily average consumption"
3 mean to you?

4 A. My understanding of the way they're using it
5 here -- I haven't looked at the study that informed
6 that statement -- is they are saying because it has
7 true twelve-hour dosing, the inference is that
8 patients --

9 JUDGE CHAPPELL: Excuse me, Doctor. You
10 started your answer with "My understanding." I want
11 you to limit your answers to what you know, not your
12 understanding.

13 BY MR. LEEFER:

14 Q. Dr. Savage, do you know what the term
15 "lower daily average consumption" means?

16 A. In fact, I do not because they don't state
17 whether it is milligrams consumed or number of tablets
18 consumed.

19 Q. In your clinical experience, Dr. Savage, are
20 there patients that are able to take -- excuse me. Let
21 me rephrase the question.

22 In your clinical experience, Dr. Savage, are
23 most patients taking Opana ER able to use it on a
24 twelve-hour dosing schedule?

25 A. Yes.

1 Q. And in your clinical experience, have you
2 encountered patients taking OxyContin that take it more
3 frequently than every twelve hours?

4 A. Yes.

5 Q. Those patients taking OxyContin more often than
6 every twelve hours, do they end up using more tablets
7 or fewer tablets than a patient taking the drug every
8 twelve hours?

9 A. They would use more tablets.

10 Q. In your experience, if a patient is taking more
11 tablets per day, does that usually result in higher or
12 lower cost for the patient?

13 A. It would depend upon their insurance. I -- the
14 cost of the medication, depending upon the relative
15 cost of the two different medications, would be more if
16 they're taking more tablets.

17 Q. I'd like to go back just briefly to the
18 CYP450 pathway that we were discussing earlier, and
19 you've mentioned a few examples from -- well, one
20 example from your experience and one example from the
21 medical literature.

22 I'd like to ask you, in your experience, how
23 common are these sorts of CYP450 interactions?

24 A. I imagine that they occur quite frequently at
25 subtle levels that don't become clinically apparent.

1 One study I reviewed recently suggested that up
2 to 30 percent of people taking an opioid that is
3 metabolized by the CYP P430 -- 450 pathway are also
4 taking a second medication that is either an inhibitor
5 or an inducer of enzymes in that pathway or also
6 metabolized by the pathway so that there's a risk of an
7 interaction between the two drugs.

8 JUDGE CHAPPELL: You started your answer with
9 "I imagine that they occur quite frequently at subtle
10 levels that don't become clinically apparent."

11 THE WITNESS: That is correct.

12 JUDGE CHAPPELL: Is that the same thing as
13 saying you don't know because you're not going to be
14 told about it?

15 THE WITNESS: This is an evolving area of
16 understanding --

17 JUDGE CHAPPELL: But my question was a yes or
18 no.

19 THE WITNESS: I'm sorry?

20 JUDGE CHAPPELL: Your own words, are you saying
21 you're not going to be aware of it because they occur
22 quite frequently at subtle levels that don't become
23 clinically apparent?

24 THE WITNESS: That is correct.

25 JUDGE CHAPPELL: Thank you.

1 THE WITNESS: That is my opinion.

2 BY MR. LEEFER:

3 Q. And is it your opinion, Dr. Savage, that in
4 some cases these interactions occur at unsubtle levels
5 that are clinically apparent?

6 A. Yes.

7 Q. And the study that you were just discussing,
8 does that study suggest that up to 30 percent of
9 patients may be at risk for these sort of CYP450 drug
10 interactions?

11 A. Yes.

12 Q. Thank you, Dr. Savage.

13 I'd like to now talk about --

14 ~~AND~~ ~~THE~~ ~~CHA~~ ~~PELL~~: The leading of your expert

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1 about some of the other available long-acting opioids.

2 Can you list a few of those other long-acting
3 opioids that you've discussed in your report.

4 A.

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1 That table is a comparison of some
2 extended-release formulations of various molecules,
3 types, in comparison according to a number of different
4 features of the medications.

5 Q. I'm sorry, Dr. Savage. Can you point the
6 microphone a little bit more back towards you so that
7 you're easier to hear.

8 Thank you.

9 And where does the information that's in this
10 table come from?

11 A. I elected to use information from the
12 prescribing -- the official prescribing information
13 for each of the formulations.

14 There is a couple of areas where it is
15 supplemented by information from the scientific
16 literature where I couldn't find the information in the
17 FDA prescribing area.

18 Q. Now, I'd like to zoom in on a portion of this
19 table and specifically the top two lines and the first
20 five columns or so.

21 A. Uh-huh.

22 Q. Dr. Savage, can you tell us what the active
23 ingredient of Opana ER is as indicated in your table.

24 A. It's oxymorphone.

25 Q. And how does that compare to the active

1 ingredient of the second line here, which is
2 OxyContin?

3 A. It's oxycodone.

4 Q. And what is the significance of the two drugs
5 having different active ingredients?

6 A. Could you repeat the question. I didn't hear
7 the end of it.

8 Q. Certainly.

9 What is the practical significance of the two
10 drugs having different active ingredients?

11 A. The significance is that different patients may
12 respond differently to the medications.

13 Q. Now, let's zoom in on a different part of this
14 table.

15 JUDGE CHAPPELL: When a patient walks in, would
16 you have any basis or reason to prescribe one of these
17 over the other, the two you've just described, in the
18 beginning?

19 THE WITNESS: In the very beginning if a
20 patient walks in?

21 JUDGE CHAPPELL: Right.

22 THE WITNESS: I would take a history of which
23 if they've had either one or the other and how they
24 responded to it to see if I could know a priori which
25 might be preferred by the patient or might be more

1 satisfactory to the patient.

2 If they had no history of using it, first of
3 all, we would start with -- generally with an
4 immediate-release form to see how they tolerated it
5 before going to a longer-acting medication, so we'd see
6 how they respond to the molecule before -- to the
7 sustained-release preparation.

8 There -- it would depend upon the type of pain
9 that they had. There is some evolving suggestion that
10 oxycodone may in fact --

11 JUDGE CHAPPELL: I'm not talking about
12 something that's evolving. I asked you a specific
13 question.

14 A patient walks in with a pain. Would you have
15 any reason to prescribe one or the other --

16 THE WITNESS: Yes.

17 JUDGE CHAPPELL: -- any difference?

18 Assuming they don't have what you call your
19 a priori information. Your a priori facts aren't
20 there. Somebody walks in with a back pain. Any reason
21 why you would prescribe one of these drugs over the
22 other or not?

23 THE WITNESS: For back pain, that's a very
24 specific type of pain. Yes. I would -- there are a
25 couple of differences that I would consider.

1 Do they -- if they told me that they take all
2 their medications at breakfast and at dinnertime, I
3 probably wouldn't use oxymorphone because you're
4 supposed to take oxymorphone an hour before meals or
5 two hours after meals.

6 If they said they take it first thing in the
7 morning, an hour before breakfast, and they take it
8 after exercising, before dinner, then that would be
9 fine.

10 There are different formulations, so there are
11 a number of clinical characteristics to consider.

12 If I thought the patient was at risk for using
13 it with alcohol, I probably would advise them not to
14 use it with alcohol, but if I had some reason --

15 JUDGE CHAPPELL: That would be either one,
16 though, wouldn't it?

17 THE WITNESS: What?

18 JUDGE CHAPPELL: That would be either of these
19 drugs. You don't want to take alcohol with either of
20 these --

21 THE WITNESS: No, you definitely do not want to
22 take alcohol, but the reality is that occasionally
23 you're concerned that a patient might use it with
24 alcohol, in which case you wouldn't want to use a drug
25 that had a black box warning against using it with

1 alcohol.

2 I'm trying to think of other reasons -- oh,
3 just I couldn't predict which was -- which would be
4 the more satisfactory molecule for them, that is
5 correct, other than those two features that I
6 mentioned.

7 JUDGE CHAPPELL: I'm not sure you answered my
8 question.

9 Would you prescribe either of those drugs at
10 the point you got to at the end of your answer, when
11 you couldn't predict?

12 THE WITNESS: Would I prescribe -- I'm sorry.

13 JUDGE CHAPPELL: Either of the two drugs you
14 were just discussing.

15 THE WITNESS: Yes.

16 JUDGE CHAPPELL: You would prescribe either of
17 them; correct? If you couldn't have your predictions
18 you talked about.

19 THE WITNESS: I could prescribe either of
20 them.

21 JUDGE CHAPPELL: Thank you.

22 Go ahead.

23 BY MR. LEEFER:

24 Q. Dr. Savage, despite the fact that you could
25 prescribe either drug in an initial consultation, are

1 there factors that you would consider in deciding which
2 one to use?

3 JUDGE CHAPPELL: We've already heard a number
4 of those. I don't want to hear them repeated.

5 You can ask her to give you any factors she
6 didn't just tell us in response to my question.

7 BY MR. LEEFER:

8 Q. Are there additional factors beyond those you
9 discussed, like the alcohol black box warning or the
10 mealtime restrictions, that you would consider?

11 A. I might consider whether the patient was going
12 to be using any strong inducers of the P450 system or
13 strong inhibitors of the P450 system, in which case
14 there would be -- I would be more inclined to use the
15 oxymorphone, which I know wouldn't interfere, those
16 inhibitors or inducers would not interfere with the
17 medication.

18 Q. Thank you, Dr. Savage.

19 Going back to this chart here, can we zoom in
20 again on the first two lines and I think the columns
21 Metabolic Pathway through T1/2.

22 And in this chart, Dr. Savage, what does "T1/2"
23 mean?

24 A. That's a half-life.

25 Q. And how does the half-life of Opana ER compare

1 to the half-life of OxyContin?

2 A. It's longer than the half-life of OxyContin.

3 Q. How much longer is it?

4 A. Repeat the question, please.

5 Q. How much longer is the half-life of Opana ER as
6 compared to OxyContin?

7 A. It's at least double the half-life. One is
8 4.5; the other is 9 to 11 hours.

9 Q. Based on this difference in half-life, which
10 drug would you expect to have a longer duration of
11 action?

12 A. I would expect oxymorphone to have a longer
13 duration of action.

14 Q. And looking at the column for metabolic path,
15 can you describe the differences between the metabolic
16 path for Opana ER as compared to OxyContin?

17 A. Yes. Again, as I mentioned, oxymorphone
18 primary metabolic pathway for degradation is through
19 glucuronidation, which is not part of the
20 CYP P450 pathway, whereas oxycodone has a black box
21 warning about using CYP P450 -- the particular enzyme
22 is 3A4 -- inducers or inhibitors.

23 Q. You've used the term "black box warning" a
24 couple times now. Can you just define that for us.

25 A. The black box warning -- the FDA puts important

1 safety information that they want to be sure gains the
2 attention of prescribers in black boxes at the
3 beginning of the prescribing information.

4 Q. And to you as a doctor, what's the significance
5 of a black box warning related to the CYP P450 pathway
6 for OxyContin?

7 A. It would steer me towards not using a drug
8 with that type of black box warning in a patient for
9 whom there was another option for treatment. It's not
10 an absolute contraindication, but I would consider it
11 very strongly.

12 Q. Now, Dr. Savage, rather than going through
13 every line of this appendix, I'd just like to ask you,
14 in general, does this identify distinguishing
15 characteristics for the opioids that are discussed in
16 your report?

17 A. Yes.

18 Q. Let's take a look at another figure in your
19 report. I'd like to direct your attention to
20 figure 4, which is page CX 5002-045.

21 And Dr. Savage, could you please explain what
22 this table is designed to show.

23 A. This is designed to show the key differences
24 between OxyContin and Opana ER.

25 Q. We've already discussed a number of these

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1 think many clinicians will -- in patients who they are
2 not a hundred percent confident are using medications
3 as prescribed will elect abuse-deterrent medications.

4 Q. Dr. Savage, I'd like to direct your attention
5 to figure 6 next in your report, and that is at
6 CX 5002-049.

7 And again, could you please explain what this
8 table is designed to show.

9 A. This is designed to show the differences
10 between Exalgo and Opana ER. The one difference it
11 doesn't show is that it's a different molecule. It's
12 hydromorphone versus oxymorphone.

13 Q. Again, I think we've discussed the difference
14 between or the significance of different opioid
15 molecules, but I want to ask you what this entry for
16 potential H-3-G neuroexcitatory effects means.

17 A. Both hydromorphone and morphine have a
18 glucuronide -- 3-glucuronide molecule which has
19 demonstrated -- H-3-G is hydromorphone-3-glucuronide,
20 and it has been shown to have neuroexcitatory effects.
21 That means it can cause irritability, hyperreflexia, in
22 patients, particularly those using high doses of
23 hydromorphone or particularly in those with renal
24 failure who aren't excreting this molecule.

25 Morphine similarly has neuroexcitatory --

1 (Admonition to slow down.)

2 BY MR. LEEFER:

3 Q. Dr. Savage, I'll -- we can get to morphine
4 later. Let's stick for now --

5 A. There was a reason that I mentioned that.

6 JUDGE CHAPPELL: Hold on a second. Don't
7 interrupt each other. One at a time.

8 MR. LEEFER: I'm sorry, Your Honor.

9 BY MR. LEEFER:

10 Q. Okay, Dr. Savage. Could you explain why you
11 mentioned morphine effects in this context.

12 A. Because seizures have been documented with
13 morphine that has similar neuroexcitatory effects, and
14 though I have not read of seizures with hydromorphone,
15 it raises a concern.

16 Q. Would you consider these sorts of effects in
17 deciding whether or not to prescribe Exalgo or morphine
18 to a patient?

19 A. Yes.

20 Q. Now, this table also indicates that all doses
21 are contraindicated in opioid-naive patients.

22 Can you please explain what that means.

23 A. Well, current recommendations of the
24 Centers for Disease Control are that we start all
25 opioids -- we start no sustained-release opioids in

1 opioid-naive patients. That is, when patients have not
2 demonstrated a tolerance to moderate doses of opioids,
3 it's recommended that we start with immediate-release
4 doses.

5 However, there are some opioids that are
6 formulated with very, very low doses so that they can
7 be started in patients, safely clinically started in
8 patients who are opioid-naive.

9 Exalgo hydromorphone is not formulated in a low
10 enough dose to make it safe to begin with the
11 extended-release.

12 Q. Is oxymorphone ER formulated in a low enough
13 dose that it co,so tegintuive.

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1 dosing that you've identified in this table?

2 A. Again, it's a different interval of
3 administration. As a matter of convenience, many
4 people would elect to have a medication that they only
5 need to attend to every 72 hours.

6 I wanted to point out on your last slide with
7 Exalgo that that's a 24-hour preparation as opposed to
8 a 12-hour preparation --

9 JUDGE CHAPPELL: That comes under the heading
10 of a question you weren't asked, ma'am. Stick to the
11 question that's pending.

12 BY MR. LEEFER:

13 Q. Dr. Savage, are there some patients that
14 prefer to take medication more often than every
15 72 hours?

16 A. Yes.

17 Q. Why would a patient ever want to take medicine
18 more often?

19 A. I think it gives patients often a better sense
20 of control that they're able to do something active to
21 manage their pain.

22 There may be times that they don't need the
23 medication and they may want to leave out a dose, and
24 if they are on a 72-hour dose, that isn't an option to
25 lower the medication.

1 Q. Rather than going through every single figure
2 in your report, I'd just like to ask, have you --
3 rather, do each of the figures in this section of your
4 report identify differences between a particular drug
5 and Opana ER?

6 A. Yes.

7 Q. And what is the information in these tables, or
8 where does this information come from?

9 A. As I said before, the information comes
10 primarily from the prescribing information approved by
11 the FDA for distribution with the medications.

12 Q. Are there any other sources for the information
13 in these tables?

14 A. Yes. It's supplemented in a couple of places I
15 believe with information from the scientific
16 literature.

17 Q. Now, we've spent a fair amount of time
18 discussing the numerous differences between Opana ER
19 and other long-acting opioids.

20 In your opinion, is Opana ER superior to these
21 other opioids?

22 A. I can't say that any opioid is superior to any
23 other opioid, so no.

24 Q. In the context of treating an individual
25 patient, are opioids superior to other opioids?

1 A. In the treatment -- in the clinical setting,
2 for individual patients with specific types of pain in
3 specific con8h9dm
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1 A. Because I think the differences between the
2 various opioids have real clinical impacts on patients
3 both in terms of pain, side effects and their quality
4 of life and their lifestyles.

5 Q. Can you give an example of a real effect that
6 these differences might have on a patient?

7 A. There are numerous examples.

8 Somebody may have nausea and vomiting on one
9 medication and not tolerate it well.

10 Some patients may prefer to take their
11 medication twice a day than every three days.

12 They may need to take an antidepressant or
13 erythromycin for infection and experience fluctuations
14 in a particular opioid that they wouldn't experience on
15 another opioid.

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1 Q. This education blueprint, is this something
2 that you considered in preparing your expert report?

3 A. It is.

4 Q. I'd like to take a look at that now. Can we
5 please bring up CX 3355.

6 And Your Honor, for the record, CX 3355 has
7 been admitted as part of JX 2 and is not subject to an
8 in camera order.

9 Dr. Savage, is this the REMS blueprint that you
10 were just discussing a moment ago?

11 A. It's the introduction to the blueprint. I
12 guess, yeah, that's the cover page of it that I'm
13 looking at.

14 Q. And what is the purpose of this blueprint?

15 A. This is to provide guidance to the development
16 of education on best practices around the use of
17 extended-release and long opi- -- long-acting opioid
18 analgesics.

19 Q. Are you familiar with the REMS blueprint from
20 your work in the field of pain management?

21 A. Yes, I am.

22 Q. And can you just explain briefly how it's
23 used.

24 A. Well, there are a number of organizations that
25 provide what's called REMS education, and it's

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1 that you chaired, which you were discussing just a
2 moment ago -- was that similar to the REMS blueprint
3 that the FDA ultimately --

4 A. It was similar, not identical by any means.

5 Q. Understood. Thank you.

6 And I'd like to direct your attention to the
7 bottom of page 6. This is CX 3355-006.

8 And specifically under the subheading Roman
9 numeral vi.

10 Now, this is kind of a long sentence, but
11 Dr. Savage, can you just summarize for us what this is
12 trying to convey.

13 A. Essentially this section says that prescribers
14 should be knowledgeable about the specific
15 characteristics of individual extended-release or
16 long-acting opioid analgesics that they prescribe.

17 Q. And do you agree with that?

18 A. I do.

19 Q. -- statement?

20 Why?

21 A. For all the reasons we've been discussing
22 because it -- the differences have a real impact on
23 the clinical effects and the quality of life that
24 patients experience when using these medications.

25 Q. I'd like to now direct your attention to

1 page 10, so CX 3355-010.

2 And Dr. Savage, can you explain what the table
3 that begins on this page is designed to show.

4 A. I believe -- I'm only looking at one page, and
5 I know it's 10 or 15 pages, but I believe that this is
6 a section that talks about the specific characteristics
7 of different extended-release opioids.

8 Q. Dr. Savage, in your opinion, are the different
9 characteristics reflected in the table beginning on
10 page 10 clinically significant to the prescription of
11 opioids for the treatment of pain?

12 A. Yes.

13 Q. I'd like to take a look specifically at
14 page 13, CX 3355-013.

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1 We're in recess.

2 (Whereupon, at 1:44 p.m., a lunch recess was
3 taken.)

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1 CX 3355-012, and then that continues onto -013.

2 Can you please pull those up.

3 And Dr. Savage, the product shown here at the
4 bottom of page 12 is Dolophine.

5 Which opioid is that?

6 A. Dolophine is methadone.

7 Q. And is methadone an opioid that you're familiar
8 with in your --

9 A. Yes.

10 Q. On page 13, under Product-Specific Safety
11 Concerns, this says "QTc prolongation."

12 What does that mean?

13 A. On an electrocardiogram the QC -- QTc -- the QT
14 interval is the area of electrical deruoenrs, BDC ean?a Td(A.)TjEM

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1 A. It is.

2 JUDGE CHAPPELL: Hold on a second.

3 Mr. Loughlin, have you issued subpoenas to
4 these witnesses?

5 MR. LOUGHLIN: We did issue subpoenas,
6 Your Honor.

7 JUDGE CHAPPELL: Have you released anyone from
8 subpoena?

9 MR. LOUGHLIN: No, Your Honor.

10 JUDGE CHAPPELL: Then they should be here.

11 MR. LOUGHLIN: Understood, Your Honor. We are
12 working with them to try to get them here on a
13 schedule that is -- that works for them and works for
14 us.

15 JUDGE CHAPPELL: Subpoena doesn't leave wiggle
16 room unless you give wiggle room, sir. You know what a
17 subpoena is; right? You know how it works?

18 MR. LOUGHLIN: I do know how it works,
19 Your Honor.

20 JUDGE CHAPPELL: You don't need to give them
21 wiggle room. When you issue a subpoena, they shall be
22 here.

23 MR. LOUGHLIN: Well, Your Honor, we're working
24 with counsel to try to make that happen, but we don't
25 have the power to send deputies to drag them to court.

1 JUDGE CHAPPELL: You bring it to me, and I'll
2 get you a deputy involved. There are ways to enforce
3 subpoenas. If you don't believe it, look at the
4 rules. I'm not saying you have a deputy, but there
5 will be a deputy -- there will be a marshal involved if
6 someone doesn't honor a subpoena. You know that;
7 correct?

8 MR. LOUGHLIN: Your Honor, yes, and that's
9 wonderful to hear. We would like nothing more than to
10 have witnesses lined up. We have not been able to make
11 that happen, but we will try harder.

12 JUDGE CHAPPELL: Thank you.

13 BY MR. LEEFER:

14 Q. Dr. Savage, in your opinion, is a factor like
15 QTc prolongation associated with methadone clinically
16 significant in deciding which opioid to prescribe?

17 A. Yes. And there are clear guidelines about not
18 prescribing methadone for patients with a QTc interval
19 that is over a certain duration.

20 Q. Does oxymorphone have a similar safety concern
21 associated with QTc prolongation?

22 A. To my knowledge, it does not.

23 Q. Okay. You can set that aside, Dr. Savage.

24 Now, the information that we were looking at in
25 the FDA REMS blueprint, is that similar to the

1 differences between opioids that you discuss in your
2 expert report?

3 A. It is.

4 Q. Dr. Savage, are you aware that Impax' expert,
5 Dr. Michna, cites to the common indication for
6 long-acting opioids in support of his position that
7 they are all essentially the same?

8 A. I'm aware of that, yes.

9 Q. Do you agree with Dr. Michna's reliance on the
10 common indication for long-acting opioids?

11 A. I agree that they for the most part -- there
12 are at least one or two exceptions, but they do have a
13 common FDA indication. That doesn't mean they have
14 identical effects and side effects.

15 Q. Why don't you believe that the common
16 indication for long-acting opioids means that they're
17 all essentially the same?

18 A. For all the reasons that I described in my
19 report and that the FDA includes in their blueprint
20 documenting that there are differences between all
21 these opioids, and the FDA recommends that it's
22 incumbent on us to understand those differences and to
23 accommodate them.

24 Q. To sum up these differences, what is your
25 opinion, Dr. Savage, about the degree of

1 interchangeability of Opana ER with the other available
2 long-acting opioids?

3 A. I don't believe that we can predict that they
4 will be reliably interchangeable with one another in a
5 particular patient. They are sometimes interchangeable
6 and often not, but we cannot know that prospectively.
7 Therefore, I believe that they're not reliably
8 predictably interchangeable.

9 Q. Thank you, Doctor.

10 Earlier, before lunch, you testified that
11 notwithstanding the significant differences between
12 opioids, it's sometimes possible to switch a patient
13 from one to another. Do you remember that?

14 A. Yes.

15 Q. Are there any complexities involved in
16 switching a patient from one long-acting opioid to
17 another?

18 A. Sometimes there are; sometimes there are not.

19 Q. And can you identify what some of those
20 complexities are?

21 A. Well, again, we can't predict whether the new
22 opioid to which one is switching is going to be
23 well-tolerated and adequate for analgesia for the
24 individual.

25 We can't predict the relative dose that will be

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1 JUDGE CHAPPELL: You said "when there's a clear
2 reason." What's a clear reason?

3 THE WITNESS: If somebody is becoming tolerant
4 to one opioid and they're having to increase and
5 increase and increase their dose, often by rotating
6 them to a different opioid, they will achieve pain
7 relief on a much lower dose of that opioid.

8 If somebody has persistent nausea or itching or
9 other side effects, we might change them to a different
10 opioid.

11 If they're on methadone and their QTc interval,
12 as we talked about, the potential for cardiac
13 arrhythmias, if we see that going up, we may want to
14 rotate them to a different opioid.

15 JUDGE CHAPPELL: What if their insurance
16 changes and they no longer can get the opioid you
17 prescribed?

18 THE WITNESS: If -- if -- it depends in that
19 case. If somebody is doing really well and they've
20 tried other opioids and they don't respond well, we
21 might seek to get authorization for the opioid even if
22 it's not one that's commonly approved by the insurance
23 company. If the insurance company denies that, we'll
24 do our best with whatever opioids are available.

25 The challenge sometimes is you end up doing

1 JUDGE CHAPPELL: So did I hear you say a
2 number of people are on two or three different
3 opioids?

4 THE WITNESS: Yes. Sometimes people will be on
5 two or three different opioids. I have seen that not
6 infrequently. I would not generally do it.

7 JUDGE CHAPPELL: And one of those might be
8 Opana ER or its equivalent and one of them might be
9 what?

10 THE WITNESS: A short-acting opioid. I have
11 seen people on a fentanyl patch and long-acting
12 oxycodone or oxymorphone and then a short-acting drug.

13 There --

14 JUDGE CHAPPELL: So like an opioid cocktail.

15 THE WITNESS: What?

16 JUDGE CHAPPELL: An opioid cocktail.

17 THE WITNESS: It's an opioid cocktail.

18 I'm not saying I'd recommend that. I'm saying
19 that patients will come to us on those.

20 And the rationale, if I may -- would you --
21 the reason that people will sometimes do that is
22 because of the fact that different opioids are
23 different and they seem to bind somewhat differently
24 to different mu opioid subreceptors, and so there is a
25 theory -- and there are number of articles on this --

1 suggesting that adding different opioids to each other
2 gives you improved analgesia.

3 The problem with that is then you become
4 tolerant to several opioids and it's difficult, if you
5 start losing your -- the effectiveness of the
6 medication, to find an opioid that works, so I
7 personally in my practice would prefer people to be on
8 a single or at most two opioids.

9 MR. LEEFER: Thank you, Your Honor.

10 BY MR. LEEFER:

11 Q. And Dr. Savage, I want to return to something
12 you were mentioning just a little bit earlier.

13 I think you mentioned that there are opioid
14 equivalent charts that allow you to calculate
15 equivalent dosages of different opioids. Is that
16 right?

17 A. That is correct.

18 Q. When you switch a patient from one opioid to
19 another, can you just cut the dose by the percentage
20 indicated by the opioid equivalent charts?

21 A. No. It's more complicated than that.

22 The equivalency charts will give you kind of
23 an average equivalency across the population, and
24 they're based on very limited studies, but they'll
25 give you some idea of the relative strength.

1 Then if the person is tolerant to the first
2 drug, you don't expect them to be tolerant to the next
3 drug, so you have to cut that dose back even further.

4 And then that doesn't take into account the
5 individual's responsiveness to either of the opioids.

6 JUDGE CHAPPELL: Are you saying that using
7 these charts is something that the AMA requires, let's
8 say, a general practitioner out here in the suburb
9 who's seeing 15-20 patients a day, kids are screaming
10 in the waiting room, climbing all over everybody, that
11 that doctor is looking at charts before he
12 prescribes -- he or she prescribes opioids to every
13 patient?

14 THE WITNESS: If he or she is rotating the
15 patient from one opioid to another, they either have
16 the equivalencies in their head if they do it quite
17 often or they do look at the chart or they just go
18 blind. And that's why, you know, I would say unless
19 there's a clinical indication and you do a lot of this,
20 you have to have -- you have to exert great care in
21 opioid rotations.

22 There are people who get profoundly sedated
23 because of overprescribing. There are people who are
24 in withdrawal because they've been underprescribed,
25 too. It's -- it is -- for high-dose opioids, it can be

1 complicated.

2 Again, I don't want to overstate it. If you're
3 taking two Percocet a day and you want to switch to a
4 couple of hydrocodone, that's not going to be a
5 complicated switch. It may or may not work as well for
6 you. But when we have people on complex regimens and
7 they're taking a number of other medications, it has to
8 be done thoughtfully and with great care.

9 JUDGE CHAPPELL: Okay. Again, is there an AMA
10 requirement or any law or regulation you're aware of
11 that requires a doctor to review these charts and apply
12 them before prescribing a different opioid?

13 THE WITNESS: I'm thinking.

14 No.

15 JUDGE CHAPPELL: Thank you.

16 THE WITNESS: May I say one caveat, though.

17 The FDA --

18 JUDGE CHAPPELL: Well, I guess so since you're
19 saying it. Go ahead.

20 THE WITNESS: The FDA in the REMS blueprint
21 suggests that you know the relative potencies of the
22 different medications. They do not provide a chart,
23 but to know the relative potencies, you need to be
24 looking at --

25 JUDGE CHAPPELL: So if I follow you, that's a

1 suggestion in the FDA REMS blueprint; correct?

2 THE WITNESS: Correct.

3 JUDGE CHAPPELL: Not a requirement by law or
4 regulation as you know about.

5 THE WITNESS: No. There may be states that
6 require it. I'm not familiar with all the state laws.
7 Many states are implementing legislation regarding how
8 to use opioids.

9 BY MR. LEEFER:

10 Q. Dr. Savage, in your capacity as an educator of
11 others in the use of opioids, do you instruct people
12 switching patients from one opioid to another to use
13 these dosage equivalency charts?

14 JUDGE CHAPPELL: When you say "people," do you
15 mean prescribing doctors who are licensed?

16 MR. LEEFER: I do mean prescribing doctors. My
17 apologies, Your Honor.

18 THE WITNESS: I do, with the caveat that I
19 usually provide three different methods for rotating.

20 BY MR. LEEFER:

21 Q. Thank you, Dr. Savage.

22 Now, getting back to the various risks that may
23 arise when rotating from one opioid to another, is
24 there a risk that new side effects may develop with the
25 use of a new opioid?

1 A. Yes.

2 Q. Given the various complexities and potential
3 risks of opioid rotation, how do you mitigate against
4 those risks when you switch a patient from one opioid
5 to another?

6 A. Well, there's several ways. Sometimes we
7 suggest that rather than giving the full dose of the
8 new medication and stopping the old medications, that
9 you give maybe a quarter of the new medication and go
10 down about a quarter of the calculated dose of the old
11 medications, and so see how somebody responds to the
12 new medication and gradual- -- it's called gradually
13 rolling them over.

14 Another method is to give no more than the
15 recommended starting dose of the new medication as
16 long-acting because we believe, based on studies, that
17 people will tolerate that new dose and then provide
18 only short-acting medications on top of it and ask the
19 person to hold that short-acting dose, don't take it,
20 if you're sedated or having other major side effects.

21 Q. Is it always complicated and difficult to
22 switch a patient from one opioid to another?

23 A. No.

24 Q. What's a circumstance in which it would be
25 relatively straightforward?

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1 healthcare costs certainly.

2 Q. I believe you touched on this earlier, but
3 given these complexities and risks, would you typically
4 rotate a patient from one opioid to another absent a
5 clinical need to do so?

6 A. No.

7 Q. And Dr. Savage, if you had a patient that is
8 doing well on a long-acting opioid like Opana ER, would
9 you prefer to keep them on that drug or switch them to
10 a new opioid?

11 A. If they're tolerating it well and it's meeting
12 their needs, I'd prefer to keep them on the drug that
13 they're using.

14 Q. Now, Dr. Savage, in your experience, would a
15 minor increase in price for an opioid that one of your
16 patients is taking cause you to switch that patient to
17 a different opioid?

18 A. It would depend upon the patient and what the
19 increase in price meant to them. Most of our patients
20 are insured and don't experience minor fluctuations in
21 price directly.

22 So generally speaking, no; in some cases, yes.

23 Q. And generally speaking, are you aware of the
24 prices of long-acting opioids?

25 A. No.

1 Q. So would you be aware if the price of a
2 long-acting opioid increased or decreased?

3 A. No. Not -- not unless I were in a healthcare
4 system where they regularly informed us of those
5 issues, which I'm not.

6 Q. Now, why wouldn't minor changes in prices
7 change your prescribing habits?

8 A. First, because I'm generally not aware of the
9 minor changes in price.

10 Second, because the -- my clinical -- my
11 concerns here are for the clinical well-being of the
12 patient, and those would take priority over more
13 abstract financial concerns.

14 Q. Understanding that you don't generally know the
15 price of opioids exactly, do you know anything about
16 relative prices of opioids?

17 JUDGE CHAPPELL: I thought she said "no" a few
18 moments ago. That was a pretty broad question you
19 asked her.

20 MR. LEEFER: Let me try and rephrase that,
21 Your Honor.

22 BY MR. LEEFER:

23 Q. Do you know any general information about the
24 prices of opioids?

25 A. Fairly limited. My understanding is that

1 short-acting opioids most often are less expensive than
2 sustained-release opioids. Methadone is a very, very
3 inexpensive long-acting opioid.

4 Q. In your experience, which tend to be cheaper,
5 generic versions of opioids or brand name versions?

6 A. Generic versions. That's the only thing I
7 know.

8 Q. Could cost information of that sort shape
9 prescribing decisions that you make?

10 A. For an uninsured patient who is -- has limited
11 financial means, certainly those would be
12 considerations.

13 JUDGE CHAPPELL: But I thought you told us
14 you're unaware of those things, so evidently you don't
15 think it's important enough to know this; correct?

16 THE WITNESS: If a patient brought to my
17 attention that they had no insurance that paid for
18 their drugs and they were concerned about their
19 finances, I would incorporate that into my clinical
20 decision-making.

21 JUDGE CHAPPELL: So that's purely
22 hypothetical?

23 THE WITNESS: And excuse me.

24 JUDGE CHAPPELL: If a patient brought it to
25 you?

1 THE WITNESS: If a patient brought it to my
2 attention, which has happened, then I would consider
3 the cost.

4 It's not that I don't care enough to notice. I
5 don't have ready access to the information of the
6 actual price of drugs.

7 JUDGE CHAPPELL: Frankly, your care is not an
8 issue, ma'am. I'm just looking at what I see to be
9 inconsistent, trying to have a complete record here in
10 this trial, so whether you care or not is not an
11 issue.

12 THE WITNESS: Well, you said that, you don't
13 care enough to know -- I'm sorry. I thought that's
14 what you said.

15 JUDGE CHAPPELL: It might have been inartfully
16 worded, but I'm trying to prevent inconsistencies in
17 our record. That's my job.

18 THE WITNESS: Thank you.

19 JUDGE CHAPPELL: We're getting at the truth
20 here whether anybody likes it or not.

21 Go ahead.

22 MR. LEEFER: Your Honor, maybe this is my
23 fault. I can try and clarify.

24 I believe Dr. Savage was drawing a distinction
25 between knowing the specific price of an opioid and

1 knowing sort of generally that generics are cheaper
2 than brand name drugs, and so she -- I believe she
3 testified that she knows that general information but
4 not the specific prices of drugs.

5 MR. ANTALICS: At some point I think I'd
6 preferred the witness to answer the questions rather
7 than the lawyer describe what he'd like her to say.

8 JUDGE CHAPPELL: He's --

9 MR. ANTALICS: Leading, Your Honor.

10 JUDGE CHAPPELL: -- in an indirect way saying
11 you're leading and suggesting an answer and coaching
12 the witness.

13 MR. LEEFER: My apologies, Your Honor. I will
14 rephrase my questions.

15 BY MR. LEEFER:

16 Q. Dr. Savage, if a patient does not raise the
17 cost of opioid medication with you as a concern, is it
18 something you independently consider when prescribing
19 drugs?

20 A. Not in the -- no.

21 Q. Dr. Savage, when you prescribe opioids, what
22 are your primary considerations in deciding which drug
23 to give to a patient?

24 A. My primary considerations are matching the
25 patient to a medication that's clinically effective for

1 them with the least amount of side effects and one that
2 meets convenience issues such as interval of dosing and
3 matches their pain needs.

4 JUDGE CHAPPELL: Have you ever testified as an
5 expert witness in a trial before?

6 THE WITNESS: Yes.

7 JUDGE CHAPPELL: Often?

8 THE WITNESS: No.

9 JUDGE CHAPPELL: Because if you do, you'll
10 understand none of this is personal, ma'am.

11 THE WITNESS: I'll understand what?

12 JUDGE CHAPPELL: None of this is personal.

13 THE WITNESS: Thank you.

14 JUDGE CHAPPELL: It's about getting to the
15 truth.

16 THE WITNESS: Thank you very much, Your Honor.

17 BY MR. LEEFER:

18 Q. Dr. Savage, if you have a patient that is doing
19 well on a long-acting opioid like Opana ER, would you
20 switch them to a different opioid based on a minor
21 change in price?

22 A. I probably would not be aware of the minor
23 change in price, and I wouldn't switch them without
24 knowing that. It depends upon what you mean by "minor"
25 and how the patient experience -- if I did become aware

1 of it, how the -- it impacted the patient and how they
2 experienced that fluctuation in price.

3 Q. If you didn't become aware of it, would it play
4 any role in your prescribing decisions?

5 A. I want to be sure I understand your question.
6 If I were not aware of the change in price, would it
7 influence my prescribing decision.

8 Q. Yes, that was my question.

9 A. No, it would not influence my prescribing
10 decision.

11 JUDGE CHAPPELL: How could it? To state the
12 obvious.

13 MR. LEEFER: That's a fair point, Your Honor.

14 JUDGE CHAPPELL: I'm glad you didn't slip up on
15 that one.

16 BY MR. LEEFER:

17 Q. Generally, Dr. Savage, in your thirty-plus
18 years of prescribing opioids, have you been aware of
19 minor changes in price in opioids?

20 A. I have not been.

21 MR. LEEFER: Thank you, Dr. Savage.

22 I have no further questions at this time.

23 JUDGE CHAPPELL: Will there be any cross?

24 MR. ANTALICS: Right, Your Honor.

25 JUDGE CHAPPELL: Go ahead.

1 THE WITNESS: Okay. I may need to do that,
2 unless it gets magnified again, but we'll see.

3 MR. ANTALICS: I think you'll recognize the
4 parts that we're looking at.

5 MR. LEEFER: Sorry. Your Honor, I object.
6 This document doesn't appear to be marked as an exhibit
7 or a demonstrative.

8 MR. ANTALICS: No, it's not an exhibit or a
9 demonstrative. It's one of the materials Dr. Savage
10 relied upon. I'm just going to ask her a couple
11 questions about it.

12 JUDGE CHAPPELL: About one of her books?

13 MR. ANTALICS: Yes. One of the materials she
14 relied on in preparing her report.

15 JUDGE CHAPPELL: That's fair game. It doesn't
16 need to be an exhibit. Depending on -- we'll see how
17 this develops.

18 BY MR. ANTALICS:

19 Q. Okay. The chapter is called Opioid Therapy of
20 Pain.

21 You were the primary author for that chapter?

22 A. Correct.

23 Q. Okay. Now, if you could turn to page 1508, and
24 we'll spend our time just on that page, 1508. It has a
25 chart with a number of opioids on it.

1 Do you recognize that chart?

2 A. I do.

3 Q. Okay. And on the top half of the page where it
4 says "Mu Agonists" --

5 A. Correct.

6 Q. -- do you see that?

7 Going down to halfway down?

8 Now, all of the --

9 THE REPORTER: I'm sorry. She keeps nodding.

10 (Discussion off the record.)

11 BY MR. ANTALICS:

12 Q. On the top half, top left corner, it says
13 "Table 97-3." Immediately under that it says "Opioid."
14 And immediately under that it says "Mu Agonists," a
15 category of opioids.

16 A. Correct.

17 Q. Okay. Now, all of the drugs listed in that
18 top category, those are all mu opioids; is that
19 correct?

20 A. That is correct.

21 Q. Okay. And all of the drugs on that page are
22 still considered opioids, though, although they're not
23 all mu opioids, mu agonists.

24 A. As far as I can see the page, they are all
25 mu opioid agonists.

1 Some have dual mechanisms of analgesia, and
2 some may have a little kappa activity, but they're
3 mostly mu agonists.

4 (Counsel and witness speaking at the same time
5 and cautioned by court reporter.)

6 JUDGE CHAPPELL: And also, it's your record,
7 but if you're going to be asking a lot about this page,

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1 Again, I don't know. You might have one
2 question and we're moving on. I don't know what you're
3 doing.

4 MR. ANTALICS: I intend to offer it,
5 Your Honor.

6 JUDGE CHAPPELL: As a demonstrative?
7 Take a moment, talk to opposing counsel --

8 BY MR. ANTALICS: Yes, I'd like to --

9 JUDGE CHAPPELL: Take a moment. Talk to
10 opposing counsel. See if you have an agreement.

11 (Pause in the proceedings.)

12 MR. ANTALICS: Your Honor, we'd like to offer
13 this as a demonstrative exhibit, I believe without
14 objection, but it will be listed as RX D-1.

15 Do we have one of those yet? I don't think
16 so.

17 JUDGE CHAPPELL: And just for better reference,
18 that is what page of what book?

19 MR. ANTALICS: The book is titled -- it is
20 page 1508 of the book called The ASAM Principles of
21 Addiction Medicine, Fifth Edition.

22 JUDGE CHAPPELL: Any objection to this as a
23 demonstrative?

24 MR. LEEFER: No objection to it as a
25 demonstrative, Your Honor.

1 JUDGE CHAPPELL: So admitted.

2 (RX Exhibit Number D-1 was admitted into
3 evidence.)

4 BY MR. ANTALICS:

5 Q. Okay. Once again, you wrote this chapter?

6 A. I did.

7 Q. Okay. Now, could we go down the list of the
8 mu agonists, and could you tell us which of these, to
9 your knowledge, has a generic drug available associated
10 with that molecule.

11 Let's start with morphine.

12 A. Okay. MD 2 B-fW-a generic dextended-release

13 Q. IAndextended-releasegeneric

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1 interchangeable if attention is paid to relative
2 potencies and onset and duration of action, individuals
3 may respond differently to different opioids in terms
4 of both analgesia and side effects."

5 Do you still agree with that sentence, Doctor?

6 A. I do.

7 Q. Okay. Thank you.

8 Now, when you talk about relative potencies
9 and onset and duration of action in the first part of
10 that sentence, you mean you may have to adjust the
11 dose of the alternative to get the same analgesic
12 effect; correct?

13 A. Yes.

14 Q. Thank you.

15 And it's also possible, as we see in the
16 second half of the sentence, that you would have to
17 give the patient some additional medication if there
18 are side effects in the alternative.

19 A. That was not what I intended. I don't mention
20 giving people additional medications.

21 Q. Okay.

22 A. I intended what's actually written -- may I
23 read it?

24 JUDGE CHAPPELL: Just so we're clear, when
25 you're saying, That's not what I intended, you're

1 talking about what's printed on this page? Or
2 testimony previous today?

3 THE WITNESS: He said that in the second
4 half -- my understanding of what you just said, if I'm
5 remembering it correctly, is that in the second half of
6 that sentence I intended to say you may need to give
7 medications for side effects and --

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1 Q. Okay.

2 A. So --

3 JUDGE CHAPPELL: Wait, wait a second. The
4 question was "they may have side effects," so is
5 your answer --

6 THE REPORTER: Wait. Can we do -- wait. I
7 didn't get any of that because she started talking
8 before you were done.

9 JUDGE CHAPPELL: My question was -- you have to
10 wait till I finish -- he asked a question and you said
11 "not only." Is your answer yes, but also?

12 THE WITNESS: Correct. Thank you.

13 JUDGE CHAPPELL: Thank you.

14 BY MR. ANTALICS:

15 Q. So if the patient has side effects, is it
16 possible that you may be able to treat those side
17 effects with some additional medication?

18 A. Yes.

19 Q. Thank you.

20 Okay. Now, in certain parts of the world,
21 morphine has been the standard of care; is that
22 correct?

23 A. That is correct.

24 Q. Okay. And they use principally morphine,
25 almost exclusively morphine.

1 MR. ANTALICS: Yes.

2 THE WITNESS: Oh, okay.

3 BY MR. ANTALICS:

4 Q. You can -- and in emergency rooms and in acute
5 care inpatient settings, in your experience, in your
6 region, hydromorphone, fentanyl and morphine are the
7 most commonly used; correct?

8 A. That's correct.

9 Q. Okay. But medical practices are very
10 regionalized, in your view; correct?

11 A. Correct.

12 Q. Okay. Practice in one hospital is very
13 different from practice in another hospital; correct?

14 A. Correct.

15 Q. And that's because medical practices are shaped
16 by many different things; correct?

17 A. Correct.

18 Q. And one of those things is knowledge of the
19 literature; correct?

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1 A. That is correct.

2 Q. Okay. And the marketing of different companies
3 for their drugs also forms an awareness of products;
4 correct?

5 A. Yes.

6 Q. Okay. And it's the relative balance of all
7 those influences that can change from region to region;
8 correct?

9 A. Correct.

10 Q. Okay. And from hospital to hospital; correct?

11 A. Correct.

12 Q. And from physician to physician; correct?

13 A. Correct.

14 Q. All right. So medical practice with respect
15 to the selection of opioids, whether it's a full mu
16 agonist opioid or a partial opioid, is different
17 across the spectrum depending on where you are;
18 correct?

19 A. The initial selection is what we're talking
20 about; correct?

21 Q. Correct.

22 Okay. Now, I believe you said opioid therapy
23 is always individualized. Correct?

24 A. Ideally it is.

25 Q. Okay. But you can't say that any particular

1 group of people need morphine or oxymorphone, because
2 it's always an individual thing; correct?

3 A. Correct.

4 Q. Now, if a patient is opioid-naive, meaning
5 they've never taken an opioid before, but they need one
6 now, doctors usually start with what they're familiar
7 with; correct?

8 A. Correct.

9 Or with a patient -- oh, they're opioid-naive.
10 Yes. Correct.

11 Q. And that could be oxycodone; correct?

12 A. Could be.

13 Q. Could be hydrocodone; correct?

14 A. Could be.

15 Q. Could be oxymorphone; correct?

16 A. Yes.

17 Q. Or any number of different opioids; correct?

18 A. Yes.

19 Q. Okay. Now, sometimes it takes two or three
20 times to get them to the right opioid, as I think you
21 said; correct?

22 A. Yes.

23 Q. Okay. And maybe somewhere in the middle,
24 somewhere in the middle, could be down to 30, could be
25 70 percent, somewhere in the middle, the doctors get

1 the right one on the first try; correct?

2 A. Correct.

3 Q. Okay. So even though they're starting with
4 different opioids, they're getting the right try half
5 the time, somewhere in that range.

6 A. I don't know if it's half the time.

7 Q. But just -- I understand you're not being
8 precise.

9 A. Yeah. Sometimes they get it right.

10 Q. Okay.

11 A. Some --

12 JUDGE CHAPPELL: When you say they're getting
13 it right, you mean the prescribing doctor?

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1 Q. Okay. With that -- with that change, is that
2 correct?

3 A. I would say yes.

4 Q. Okay. For example, based on a study you've
5 seen, you believe that most patients on oxymorphone --
6 and by that I mean more than 50 percent -- could
7 successfully be switched to oxycodone; correct?

8 A. I don't know that to be true. I -- weighing
9 my own personal experience, I can't give you a number.

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1 MR. ANTALICS: I'm not sure, Your Honor.

2 THE WITNESS: I can't say --

3 BY MR. ANTALICS:

4 Q. But it's your belief -- I think it's your
5 belief that you can't say if 90 percent could
6 successfully be switched; correct?

7 A. I can't say if 30, 40, 50, 60, 70, 80,
8 90 percent could successfully switch.

9 Q. Did you once before tell me --

10 JUDGE CHAPPELL: Wait, wait, wait. She was
11 still talking.

12 THE WITNESS: I believe that I said, after
13 being pressed to give some kind of an answer, probably.
14 I believe that's what I said.

15 So probably 50 percent, but I don't say that
16 with certainty that I am correct.

17 BY MR. ANTALICS:

18 Q. Okay.

19 A. I have to see the study.

20 Q. Okay. In your own personal experience, though,
21 you have switched patients from oxymorphone to other
22 opioids; correct?

23 A. Yes.

24 Q. Okay. And in fact, you've never seen a
25 situation where somebody had been on oxymorphone ER and

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1 JUDGE CHAPPELL: We didn't hear the last thing
2 you said. You said it is not --

3 THE WITNESS: It is metabolized in the liver,
4 but it is not -- does not utilize the CYP P450 system.

5 BY MR. ANTALICS:

6 Q. Okay. And it's because it doesn't utilize the
7 CYP450 system that you don't have to worry about
8 certain drug interactions; correct?

9 JUDGE CHAPPELL: Wait a minute, wait a minute.
10 To me that question is vague because you say

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1 that also is not metabolized via the CYP450 system;

2 correct?

3 A. That's correct. And --

4 Q. So --

5 A. -- hydromorphone as well.

6 Q. I'm sorry. Which one?

7 A. And hydromorphone as well.

8 Q. Okay. So both of those you wouldn't have to

9 worry about the drug interactions either, would you?

10 A. That's correct.

11 Q. Okay. And with respect to the other opioids

12 that are metabolized via the CYP450 system, they can

13 still be used with that interaction with proper care

14 and attention to dosing; correct?

15 A. They can be.

16 Q. Okay.

17 A. Some of them carry black box warnings not to,

18 but they can be, yes, as long as you adjust dose.

19 JUDGE CHAPPELL: Hang on a second.

20 Just so -- for people that may read the record

21 that don't live with drugs every day --

22 THE WITNESS: Uh-huh.

23 JUDGE CHAPPELL: -- would you be a450 sy

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1 JUDGE CHAPPELL: That's Opana ER.

2 I think those are the common ones. Thank you.

3 THE WITNESS: Yep. Sorry for not making it
4 clear before.

5 JUDGE CHAPPELL: It wasn't just you. We've
6 been here a few days and nobody had done that.

7 THE WITNESS: Yeah.

8 BY MR. ANTALICS:

9 Q. Now, in your report, one of your reports Ins and noALIC0 1
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1 record is clear on part of your previous question.

2 MR. ANTALICS: Okay.

3 JUDGE CHAPPELL: You asked her about someone
4 in a hospital gets an injectable form and then an
5 entirely different molecule upon release.

6 What I want to make clear is, are we talking
7 about an injectable form being drug A and a different
8 molecule upon release being drug B, or is it -- is
9 there a drug that has an injectable form and a
10 take-home capsule or pill form that's the same drug?

11 I want to make sure you understood his question
12 and we understand her answer.

13 THE WITNESS: I did understand --

14 MR. ANTALICS: I was going to get into that a
15 little bit more, Your Honor, but --

16 JUDGE CHAPPELL: Well, that question has
17 already been asked, so I'd like for that to be clear.

18 MR. ANTALICS: Yeah. No. Certainly.

19 THE WITNESS: Would you like clarification?

20 JUDGE CHAPPELL: Yes.

21 THE WITNESS: I was tempted to clarify, but I
22 don't want to talk too much.

23 So in general, yes, it's common practice to
24 provide an IV drug, whatever the favored drug is or
25 what works for that patient in the hospital, and

1 then -- it might be morphine, it might be fentanyl, it
2 might be hydromorphone, and then often practice is to
3 discharge people home on Vicodin or Percocet,
4 oxycodone or hydrocodone, so there is a change in
5 molecule.

6 All I said -- and it's not a point that --

7 JUDGE CHAPPELL: Well, no. Back up. When you

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1 My only point in my report is that you reduce
2 one more uncertainty when you have somebody on the
3 same molecule in the hospital that you discharge them
4 on.

5 JUDGE CHAPPELL: When you say "same molecule,"
6 I just -- I'm not trying to beat a dead horse -- maybe
7 it's been done already -- but when you say "not the
8 same molecule," you mean a different medicine, a
9 different opioid?

10 THE WITNESS: Well, the reason I use the term
11 "molecule" -- I'm sorry -- is because -- because there
12 are different brands of drugs and --

13 JUDGE CHAPPELL: Right. That's how we have the
14 various patents. I understand that.

15 THE WITNESS: Yeah.

16 JUDGE CHAPPELL: But if you were going to say,
17 I'm on IV heroin -- or heroin, jeez -- morphine --

18 THE WITNESS: Morphine.

19 JUDGE CHAPPELL: -- and -- I'm hoping there's
20 not a tablet form of heroin -- I'm on IV morphine and I
21 go home and the doctor says, Everything else makes him
22 vomit, give him tablet-form morphine, if that happened
23 to me, I've got an IV morphine, I go home and I've got
24 a bag of morphine tablets.

25 THE WITNESS: Yes.

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1 that there is an injectable form of Opana ER, don't
2 know who makes it, don't know who sells it, don't know
3 anything else. Maybe some witness will know.

4 MR. ANTALICS: I think Dr. Savage --

5 THE WITNESS: It's not under that brand name.

6 Is it?

7 BY MR. ANTALICS:

8 Q. Did you just say --

9 (Counsel and witness speaking at the same time
10 and cautioned by court reporter.)

11 BY MR. ANTALICS:

12 Q. Did you just say the injectable form of
13 oxymorphone is not commonly used --

14 A. I don't know -- oh.

15 JUDGE CHAPPELL: Well, let's start it this
16 way.

17 Is there an injectable form of Opana ER?

18 THE WITNESS: It's my understanding that there
19 is an injectable form of Opana ER.

20 JUDGE CHAPPELL: But that's all you know about
21 it?

22 THE WITNESS: It's not widely used, to my
23 knowledge, at least in the systems that I work in.

24 BY MR. ANTALICS:

25 Q. Okay. Okay.

1 Okay. I'd like to speak briefly with you about
2 formularies.

3 Now, I think you acknowledged that you know
4 very little about formularies having different tiers
5 and copays; correct?

6 A. That is correct.

7 Q. You don't have much experience dealing with
8 insurance companies; correct?

9 A. That is correct.

10 Q. You're a consultant in your practice area, and
11 it's the staff positions who are the ones that deal
12 with the insurance companies and write the
13 prescriptions; correct?

14 A. That is correct.

15 Q. Okay.

16 A. It's only part of the reason that I'm not as
17 familiar. It also is the practice context.

18 Q. But you do understand that formularies
19 encourage clinicians and patients to work out a
20 therapeutic plan that is the least costly for the
21 patient in terms of copays; correct?

22 MR. LEEFER: Your Honor, I'm going to object
23 for a lack of foundation.

24 JUDGE CHAPPELL: Response?

25 MR. ANTALICS: Well, in both Dr. Savage's

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1 terms of copays; correct?

2 MR. LEEFER: Your Honor, I have the same
3 objection. Mr. Antalics elicited from the witness that
4 she has very little knowledge of formularies. Now I
5 believe he's asking what formularies encourage
6 clinicians and patients to do.

7 MR. ANTALICS: Your Honor? Could I respond
8 briefly, Your Honor?

9 JUDGE CHAPPELL: Go ahead.

10 MR. ANTALICS: I think the language that I used
11 was almost precisely what Dr. Savage used in her
12 deposition, so I'm not sure why we're asking whether
13 she can --

14 JUDGE CHAPPELL: What we have here is an expert
15 witness under cross-exam being tested for depth of
16 knowledge and understanding. Overruled.

17 THE WITNESS: Would you ask the question
18 again. I'm sorry. I was looking at my report, and I

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1 is so we can save a little time.

2 MR. ANTALICS: Okay.

3 JUDGE CHAPPELL: If you are.

4 MR. ANTALICS: I am.

5 BY MR. ANTALICS:

6 Q. It's in your report at paragraphs 176 through
7 179, the initial report, deals with formularies. And
8 in her rebuttal report, paragraphs 31 through 34 deal
9 with formularies and insurance coverage.

10 A. I'm sorry. I only see one paragraph, and it's
11 really just the first part of it that deals with
12 formularies.

13 And I don't know what I'm -- I've been
14 requested to only respond to questions that are asked
15 me, so I'd prefer not to give unwelcome commentary.

16 177?

17 Q. 176 through 17- -- oh, it may have been in the
18 uncorrected version. You have a whole section on
19 insurance, pricing effects on long-acting opioids.

20 (Pause in the proceedings.)

21 JUDGE CHAPPELL: Well, I didn't mean to throw a
22 wrench in the works, but if you asked the witness about
23 something in her report and she wanted to look at it
24 and find it, we would have to wait for her to do that
25 anyway.

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1 BY MR. ANTALICS:

2 Q. "QUESTION: Do you understand what the concept
3 of having different tiers with different copays is
4 for?

5 "ANSWER: My understanding is that it
6 encourages clinicians to start -- and patients to work
7 on a therapeutic plan that is the least costly for the
8 patient in terms of copays, and so the preferred drugs
9 would be put on the most available tier."

10 Do you recall saying that?

11 A. I do recall saying that.

12 Is that all I said there?

13 Q. That was your complete answer to that
14 question.

15 A. Okay. That's fine.

16 Q. Is that accurate?

17 A. That's accurate.

18 MR. ANTALICS: Okay. That's the only thing I
19 was trying to get at, Your Honor.

20 THE WITNESS: I thought you said I addressed it
21 in my report, and I don't find anything in my report.

22 BY MR. ANTALICS:

23 Q. And you understand that the insurance
24 companies put drugs on the most available formulary
25 tier in -- that are, in the opinion of the insurance

1 company, adequate to provide the relief that's
2 contemplated; correct?

3 MR. LEEFER: Sorry, Your Honor. I object. It
4 seems like Mr. Antalics is asking Dr. Savage to testify
5 what's in the mind of insurance companies, and I object
6 on lack of foundation.

7 MR. ANTALICS: I think I asked her
8 understanding.

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1 on the most available formulary tier that are intended
2 to be adequate to provide the relief contemplated?

3 A. I don't know the criteria that insurance
4 companies use to determine how many or what drugs they
5 put in a tier. My understanding is that they --

6 JUDGE CHAPPELL: Hold on, hold on. We don't
7 want to hear your understanding.

8 THE WITNESS: Oh, okay. Thank you. I don't
9 know.

10 BY MR. ANTALICS:nding.

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1 A. Correct.

2 Q. Now, you agree that when you walk down the
3 aisle in a drugstore you can find aspirin right next to
4 ibuprofen, Advil; correct?

5 A. Correct.

6 Q. And those drugs are right next to Tylenol,
7 which is acetaminophen; correct?

8 A. Correct.

9 Q. And those drugs are right next to Naprosyn,
10 which is Aleve; correct?

11 A. Correct.

12 Q. Okay. Now, each of those four relieves mild to
13 moderate pain; correct?

14 A. Correct.

15 Q. But they each do it differently; correct?

16 A. They have different mechanisms of action.

17 Q. Okay. Acetaminophen acts at the level of the
18 spinal cord to block pain transmission; correct?

19 A. Correct.

20 Q. And the other --

21 A. We think. We think. It's not certain, but we
22 think, yes.

23 Q. And the other three, ibuprofen, Naprosyn and
24 aspirin, they act closer to the site of the injury;
25 correct?

1 A. That's their major mechanism. Yes.

2 Q. But even those three act differently from one
3 another in terms of where they interact to meet the
4 pain; correct?

5 A. That is correct.

6 Q. Okay. And they also have differences in how
7 often you should take them; correct?

8 A. Correct.

9 Q. Aleve, for example, says it can be taken every
10 twelve hours; correct?

11 A. Correct.

12 Q. Ibuprofen every four to six hours; correct?

13 A. I believe so.

14 Q. And aspirin every four hours?

15 A. I believe so.

16 Q. Okay. And they each have different toxicity
17 profiles; correct?

18 A. Correct.

19 Q. And they all act differently in different
20 individuals; correct?

21 A. Correct.

22 Q. Okay. And that's because people are
23 biogenetically slightly different in the way our
24 bodies' pathways lead to pain; correct?

25 A. Yes.

1 Q. Okay. So the bottom line is, just like
2 opioids, some people respond to one of the four better
3 than others; correct?

4 A. Correct. Some people respond better to one
5 than to others.

6 Q. Now, despite that, all four of those products
7 have on their labels that they can be used for
8 headaches; correct?

9 A. Yes.

10 Q. And they can -- all four say they can be used
11 for toothaches; correct?

12 A. I -- I haven't looked at labels recently, but I
13 would believe you if you tell me that is true. Yes.

14 Q. Okay.

15 A. They're certainly used for those --

16 Q. Let me list -- give you a list of other
17 indications, and you tell me if you think I missed
18 any.

19 A. Okay.

20 Q. They can each be used for muscle aches, each be
21 used for back pain, the common cold, minor pain of
22 arthritis, menstrual cramps, and all four say they
23 reduce fever; correct?

24 A. Tylenol doesn't reduce -- yes.

25 Q. Okay.

1 A. Sorry. Yes.

2 Q. Okay. So all four of them are out there right
3 next to each other in the aisle, and they're competing
4 for people who have headaches; correct? Even though
5 they do it differently.

6 A. Yes.

7 Q. Okay. And for all of those indications;
8 correct?

9 They do it differently, but they're competing
10 for the same patients.

11 A. I want to make sure -- what I started to say
12 is Tylenol doesn't reduce inflammation, and I think I
13 erroneously said "yes" when you listed inflammation in
14 that list, so I wanted to make sure that I corrected
15 that.

16 Q. Okay. I don't think I mentioned inflammation.

17 A. Okay. That's what I was thinking. Thank you.

18 JUDGE CHAPPELL: Fever. It was fever he
19 mentioned.

20 THE WITNESS: Fever -- what?

21 JUDGE CHAPPELL: Fever.

22 BY MR. ANTALICS:

23 Q. Okay. So they're out there, those companies
24 that produce those products, they're competing for the
25 same consumers; correct?

1 A. Yes.

2 Q. Okay. And in the same fashion the makers of
3 the opioids, even though they do things differently,
4 are competing generally for the same consumers;
5 correct?

6 A. I believe so.

7 Q. Okay. Now, you're familiar with Endo's
8 crush-resistant formulation of oxymorphone?

9 A. Yes.

10 Q. You're aware that it's off the market now;
11 correct?

12 A. Yes.

13 Q. Impax, though, still has its generic version of
14 oxymorphone ER on the market; correct?

15 A. Correct.

16 Q. Now, for the patients that had been on the
17 crush-resistant formulation that was just taken off the
18 market, those patients have had to go either to Impax'
19 generic version of oxymorphone ER or to another opioid;
20 correct?

21 A. Correct.

22 Q. Okay.

23 A. If they continued on opioids.

24 Q. Right.

25 So in your view, there's been a benefit to

1 patients who like oxymorphone because Impax' generic
2 oxymorphone ER is still on the market; correct?

3 A. I didn't hear the first part of your statement.
4 Could you repeat it, please.

5 Q. In your view, there has been a benefit to
6 patients who like oxymorphone ER because Impax'
7 generic oxymorphone ER is still on the market;
8 correct?

9 A. Yes.

10 Q. Okay. If a physician wanted to rotate a
11 patient to another opioid rather than going to Impax'
12 generic, the physician might try a trial rotation to
13 any of the opioids listed in that chart that we looked
14 at earlier; correct?

15 A. Depending upon the individual's prior
16 experiences and comorbidities and other issues that
17 might impact the decision, but yes.

18 Q. Okay. And if Impax' generic version of
19 oxymorphone ER was for some reason taken off the
20 market, you would expect that the physicians would
21 rotate their patients to the other opioids; correct?

22 A. As long as they still needed an opioid,
23 correct.

24 Q. But that, in your view, would increase risk of
25 some discomfort or side effects potentially; correct?

1 A. Potentially, yes.

2 Q. Okay. It might create some anxiety; correct?

3 A. Yes.

4 Q. Okay. So you would expect in that instance, if
5 Impax' version of oxymorphone ER was taken off the
6 market, that there would be negative effects for some
7 patients; correct?

8 A. Correct.

9 Q. Oxymorphone came on the market just several
10 years ago; correct?

11 A. Yes.

12 Q. You were able to treat patients before it came
13 on the market, though; correct?

14 A. Yes.

15 Q. Okay. But for some patients today you think
16 it's been an especially good medication; is that
17 right?

18 A. Yes.

19 Q. Okay. And it's a benefit to those patients,
20 and you would prefer to have it as an option in the
21 market; correct?

22 A. I believe having diversity in our choice of
23 opioids improves patient care and outcomes.

24 Q. So --

25 A. Yes.

1 Q. -- is the answer yes? Okay.

2 A. Sorry.

3 Q. And you'd be concerned if Impax' generic
4 oxymorphone ER was not on the market; correct?

5 A. Define "concerned."

6 I -- I think I answered your question that it
7 would create some anxiety and at least transient
8 negative changes for some patients.

9 Q. Okay. And because it's a benefit then for
10 some patients, there's a benefit to having it on the
11 market.

12 A. I believe so.

13 MR. ANTALICS: Okay. I have nothing further,
14 Your Honor.

15 JUDGE CHAPPELL: Redirect?

16 MR. LEEFER: Your Honor, I think I have a
17 couple things I want to ask about. May I have a moment
18 to confer with co-counsel?

19 JUDGE CHAPPELL: Go ahead.

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2 REDIRECT EXAMINATION

3 BY MR. LEEFER:

4 Q. Dr. Savage, do you remember Mr. Antalics asking
5 you whether it was possible to treat opioid side
6 effects with additional medications?

7 A. Yes.

8 Q. In your view, is it desirable to treat
9 opioid-related side effects with additional
10 medications?

11 A. No.

12 Q. Why not?

13 A. It's preferable to find an opioid that has
14 lesser side effects that don't require treatment.
15 Anytime we add a new medication in, we have risks of
16 additive side effects, toxicities.

17 Simple is better. When you can accomplish the
18 same thing with one medication, it's preferable not to
19 begin adding. That can go on and on.

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1 as few side effects as possible and as few medications
2 as possible.

3 Q. Thank you.

4 A. In most cases.

5 Q. I believe you were also asked about small
6 villages that might only have access to a single opioid
7 like morphine. Do you remember that?

8 A. Yep.

9 Q. And if you were in a small village like that,
10 would you try to make due as best you could with that
11 single opioid?

12 A. Yes.

13 And we did that before we had many different
14 kinds of opioids, but we've been able to improve
15 patient care I believe from having a diversity of
16 options.

17 Q. And in the United States, in your experience
18 with thirty years treating pain with opioids, is it
19 better to have more options to treat patients?

20 A. More opioids from which to select, not
21 necessarily more opioids out there in the world, but
22 more opioids from which to select.

23 Q. Thank you. I appreciate that clarification.

24 A. Yes.

25 Q. Now, Mr. Antalics also asked you if you had

1 ever had a patient who was unable to rotate from

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CERTIFICATE OF REPORTER

I, JOSETT F. WHALEN, do hereby certify that the foregoing proceedings were taken by me in stenotype and thereafter reduced to typewriting under my supervision; that I am neither counsel for, related to, nor employed by any of the parties to the action in which these proceedings were taken; and further, that I am not a relative or employee of any attorney or counsel employed by the parties hereto, nor financially or otherwise interested in the outcome of the action.

s/Josett F. Whalen

JOSETT F. WHALEN

Court Reporter