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IN THE UNITED STATES DISTRICT COURT
IN AND FOR THE DISTRICT OF DELAWARE

- - -

ELAN PHARMA INTERNATIONAL : Civil Action
LIMITED, :
 :
 Plaintiff, :
 :
 v. :
 :
 ABRAXIS BIOSCIENCE INC., :
 :
 Defendant. : No. 06-438-GMS

- - -

Wilmington, Delaware
Tuesday, June 10, 2008
8:45 a.m.
SEVENTH DAY OF TRIAL

- - -

BEFORE: HONORABLE GREGORY M. SLEET, Chief Judge,
and a Jury

APPEARANCES:

JOHN G. DAY, ESQ.
Ashby & Geddes
-and-
STEPHEN SCHEVE, ESQ.,
LINDA M. GLOVER, ESQ.,
JEFFREY SULLIVAN, ESQ.,
ROBERT RIDDLE, ESQ., and
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-and-
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Counsel for Plaintiff

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12

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15

THE COURT: Good morning.

16

(Counsel respond "Good morning.")

17

THE COURT: I understand we have an issue.

18

MR. JACOBS: A couple of things, Your Honor.

19

THE COURT: I hope they are short.

20

MR. JACOBS: Two are short and one may take a

21

few minutes. No. 1, we have reached a stipulation on a

22

person of ordinary skill in the art.

23

THE COURT: Good. I was wondering whether we

24

were going to hear about that mystic person.

25

MR. JACOBS: Procedurally, Your Honor, would you

26

like Ms. Kruze to read it? It would have come up in

27

Dr. Amiji's testimony. Ms. Kruze could just read the

28

stipulation into the record, if that would be appropriate.

29

MR. SCHEVE: Fine.

30

1 MR. JACOBS: No. 2, documents in evidence. How
2 do we work? I am still a little confused. I know we have
3 heard several times how this is supposed to work but we are
4 at the level of mechanics, understanding what is in and what
5 isn't, especially documents that are --

6 THE COURT: All objections were overruled to
7 documentary exhibits, unless raised again. I have not
8 entertained any additional objections. So it's in.

9 MR. JACOBS: On the original exhibits list, all
10 those exhibits are in evidence.

11 THE COURT: Are in. What you want the jury to
12 consider is another matter. Is that where we are going with
13 this?

14 MR. JACOBS: No. I think there are documents --

15 THE COURT: For your record, they are in.

16 MR. JACOBS: For closing --

17 THE COURT: That's evidence.

18 MR. JACOBS: Terrific.

19 THE COURT: Mr. Scheve, do you have any
20 questions?

21 MR. SCHEVE: That's exactly what I have
22 understood, Your Honor.

23 MR. JACOBS: Dr. Brittain, two alternative
24 paths, from our standpoint.

25 No. 1, we put him on the stand, he is here in

1 the courtroom, by the way. We put him on the stand, and we
2 examine him pursuant to the second Bench memo we filed
3 yesterday, in which we elicit only -- I can hand Your Honor
4 a copy.

5 THE COURT: I got it yesterday, you say?

6 MR. JACOBS: Yes. We didn't focus on it
7 yesterday.

8 THE COURT: Have you seen the Bench memo,
9 Mr. Scheve?

10 MR. SCHEVE: Yes.

11 MR. JACOBS: We gave it to them yesterday, Your
12 Honor.

13 The main point of this Bench memo, Your Honor,
14 is that when we ask him questions, we do not want him
15 volunteering, we do not want counsel for Elan eliciting
16 testimony beyond the specific and narrow facts that are
17 already in the record from his deposition or from the
18 documents.

19 THE COURT: You know, counsel and those in the
20 well, you can sit. It seems like this is going to take a
21 few minutes. There is no reason for you to have to stand.

22 Mr. Jacobs.

23 MR. JACOBS: There is only one question from the
24 deposition that I need to ask him, which is, Did you perform
25 studies on Abraxane? Beyond that, I don't believe counsel

1 for Elan should be allowed to elicit additional testimony
2 about what he did because he was instructed not to answer a
3 whole range of questions about what he actually did at his
4 deposition.

5 Actually, the second path is that we do not put
6 Dr. Brittain on the stand, and the Court explains to the
7 jury what happened with the privilege log and why we are
8 where we are. I prepared and gave to counsel for Elan
9 yesterday a proposed statement from the Bench that would
10 just lay out, very briefly, lay out exactly what happened.
11 That way, we don't have to deal with uncertainties about
12 what Dr. Brittain might say when he testifies on this issue.

13 THE COURT: I got to believe that Mr. Scheve
14 probably doesn't want the jury hearing about that from me.
15 Maybe I am wrong about that.

16 MR. SCHEVE: Well, after all day yesterday
17 asking witnesses, What did you have for breakfast?, and
18 hearing, Well, I had eggs right next to an order of
19 amorphous paclitaxel contained in Abraxis, all day, and now
20 to have counsel say, We really don't want any gratuitous
21 answers, or to go beyond -- they are now the sponsoring
22 witness, Your Honor. There is no expert report from him.
23 If they are going to ask fact questions, you know, it's my
24 decision, I would think, whether or not I wade into
25 something. I will be very cautious about that. The idea

1 that counsel can say, in advance, that I am restricted to
2 what I may ask --

3 THE COURT: I am not going to do that,
4 Mr. Jacobs. You will have to object.

5 MR. JACOBS: To be clear, Mr. Scheve instructed
6 Dr. Brittain at his deposition not to answer additional
7 questions.

8 THE COURT: I think both sides know what the
9 issue is with Dr. Brittain. We have had an extensive
10 discussion about this. I am tired of it. Let's move on.
11 Let's get this trial back underway.

12 Ms. Walker, bring in this jury.

13 MR. SCHEVE: I do have an issue, Your Honor.
14 They have tendered something they want to either read to the
15 jury or give to them that talks about your ruling that says,
16 Your Honor has ruled --

17 THE COURT: That was the second path that he was
18 just talking about. Right?

19 MR. SCHEVE: They have offered an instruction
20 which would --

21 THE COURT: I just rejected --

22 MR. SCHEVE: It is a separate issue. On this
23 inference, they have offered an instruction, and they also
24 now want to read or show the jury, in writing, that Your
25 Honor has found that Elan, my client, has willfully or

1 wrongfully --

2 THE COURT: We are not going to do that, either.

3 MR. SCHEVE: It would be two comments on the
4 inference. That should be in the jury instructions.

5 THE COURT: That is where it will be.

6 MR. JACOBS: I need to know what you have
7 decided on the jury instructions.

8 THE COURT: Are you talking about the final jury
9 instructions?

10 MR. JACOBS: I am sorry, Your Honor. I thought
11 you said to Mr. Scheve, on the jury instructions --

12 THE COURT: I am instructing this jury at this
13 point on Dr. Brittain. I am going to give an instruction on
14 the final jury instruction -- you are going to be trial
15 lawyers and we are going to try this case with this witness
16 on the stand. You will interpose objections. I will rule
17 on those objections. It is not unduly complicated.

18 MS. KRUZE: Your Honor, shall I read into the
19 record the person of ordinary skill?

20 THE COURT: Don't you want the jury to hear it?

21 MS. KRUZE: Yes.

22 THE COURT: I certainly would like to hear it.
23 I think the jury would like to hear it.

24 We had a witness on the stand, Dr. Amiji.

25 Dr. Amiji, please.

1 Doctor, you are still under oath. Good morning.

2 (Jury enters courtroom at 9:07 a.m.)

3 THE COURT: Good morning on yet another hot day,
4 ladies and gentlemen. Have a seat. You will be comfortable
5 today, hopefully.

6 Ms. Kruze, you may continue with Dr. Amiji.

7 ... MANSOOR AMIJI, having been previously sworn
8 as a witness, was examined and testified further as
9 follows...

10 THE COURT: Do you want to start out with a
11 stipulation?

12 We have arrived at one of those stipulations I
13 talked with you about in the preliminary instructions, that
14 is an agreement, one of those rare events in this case
15 between the parties. Ms. Kruze is now going to tell you who
16 the ordinary person of skill in the art is, that is, give
17 you the definition of this person you have heard about, this
18 person of skill.

19 MS. KRUZE: The person of ordinary skill in the
20 art would have a Ph.D. or the equivalent in pharmaceutical
21 sciences, chemistry, chemical engineering, or biological
22 sciences, and at least two years of practical experience in
23 formulating drug compositions at the time the application
24 for the '363 patent was filed.

25 Alternatively, the person of ordinary skill in

Amiji

1 the art could be someone with a Master's degree in
2 pharmaceutical sciences, or the equivalent, with two or more
3 years of practical experience, specifically in the
4 development of nanoparticulate pharmaceutical compositions.

5 THE COURT: Let me see counsel for just a second
6 before I say what I am thinking about saying. It doesn't
7 need to be on the record.

8 (Sidebar conference not reported.)

9 THE COURT: Perhaps Ms. Kruze will direct you to
10 the place. You don't have to worry about having made notes
11 as to that definition. It has been or will be provided to
12 you.

13 DIRECT EXAMINATION CONTINUED

14 BY MS. KRUZE:

15 Q. Good morning, Dr. Amiji.

16 A. Good morning, Ms. Kruze.

17 Q. Yesterday we were discussing enablement of the patent
18 relating to drug and surface modifier combinations. I
19 believe where we left off was Defendant's Exhibit 193. This
20 was the memo from Sarptodar and your comparison of that memo
21 to the patent claims.

22 A. Yes.

23 Q. And we were discussing, did the patent applicants
24 disclose, for example, that Tween 80 reached 3,000
25 nanometers?

Amiji - cross

1 A. No, they did not.

2 Q. Let's take a quick look at what the patentees did tell
3 the Patent Office. That's JX-81 at Columns 3 through 4. I
4 believe it's in Column 4, in the second paragraph.

5 Did the patentees tell the Patent Office that
6 Tween 80 was a particularly preferred surface modifier?

7 A. Yes, they did.

8 Q. But internally, that surface modifier had failed?

9 A. That's correct, yes.

10 Q. Let's switch to DD106.

11 Did you review any other documents regarding
12 Elan's efforts to make a nano-piposulfan product?

13 A. Yes, I reviewed several other documents.

14 Q. Could you read some of the statements that you found
15 in those documents? This, for the record, is JX-47, JX-55,
16 JX-81, DX-258 and DX-286.

17 MR. SCHEVE: Your Honor, I object to just
18 reading documents. It's inappropriate form.

19 THE COURT: I will sustain the objection.

20 BY MS. KRUIZE:

21 Q. Did you review any other documents regarding Elan's
22 efforts to make a piposulfan project?

23 A. Yes, I did.

24 Q. What did those documents say to you?

25 A. So here we can see from the different time points, we

Amiji - cross

1 have, in the case of August of '92, the '363 inventors
2 discuss that pivosulfan is physically unstable. In '93, the
3 inventors of pivosulfan, was difficult to stabilize. In '96
4 here, again, same problems with generating a stable
5 nanocrystalline suspension proved to be challenging.

6 In '96, formulation does have its problems.

7 And even today, in 2008, we still do not have a
8 nano-pivosulfan product.

9 Q. Dr. Amiji, did Elan also try to make a NanoCrystal
10 formulation of paclitaxel using albumin?

11 A. Yes.

12 Q. Did you review laboratory notebooks regarding those
13 experiments?

14 A. Yes, I reviewed several different laboratory
15 notebooks.

16 Q. Was Elan successful in making a NanoCrystal version of
17 paclitaxel in albumin?

18 A. No, they were not.

19 Q. What is the significance to you that as late as 2006,
20 Elan couldn't make a NanoCrystal version of paclitaxel in
21 albumin?

22 A. Well, because of the technology involved in the
23 milling process, I believe that a protein stabilizer such as
24 albumin would not be very effective in making a
25 nanocrystalline because of the fact that it requires 120

Amiji - cross

1 hours of milling. The protein, typically, would not be a
2 very effective stabilizer under those conditions, having to
3 have to mill for that long a time.

4 Q. Did you review any other documents regarding Elan's
5 efforts to make a NanoCrystal version of just paclitaxel in
6 general?

7 A. Yes, I have.

8 Q. Can you please bring up, Mr. Broyles, DD41.

9 Are you familiar with this interrogatory, this
10 is a legal question that Abraxis asked Elan?

11 A. Yes, I am.

12 Q. What did Abraxis ask Elan?

13 A. Abraxis asked Elan if they had made a NanoCrystal
14 paclitaxel formulation.

15 Q. Are you familiar with Elan's answer to that?

16 A. Yes.

17 Q. Can you bring up DD42, Mr. Broyles.

18 Is this the answer that Elan gave that you are
19 familiar with?

20 A. Yes. This is the response to the interrogatory that,
21 for almost 20 years Elan has been trying to make
22 nanocrystalline paclitaxel. And these are the different
23 types of products that have been tried.

24 Q. And we have --

25 MR. SCHEVE: Your Honor, if I may, since the

Amiji - cross

1 rules allow us under Rule 34, in response to a discovery
2 request, to provide citation to specific documents, I would
3 ask that at least that be explained to the jury. Because
4 what this is --

5 THE COURT: Let me see counsel for a moment.

6 (The following took place at sidebar.)

7 THE COURT: I really don't want to get into
8 having to describe and explain to the ladies and gentlemen
9 of the jury the Federal Rules of Civil Procedure. It
10 shouldn't be necessary in the case.

11 MS. KRUZE: Maybe I should explain where I am
12 going with this.

13 Basically, what we want to do is we want to
14 enter into evidence DX-44, which is a compilation of all
15 those documents, which Elan, it's a party admission, has
16 admitted with all their paclitaxel documents. That's what I
17 am trying to get across.

18 THE COURT: But is there something more
19 expressive, more descriptive, more helpful that you might
20 have?

21 MS. KRUZE: We have the documents.

22 THE COURT: I am not sure the documents are
23 helpful. I am not sure it is really worth the trouble. You
24 try the case the way you want to try it.

25 But why don't you react to this.

Amiji - cross

1 MR. SCHEVE: My objection is they have shown an
2 interrogatory answer where my client under Rule 33 and 34
3 referred them to the specific documents in this list.

4 THE COURT: I don't want a discovery dispute in
5 front of the jury. Go ahead.

6 MR. SCHEVE: So we would object that it is
7 prejudicial, it's confusing, under Rule 403, to just put
8 that up, if the jury is not allowed to understand that we
9 satisfied our discovery obligations.

10 MS. KRUIZE: My response is it is a party
11 admission, Your Honor. We are entitled to use it in court.
12 It is a binding response that Elan made.

13 MR. SCHEVE: We don't deny that we made the
14 response. It doesn't change the fact that it's confusing to
15 the jury, likely to mislead the jury, when all you do is
16 show an answer to interrogatory that is five columns of
17 citations to Bates numbers of the documents that in any way
18 might relate to what was done with paclitaxel.

19 THE COURT: Is there a contention -- I guess
20 it's not your contention that there was anything wrong
21 procedurally with the response. It's, this is the response,
22 and we want you to draw an inference from this response,
23 directly from this response that they had difficulty.

24 MS. KRUIZE: My next question may clear this up.
25 It was simply are these documents all collected in the

Amiji - cross

1 courtroom. Then they can just see the five boxes of
2 documents. That way they don't have to focus on the
3 numbers. The idea is that Elan tried very hard to do this.

4 THE COURT: Do you object to them having a
5 visual aid, the jury?

6 MR. SCHEVE: No. That would be the next
7 question, Your Honor. I take it question by question. I
8 was objecting to put up a discovery response.

9 THE COURT: I am going to sustain the objection
10 to this question. I understand what you are trying to do.
11 I think you are entitled to do it. Quite frankly, I think
12 it is a better avenue.

13 Why don't you go ahead.

14 (End of sidebar conference.)

15 BY MS. KRUZE:

16 Q. Dr. Amiji, if I could direct your attention to DX-484,
17 which is the five boxes --

18 THE COURT: We are going to take this down.

19 BY MS. KRUZE:

20 Q. There are five boxes of documents. I don't want to
21 roll them into the courtroom.

22 THE COURT: Ladies and gentlemen, may I see a
23 banker's box, please? Would you display one to the jury
24 that is representative of the boxes of documents that
25 Ms. Kruze is referencing. Just hold it up, if you would.

Amiji - cross

1 (Banker's box held up.)

2 That is a banker's box. That is what they are
3 talking about, five of those filled with paper.

4 BY MS. KRUZE:

5 Q. Do these five boxes of documents, do they contain any
6 failures that Elan had with paclitaxel?

7 A. Yes. There were a lot of failures.

8 Q. Did Elan disclose those five boxes of failures to the
9 Patent Office?

10 A. No, they did not.

11 Q. Why is this important?

12 A. Well, because, you know, in the patent itself, there
13 is an example of the paclitaxel that did work, whereas you
14 had all these other failures that were not disclosed.

15 Q. Based on your review of all these Elan documents, how
16 long has Elan been trying to make a NanoCrystal version of
17 paclitaxel?

18 A. I believe it's been about 20 years now.

19 Q. Dr. Amiji, to summarize, can many of the possible
20 combinations covered by the '363 patent form usable
21 pharmaceutical compositions?

22 A. No, they cannot.

23 Q. And in your opinion, will many of those combinations
24 of drugs and surface modifiers fail to form usable
25 compositions?

Amiji - cross

1 A. Yes, they will.

2 Q. Do you have an opinion today that is relevant to the
3 requirement that the '363 patent be enabled like we saw in
4 the patent video?

5 A. Yes.

6 Q. And do you hold that opinion to a reasonable degree of
7 scientific certainty?

8 A. Yes, I do.

9 Q. At the time the patent was filed, did the '363 patent
10 enable ordinary scientists to make and use the claimed
11 inventions without undue experimentation?

12 A. No, they wouldn't.

13 Q. Do you have an opinion today that is relevant to the
14 requirement that the '363 patent have an adequate written
15 description?

16 A. Yes, I do.

17 Q. Do you hold that opinion to a reasonable degree of
18 scientific certainty?

19 A. Yes, I do.

20 Q. Could you tell the jury what your opinion is?

21 A. That it wouldn't enable.

22 Q. At the time the patent was filed, did the patent
23 convey that Elan was actually in possession of the full
24 scope of the patent claims?

25 A. Yes.

Amiji - cross

1 Q. In other words, at the time the patent was filed, was
2 Elan in possession of all the drug and surface modifier
3 combinations?

4 A. No, they were not.

5 Q. And while the patent application was pending, did Elan
6 tell the Patent Office about these bad tests that we
7 reviewed or all the failures that you were speaking of?

8 A. No, they did not.

9 Q. And did these bad tests or failures contradict
10 statements that Elan was making to the Patent Office?

11 A. Yes.

12 Q. Dr. Amiji, let's talk about contamination.

13 Mr. Broyles, if you could bring up JX-81 on the
14 screen, Column 6. Do you have testimony today relevant to
15 the enablement requirement in terms of contamination?

16 A. Yes, I do.

17 Q. What is the method for making nanoparticles that's
18 disclosed in the '363 patent?

19 A. So the '363 patent mentions this grinding process, the
20 wet grinding process, which uses the grinding media, and
21 reduces the particle size from larger crystals into smaller
22 crystals.

23 Q. Could you bring up DD107, which is from Elan's
24 website.

25 Is this a depiction of how the large crystals

Amiji - cross

1 become smaller?

2 A. Yes, it is.

3 Q. And if you could go to JX-81 again at Column 6. What
4 types of instruments does the patent tell one to use to make
5 these crystals go from smaller to -- or bigger to smaller?

6 A. So it uses the milling equipment, which is a ball
7 mill, and then there is the grinding media. The grinding
8 media or these beads are made from zirconium oxide,
9 zirconium silicate, and glass.

10 Q. And let's turn to Column 7. How long does the patent
11 teach one to grind?

12 A. In the simple screening method, for instance, it says
13 up to 120 hours, which is more than five days.

14 Q. Just to clarify for the jury, what is zirconium oxide?

15 A. Zirconium oxide is a metal, a heavy-metal oxide. It
16 has this oxygen and a heavy metal.

17 Q. Silicate, what is that?

18 A. Silicate is, again, a compound from silica. Silica is
19 one of the major constituents of sand.

20 Q. Do you have an animation that illustrates the
21 manufacturing process of the '363 patent that would help the
22 jury's understanding?

23 A. Yes, I do.

24 Q. Let's play that animation.

25 Can you narrate what's happening?

Amiji - cross

1 A. This is Abraxane.

2 Here is the animation, ladies and gentlemen, for
3 the NanoCrystal technology based on the documents that I
4 reviewed from Elan.

5 This is the ball mill that we are talking about,
6 which has this report, and these are the grinding media that
7 we have talked about. And these are about one to three
8 millimeters in diameter. And they are put inside this ball
9 mill. The report here is going to be the one that will
10 basically create the tumbling action.

11 The next thing here is the premix, which the
12 inventors call the premix. That is basically water and
13 these larger drug crystals. These are the starting material
14 for making the NanoCrystal product. Here we start with
15 larger crystals. These crystals are then suspended or put
16 in water. That's what leads to this premix; the product
17 that is then put inside the ball mill.

18 Because of the size differences, we depict that
19 as simply a green hue.

20 Now we will see the starting of this ball mill.
21 See them tumbling, the rotor is tumbling and these beads,
22 the larger grinding beads, are starting to then get
23 suspended in the premix. As they get suspended, and they
24 get in contact with the crystal, the drug crystal and these
25 other grinding beads, they will start to collide with one

Amiji - cross

1 another, as you see. And as these collide, they break up
2 into smaller particles.

3 That collision continues. This milling process
4 continues for a long time. And each time this leads to more
5 and more fragmentation of the crystals into smaller and
6 smaller particles.

7 Eventually, it creating these very, very tiny
8 particles or nanoparticles.

9 Q. And those grinding beads, again, in terms of the '363
10 patent, are made out of?

11 A. Zirconium oxide, zirconium silicate, or glass.

12 Q. Dr. Amiji, can milling with metal or glass beads cause
13 any problems?

14 A. Yes. Again, this milling procedure, especially
15 because it is ongoing for such a long time, will cause
16 contamination.

17 Q. How does this contamination occur exactly?

18 A. So here, again, we have an animation that illustrates
19 that.

20 Q. Let's play that.

21 A. So the animation here will show you exactly how the
22 contamination occurs. So we are starting here from where we
23 left off in the previous animation. The grinding media and
24 the ball mill with the crystals being basically broken into
25 smaller and smaller fragments.

Amiji - cross

1 But as you enlarge this, what you observe is
2 that, yes, there is going to be decrease in the size of the
3 crystals. But at the same time, these grinding media will
4 collide with each other. As they collide with each other,
5 they fragment as well. Especially as you get into longer
6 and longer time points.

7 So this grinding media colliding with each other
8 causes the contamination because of these metal and glass
9 grinding media that is present inside this ball mill.

10 Q. What were those white flakes or silver flakes that we
11 just saw?

12 A. That is the contamination that occurs because of the
13 fact that two grinding, two or more grinding media colliding
14 with each other.

15 Q. What are some of the problems with contamination in
16 pharmaceutical compositions?

17 A. Contamination is a big problem in pharmaceuticals
18 because you clearly want this product to be safe and
19 effective. And safety, not only from the drug point of
20 view, but from the purity and from the quality control point
21 of view. You want to make sure that the product will not
22 have any contamination, any type of contamination.

23 Pharmaceutical products, especially those are intended for
24 administration into the bloodstream you really have to be
25 very careful about making sure that the quality is as pure

Amiji - cross

1 and as best as possible.

2 Q. When we are talking about intravenous administration,
3 things that go directly into the bloodstream, are the risks
4 greater with contamination?

5 A. Yes, they are, because, first of all, the FDA requires
6 a much more stringent requirement for any product that is
7 given into the bloodstream. And the reason is you don't
8 have any way to reverse the problems.

9 If you take a pill orally, one could easily
10 either give another product and have that drug stop being
11 absorbed. But once you give a product in the bloodstream,
12 it is always going to be there. There is not an opportunity
13 to take that product out.

14 The other thing is that contamination in
15 product, in pharmaceutical product, even if it occurs in one
16 product, one vial of a large number of vials, it is not
17 possible to tell which vial has that contamination and the
18 patient who will get that.

19 So it is an unpredictable event and you don't
20 want that kind of risk.

21 Q. What about with drugs that are administered routinely,
22 like most anticancer drugs?

23 A. Again, the problem of contamination becomes even more
24 magnified, because once you give a product, as it is given
25 continuously to patients, what you find is that the

Amiji - cross

1 contaminant level starts to increase in the body. And
2 especially in the cases like zirconium, which concentrates
3 in organs like the ovaries, the contamination will start to
4 increase in those organ systems.

5 Q. Let's start with the patent and pull up DD-102. Does
6 the patent require that the particles be free of
7 contamination?

8 A. Yes, it does.

9 Q. And do the patent examples in the '363 patent disclose
10 the level of contamination?

11 A. No, there is not any mention of contamination in the
12 patent examples.

13 Q. Let's pull up JX-81. Let's go to Column 8, second
14 paragraph.

15 Were you here in the courtroom when
16 Dr. Liversidge testified to some sort of cleaning method?

17 A. Yes, I was.

18 Q. What was he referring to?

19 A. So in the example, Example 1, there is a cleaning
20 method that is present. And this cleaning method is using
21 sulfuric acid, I think further down.

22 Q. I think it's around -- there. That looks like it.

23 A. So it starts out right here. It says the zirconium
24 oxide beads are first cleaned using one normal sulfuric acid
25 and rinsing with several rinses of deionized water.

Amiji - cross

1 This cleaning method is going to clean the beads
2 before they are put into the grinding media, but it doesn't
3 stop the grinding media from colliding with each other and
4 producing this contamination.

5 Q. Is this sufficient to avoid contamination?

6 A. No, it is not.

7 Q. Dr. Amiji, did you review any internal documents
8 regarding contamination problems that Elan was having?

9 A. Yes, I did.

10 Q. And what did these documents show?

11 A. They showed significant levels of contamination,
12 especially zirconium, silica, and other types of metal
13 contamination.

14 Q. Let's go to DD110. Dr. Amiji, you can turn to DX-243,
15 also.

16 What did Elan's toxicology department tell the
17 patent applicants?

18 A. So here is a memo from the toxicology department
19 saying that zirconium oxide and zirconium silicate are
20 acceptable in one record, but then they cause the zirconium
21 levels that are produced, that accumulates in the organs,
22 such as the ovaries.

23 Q. Just to confirm for the jury, I don't think that
24 zirconium oxide is acceptable because --

25 A. Correct. Yes, I don't think that zirconium oxide is

Amiji - cross

1 acceptable.

2 Q. So Elan's toxicology department was telling the
3 patentees that this type of technology was not acceptable?

4 A. That's correct, yes.

5 Q. And can you confirm that the date of this is 1990?

6 A. Yes, it is. It is the September 12th, 1990.

7 Q. Let's turn to DD1? Can you tell the jury what this
8 is?

9 A. These are other memos and other documents from Elan.
10 Again, looking at the issue of toxicology of various
11 contaminants from these grinding media. ZR stands for
12 zirconia. It says toxicology has recommended the non-use of
13 zirconium grinding media. This leaves us with glass as an
14 acceptable alternative. At the bottom you can see it says
15 high levels of lead being found in dispersions from the
16 lead-free glass. Even in the case of lead-free glass,
17 because of this long milling period, there is actually lead
18 contamination.

19 Q. So even lead-free glass is causing lead contamination?

20 A. Right. Because in many of these so-called lead-free
21 glass, there is actually a low level of lead that's present.

22 Q. And can you tell the jury what the date of this
23 document is? You may have to flip to DX-206. I don't know
24 if you can see it, Mr. Broyles, if you could blow that up,
25 then the next page.

Amiji - cross

1 A. Right. This is June 16, 1993.

2 Q. So that was while the Patent Office was working on the
3 patent?

4 A. That's correct, yes.

5 Q. And let's pull up DD-100. Could you please tell the
6 jury what this is?

7 A. This is a presentation in Elan from November of '93.
8 And again, the highlighted statement is that roller and
9 media milling using zirconium and glass beads generates
10 unacceptable contamination.

11 Q. The source of this document -- there is actually
12 two -- is DX-238 and DX-607.

13 Can you see when the document was dated?

14 A. Yes. November of '93.

15 Q. And did Elan tell the Patent Office about this
16 problem?

17 A. No, they did not.

18 Q. Let's turn to DX-238 at 85245.

19 Were you in the courtroom when Dr. Liversidge
20 testified about polymeric milling media and things like
21 microfluidization?

22 A. Yes, I was.

23 Q. Are those things relevant to solving the problem in
24 the '363 patent?

25 A. Right. So in order to -- in the '363 patent it is

Amiji - cross

1 clear that it describes the use of zirconium and glass
2 beads. But to reduce this contamination issue, the same
3 investigator switched to these polymeric milling media,
4 hoping that they will have lower levels of contamination.
5 And using microfluidization and control precipitation
6 methods instead of this wet milling technique which requires
7 a long period of time.

8 Q. So, in other words, their solution was to move away
9 from the '363 patent?

10 A. That's correct, yes.

11 Q. Let's go to DD-101. Did you review some other
12 documents that some of Elan's formulations were seriously
13 contaminated?

14 A. Yes, I did. And here, just a summary of a few that I
15 reviewed in the case of pivosulfan, there was about 140
16 parts per million; paclitaxel had 16,000 parts per million;
17 other paclitaxel -- even reproducibility is a concern. In
18 certain cases you get very high, another case, like 1200, it
19 is still very high levels. But it is not reproducible, so
20 you can't even tell if they are going to get the same levels
21 of contamination each time the product is made. So in three
22 different cases of paclitaxel we find that you have very,
23 very high levels.

24 Q. 16,000, just as an example, ppm of zirconium, how
25 dangerous is that?

Amiji - cross

1 A. That is very, very dangerous. The limits in those
2 most of the Pharmacopedia is about ten to 20 parts per
3 million at the most. But again, you try to be as
4 conservative as possible when you are dealing with
5 contamination.

6 Q. Let's go to DD93 -- I am sorry, DD99. What is this?
7 The source of this is JX-53.

8 A. Here we see what is called a scanning electron
9 micrograph, that looks at these nanoparticles under very
10 high magnification.

11 What you see in the scanning electron
12 micrographs is the zirconia and paclitaxel NanoCrystals.
13 Unfortunately, because the zirconium contamination has the
14 same size and same, almost looks exactly like these
15 NanoCrystals, you can't tell them apart.

16 Q. Let's pull up JX-53 at Elan P-18468. That actual
17 document.

18 A. Right. So here is the combined, both the scanning
19 electron micrograph we just saw a few seconds back, then the
20 summary of the contamination levels. And really striking is
21 to look at the silica, which is SI, and zirconia. And what
22 I found to be very interesting is the formulation that comes
23 out of the rolling media has around 1100 parts per million
24 of zirconia. Then we have heard in this trial the
25 centrifugation process. This is the process where the

Amiji - cross

1 particles are spun down and collected as a pellet.

2 What happens is that these, contamination
3 actually increases because we are now bringing the same
4 contaminant particles together with the crystalline
5 paclitaxel. So we find that the contamination increases.

6 In the supernatant, which is the clear liquid,
7 there is very, very little of that contamination. So the
8 contamination gets held on with these NanoCrystals.

9 Q. The contamination sticks on the particles?

10 A. Right. It is spun together with the NanoCrystals when
11 they are centrifuged.

12 Q. Were you here when Dr. Liversidge mentioned filtering
13 out these contaminants somehow?

14 A. Yes, I was.

15 Q. Do you agree with him?

16 A. No, I don't believe you can, especially as you go down
17 to the 200 or 400 nanometer particle size. And the
18 contaminants having the same size, you are not going to be
19 able to filter that out.

20 Q. Dr. Amiji, did you hear both Liversidges testify that
21 contamination wasn't an issue because they have FDA-approved
22 products for oral --

23 A. Yes, I was here.

24 But contamination is a serious issue, especially
25 with this type of product and what is taught in the '363

Amiji - cross

1 patent.

2 Q. To the best of your knowledge, do any of these
3 products that they refer to use the zirconium media that's
4 disclosed in the '363 patent?

5 A. No. The technology that Elan has now moved away from
6 or is now using are these polymeric media, the grinding
7 media. And they are not using the zirconia or glass beads.

8 Q. Did Elan ever disclose the contamination problems it
9 was having to the Patent Office?

10 A. No, they have not.

11 Q. Let's bring up DD98.

12 Are the internal documents that you reviewed
13 consistent with what Elan told the Patent Office?

14 A. No, they are not. Here is an example. For instance,
15 we see that in the patent, it says the level of
16 contamination which are believed to be acceptable. Whereas
17 internal documents contradict that and say the levels are
18 unacceptable.

19 Q. Let me ask you to consider the '363 patent technology
20 in the context of a scientific publication.

21 Would scientists consider the internal Elan
22 documents you reviewed concerning contamination something
23 that was important to disclose?

24 A. Yes, absolutely.

25 Q. And do you have an opinion today that is relevant to

Amiji - cross

1 enablement?

2 A. Yes, I have.

3 Q. Do you hold this opinion to a reasonable degree of
4 scientific certainty?

5 A. Yes, I do.

6 Q. To summarize, does the '363 patent teach, at the time
7 it was filed, how to make drug particles or compositions
8 that are essentially free of contamination?

9 A. No, they do not.

10 Q. And did some of the internal documents you reviewed
11 about contamination problems contradict what Elan told the
12 Patent Office?

13 A. Yes.

14 Q. And with these problems in mind, what real-world
15 usefulness does the patent have?

16 A. In my opinion, not a lot, because these are some of
17 the serious problems with having a pharmaceutical product
18 that actually can have such high degree of contamination.

19 Q. Let's back up just for a quick moment and talk about
20 the '363 patent and mention, just because I think it's easy
21 to get confused. DD-86.

22 Did Elan invent crystalline paclitaxel?

23 A. No. Crystalline paclitaxel has been around for a long
24 time.

25 Q. And did Elan invent nanoparticles?

Amiji - cross

1 A. No. Again, nanoparticles, nanoformulations or
2 nanoparticles have been around for a long time.

3 Q. Did Elan invent nano-sized drugs?

4 A. No. Again, there have been many others that have
5 preceded Elan in that.

6 Q. So what, exactly, does Elan say it invented?

7 A. Well, it claims to have invented this huge list of
8 anticancer drugs, very, very large list of surface
9 modifiers, and ratios of the two, going from having .1 of
10 surface modifier to 90 percent and 10 percent drug up to
11 99.9 percent drug. In reality, in my opinion, it is not
12 really enabled.

13 Q. Dr. Amiji, if Elan had invented all those combinations
14 of drugs and surface modifiers, would that be a significant
15 breakthrough?

16 A. Absolutely. Cancer is one of those areas where we
17 direly need newer drugs, newer methods of treatment. Even a
18 few of those, that were in the clinic and really helping the
19 patient, it would be a huge breakthrough and huge
20 significance in cancer treatment.

21 Q. Did Elan, in fact, invent that?

22 A. No, they did not.

23 MS. KRUZE: Thank you.

24 THE COURT: You are done, Ms. Kruze?

25 MS. KRUZE: Yes. No more questions.

Amiji - cross

1 THE COURT: Mr. Scheve.

2 MR. SCHEVE: Thank you, Your Honor.

3 CROSS-EXAMINATION

4 BY MR. SCHEVE:

5 Q. Sir, how many patents do you have to your name? List
6 you as an inventor?

7 A. I am an inventor on four patents that are issued. And
8 I also have about five or six patent applications that I
9 have that are being interviewed by the U.S. Patent Office.

10 Q. Have you in the 14 years you have been at Northeastern
11 University, have you or anybody coming out of your lab been
12 able to license any of that technology?

13 A. In our case, academia, we tend to usually do
14 preclinical research and we then, if there is an invention,
15 we patent it.

16 But we do not have resources in academia to
17 carry additional, especially safety and efficacy studies as
18 they get into larger and larger animals.

19 So we tend to find licensing or partnership
20 agreements. I have been very active in finding partnership
21 agreements for the technologies that we have patents on.

22 Again, you know, industry sometimes looks at
23 these patents, other times they will say, yes, we will
24 consider it. It's an ongoing process. At present, I do not
25 have any licenses from my lab. But it's an ongoing process

Amiji - cross

1 and we are talking to various parties.

2 Q. So the answer is in 14 years no one has found your
3 technology sufficiently attractive to license it. Correct?

4 A. No, it's not that, that it's not sufficiently
5 attractive. There are other reasons. For instance --

6 THE COURT: I think you had some books you
7 wanted to pass up behind you.

8 BY MR. SCHEVE:

9 Q. Sir, in 14 years, has anybody licensed your patents?

10 A. No. Again, as I said, we haven't had the opportunity
11 to license them.

12 Q. Did you try to sell your technology to Abraxis?

13 A. No, I have not.

14 Q. Would you please dial up the video.

15 Do you know Dr. Desai?

16 A. I have met Dr. Desai in 2007.

17 Q. Would you play it, please.

18 "Question: When is the first time you
19 interacted with Dr. Amiji?

20 "Answer: The last year at some point, 2006.

21 "Question: What was the context in which you
22 interacted with him?

23 "Answer: He had some interesting technology in
24 a related field, and he had sent me a presentation to
25 review.

Amiji - cross

1 "Question: Was he trying to market that
2 technology?

3 "Answer: I suppose you could use that word.

4 "Question: And what was the technology?

5 "Answer: Varying pieces of different types of
6 technology but related to drug delivery in general.

7 "Question: And did you or Abraxis find his
8 technology to be sufficiently interesting to take steps to
9 try to acquire it or employ it in the drug delivery arena?

10 "Answer: No, not at that point."

11 Now, sir, you were at Northeastern University.
12 Let's help the jury understand just a bit about Northeastern
13 University.

14 Did the president there, in the early 1990s, try
15 to implement what he called a turnaround plan for
16 Northeastern?

17 A. Yes. I believe Dr. Richard Freeland, who was the
18 president at the time, was brought in with the idea of
19 having a turnaround plan.

20 Q. Isn't it true, sir, that in about 1982 his plan was
21 that over the next 18 years, in other words, by the year
22 2010, he hoped that he could get Northeastern University to
23 crack the top 100 universities in the United States? Isn't
24 that correct?

25 A. Yes. Many of these presidents of institutions

Amiji - cross

1 typically have these types of plans and they try to bring
2 the institution to greater recognition and try to do the
3 kinds of things that enhances the recognition of the
4 university.

5 Q. In fact, in 2002, there was yet another initiative by
6 the then new president where he announced the spending of an
7 ambitious 18.3 million dollar spending plan and other
8 strategic steps that they hoped would vault the university
9 from 150th ranked in the country to in the top 100.

10 Has Northeastern University ever gotten above
11 150th in rank in the country?

12 A. Yes, actually, they have. I am very proud to say we
13 have cracked the top 100 in the U.S. News and World Report
14 ranking. The momentum is continuing. There was an article
15 in the Boston Globe just about a year and a half back that
16 showed the momentum of Northeastern being in the center of
17 Boston and being in this very vibrant city, and being able
18 to do some amazing things in research, in teaching, and in
19 developing relationships, especially with our surrounding
20 community in the Boston area.

21 Q. In the Boston area there are 13 academic institutions,
22 aren't there, sir?

23 A. Yes, there are.

24 Q. Among those 13, Northeastern is ranked 11th in terms
25 of government funding. Correct?

Amiji - cross

1 A. Not true, Mr. Scheve. Actually, it's climbing up. We
2 are going up in the ranking, even within the Boston area.

3 Q. During your deposition that was taken here three
4 months ago, didn't you tell me it was ranked 11th out of the
5 13 in the Boston area?

6 A. I don't believe I said it was ranked 11th. I said --
7 in terms of the institutions that are in the Boston area,
8 like Harvard and MIT, certainly they are ranked higher than
9 us. But Northeastern right now is around the same ranking
10 as Tufts. It's a little below BU, but it's right near
11 Brandeis and others.

12 Q. Let's make sure the jury understands.

13 Does your pharmacy school which you are a part
14 of, does it own any equipment?

15 A. Yes, we do. We do own a lot of equipment.

16 Q. The pharmacy school does?

17 A. No. The way, in academia, what we have is, we have
18 equipment that is owned by investigators themselves. For
19 instance, my lab, if there is equipment that I need for
20 research that is routinely used in my lab, I would have
21 them.

22 On the other side, we also have what are called
23 shared facilities. So certain equipment, especially large
24 equipment, we would have a shared facility. Depending on
25 the usage, sometimes those shared facilities will either be

Amiji - cross

1 in the department, in the school, or even within certain
2 colleges. So we have several equipment that are in these
3 shared facilities.

4 Q. Does the pharmacy school own equipment, sir?

5 A. Again, as I said, pharmacy school is the department
6 within the pharmacy school do own. Every investigator owns
7 and these equipments are in these shared facilities.

8 Q. So the pharmacy school doesn't own any. It's the
9 individual labs run by the individual faculty members that
10 own equipment. Correct?

11 MS. KRUIZE: Asked and answered.

12 THE COURT: Overruled.

13 THE WITNESS: So, as I said, the way this -- the
14 university, sometimes the equipment is bought by the
15 university and they are then put into the shared-use
16 research. Other times we get equipment based on grants that
17 we write. For instance, I write a grant. It could be
18 either a regular grant that supports research and I would
19 put in a equipment request, or I would write a grant which
20 is specific for the equipment. And we have done both. We
21 have written grants where, a regular grant and we have been
22 awarded grants specific for equipment.

23 Those equipments will be kept with the grant
24 funding. I am not sure if I understand your question
25 correctly; does the school of pharmacy own equipment?

Amiji - cross

1 Q. Right.

2 A. I don't -- again, I would say that, you know, there
3 are equipments within our purview and what we can use. I am
4 not sure who owns them, because, you know, it's part of
5 our -- we use these equipments. It is in our daily use.

6 Q. Is there a solid-state NMR capabilities anywhere in
7 your program, sir

8 A. We have liquid NMR. We don't have solid-state NMR,
9 because, again, our research does not, at least current
10 research does not use solid-state NMR. But we do have
11 liquid NMR. We actually have three very state-of-the-art
12 NMR equipments now at Northeastern that does various types
13 of characterization.

14 Q. So the answer is you don't have solid-state NMR?

15 A. No, we don't have solid-state NMR.

16 Q. Does your lab even have an x-ray diffraction machine?

17 A. No. Again, there is an x-ray diffraction in one of
18 these user facilities that I mentioned.

19 Q. Your lab doesn't even have an diffraction machine.
20 Correct, sir?

21 A. Yes. As I said, we have equipment within our usage on
22 a daily basis. Sometimes this equipment is very expensive.
23 So you don't want to have these in your lab if there is
24 going to be equipment that is going to be used on campus,
25 and it is not routinely used, especially in our case. We

Amiji - cross

1 don't use x-ray diffraction routinely. So there is no need
2 to buy that type of equipment and have it in your lab and
3 occupy space.

4 What we do is we find common users and create a
5 shared facility, where the equipment is then placed in that
6 shared facility. And most of the time we would hire a
7 technician, so that we can then have somebody who is
8 qualified to run that equipment and be able to then analyze
9 the results and give us that.

10 Then we would take those results and use them.

11 Q. Now, when this Liversidge '363 patent was filed, all
12 you had was a Bachelor's degree. Right, sir?

13 A. Yes, I did have a Bachelor's degree and I was at
14 Purdue University at the time.

15 Q. Now, while an undergraduate, none of your research
16 involved applying or utilizing a surface modifier adsorbed
17 onto the surface of a molecule. Is that correct, sir?

18 A. Sir, when I was an undergraduate at Northeastern, I
19 was privileged to work in a laboratory, and it was one of
20 the reasons that I chose to go to graduate school. I worked
21 on a research project with an anticancer drugs called
22 doxorubicin. This is a very potent drug, but it has one of
23 the most horrendous side effects.

24 So I was able to develop nanoparticles of
25 doxorubicin. Then analyze them, did a little bit of work --

Amiji - cross

1 then that persuaded me to go to Purdue.

2 Q. Was that a yes or a no?

3 A. The answer to your question, did I use surface
4 modifier to --

5 Q. While an undergraduate, sir, isn't it true that none
6 of your research involved applying or utilizing a surface
7 modifier adsorbed onto the surface of a molecule?

8 A. Not as an undergraduate. But subsequent to that I
9 have done a lot of work in this area. Nanotechnology, I
10 have done work in surface modification of materials. My
11 Ph.D. thesis was on surface modification of materials, which
12 is, you know, a four-year work on various types of
13 modifiers, various types of surfaces. And I have
14 subsequently published extensively in the area of
15 nanotechnology. Including the book that you saw.

16 Q. Actually, your dissertation dealt with glass.

17 A. Not necessarily, Mr. Scheve. Actually, you know, what
18 happened in my dissertation was that we looked at surfaces.
19 We looked at surfaces that were hydrophobic. You, members
20 of the jury, have heard about hydrophobic surfaces. These
21 are surfaces that do not like water.

22 So we are interested in looking at surface
23 modification of these hydrophobic, model hydrophobic
24 surfaces with the intent that these will be able to resist
25 blood interactions, will resist platelets. These are cells

Amiji - cross

1 in our blood that clot, prevent them from attaching to these
2 surfaces and forming a clot. Prevent bacteria from adhering
3 to the surface and forming an infectious site. My Ph.D.
4 thesis was on a hydrophobic model surface and hydrophilic or
5 water-loving surface. And allowed them to be modified.

6 Q. Let's tell the jury what those models were. They were
7 plastic, modified plastic, hydrophobically modified plastic,
8 and hydrophobically modified glass, and hydrophobic
9 plastics. That's what your models were for your thesis.
10 Isn't that correct, sir?

11 A. Right. Again, these hydrophobic materials, basically
12 anything that doesn't like water behaves similarly. So even
13 if you have a drug crystal that doesn't like water, it
14 behaves exactly the same as a hydrophobic polymer that
15 doesn't like water or hydrophobic glass that doesn't like
16 water.

17 Q. Your Ph.D. did not involve surface modification of a
18 hydrophobic anticancer agent, did it, sir?

19 A. No. Again, my Ph.D. thesis was on surface
20 modification of hydrophobic model surface where it
21 represents, and any hydrophobic surface is a hydrophobic
22 surface.

23 Q. Now, when you went to Purdue you were in the
24 industrial and physical pharmacy program. Correct?

25 A. Yes, I was.

Amiji - cross

1 Q. You weren't in the medicinal chemistry department at
2 Purdue. Correct?

3 A. No, the pharmaceuticals program at Purdue is in the
4 industrial and physical pharmacy program.

5 Q. Do you agree with me, sir, or not, did you or did you
6 not go through the medicinal chemistry department or
7 curriculum at Purdue?

8 A. No. I went through the industrial and physical
9 pharmacy program, which trains students to get degree in
10 formulation development.

11 Q. Did you go through any curriculum in medicinal
12 chemistry while at Purdue?

13 A. No, I did not. My training is in the physical
14 pharmacy. It's on formulation development, biomaterials,
15 which is in the area of my thesis. And that's what my
16 training was.

17 Q. You don't hold any degree in medicinal chemistry.
18 Correct?

19 A. No. My degree from Purdue is a Doctor of Philosophy
20 degree. Purdue designates that as purely a Doctor of
21 Philosophy degree. Then my thesis, which is what defines me
22 based on my work that I did at Purdue, is in the area of
23 surface modification of biomaterials.

24 Q. Those biomaterials being modified plastic, plastic --

25 THE COURT: We have done that, Mr. Scheve.

Amiji - cross

1 MR. SCHEVE: All right.

2 BY MR. SCHEVE:

3 Q. You didn't do any work at Purdue on nanoparticulate
4 formulations. Correct?

5 A. No, I did not work on nanoparticulate formulations at
6 Purdue. But I did take courses at Purdue that was on
7 dispersed phenomena. And dispersed phenomena is this idea
8 of having colloidal or nanoparticulate systems. I took
9 courses on rate processes, which is another term for looking
10 at these nanoparticles interacting with each other and
11 either forming a stable system or an unstable system.

12 Q. So the answer is you didn't work on any
13 nanoparticulate formulations at Purdue?

14 A. I didn't work specifically. But I did take courses on
15 that.

16 Q. You didn't work to formulate any anticancer drugs
17 while at Purdue. Correct, sir?

18 A. No. Again, my thesis was on this unique area of
19 biomaterial surface modification. I was interested in
20 looking at how blood interacts with these types of materials
21 and how they form usable devices and usable implantable
22 devices that can benefit patients.

23 Q. When you say no, sir, I asked you if that's correct,
24 and you said no. I am trying to understand, sir.

25 Is it correct or not that you did not formulate

Amiji - cross

1 any anticancer drugs while at Purdue?

2 A. Yes, I did not formulate anticancer drug. But my
3 thesis was in the area of biomaterials.

4 Q. After you left Purdue, you went to a company called
5 Columbia Research Laboratories?

6 A. Yes. This was a small company that was in Madison,
7 Wisconsin. It was a great opportunity, because it was a
8 startup company by a faculty member that I admired a lot,
9 the late Professor Joseph Robinson. He is my academic
10 grandfather. My advisor graduated from his lab. And he
11 started this company. It was my first opportunity to go and
12 work in a private company.

13 Q. Now, while at this Columbia Research Laboratories, is
14 it not true, sir, or is it true, sir, that you had no
15 involvement with anticancer agents, no involvement with
16 paclitaxel, no involvement with efforts to utilize surface
17 modifiers on nanoparticulate anticancer drugs, and, in fact,
18 had no involvement in any nanoparticulate technology while
19 there?

20 A. Again, you know, when you work for a company, you are
21 obviously going to focus on a specific product. Our product
22 was not in the nano area. We were interested in other types
23 of products when I was at Columbia.

24 But the training that I had and work that I have
25 done subsequent to that shows that once you develop as a

Amiji - cross

1 pharmaceutical scientist, especially from a school like
2 Purdue, which has an incredible richness of the experience
3 that you get from Purdue, it is just absolutely amazing, you
4 come out with very excellent skills that you can adapt to
5 different research environments.

6 So as I continued my career, I am able to work
7 on nanotechnology. I am able to work on paclitaxel. I am
8 able to work on all these different systems that Mr. Scheve
9 is talking about.

10 Q. Is the answer, you didn't do any of that at that
11 Columbia Research Laboratory, sir?

12 A. Yes, the answer is I didn't do it. Again, the company
13 was focused on a very specific product.

14 Q. Then it went out of business and you had to find a new
15 job?

16 A. No. Actually -- I mean, the company did go out of
17 business. But I had the opportunity to come back to my alma
18 mater at Northeastern. And I did get the job even before I
19 took the position at Columbia, I had a job at Northeastern.
20 But I didn't accept it.

21 I then, I heard that this company is in
22 financial difficulty, I decided to move into academia and
23 get, at least for the time being, what was considered to be
24 a more secure job.

25 Q. You joined Northeastern in 1993?

Amiji - cross

1 A. Yes, I did.

2 Q. Isn't it true, sir, that Northeastern didn't offer its
3 first what's called Pharma D or pharmacy doctorate degree
4 until the year 2002?

5 A. Well, let me clarify that for the jury.

6 So --

7 MR. SCHEVE: Your Honor, I have to object. Can
8 I ask him to answer the question.

9 THE COURT: Doctor, please, endeavor to respond
10 directly to the question posed.

11 Ms. Kruze will have an opportunity to ask you
12 additional questions. We will get through this a lot
13 quicker if you do that.

14 THE WITNESS: Thank you, Your Honor.

15 So pharmacy schools in the time that I joined
16 were offering a Bachelor of Science degree.

17 Subsequent to that, in the year 2000, around
18 that time frame, the American Association of Pharmacy, which
19 is an organization that has membership of all the colleges
20 of pharmacy, as well as the American Council of
21 Pharmaceutical Education, which is the accrediting agency of
22 all pharmacy schools, mandated that every school of pharmacy
23 move to this Doctor of Pharmacy program.

24 So before then, there were very few Doctor of
25 Pharmacy programs in the nation. Only in California mostly.

Amiji - cross

1 But then, after this mandate, all schools of pharmacy had to
2 move into the Doctor of Pharmacy school.

3 BY MR. SCHEVE:

4 Q. The answer as you didn't offer it until 2002.

5 Correct?

6 A. Yes. Again, what we started out was that we will have
7 a Bachelor's degree program and have a tracking option for
8 students, either they can track into the Pharma D or they
9 can continue with the Bachelor's degree and gradually move
10 more and more into the Pharma D as they continue to show
11 interest. And then eventually turn over and have a complete
12 Pharma D degree.

13 Q. Now, the U.S. News and World Report ranks pharmacy
14 programs?

15 A. Yes, they do.

16 Q. They rank yours 46th?

17 A. No. I believe again, you know, these are maybe dated.
18 If you have something that you can show me.

19 Q. Didn't you testify, sir, that the 2005 ranking by U.S.
20 News and World Report ranked Northeastern at 46th?

21 A. Again, these rankings, they continue to be -- we see
22 ourselves going higher and higher. Again, these rankings
23 are, to some degree, subjective. The U.S. News and World
24 Report looks at one criteria for ranking, which may be a
25 specific thing, for instance, grant funding. Others who

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1 grant rank use different criteria, such as success rates of
2 students. I think each one is very subjective.

3 My issue is that I am a faculty member in the
4 department, in a school of pharmacy. I love my job. I love
5 the fact that I can go to work every day, and interact with
6 students and mentor them and make sure that they are
7 successful in what they have sought out to achieve.

8 That's really what I care about most. I really
9 don't get too much involved in these rankings.

10 Q. 2005, did they rank them 46th, sir?

11 A. Again, you know, maybe I don't know, I don't pay too
12 much attention to these rankings. I am concentrating on
13 what my sphere of influence is. How I can educate these
14 students. What I can do to affect their lives.

15 Ranging, whatever it is, you know, that's very
16 subjective. It's based by somebody else. I pay attention
17 to what I can do to help my students and make sure they are
18 successful.

19 Q. Have you testified, at Page 39, Lines 14 through 21 of
20 your deposition, that Northeastern was ranked by U.S. News
21 and World Report as 46th in 2005? Is it your testimony --
22 are you changing your testimony? Or is that still true?

23 A. Again, Mr. Scheve, I don't know exactly what the
24 ranking was in 2005. But, you know, these are arbitrary
25 things that, you know -- yes, maybe 46 out of whatever you

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1 mentioned.

2 Q. U.S. News and World Report, you would call that pretty
3 arbitrary. Is that correct?

4 A. Well, I mean, you know, it's a subjective ranking.
5 That's what it is. It is based on somebody at U.S. News and
6 World Report making --

7 THE COURT: We are never going to agree on this
8 particular point. It's probably time to move on.

9 BY MR. SCHEVE:

10 Q. Now, this Center for Pharmaceutical Biotechnology
11 Nanomedicine that you told the jury about, that didn't come
12 into existence until 2006. Correct?

13 A. Yes. There are two things. One is the Center for
14 Pharmaceutical Biotechnology and Nanomedicine, which the
15 director of that center is our department chair. The other
16 that I am a member of is actually called the Nanomedicine
17 Education and Research Consortium. It's different from the
18 two.

19 Q. That's what I want to establish. You don't even
20 belong to Northeastern's Center of Pharmaceutical
21 Biotechnology and Nanomedicine program. Correct?

22 A. No. I am an affiliate of that center, because it was
23 started by a faculty, my chair, his name is Professor
24 Vladimir Torchilin. He has his own program, and he has his
25 own students, his own postdoctoral associates. He does his

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1 own. We have a different center, a consortium. Our
2 consortium that I am a part of involves both research as
3 well as training of graduate students.

4 What we are doing is including not only the
5 Department of Pharmaceutical Science that I am a member of,
6 but six other departments on campus. And also creating
7 links with various medical centers in the Boston area,
8 various other institutions, such as Harvard, MIT and so
9 forth. That's really what the Nanomedicine Consortium is.

10 Q. Now I want to talk about the Nanomedicine Consortium
11 that you do belong to. Isn't it true, sir, that that is
12 just a group of faculty members who individually have their
13 own research funding, and they formed this consortium that
14 you call the Nanomedicine Consortium?

15 A. It's a group of faculty who are united by this theme
16 of nanomedicine. We see a tremendous potential in this area
17 in treatment and diagnosis of diseases.

18 So united, we found interest from physics
19 faculty, from chemistry faculty, from pharmaceutical
20 scientists like myself, from biology and all these different
21 disciplines, engineering disciplines, we formed this
22 uniquely. And we said, we want our students not to be
23 trained in a specific area but maybe we can have a way to
24 train them in a problem-based training that looks at a
25 specific type of problem and says, you know, maybe a

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1 solution comes from physics. And maybe a solution comes
2 from biology. How can we make this interdisciplinary?
3 That's really what the consortium is all about.

4 Q. The answer is yes?

5 A. It is a group of faculty. Like any other consortium,
6 it is a group of faculty. But the real emphasis here is how
7 can we ask each other to help our students become better
8 scientists.

9 Q. That consortium itself did not have and still doesn't
10 have any funding. Correct?

11 A. Oh, no, absolutely not, Mr. Scheve. The consortium is
12 funded through the training grant that I mentioned. It's a
13 3.3 million dollar training grant that we received from the
14 National Science Foundation and the National Cancer
15 Institute.

16 The students that we are training in that get
17 support, financial support. They get complete free tuition
18 to take courses whenever they want to take courses. If they
19 want to travel, we subsidize their travels overseas. And we
20 had a wonderful opportunity last year when one of our
21 trainees went to Macao and spent time to learn how to work
22 with human stem cells.

23 MR. SCHEVE: May I approach, Your Honor?

24 THE COURT: Counsel, you may.

25 BY MR. SCHEVE:

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1 Q. Sir, did you give your deposition in this case?

2 A. Yes, I did.

3 Q. At that deposition, sir, were you asked this question,
4 beginning at Page 173, Line 14?

5 A. Yes, I did give this.

6 Q. Did you give the answer that follows it?

7 A. Yes. So let me clarify for the jury.

8 MR. SCHEVE: May I ask the question, Your Honor.

9 THE COURT: Yes.

10 BY MR. SCHEVE:

11 Q. Were you asked the following:

12 "Question: So the actual funding for this
13 Nanomedicine Consortium program now known as the
14 Nanomedicine Education Research Consortium came in to
15 existence in 2005?"

16 Did you give the following answer, sir:

17 "No. Let me clarify. The nanomedicine, the
18 consortium is a group of faculty members who had
19 individually had their own research funding. And we formed
20 this consortium in order to collaborate within the
21 department. The consortium itself did not have and still
22 does not have its own funding. We never got funding
23 specifically for the consortium. We have obtained funding
24 through various collaborative efforts."

25 Did you give that answer or not give that answer

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1 under oath, sir?

2 A. Yes, I did.

3 Again, I think it requires a little bit of
4 clarification for the jury, Your Honor.

5 THE COURT: You will get a chance to respond to
6 questions from Ms. Kruze.

7 MS. KRUZE: I was going to object. I will
8 let --

9 THE COURT: Object to what?

10 MS. KRUZE: I don't believe it's contradictory.

11 THE COURT: I disagree, as to whether it is an
12 appropriate question. As to whether it is contradictory,
13 that is up to the jury to decide.

14 The jury will disregard Counsel's comment as to
15 what she believes as to whether it is contradictory or not.
16 You will have to make that determination.

17 BY MR. SCHEVE:

18 Q. Now, with regard to its Ph.D. program, sir, when
19 did Northeastern first start offering a Ph.D. program in
20 nanotechnology?

21 A. The nanotechnology program -- we have Ph.D. programs
22 in various departments. We have Ph.D. program in
23 pharmaceutical science. We have a Ph.D. program in
24 chemistry. Ph.D. in physics. Ph.D. in biology and other
25 engineering disciplines. Nanotechnology is a new field. So

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1 not a lot of schools even offer a nanotechnology Ph.D. The
2 reason is that, basically, having a student graduate with a
3 nanotechnology doesn't give them a job. Nobody understands
4 what they did in their Ph.D. thesis.

5 So we have kept the traditional Ph.D. programs
6 at Northeastern where these students can continue to
7 graduate and have a distinction based on what they have
8 done.

9 But we have created this nanomedicine training
10 program where we give students stipends to work on projects
11 that are related to nanomedicine. And based on that, we
12 then ask them that they will have their Ph.D. in their
13 designated department, with their nanomedicine minor, so to
14 speak.

15 Q. You heard the testimony of Dr. Liversidge that they
16 were working on nanotechnology in late 1980s?

17 A. I was here. Again, you know, he was working for his
18 thesis. I don't believe Dr. Liversidge mentioned that he
19 received a Ph.D. in nanotechnology.

20 Q. My question is, sir, you heard the testimony that he
21 and his colleagues were working on nanoparticulate
22 technology as early as late 1980s?

23 A. Yes, I heard the testimony.

24 Q. Isn't it true that Northeastern now, where you are a
25 faculty member, first began training Ph.D. students in

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1 October 2005?

2 A. Again, you know, this area of nanotechnology is
3 relatively new. And offering a Ph.D. specifically in this
4 area, you know, it doesn't really make a lot of sense from a
5 faculty point of view.

6 So we offered Ph.D., just as Dr. Liversidge's
7 Ph.D. is in pharmaceutical chemistry, we have a Ph.D. in
8 pharmaceutical science. We have a Ph.D. in chemical
9 engineering.

10 So I don't believe that, you know, anyone has --
11 maybe there are one or two schools that have offered a Ph.D.
12 in nanotechnology. But I don't believe there is any
13 pharmacy school that is offering a Ph.D. in nanotechnology
14 or nanomedicine.

15 Q. Is that yes?

16 A. I am sorry. Yes. We didn't offer in 1980s a
17 nanotechnology Ph.D.

18 Q. My question, sir, was, didn't your program begin in
19 October of '05?

20 A. The nanomedicine program based on the funding that we
21 received, yes, began in October of '05.

22 Q. Has your first person yet achieved a Ph.D. from
23 Northeastern?

24 A. Yes, sir. Actually, we have had two students graduate
25 from our nanomedicine program. One of them was my own

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1 student. Her name is Lillian VanVlerken. She graduated in
2 January of this year. We had a second student graduate this
3 May, again receiving a Ph.D. in pharmaceutical science with
4 this nanomedicine designation.

5 Q. So, the first Ph.D. to ever come through Northeastern
6 in nanotechnology wasn't until the year 2008. Is that
7 correct?

8 A. Again, as I said, in the pharmaceutical sciences area,
9 we have worked on nanotechnology and medical application of
10 nanotechnology --

11 THE COURT: Doctor, that is a relatively
12 straightforward question. Please, attempt to direct your
13 response.

14 Could you re-put the question.

15 BY MR. SCHEVE:

16 Q. So, the first Ph.D. awarded from Northeastern in this
17 technology occurred in 2008. Correct?

18 A. Right. Students who have learned in nano--

19 THE COURT: Is that a yes, Doctor?

20 THE WITNESS: Yes.

21 MR. SCHEVE: Thank you.

22 BY MR. SCHEVE:

23 Q. Northeastern doesn't even have a medicinal chemistry
24 department within the pharmacy school, does it, sir?

25 A. No, we have a center for drug discovery, which is

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1 where the medicinal chemistry research is done.

2 Q. Sir, when I asked you isn't that correct? And you say
3 no, are you agreeing with me or not agreeing with me?

4 A. Yes. We don't have a designated medicinal chemistry
5 program. But we do have a center for drug discovery where
6 medicinal chemistry is done.

7 Q. Now, sir, did you sign an agreement when you became
8 involved in this case, where you agreed that you wouldn't
9 take on a case or take on any work or perform any services
10 that, if it were adverse to the attorneys, called Morrison &
11 Forester?

12 A. Yes, I did. This is the letter of agreement that I
13 signed.

14 Q. So if, hypothetically, one of my clients wanted to
15 hire you, you would have to go to these lawyers first and
16 find out whether they are on the other side, and then if you
17 found out that they are on the other side, then you would
18 have to get their permission, no matter how meritorious my
19 client's position is, no matter how correct the science, you
20 would have to go to their lawyers and get permission before
21 you could take it on? Is that what you contractually
22 obligated yourself to?

23 A. Yes. But as you look at the line just below where you
24 have highlighted, the agreement can be terminated at the
25 discretion of either party within ten days of notice. So I

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1 can terminate this agreement that I have with Morrison &
2 Foerster within ten days of notice.

3 Q. Of course, if you terminate, then you are no longer
4 working in this lawsuit. Right, sir?

5 A. Right, yeah.

6 Q. So the only way -- by the way, were you being paid for
7 your time in this lawsuit, for your involvement?

8 A. Yes. I am paid.

9 Q. The only way while you are involved in this lawsuit is
10 to go ask them for permission so that you could take on some
11 other client?

12 A. Yes. That's what I have signed. But there is an
13 appendix, there is again the clause in the agreement that I
14 can terminate the agreement.

15 Q. Now, did the FDA ever call you and say, Dr. Amiji, we
16 would sure like you to come and teach us something?

17 A. No. I have not had the pleasure of going to the FDA.
18 But I have been involved with this Alliance For
19 Nanotechnology in Cancer. It's an active alliance. It
20 started in 2005, by the National Cancer Institute. And one
21 of their responsibilities of this alliance is to interact
22 with the FDA, to make sure that the FDA understands
23 nanotechnology, especially as it applies to cancer
24 prevention, diagnosis and treatment.

25 So I have gone to various meetings and met with

Amiji - cross

1 various FDA representatives to interact with them and try to
2 understand some of the issues with nanotechnology.

3 Q. Now, has the FDA, sir, ever communicated to Elan that
4 it saw any contamination problem with any product that it
5 was reviewing?

6 A. No. Again, the products that FDA has reviewed for
7 Elan are based on these oral tablets that we heard about,
8 drugs like Megace, and Elan has moved away from the
9 zirconium B's. So Elan is using polystyrene beads for
10 instance in wet milling, they might not have contamination.
11 But the '363 talks about beads of zirconia or glass beads.
12 That's where we see the contamination.

13 Q. Well, that begs several questions, sir.

14 Isn't it true that Johnson & Johnson is using
15 zirconium beads today for the manufacturer of itraconazole?

16 A. Again, I am --

17 Q. Yes or no, sir.

18 A. I don't know if Johnson & Johnson is using it.

19 Q. How many injectable drugs are under development that
20 incorporate the '363 patent?

21 A. Again, it could be many. The point is that, you know,
22 once these drugs -- they are under development. That is the
23 keyword here in this issue, this question. The FDA looks at
24 this very carefully, and contamination is a huge issue. We
25 heard here about contamination in products like Heparin from

Amiji - cross

1 Baxter and other types of products.

2 This is not something to take very trivially.

3 Q. The FDA is very, looks at that very closely, don't
4 they, sir?

5 A. Absolutely, they do look at it very closely.

6 Q. Now, when is the Johnson & Johnson drug that
7 incorporates the '363 technology going to be approved --
8 launched?

9 A. Again, you know, based on the testimony that I heard,
10 it was to be launched soon. But we don't know exactly what
11 the product -- it may say one of the technologies from the
12 '363, but it could have other technologies as well from the
13 other patent that Elan has. The milling media may be
14 different. I am not privileged to know exactly what is
15 going on in the product that Johnson & Johnson is making.

16 Q. What about the other two? There was testimony that
17 there is a second drug that is in Phase 2 trials. What is
18 that drug?

19 A. Again, I am not sure. I don't know which one is in
20 Phase 2 trials.

21 Q. What is the one in Phase 1? I am talking about
22 injectable forms of anticancer agents that are now being
23 given to humans utilizing the '363 patent.

24 A. Right.

25 Q. What are those drugs?

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1 A. The Phase 1 drug, I believe, when I heard
2 Dr. Liversidge's testimony, is, he did not disclose what
3 drug it was. He basically said that it's in Phase 1
4 clinical trial. Because of the contractual agreement with
5 Johnson & Johnson or some other company, Bristol Myers,
6 excuse me --

7 Q. Let's help the jury understand; what is an
8 investigational new drug exemption?

9 A. I am sorry. What is an investigational new drug
10 exemption?

11 Q. Yes, sir. Some people call it application.

12 A. Right. It's an INDA or Investigational New Drug
13 Application. This is the first step to going for clinical
14 approval of any type of drug. So Investigational New Drug
15 Application is submitted to the FDA with all the documents
16 that have been collected based on what we call preclinical
17 studies. These are studies that are done before the first
18 to man or first to person trial.

19 What happens is you collect all these documents
20 and you present it to the FDA and make a case that, yes, we
21 have a product that may be safe and efficacious, and we can
22 start human studies.

23 Q. Now, does it contain something called a CMC section?

24 A. Yes, it does.

25 Q. Does CMC stand for chemistry, manufacturing, and

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1 control?

2 A. That's correct.

3 Q. Now, that chemistry, manufacturing and control segment
4 of the IND submitted for each one of these injectables, does
5 it have to communicate in very precise detail any sorts of
6 information about contamination to the FDA?

7 A. It does. And again, you know, we are looking at this
8 purely from the '363 patent. The technology that's adopted
9 may involve more than one patent, may involve other secret
10 methods that may be present within the company. But in the
11 context of the '363 patent, there is contamination. In
12 zirconia, glass, in zirconium silicate that is in the '363
13 that is causing contamination.

14 Q. Have you seen the contamination levels or any part of
15 the CMC for those three injectable drugs that we have just
16 talked about?

17 MS. KRUIZE: Your Honor, objection. Sidebar.

18 THE COURT: Yes.

19 (The following took place at sidebar.)

20 MS. KRUIZE: Your Honor, there is no foundation
21 for any of these questions. We have no documents
22 supporting -- the misleading part of his --

23 THE COURT: Sustained.

24 (End of sidebar conference.)

25 BY MR. SCHEVE:

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1 Q. If the FDA thought for a minute that there was a
2 contamination issue with these three injectables that are
3 currently in clinical trials, would they have let that go
4 forward?

5 A. Again, you know, I am not privileged to see what the
6 FDA has reviewed. So I don't know what the FDA saw.

7 What I have reviewed is the documents that are
8 relevant to the case here, which is the '363 patent, and
9 other documents that came through Elan, very much specific
10 in this area.

11 I can't speak for what the FDA has reviewed and
12 how much levels of contamination has been disclosed.

13 Q. If the FDA thought there was any safety issues, sir,
14 would they have allowed that to be given to human beings?

15 A. Again, based on my experience with the FDA, the
16 TOLERANCE is very low.

17 MS. KRUIZE: Same objection. There is no
18 foundation.

19 THE COURT: Sustained. Continue on, Mr. Scheve.

20 BY MR. SCHEVE:

21 Q. What pharmaceutical companies do you consult with?

22 A. I consult with several. I do have an active
23 consulting agreement with General Enzyme Pharmaceutical,
24 which is in Boston, the Boston area. I also have a
25 consulting agreement with other companies, a few other

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1 companies, smaller companies in the Boston area.

2 Q. Those smaller companies, sir, you told me their names
3 during the deposition. Who are they?

4 A. There is one called, Cequent Pharmaceutical. Maybe I
5 can pull up my CV. Do you have my CV in one of these
6 binders?

7 Q. I do not, sir, sorry.

8 Maybe I do. Let me see if I can find the
9 companies. It was Novavax, Zydus and Biocure?

10 A. Biocure, I do consult. Novavax, I used to consult.
11 It's in Pennsylvania, Malvern, Pennsylvania. I do not
12 anymore. And Zydus is an Indian company. They asked me to
13 be on their scientific advisory board, but I do not have any
14 consulting with they mean.

15 Q. Sir, do you consult with Merck?

16 A. No, I do not consult with Merck.

17 Q. Abbott Labs?

18 A. No, I do not consult with them.

19 Q. Roche?

20 A. No.

21 Q. AstraZeneca?

22 A. No.

23 Q. Sanofi-Aventis?

24 A. No, I do not have consulting.

25 Q. BMS or Glaxo?

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1 A. No, none of those.

2 Q. You heard the testimony that all of those companies
3 have licensed the nanocrystalline technology?

4 A. Yes.

5 Q. Do you think their lawyers and their scientists
6 internally are licensing invalid patent technology?

7 A. Again, you know, I can't speak for, what I can speak
8 for is really what I saw as the exhibits that were submitted
9 to me. And based on the exhibits, I feel that the '363
10 patent is invalid.

11 Q. Do you have my question in mind, sir? Do you think
12 they got it wrong?

13 A. Again, I can't speak for the lawyers in these
14 different companies.

15 Q. In your experience, sir, are the scientists within
16 each one of those companies going to do due diligence before
17 they sign a license agreement to license that kind of
18 technology?

19 A. Again, you know, many of them may do. I don't know
20 exactly how each company operates. I don't have any
21 information related to their process and procedure.

22 Q. All right, sir.

23 Let's go to a new topic then.

24 Isn't it true, sir, that up through the year
25 2000 you had not published any paper specifically on

Amiji - cross

1 nanoparticle formulations?

2 A. Up to 2000 we had worked on various drug delivery
3 systems. At that time, when I first joined Northeastern, I
4 was interested in looking at oral drug delivery. In oral,
5 you don't need a nanoparticulate because you can take a
6 larger pill. So we worked with other types of drug-delivery
7 systems. But as I got more and more interested in systemic
8 delivery or delivery of drugs into the body, so we started
9 to work with nano.

10 At present, as I mentioned already, I have about
11 80 peer-reviewed publications and out of that about at least
12 50 or so is in the nano area.

13 Q. Is it true, sir, that up through 2000 you hadn't
14 published any paper on nano?

15 A. Yes, as I mentioned before.

16 Q. Is it true that up through 2000 you had not even
17 looked at surface modification of an anticancer agent?

18 A. Again, my thesis -- my Ph.D. thesis was in the area of
19 surface modifications of hydrophobic material. That is my
20 entire Ph.D. thesis. I worked on that extensively at
21 Purdue. And based on the same surface modifiers that we had
22 in this, some of the same surface -- like chloride which is
23 in the '363 patent, I worked extensively on chloride. I
24 worked extensively on albumin, both human albumin as well as
25 the animal-derived albumin.

Amiji - cross

1 Q. Was it an anticancer agent in your thesis, sir?

2 A. No. Again, hydrophobic surfaces that become
3 implantable devices. We were interested in studying how
4 these interact with blood.

5 Q. Isn't it true, sir, that you have not used any
6 anti-tumor agent or attempted to modify the surface of any
7 anti-tumor agents with a protein?

8 A. Again, you know, we have worked on area of drug
9 delivery and we have used polymeric drug delivery. We have
10 used a number of different types of other nanoparticulate
11 concepts.

12 But not specifically in the protein drug -- no.

13 Q. Is it true you have never used human serum albumin in
14 any research on a nanoparticle?

15 A. No. My work on human serum albumin has been on
16 modification of surfaces in my Ph.D. thesis. And then we
17 have used human serum albumin for other types of
18 applications. We have also used obal human, which is a
19 derivative of albumin, recently in studying some of the
20 properties as a vaccine model.

21 Q. To boil this down, sir, isn't it true that none of
22 your research involves proteins adsorbed under the surface
23 of an anticancer nanoparticulate formulation?

24 A. Yes. Mr. Scheve, that is a very specific area. As I
25 said before, scientists are focused on problem solving.

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1 That's really what we do. We try to find problems that are
2 very important, and we try to solve them.

3 The answer to Mr. Scheve's question, not in that
4 very, very narrow area of proteins on the surface of a
5 nanoparticle. But as a scientist, as a pharmaceutical
6 scientist specifically, worked on extensively so many
7 different areas, from looking at delivery of anticancer
8 drugs like paclitaxel, looking at how to enhance their
9 delivery into tumors. Looking at gene therapy. This is a
10 really exciting area. Now we can take a molecule, in gene
11 construct, and actually have the drug produced in the body
12 itself and have the drug suppress the blood vessels in the
13 tumor and completely starve the tumor.

14 I have done all that.

15 Q. Isn't it true, sir, that the Vuone Trieu paper that
16 Ms. Kruze put up for you has never been submitted to the
17 FDA?

18 A. I mean, it's a study that was done at Abraxis, to
19 confirm the cross-linking that occurs in these albumin
20 molecules on the surface of the nanoparticle.

21 Since the particles are not what FDA regulates,
22 FDA regulates the final product. They regulate how much --
23 what is the final product, what is the safety and efficacy
24 of the final product.

25 Abraxane has submitted all the documents for --

Amiji - cross

1 Abraxis has submitted all the documents for Abraxane. But
2 once you isolate the nanoparticle, the FDA is not regulating
3 the nanoparticle part of the Abraxane.

4 Q. Sir, isn't it true that that paper was never submitted
5 to the FDA?

6 A. Again, as I mentioned, there is no need to submit to
7 the FDA because --

8 THE COURT: Doctor, was it submitted?

9 THE WITNESS: No, it wasn't.

10 BY MR. SCHEVE:

11 Q. So the data -- let me back up.

12 Isn't it true that Abraxis reported for the FDA
13 monomer content for two stability batches, one from Illinois
14 and one from New York, that was submitted as part of the CMC
15 portion of both the IND and the New Drug Application.

16 Correct?

17 A. Correct. Again, it is the entire formulation of
18 Abraxane. So it has the free albumin as well as what's on
19 the surface of the nanoparticle.

20 Q. This piece of paper that you relied upon, this
21 Vuone Trieu document, it was created internally at Abraxis
22 after this litigation was filed. Correct?

23 A. That's correct. Yes, it was created in July of 2007.

24 Q. It's never been submitted to the FDA, has it, sir?

25 A. Again, because this is now going to be a product out

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1 of a product. It is actually a nanoparticle that is out.
2 FDA doesn't require --

3 THE COURT: Doctor....

4 Would you repeat the question.

5 BY MR. SCHEVE:

6 Q. It's never been submitted to the FDA. Right, sir?

7 A. Yes.

8 MR. SCHEVE: Pass the witness.

9 THE COURT: Ms. Kruze, you may redirect.

10 REDIRECT EXAMINATION

11 BY MS. KRUZE:

12 Q. Is this your book, Dr. Amiji (indicating)?

13 A. Yes. This is what I call my pride and joy.
14 Nanotechnology for cancer therapy.

15 Q. And are you a representative for the USP?

16 A. Yes, I am. I have been fortunate to be elected by the
17 school of pharmacy at Northeastern to be the faculty
18 designate in the United States Pharmacopeia. So I attend
19 their meetings, usually every year.

20 Q. And did you want to clarify anything regarding the
21 funding issue for the Nanomedicine Consortium for the jury?

22 A. Yes, I would. Thank you for the opportunity.

23 So the consortium is, as Mr. Scheve mentioned,
24 faculty members. We come together. We work and collaborate
25 and talk about and try to help our students learn each

Amiji - redirect

1 other's discipline. The way he asked that question during
2 the deposition was, does the consortium have its own
3 funding. And consortiums usually do not, because we have
4 faculty members who apply for grants.

5 My understanding of his question at the time
6 was, does the entity that we have created somehow, you know,
7 has its own funding. Usually, it's the faculty members. So
8 I have applied for grants and I have a grant -- I am a
9 member, actually director of the consortium. There are
10 other faculty who work -- they apply for grants and they get
11 money and they are then part of our consortium because we
12 have this common theme in the area of nanomedicine.

13 Q. Elan's counsel also showed a video of Dr. Neil Desai.
14 Would you like to clarify anything about your meeting with
15 him then?

16 A. Yes. Let me, first of all, I have to correct myself.
17 I did meet Neil in 2006. So Dr. Desai, in 2006, not 2007.
18 Because we had this conference in Boston. My colleague that
19 I mentioned, Professor Torchilin, organized that conference
20 in nanomedicine, and we had Dr. Desai come and present on
21 that conference. I had a brief, maybe about two-minute
22 interaction with him. We said hello. And then he proceeded
23 with his presentation and then left the meeting.

24 Q. Talking briefly about contamination, did Elan's
25 counsel offer you any documentary support for what he was

Amiji - redirect

1 implying in his questions?

2 A. No. I have not seen a single documentary support.

3 MR. SCHEVE: Objection. Foundation.

4 THE COURT: Sustained.

5 BY MS. KRUZE:

6 Q. Based on the documents you have seen, Dr. Amiji, was
7 contamination a significant problem with the '363 patent?

8 A. Yes, it is.

9 Q. And were any of the products that Elan's counsel
10 referred to, were any of them around at the time that the
11 patent was filed?

12 A. No, I don't believe they were.

13 Q. And the issue of enablement, that's determined at the
14 time the patent was filed. Correct?

15 A. Yes, that's correct.

16 Q. For cross-linking, did Elan's counsel ask you any
17 substantive questions about your opinion that Abraxane is
18 substantially cross-linked?

19 MR. SCHEVE: Objection. Form.

20 THE COURT: Sustained.

21 BY MS. KRUZE:

22 Q. Did Elan's counsel ask you any questions --

23 THE COURT: Same ruling.

24 MS. KRUZE: All right. No further questions.

25 THE COURT: You are excused, Doctor. Thank you.

Amiji - redirect

1 THE WITNESS: Thank you very much, Your Honor.

2 THE COURT: You are excused.

3 Ladies and gentlemen, let's take our break a
4 little early.

5 THE COURT: I would like to speak with counsel.

6 (Jury leaves courtroom at 10:35 a.m.)

7 THE COURT: Counsel, for reasons you might
8 understand, I didn't take home with me yesterday the
9 submissions regarding the proposed final jury instructions
10 and verdict form. I have had a chance to at least peruse
11 the final instructions and glance at the proposed verdict
12 forms.

13 To say that I am disappointed is a vast
14 understatement. I am going to cut to the chase. Lead
15 counsel are going to have to get involved in this. Clearly,
16 you haven't been. I understand why.

17 But we have 33 -- maybe half, if that is the
18 case, you know, I will say what I am going to say, I have 33
19 proposed final instructions, as I count them, 25 are in
20 dispute. That leaves eight that there is agreement upon.

21 It's me and my clerk, ladies and gentlemen. You
22 have got vast legal teams out there on both sides, that
23 directly are involved or in town, never mind who is down at
24 Baker in Texas, out in San Francisco with Morrison. You are
25 going to have to do a better job than you have of coming to

1 some reasonable agreements.

2 I don't have a problem making rulings. You know
3 that by now, I would imagine.

4 But my goodness, this is just not tenable. I
5 could never get through all of these. And the separate
6 submission with all of the law, 25 pages of, I think -- yes,
7 there is a submission of 104 which is a supposed clean copy
8 and a submission of 125 pages, which is a supposed unclean
9 copy.

10 I gather that has the citations to the various
11 legal authority, pieces of legal authority that supports
12 your various positions, which is helpful to have. But only
13 in the instance of a reasonable number of disputes. The
14 number of disputes that are still extant in this case, with
15 regard to the final jury instructions, is entirely
16 unreasonable. Quite frankly, at this stage of the
17 proceeding, in a patent case, I have never seen this many.

18 You are going to have to do a better job and
19 submit me a joint verdict form. I am not going to -- I see,
20 I have been able to glance at it, I see some of the
21 differences. Quite frankly, some of these differences are
22 very subtle, very subtle. And involve lawyers who have
23 intimate knowledge of the subject matter, and are going to
24 be entirely lost on a jury and are not necessary, quite
25 frankly, for the purpose of preserving your positions on

1 appeal to the Federal Circuit.

2 So let's get it together and do a better job and
3 make this a reasonable exercise in judging and lawyering.

4 We are in recess.

5 (Recess taken.)

6 THE COURT: All right. Ms. Walker.

7 (Jury enters courtroom at 10:59 a.m.)

8 THE COURT: Please take your seats, ladies and
9 gentlemen. Next witness.

10 MR. JACOBS: The defendants will present by
11 videotape testimony the testimony of Dr. Pramod Sarpotdar,
12 one of the named inventors on the '363 patent.

13 THE COURT: All right.

14 "Question: Dr. Sarpotdar, could you state your
15 name for the record?

16 "Answer: Pramod. My middle name is P., for
17 Purushottam, Sarpotdar.

18 "Question: Doctor, do you still have in front
19 of you Exhibit 7, which is U.S. Patent No. 5,399,3637?

20 "Answer: Yes.

21 "Question: Why are you listed as an inventor on
22 this patent?

23 "Answer: I cannot answer the legal aspect of
24 why am I listed, but I'm a co-inventor, as I understand, on
25 this patent.

Sarpotdar - depo.

1 "Question: When you were looking into
2 feasibility of different formulations then, were you
3 actually making particles?

4 "Answer: We were generating particles, yes,
5 from course particles.

6 "Question: When you would generate particles,
7 how would you determine whether or not particles that you
8 generated were feasible?

9 "Answer: Well, we talked about a couple of
10 things so far, right? I mean, we were talking about
11 particle size. We were talking about stability.

12 "Question: Are those the only two factors you
13 considered?

14 "Answer: From my perspective in developing
15 compositions, those were the two important factors.

16 "Question: So, in your work, were you
17 considering factors such as toxicity or efficacy?

18 "Answer: You want me to split the question?

19 "Question: Sure.

20 "Answer: Toxicity, no. Efficacy, no. Efficacy
21 as defined in humans. Again, I mean, what's the definition
22 of efficacy? When I said no to is testing in humans.

23 "Question: Referring, again, to Sarpotdar
24 Exhibit 7, the '363 patent, to the surface modifiers listed
25 at the bottom of Column 3 and in Column 4, will every one of

Sarpotdar - depo.

1 the surface modifiers listed here be useful in making
2 nanocrystalline composition according to the invention?

3 "Answer: It also is a very broad question. I
4 mean, you are asking me to say will everything work with
5 everything else. I cannot answer that question.

6 "Question: Why not?

7 "Answer: I simply don't know.

8 "Question: Can you predict in advance which
9 combinations will work?

10 "Answer: Again, you are making a very broad
11 statement that requires me to speculate, and I would rather
12 not.

13 "Question: You're here to answer the questions
14 put to you. And I would appreciate it if you could just let
15 me know if the surface modifiers listed in columns 3 or 4,
16 if every one listed is useful in making nanocrystalline
17 compositions according to the invention of the '363 patent.

18 "Answer: I'll try to repeat and explain what
19 I'm trying to say here. I think your question is too broad
20 for me to say, yes, no, or whatever. I think if every one
21 of these will work with every one of the anticancer agents,
22 the answer is I don't know.

23 "Question: Doctor, during your time at
24 Sterling, did you ever try to make NanoCrystals with
25 piposulfan?

Sarpotdar - depo.

1 "Answer: Again, I think you are asking me a
2 very broad definition. Could you be me more specific one
3 what I did with the piposulfan?

4 "MR. COYNE: Could you reread the question,
5 please.

6 "(Record read.)

7 "Answer: I think 'try to make' is key. Yes, I
8 worked on it.

9 "Question: Doctor, you have just been handed
10 what has been marked as Sarpotdar Exhibit 3, Bates No.
11 ELANP0007472 through ELANP0007695.

12 "Answer: Okay.

13 "Have you seen this document before?

14 "Answer: I need to browse through it. The
15 first page says it's a laboratory notebook, I'm the author
16 on that. So are all the pages the laboratory notebook, or
17 dye need to go through the pages?

18 "Question: And was this notebook authored by
19 you in the ordinary course of your employment at Sterling?

20 "Answer: Yes.

21 "Question: Was it part of your duties as a
22 Sterling employee to author laboratory notebooks such as
23 this one?

24 "Answer: Yes.

25 "Question: Could you turn to page 96 of

Sarpotdar - depo.

1 Sarpotdar Exhibit 3, which is Bates numbered ELANP0007588.

2 Have you found that page, Doctor?

3 "Answer: Yes, I have. 88, correct?

4 "Question: Could you read the title of this
5 page on the line that begins with "Title."

6 "Answer: 'To determine the feasibility of
7 making stable pi po' -- in quotes -- "'N' nanocrystals.'

8 "Question: I'm asking you to tell me what this
9 experiment from your own laboratory notebook is.

10 "Answer: Pipo -- in quotes -- 'N' nanocrystals.
11 So, obviously, I was looking for the feasibility of making
12 piposulfan nanocrystals.

13 "Question: Now, based on the experiment as of
14 the point at which you measured the particle size here,
15 was -- were these particles feasible?

16 "Answer: Could you define 'feasible' in a more
17 appropriate manner.

18 "Question: As you read earlier, the title of
19 this page of Sarpotdar Exhibit 3, Bates No. ELANP0007588, is
20 to determine the feasibility of making stable pipo 'N'
21 nanocrystals.

22 "Answer: So the way I'm defining it,
23 feasibility of nanocrystals, I would not call this a
24 success.

25 "Question: Dr. Sarpotdar, you have been handed

Sarpotdar - depo.

1 a copy of United States Patent No. 5,340,564, which has been
2 marked, a copy, as Sarpotdar Exhibit 2. Have you seen this
3 document before?

4 "Answer: I must have, but I haven't seen it in
5 the last 15 years, so I don't recall.

6 "Question: Why do you say you must have seen
7 it?

8 "Answer: Because my name is on it.

9 "Question: Remaining in the same Column 1 of
10 the '564 patent, Sarpotdar Exhibit 2, at Line 37, it's a new
11 paragraph, beginning with 'Shelf stability of nanoparticles
12 also is a problem.' Do you see that, Doctor?

13 "Answer: Yes, I do.

14 "Question: Why is shelf stability a problem?

15 "Answer: I cannot answer in the context of this
16 patent. I can answer in the context of the science that any
17 pharmaceutically trained scientist would know. When you
18 make a product, it doesn't matter if it is good only on day
19 one. Where the patient consumes it, it needs to be good.
20 So stability is a crystal aspect.

21 "Question: What did you mean by the term
22 non-crosslinked?

23 "Answer: Again, I cannot give the legal
24 definition of non-crosslinked. I can give you my
25 understanding of non-crosslinked.

Sarpotdar - depo.

1 "Question: Yes.

2 "Answer: This is one perspective. I'm not
3 necessarily saying this is all-inclusive or all-exclusive,
4 for that matter. To me, chemistry-wise, when cross-linking
5 occurs, the properties of the polymer change. There could
6 be intermolecular bonds within the same molecule or same
7 compound. If there are no intermolecular bonds, then it is
8 non-cross-linked.

9 "Question: And what kind of intermolecular
10 bonds are you referring to?

11 "Answer: Are you asking me a question of
12 chemistry, as my understanding of chemistry?

13 "Question: Yes.

14 "Answer: Okay. So, again, I'm not going to
15 give you a legal opinion here. Just thinking in terms of
16 chemistry, I think there could be any kind of attractive
17 forces. I think one can form covalent bonds or other types
18 of bonds, but anything that is linking two molecules of the
19 same compound, that could be considered cross-linking."

20 MR. JACOBS: For clarity, the exhibits referred
21 to in that deposition testimony were his notebook, which is
22 JX-67, and a patent, which is D-652.

23 Defendants now call Dr. Patrick Soon-Shiong.

24 ... Patrick Soon-Shiong, having been duly sworn
25 as a witness, was examined and testified as follows ...

Soon-Shiong - direct

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DIRECT EXAMINATION

BY MR. JACOBS:

Q. Dr. Soon-Shiong, do you have your pointer there?

A. Yes, I do. Thank you.

Q. Could you please introduce yourself to the jury, now that you are seated and in front of the microphone?

A. My name is Dr. Patrick Soon-Shiong. I am CEO of Abraxis Bioscience and CEO of American Pharmaceutical Partners.

Q. Could you tell the jury a little about how you were raised and how you happened to come to the United States?

A. My parents left China, and I was born in South Africa. And I left South Africa after having graduated as an M.D. and came to this country. First through Canada, then to this country.

Q. Let's talk a little bit about your professional training.

Could we have DX-98 on the screen. DX-98 is your CV, Dr. Soon-Shiong?

A. Yes, it is.

Q. Talk a little bit about your educational background.

A. Well, my degree is M.D., MSc, FRCS(C), and FACS. That is a lot of letters. Let me try to explain some of them to you.

The M.D. degree, is M.B., B.Ch. is the English

Soon-Shiong - direct

1 version of the M.D. degree. So I graduated in 1975 at the
2 University of Witwatersrand then was able to achieve a job
3 in Canada as a surgical resident. And I entered into the
4 Master's of science program and achieved my M.Sc. degree.
5 And while a resident in Canada got recruited to UCLA as a
6 resident, and finished as a surgical resident there, and
7 obtained my Fellow of American College of Surgeons, was a
8 board-certified surgeon in the United States. But at the
9 same time, I was able to be a board-certified surgeon in
10 Canada. So the FRCS(C) in 1983 is the board certification
11 by the Royal College of Surgeons in Canada. And the FACS is
12 a Fellow of the American College of Surgeons.

13 So I am a board-certified surgeon in both Canada
14 and the United States.

15 Q. How old were you when you graduated from medical
16 school, Dr. Soon-Shiong?

17 A. Twenty-three years old.

18 Q. Where did you go after graduating from medical school?

19 A. From medical school, as I said, I was able to receive
20 an offer to go to Canada, Vancouver General Hospital, and
21 the University of British Columbia in Vancouver, Canada.
22 And took my Master's degree in science and also a surgical
23 residency there.

24 Q. How did you happen to come to the United States from
25 that -- what was the next step?

Soon-Shiong - direct

1 A. Well, while I was a surgical resident in Canada, I was
2 fortunate enough to be recruited to the surgical residency
3 program at UCLA. And then I completed my surgical residency
4 at UCLA.

5 I was offered then, while I was a chief
6 resident, an assistant professorship position at the
7 department of surgery in UCLA.

8 Q. What were your duties as assistant professor at UCLA
9 medical school?

10 A. So I was also interested, obviously, in basic
11 research. During that time at UCLA, I had multiple hats.
12 During my surgical residency my mentor and the person who
13 trained me, Dr. Don Morton, who is the world-renowned
14 melanoma surgical specialist, and I did my training, as I
15 said, as a GI certain, what they call a GI surgeon.

16 My area of interest was I did all the pancreatic
17 cancer, the colon cancer and breast cancer procedures at
18 UCLA. But at the same time I also had responsibility to
19 teach and I taught residents and interns.

20 Then the third hat I had is I also had an NIH
21 research grant, an RO1-equivalent research GRANT. And I did
22 basic research lab.

23 So my days were spent, one day in surgery doing
24 gastric surgery, one day doing breast cancer. And the rest
25 in my research lab.

Soon-Shiong - direct

1 Q. Did you work with the pancreas, Dr. Soon-Shiong?

2 A. Yes.

3 Q. Could you tell the jury a little bit about that work?

4 A. From my residency days or intern days, I had a
5 fascination with the organ called the pancreas. While a
6 surgical resident, there was a patient with pancreatitis.
7 We performed the country's first total pancreatectomy and
8 transplantation of that organ into the patients leg so the
9 patient could be relieved of the pain.

10 When I got to UCLA, I was involved in mainly the
11 pancreatic cancer surgery, which is a very technically
12 difficult procedure.

13 Through that interest, I got involved in doing
14 whole organ pancrease transplants for diabetic patients. So
15 the department of surgery, the dean gave me an appointment
16 to the department of medicine, so I could also see diabetic
17 patients.

18 After training to do that in 1986, I did Los
19 Angeles', UCLA's first whole organ pancreas transplants in
20 diabetic patients.

21 Q. Let's go to Page 3 of your curriculum vitae, Dr.
22 Soon-Shiong, and look at some of the recognition you
23 received after you completed some of your formal training.

24 Could you tell the jury about a few of these?

25 A. Well, the recognition was really for a multitude of

Soon-Shiong - direct

1 different activities. One of them was to do with the
2 surgery. And one of them was to do with the science.

3 After doing the whole pancreas transplant, to
4 me, the concern that I had was whether the patient would now
5 have to take rejection drugs antirejection drugs, and,
6 unfortunately, in diabetic patients, if you do a transplant,
7 the antirejection drugs can cause cancer.

8 So you, unfortunately, now substitute one
9 terrible disease with another terrible disease. And an
10 opportunity was to actually avoid rejection drugs if you
11 could encapsulate living cells and inject that into a
12 patient.

13 So I spent time at MIT, and pursued then islet
14 cell transplants or insulin-producing cell transplants.
15 Maybe I will come back to that. I will just identify some
16 of these.

17 The first set is basically the research awards.
18 As a resident, I won the Association For Academic Surgery
19 Award, which is a national award of the United States. I
20 won the Royal College of Physicians and Surgeons Canada
21 Research Award, which is a national award in Canada.

22 I then won the American College of Surgeons
23 Award. Then I entered into my assistant professorship, and
24 I won the NIH New Investigator Research Award.

25 Then, as you said, I did islet and pancreas

Soon-Shiong - direct

1 transplant. And for my work in which we performed the
2 country's first encapsulated islet cell transplant, where we
3 injected just these microcapsules of living cells without
4 the need for antirejection drugs, I won the International
5 Award For Service to Mankind by the Society of Plastics
6 Engineers.

7 As we worked our way into cancer, I was invited
8 by Dr. Hedelbaumus, who was head of NIH then, to speak as a
9 keynote speaker with a vision for the future of both cancer
10 and diabetes work. And as I developed, we developed as a
11 team together this area on Abraxane. And I was awarded by
12 the Gilda's Club of New York the award for the Advancement
13 of Cancer Medicine. This is a club in New York in which
14 together I and Dr. Larry Norton, who was the head of Sloan
15 Kettering, won the word together.

16 Most recently, in 2007, I was awarded the Ellis
17 Island Medal of Honor.

18 Q. The Ellis Island Medal of Honor is awarded to what
19 kind of person, Dr. Soon-Shiong?

20 A. I think it's really for immigrants who actually made a
21 contribution to the country.

22 Q. How many patents are you a named inventor on,
23 Dr. Soon-Shiong?

24 A. About 50 patents.

25 Q. How many publications are you an author on?

Soon-Shiong - direct

1 A. I have about a hundred, over a hundred publications.

2 Q. You mentioned your islet cell work, Dr. Soon-Shiong.
3 Can you describe for the jury how the islet cell work that
4 you did ultimately translated into the initial development
5 efforts for Abraxane?

6 A. It's a span of a decade.

7 Your Honor, may I go up to the board?

8 THE COURT: Yes, sir.

9 (Witness steps down from stand.)

10 A. So I think the issue is how did it connect, the work
11 involving pancreas transplants, how did that get to
12 Abraxane. What is exciting about science, there is always a
13 continuum of thought. The area, I will draw a diagram, this
14 is the pancreas.

15 THE COURT: Doctor, hold on just a second. We
16 are going to mike you up.

17 THE WITNESS: Sorry.

18 THE COURT: That's okay.

19 THE WITNESS: So the area of pancreas transplant
20 and pancreatic cancer is where I started my work. As I
21 said, within the pancreas there is a cell called the islet
22 cell, which secretes insulin. The idea is diabetic
23 patients, unfortunately, have destruction of the cell and
24 the opportunity to transplant this whole organ.

25 Q. Let's break that down. What cell is destroyed?

Soon-Shiong - direct

1 A. This is the cell within the body of the pancreas
2 called the islet cell. So there is two percent gland, it's
3 called the I-S-L-E-T, islet cells. These cells specifically
4 make insulin to secrete into the blood and keep the patient
5 non-diabetic.

6 Q. The problem that you were addressing was the death of
7 those cells?

8 A. Correct. These patients from juvenile, from children
9 on, have a family history of diabetes, have antibodies that
10 attacks these cells. And then these patients then would
11 have diabetes and would inquire insulin. Unfortunately,
12 kidney disease, blindness, and death ensues, despite the
13 insulin.

14 So in 1986, we performed the first whole organ
15 pancreas transplant in a diabetic patient. And then I was
16 made director of the pancreatic transplant program at UCLA.
17 And then we performed the first kidney-pancreas transplant.
18 And so we did the first three patients, and they were highly
19 successful. However, this bothered me because these
20 patients required antirejection drugs, and the opportunity
21 for these patients to convert diabetes to cancer was high.

22 So we came up, then, with a concept, at that
23 point was, if we could take these islet cells out of the
24 pancreas or make human cadaver pancreases and again just
25 extract out these islet cells, and this is when I had UCLA

Soon-Shiong - direct

1 started working, bringing scientists together that were in
2 different fields. So I worked with a scientist at the jet
3 propulsion lab who was working with NASA on magnetic
4 microspheres.

5 Q. Let's just pause for a moment. A jet propulsion lab
6 is what kind of institution?

7 A. It is an institution, clearly a highly scientifically
8 driven, quasi-academic government institution working with
9 NASA to do the Space Shuttle, as you can see now. There is
10 an eminent scientist there, Dr. Alan Limbach, who has since
11 passed away, and was dying of cancer and said he wanted me
12 to take over his work.

13 One of the things he was dealing with was these
14 magnetic microspheres -- let me digress a minute. Putting
15 it on submarines to make submarines stealth.

16 Q. So we are seeing some science in very different areas
17 here?

18 A. Very much so, because those magnetic microspheres, the
19 way to make the submarine stealth is you have proteins cover
20 it and you have -- you'd think it's a whale. It sounds
21 crazy, but that's exactly what it was. I took those
22 magnetic microspheres and put an antibody on to those
23 magnetic microspheres and allowed the antibody to pull out
24 the islet cells. All of a sudden I had an enrichment of
25 islet cells in my hands, which is literally a thumbnail for

Soon-Shiong - direct

1 it. Now you can inject these cells as opposed to a whole
2 transplant. Now you would still be faced with the problem
3 of these patients having these rejection drugs.

4 We then came up with a concept, if we could take
5 these cells and protect them in what we called then a
6 microcapsule, in which these cells would be within the
7 capsule and this insulin, that is inside these cells, would
8 be able to secrete like a tea bag through this capsule.

9 So the only way to do that is to create these
10 cross-links inside this microcapsule. And this material we
11 used was seaweed. So we made a seaweed and we cross-linked.

12 This would serve what we call encapsulated islet
13 cell transplant. This would serve, two things. It would
14 give insulin. We would put an injection, and the body could
15 not get to the cells, so rejection --

16 THE COURT: Doctor, let's see if we can make the
17 sound a little clearer. Put that mike on your tie.

18 THE WITNESS: I am sorry, Your Honor. I will
19 put it closer.

20 Thank you, sir.

21 I will try and speak up. The encapsulated
22 islets, so if we could overcome rejection with a single
23 injection and not do a whole major procedure, this would
24 have been an important innovation.

25 We were excited to say that together with Dr.

Soon-Shiong - direct

1 Felner at the University of Davis, we were able to cure
2 diabetic dogs who were pets of the veterinary school, with a
3 single injection.

4 And we went on in 1993 then to do the country's
5 first encapsulated islet cell transplant at UCLA and at St.
6 Vincent's Medical Center. And we published this in Lancet
7 in 1993.

8 So to me this was a --

9 BY MR. JACOBS:

10 Q. I think the battery may be going.

11 (Pause.)

12 Q. Let's just catch the jury up with what you are
13 describing right now.

14 A. Okay. So we conceived of, developed, successfully
15 developed a cross-linked capsule, which acted like a tea
16 bag, placed living cells in, kept the cells alive. Placed
17 them into the abdominal cavity with a single injection into
18 a patient, literally a ten-minute procedure. Now the
19 patient could have insulin being secreted and the body
20 cells, rejection cells, could not reach the cells to reject
21 it.

22 This was the country's first transplant ever of
23 an encapsulated islet cell.

24 So this, clearly, was to me an exciting moment.
25 And the idea was, now, the problem and the frustration was

Soon-Shiong - direct

1 there were not enough human pancreases to treat a million
2 diabetics.

3 Q. The reason that was important is because the
4 pancreases were the source of the islet cells?

5 A. That's correct, sir.

6 So the next innovation was could we identify
7 within this pancreas the stem cell. So by 1991 to 1992, I
8 applied to NASA, and NASA had, as I said, I was working
9 earlier with NASA, a tissue engineering division in which
10 they wanted to create tissue for Mars and to grow tissue.

11 So I applied for a grant to NASA and received a
12 two-million-dollar grant from NASA and started working on
13 stem cells, in which we could actually grow and proliferate
14 these cells.

15 So you could take one cell, as a stem cell and
16 grow them. What was exciting about that, one then could
17 then have an unlimited supply of cells for mankind.

18 So these cells then actually started to make
19 insulin and died. It made insulin, and died.

20 As these cells grew, they grew rapidly. They
21 made insulin, and they died. This was a puzzle to us. This
22 was the mystery that we couldn't solve.

23 It turns out that at the same time, NASA was
24 also taking albumin up into the Space Shuttle, because
25 albumin was an important nutrient for living cells, to

Soon-Shiong - direct

1 understand the chemical structure of albumin.

2 Then, truly, the light bulb went on. It was,
3 maybe these cells were dying because they needed a blood
4 supply. And if, indeed, albumin was a very important
5 nutrient that these cells were not getting albumin, and it
6 turned out exactly the case, that in order for these cells
7 as they grow, they needed to feed. In order for them to
8 feed, they needed albumin, because albumin brought with it
9 vitamins, fatty acids, nutrients. And we then grew these
10 living cells with blood vessels. And they survived.

11 So --

12 Q. At this point the purpose of feeding these cells the
13 albumin is that you want these cells to flourish. You want
14 them to grow so that they can secrete --

15 A. Insulin.

16 So when you looked at this, we looked at this,
17 and then, if you looked at this itself, while on the one
18 hand we are trying to treat diabetes, this actually looked
19 to me, and I say remember I was working on cancer as well,
20 what I would see when I would see a patient with cancer.
21 That a patient with a cancer had cells that would
22 proliferate and grow. That's how they would spread. And
23 around all the cancer tissue, there would be a huge number
24 of blood vessels. We think we now know its angiogenesis.

25 It dawned upon me, that is what was happening

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1 with cancer biology. As the cancer was spreading, the way
2 that cancer was spreading, it was actually drawing to itself
3 albumin to feed itself to the detriment of the rest of the
4 body.

5 That's why, I believe, we lose weight when we
6 have cancer. You can have the smallest cancer and lose a
7 huge amount of weight because the tumor had a mechanism of
8 extracting all the nutrients to itself. And the key
9 nutrient it was extracting was albumin.

10 So from that, then, came the concept, if,
11 indeed, that were the case, we would be able to then take
12 this albumin and cross-link it, just like my cross-linking,
13 and place within this albumin an amorphous drug, any drug.
14 And now, if that were inside and injected inside the blood
15 vessel, the tumor would, by its natural biology, rapidly
16 pull it out of the bloodstream to itself.

17 To me, that to me was just an epiphany in the
18 sense that the dogma at that time and the dogma still is,
19 frankly, that to give chemotherapy, you just want it in the
20 blood.

21 But to me, the dogma was, you didn't want it in
22 the blood. You wanted it out of the blood. You wanted it
23 rapidly into the tumor cell. How would you get it there?
24 It turns out, the tumor cell was actually asking for it by
25 putting albumin in.

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1 So then if you then could make an albumin
2 nanoparticle, cross-link it, and put inside an amorphous
3 paclitaxel, which would actually dissolve or make rapidly
4 bioavailable, if you then take this albumin and you actually
5 cross-linked it, and made this amorphous, you would then
6 have a particle that could forever change chemotherapy.

7 So by '92, we started developing actually this
8 cross-linked, we started developing this amorphous form.
9 And by 1992, I got invited by the NCI, who had actually
10 invented the taxol --

11 Q. Th CIS is?

12 A. The National Cancer Institute.

13 Q. A government funded, or government organization?

14 A. It is the government organization that is charged with
15 discovering cancer drugs for this country.

16 They had identified taxol since 1970s. The
17 problem is, taxol, the only way they could deliver Taxol was
18 in a toxic solvent Cremophor. And I saw yet another
19 opportunity to better treat the patient without the
20 toxicities, whether with rejection drugs or Cremophor, by
21 putting it into a nanoparticle without Cremophor and more
22 importantly drive it to the tumor.

23 So they introduced us to Bristol Myers, and we
24 created this compound called Capxol. Why was it Capxol?
25 Because it was encapsulated taxol. That was our first

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1 prototype that we handed to Bristol Myers in 1995.

2 So if you look, then, at -- sorry to put my back
3 to you. But 1986, whole organ pancreas transplant. 1991
4 to -- 1989 to 1993 doing islet cell transplant.

5 And by 1991, 1992, understanding the albumin,
6 and creating the first prototype in 1992. And handing the
7 first molecule to Bristol Myers in 1995.

8 While this looks like almost a decade of work,
9 of discontinued thought, it was absolutely connected, that
10 is exactly how science works, you build on your knowledge
11 from one to the other.

12 By this time, we really had a wonderful team
13 working with NASA. We had about 50 scientists here. And
14 around this time is when Neil Desai joined our group. And
15 we evolved that concept down to that concept.

16 So at the end of the day, this then became
17 Abraxane. So this is how diabetes converted to Abraxane.

18 Q. Thank you, Dr. Soon-Shiong.

19 I would like to ask you now to explain to the
20 jury your understanding of how Abraxane actually works in
21 the body?

22 A. Your Honor, I have got a videotape. The way I would
23 like to do it is present the videotape. May I go up to
24 that?

25 THE COURT: You may.

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1 MR. SCHEVE: Your Honor, has a copy been
2 provided for us?

3 THE COURT: I assume that this was all --

4 MR. JACOBS: Absolutely, Your Honor.

5 MR. SCHEVE: I guess it was. My fault.

6 THE COURT: All right.

7 THE WITNESS: What I would like to do, this is a
8 videotape with, actually, not prepared for this case. We
9 had prepared this videotape for the scientists and the
10 doctors at the -- the cancer doctors, because we wanted to
11 explain this new science. This is a total new science with
12 regard to chemotherapy.

13 I think we created this tape around 2003-2004,
14 with the idea that this would be an explanatory tool.

15 So for the purpose of this case -- obviously,
16 that tape was fairly long -- we reduced it to maybe
17 one-fourth of that. All we have done is just put labels,
18 just so that would be clear.

19 What I would like to do is take you through --

20 BY MR. JACOBS:

21 Q. Before you do that, I think it might help if we dim
22 the lights some.

23 A. What I would like to do is take you through this
24 videotape first rapidly so you can see where you are inside
25 the body system. Then replay it slowly to explain how I

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1 believe Abraxane works.

2 So if we could start the tape. What we have
3 here is a solid tumor. As I said, within cancer, one of the
4 things that you see, blood vessels feeding the tumor. We go
5 now rapidly into the blood vessel, as you inject the drug.
6 Now you are inside the blood vessel. And here is the red
7 cell and here is our nanoparticles inside the blood vessel.

8 I will come back to this as we go through it in
9 detail. This is the structure of the nanoparticle. It's
10 amorphous paclitaxel. And in order to contain amorphous
11 paclitaxel, it needs to be cross-linked. This amorphous
12 paclitaxel dissolves once injected. Now you are inside the
13 blood.

14 The question you want to get from there to the
15 other side, this is the blood vessel and the tumor is on the
16 other side.

17 And the amorphous paclitaxel dissolves inside
18 the blood vessel. The question is, then, how does it get to
19 the other side? You are now inside the blood vessel. I
20 will speak a little to this receptor activates. And it
21 creates an elevator, a physical elevator, within the blood
22 vessel wall itself. That's the beauty of this science.
23 This is what the tumor does to extract albumin to itself, so
24 it gets to the tumor .

25 Then the albumin gets into the tumor and feeds

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1 the tumor. However, if we put a drug inside this albumin,
2 it will kill the tumor.

3 So, in a rapid run-through, that was how
4 Abraxane worked. If I may now take you through this a
5 little slower and start it again, Your Honor.

6 So, as I said, one of the ideas is, it's very
7 clear that when you have the tumor, the tumor grows blood
8 vessels around itself. It's called angiogenesis. Why is it
9 doing this? It's doing this to feed itself.

10 So the idea came to us, rather than starve the
11 tumor, which by the way, Avestin and Genentech and other
12 mechanisms were trying to do, kill these blood vessels.
13 Another way to do it is to feed the tumor, but feed the
14 tumor poison. Why this to us was important was, to me, this
15 was ubiquitous to all tumor types, meaning any tumor,
16 whether breast, lung, pancreatic, would actually have this
17 mechanism.

18 You are then now inside the blood vessel. Now,
19 when you are inside the blood vessel, as you inject this
20 particle, it has to be small enough, the nanoparticle has to
21 be small enough for many reasons. One, small enough so it
22 can get through a sterile filter. A sterile filter is 220
23 nanometers. So it needs to be below that so you can
24 actually filter this and you can inject this into human
25 beings, because you cannot sterilize albumin. If you

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1 sterilize albumin you would actually destroy it. The only
2 way to sterilize it is put it through a filter and remove
3 any contaminants.

4 The other reason you need it to be small enough,
5 so you can get it into the smallest blood vessel. This is a
6 single red blood cell inside the blood vessel.

7 As you can see, a nanoparticle is 1/80th the
8 size of a single red blood cell.

9 There is a tremendous challenge here. You
10 needed to make it small. You needed to make it stable. And
11 you needed to keep it so that you can actually filter it.

12 The particle is injected, and let me now explain
13 to you the structure of this particle.

14 In order for us to accomplish that goal of
15 making it small enough, and yet when it gets in to rapidly
16 dissolve, you needed to make the paclitaxel amorphous.

17 As we described in our papers, that in order to
18 make this dissolve, it needs to be amorphous, like cotton
19 candy. If you made it crystalline, you would actually
20 design it not to dissolve, like rock candy, just to stay
21 there.

22 So we had two different paths. We wanted ours
23 to dissolve rapidly and not stay inside the blood. So,
24 therefore, ours had to be amorphous, not crystalline. But
25 because it's amorphous, you had to contain it. And the only

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1 way to contain it, you could put it with the albumin, but
2 you need to cross-link the albumin.

3 So this was the albumin cross-linked, like a
4 weave.

5 And this contained the nanoparticle in its
6 cross-linked form.

7 But then the albumin would actually be able to
8 now see these receptors.

9 So once injected, it would then go and rapidly
10 dissolve. So here is the amorphous nature, taking in space,
11 now you have paclitaxel and albumin together.

12 Now the question is, how does it get out?

13 Well, what it does, it now seeks -- how does it
14 go from here magically to here? We needed to cross this
15 physical blood vessel wall. The way it does that is it
16 seeks out on the inside of the blood vessel a receptor. If
17 you could hold this right here. Now we are inside the blood
18 vessel. It is dissolved. It turns out that this thing
19 called a gp60 receptor is overexpressed in cancer. By that
20 we mean, as these cancer cells grow and these blood vessels
21 grow around it, these blood vessels are a little abnormal.

22 What they do, they actually express all these
23 little receptors, so it can pull albumin to itself.

24 What is exciting to us, then, we have now a
25 tumor-selective mechanism. It goes to the tumor, not to the

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1 rest of the body, so we can reduce the toxicity, increase
2 the tumor concentration, increase the efficacy, by virtue of
3 this interaction between this albumin and this receptor that
4 the tumor overexpresses.

5 So what happens when it actually locks in here?
6 It then activates this key called caviolin-1. Once it
7 activates this key, it opens the elevator door, and in comes
8 all the albumin molecules, and it goes through. It
9 literally physically creates this hole called a caviolin.
10 It literally creates this hole, and physically transports it
11 to the other side.

12 This occurs literally within minutes of
13 injection. So to us, this was what I considered the
14 transforming event for chemotherapy, because now, rather
15 than the dogma of keeping it in the blood, the transforming
16 event is to get it out of the blood because if you want to
17 kill a cancer, you don't want it there. You want it here.

18 And you want it here rapidly.

19 We achieved that through this mechanism. Now it
20 gets to the tumor cells, and when it gets to the tumor
21 cells, this fatty acid membrane takes this albumin, unlocks
22 the drug, takes it into its nucleus, and shrinks the tumor
23 rapidly.

24 So that is the mechanism of Abraxane. And by
25 supplying the tumor with albumin-bound nanoparticles, this

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1 is what we had approved first in breast cancer.

2 BY MR. JACOBS:

3 Q. Thank you, Dr. Soon-Shiong. You can resume your seat.

4 (Witness resumes stand.)

5 Q. I need to bring you now to the specific patent issues
6 in this case. You became aware of Elan's '363 patent
7 sometime toward the end of August 1996. You followed Elan's
8 technology over the years.

9 Do you believe that Abraxane infringes the '363
10 patent?

11 MR. SCHEVE: Objection, Your Honor, to there
12 being no foundation for this witness to express an opinion
13 without a foundation about even the claim construction terms
14 that Your Honor has provided.

15 THE COURT: Please, Mr. Jacobs.

16 BY MR. JACOBS:

17 Q. Did you form a judgment at that time, did you form an
18 opinion yourself, when you have seen the '363 patent,
19 whether you were infringing that patent?

20 MR. SCHEVE: Same objection, Your Honor.

21 THE COURT: I don't have to tell you how to do
22 this, Mr. Jacobs, you have to establish that he has seen the
23 '363 patent and he is familiar with the claims.

24 BY MR. SCHEVE:

25 Q. Did you see the '363 patent?

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1 A. Yes.

2 Q. Did you form a judgment about whether Abraxane and
3 whether Abraxis would be infringing it?

4 A. Yes.

5 Q. What was that judgment?

6 A. I was very clear, not at all.

7 Q. Why is that? What was the basis for that belief?

8 A. Well, firstly, our design was totally opposite,
9 clearly, I think, as I tried to express. Maybe it would be
10 easier if I may just go to two pictures on that to express
11 that, if I may.

12 (Witness steps down from stand.)

13 THE WITNESS: Sorry, Your Honor. Our design was
14 such that we wanted our drug rapidly out of this, rapidly
15 out of the system.

16 So from a purpose or focus of our design is we
17 wanted our drug rapidly out. My understanding of Elan's
18 strategy is they wanted to prolong the drug inside the
19 vascular system, 180-degree opposite strategy.

20 In order for us, however, to get our drug out
21 rapidly, the only way we could get out rapidly is by
22 designing an amorphous system. The only way they could get
23 it to stay inside the drug for a long time is to keep it
24 crystalline. So the crystalline nature and the amorphous
25 nature achieves two direct opposite purposes. And if I may,

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1 then, show it.

2 So we wanted it amorphous so we can get it out.
3 They wanted it crystalline so they could keep it in. And in
4 order for us to make it, keep it amorphous, we needed to
5 keep it cross-linked. They had theirs non-cross-linked.

6 So if one is amorphous, the other is
7 crystalline, the other is cross-linked, another one is
8 non-cross-linked, to me, it was very clear. These were two
9 different paths, two different missions.

10 BY MR. JACOBS:

11 Q. Thank you.

12 (Witness resumes stand.)

13 Q. You mentioned in the first part of your remarks the
14 contact you had with Bristol Myers Squibb in 1995. Can you
15 describe that contact and what came of it?

16 A. Yes. The NCI introduced us to Bristol Myers Squibb in
17 1992-1993 time frame. They gave us paclitaxel. It was a
18 rare opportunity for us to get our hands on the paclitaxel.
19 We made the nanoparticle, provided it to Bristol Myers.
20 They tested it. And they found it to be active. And then
21 turned around and said, unfortunately, they didn't believe
22 we could manufacture this.

23 So nobody ever manufactured a human protein
24 nanoparticle in large scale. We are talking about
25 kilograms, thousands of grams of paclitaxel and nobody had

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1 ever done this on a commercial scale. And they declined.

2 Q. How did that affect your plans or thinking about the
3 development of Abraxane?

4 A. It was a very, very difficult time for us, because we
5 now had 50 people. And the choice to us was, do we drop
6 this drug? And we did not have expertise in scale-up or
7 large scale-up as a pharmaceutical company.

8 So we had to make a choice, and I took the
9 choice of taking the risk at that point, and approaching a
10 company in Chicago, owned by the Japanese, that had the
11 largest plant in the United States that did all anticancer
12 drugs, a large number of FDA approval for injectables. And
13 they had this plant in Chicago with 500 people. But they
14 were losing a million and a half a month, truly losing
15 money.

16 They wanted to sell this plant. They put it up
17 for sale with JP Morgan. And I had to convince investors to
18 say, please buy this plant, it's losing one and a half
19 million a month, because it is important for me to figure
20 out a way to scale this and manufacture this because we
21 cannot let this go.

22 So we went ahead and, this is what became APP.

23 Q. And APP was a predecessor company to Abraxis?

24 A. Well, it was the other way around. Abraxis owned the
25 technology. We created within Abraxis a subsidiary called

Soon-Shiong - direct

1 APP. And the purpose of APP was solely to take in
2 injectable drug expertise and invent new scale-up
3 technologies so that we could scale this.

4 They had about 500 people. So by 1998, we had
5 about 550 people in our organization.

6 Q. What was the next major milestone in the development
7 of Abraxane?

8 A. So the next major milestone was, obviously, a full
9 commercial, we actually succeeded in scaling this up very
10 rapidly. And then filed an IND with the FDA. We met with
11 the FDA around 1996. And we filed the IND with the FDA,
12 having completed all the animal safety studies, the
13 scale-up, the stability lots. And filed the IND in 1998.

14 Q. What does the IND allow you to do once it's approved?

15 A. The IND allows you to do the first patient testing,
16 because what we wanted to do was actually increase the dose.
17 Taxol can only be given at 175 milligrams because of the
18 toxicity of the Cremophor. We wanted to give 300 milligrams
19 of paclitaxel, same drug, because we didn't have Cremophor,
20 and more importantly, we felt we could get more drug into
21 the tumor.

22 So the Phase 1 was actually to address this
23 question, could we safely get to 300 milligrams?

24 Q. What kind of patients did the FDA allow to be treated
25 with Abraxane in the Phase 1 study?

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1 A. The Phase 1 study is designed such, unfortunately,
2 these patients have no more choices. These are last-resort
3 patients who have had every chemotherapy administered to
4 them. So our Phase 1 study was performed at MD Anderson, a
5 large cancer center in Texas. There we had patients, our
6 first set of patients, patients with melanoma and patients
7 with breast cancer. These patients with melanoma and breast
8 cancer had gone through every chemotherapy available to them
9 and then went on to our drug.

10 What is very exciting is we got to this high
11 dose and not only did we stabilize these diseases, we
12 actually had patients improve and regress the tumor in the
13 Phase 1, both melanoma and breast cancer patients.

14 Q. Then what was the next step?

15 A. The next step was to go to Phase 2. Now that we had
16 established that we could get to 300 milligrams safely, we
17 now needed to say, okay, which cancer would we now attack
18 first. And I wanted to attack breast cancer first. The
19 reason for that is that this Cremophor in Taxol had a black
20 box that women may survive the breast cancer, get the drug,
21 and die from anaphylaxis.

22 Q. Anaphylaxis is?

23 A. Anaphylaxis is an allergic reaction to this Cremophor,
24 such that patients would need steroids, and despite
25 steroids, in the black box of the FDA of taxol, despite

Soon-Shiong - direct

1 steroid medication, the patients may die from anaphylactic
2 reaction. To me, that was a tragedy. You would survive your
3 cancer and die from an allergic reaction to a chemical that
4 is added. So we decided, we should first go after breast
5 cancer.

6 So we went after breast cancer first, where we
7 would take patients first that were in what we call first
8 and second lines of chemotherapy with 300 milligrams, as we
9 described.

10 Q. That was the Phase 2 study?

11 A. That was the Phase 2 study. It's a memorable moment
12 for me, because the first patient was actually our employee.
13 And this was the 300 milligram per meter squared, never been
14 done before. As you recall, I acquired this company with
15 500 employees. And my top marketing person came to me and
16 said, I have breast cancer throughout my body. Please, put
17 me on your trials as your first patient.

18 She had failed chemotherapy. We put her on our
19 trial as our first patient, 300 milligrams, and she had a
20 complete response. She lived seven years from that.

21 Q. Could you describe the Phase 3 study, please?

22 A. We then went on to do, now that we knew that we could
23 do it not only safely, we actually showed we had a 64
24 percent response rate in our Phase 2, a remarkable response
25 rate. So to actually scientifically prove that, we then

Soon-Shiong - direct

1 needed to take taxol and Abraxane and do head-to-head
2 studies in breast cancer and compare them.

3 So we did taxol and Abraxane head-to-head
4 studies. Not only did we prove what we proved in Stage 2,
5 that we actually doubled the response rate when compared to
6 taxol. We had no adverse reactions in terms of anaphylaxis,
7 despite not having to give any steroids. And more
8 excitingly, we actually statistically improved survival with
9 the same drug. So that to us was the Phase 3, which allowed
10 us to get approval.

11 Q. You got approval in January 2005?

12 A. Correct.

13 Q. Then once you have approval, you can actually market
14 and sell the drug on the market, as it were?

15 A. That's correct.

16 Q. Have clinical trials continued for Abraxane since
17 then?

18 A. Yes. As I said, the opportunity for this drug now is
19 not limited to any one cancer, because all cancers need to
20 feed or die.

21 So we went then after lung cancer, we went after
22 all the cancers. We believe that there are huge unmet
23 needs, meaning that we have not yet been able to, as
24 physicians and oncologists, attack these diseases, lung
25 cancer, melanoma, pancreatic cancer.

Soon-Shiong - direct

1 As some of you may know, these are cancers for
2 which, unfortunately, we have made very little progress.
3 Lung cancer, the response rate is only like 16, 15 to 16
4 percent, no matter what drug you give.

5 Q. For existing drugs?

6 A. Correct. For existing drugs.

7 So we did this first in lung cancer and
8 presented it in ASCO, we got 50 percent rate.

9 Q. ASCO, what is that?

10 A. ASCO is the largest collection of doctors,
11 oncologists, in a meeting together every year. They just
12 had one in Chicago, 30,000 oncologists come together, where
13 we share scientific, clinical information. And I think
14 around 2004, '5, I forget, '6, that time frame, we presented
15 our lung cancer data.

16 We also then did trials in patients who were
17 actually growing their tumor in breast cancer while on taxol
18 and while on paclitaxel, and then gave them Abraxane, and
19 they responded.

20 We then also did trials in patients with
21 melanoma, where there is no treatment, unfortunately. And
22 we doubled the progression-free survival, the time before
23 they got a recurrence when compared to other drugs.

24 Now most excitingly, we have done this in
25 pancreatic cancer. Now we have patients with pancreatic

Soon-Shiong - direct

1 cancer with a 70-percent response rate. Some of the work
2 was done at Johns Hopkins and University of Arizona, and I
3 think 14 to 15 consecutive patients now had a response rate
4 with pancreatic cancer.

5 Q. Where do you see this for the future? What is the
6 future for Abraxis in your view, Dr. Soon-Shiong?

7 MR. SCHEVE: Objection. Foundation.

8 THE COURT: Overruled.

9 THE WITNESS: I got to tell you, I just came
10 back from ASCO last week. I was in ASCO, and the
11 investigators met with me privately in the room to share
12 with me the results on pancreatic cancer. They were so
13 overwhelmed by the findings of 77 percent. They feel that
14 by adding one more drug, and we designed their protocol now,
15 in combination with Abraxane, we could eradicate pancreatic
16 cancer. To me, that would be the most exciting thing we
17 could have contributed to.

18 But I think what is truly exciting is that not
19 just paclitaxel, this is other drugs that we can put into,
20 and more importantly, it's available not just for one cancer
21 but a broad range of cancers, whether it be breast, lung,
22 melanoma, head and neck cancer, pancreatic cancer.

23 MR. JACOBS: Thank you very much. No further
24 questions.

25 THE COURT: Mr. Scheve.

Soon-Shiong - cross

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CROSS-EXAMINATION

BY MR. SCHEVE:

Q. Sir, could I just make a couple marks on your chart. 1986, what did you say this reflected?

THE COURT: I think you need a particular type of marker.

MR. JACOBS: Could we mark the version of it as is as an exhibit?

THE COURT: You can do it all.

MR. JACOBS: We have captured it as of this moment, noon. Now Mr. Scheve can work with it.

THE COURT: Have at it, Mr. Scheve.

CROSS-EXAMINATION

BY MR. SCHEVE:

Q. You were describing these dates, Doctor. What was 1986?

A. 1986, '87, I think, when we did the first West Coast pancreas contrast transplant, at Los Angeles, at UCLA.

Q. '89-'93?

A. 89-'93 is when we were working on understanding developing a cross-linked capsule for islet cells.

Q. This is pancreatic islet cells?

A. Correct, as well as understanding the area of proliferation cells in albumin.

Q. '91 to '92, what was that, sir?

Soon-Shiong - cross

1 A. That was my insight into working with jet propulsion
2 lab working with monodispersion, knowing particle size
3 matters is important with regard to nanoparticles, working
4 with that. And also working on albumin and working on the
5 proliferation stems cells.

6 Q. Stem cells?

7 A. Correct.

8 Q. 1992, what was that?

9 A. Same. I am sorry. I have repeated myself. That was
10 all in that same time frame, working on albumin,
11 understanding the concept that albumin actually will maybe
12 feed the proliferating cells.

13 Q. Here you wrote 1992 taxol, is this when you began your
14 work with paclitaxel, in '92?

15 A. We began our work before that. That's when I went to
16 the NCI conference. I was first invited to the NCI
17 conference because we were working on taxol.

18 Q. When did your work with taxol begin?

19 A. I think, as I said, probably around 1990, 1991.

20 Q. 1991?

21 A. In that time frame. I know it was before the '92
22 conference because, obviously, we were invited because we
23 were working on taxol. I would say roughly 1990 to 1991.

24 Q. Now --

25 A. When I say working, we didn't have the raw material.

Soon-Shiong - cross

1 We may have got some from some -- you can buy chemical
2 grade, non-pharmaceutical grade material. In 1992, the
3 importance of the NCI is they introduced me to Bristol Myers
4 so I could get the material as being used in man.

5 Q. This islet research, actually, those people that got
6 the implants, there were deaths that occurred. Correct?

7 A. No.

8 Q. Where is this today? Has it gone anywhere?

9 A. No -- well, gone anywhere? There were two reasons.
10 One, the limitation -- islet cell transplant, the NIH
11 actually then stepped forward and said islet cell transplant
12 is now an established procedure and actually created seven
13 centers in the country. However, because of this capsule
14 and the ability to get enough cells -- patients now have
15 been cured of diabetes with islet cells.

16 Q. My question was, in terms of your research today, did
17 you get rid of that part of your business?

18 A. No, I did not.

19 Q. What was that business called? You formed a company
20 called VivaRex. Correct?

21 A. Correct.

22 Q. Did VivaRex only deal with cancer?

23 A. There were two organizations, one was VivaRex Diabetes
24 and one was VivaRex Pharmaceuticals.

25 Q. Did VivaRex Diabetes have this islet specimen

Soon-Shiong - cross

1 research?

2 A. Correct.

3 Q. Where is VivaRex Diabetes today?

4 A. That is now disbanded because the problem was
5 developing stem cells. But the other problem, the most
6 important problem, was the alternative other than stem
7 cells, but to actually put pig cells.

8 Unfortunately, in 1998, there was a discovery
9 made that within pigs there is a virus equivalent to the
10 AIDS virus called the perv virus.

11 We had the country's first FDA approval to go
12 from using pig cells into man. But I worked with the FDA to
13 say we should ethically shut this down because there is no
14 way for us being able to prevent the transmission of pig
15 viruses into man. As you may know, about the issue of SARS.
16 In 1998, I participated on the FDA biological board to
17 actually establish new standards for safety of pigs to man,
18 and they shut down in vivo transplants in the United States
19 as a result of that. Correctly so.

20 The irony of that is, because of that work, we
21 now as a company, APP, are the only supplier of Heparin to
22 the United States, this blood thinner, because it comes from
23 pigs. And we've established with the FDA a safe supply
24 chain starting in 2000, 2005. As a consequence, the irony
25 of all of this is that science prevails, we now have the

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1 only safe supply of Heparin through APP in the United States
2 as a result.

3 Q. So this VivaRex Diabetes is no longer in the picture.
4 Correct?

5 A. I will personally continue this work on the stem cell.
6 But --

7 MR. SCHEVE: Your Honor, may I ask that he
8 answer my question.

9 THE COURT: He is answering the question.

10 THE WITNESS: The answer is correct. VivaRex
11 Diabetes company, that is no longer here.

12 MR. SCHEVE: Your Honor, may I approach?

13 THE COURT: Yes, sir.

14 (The following took place at sidebar.)

15 MR. SCHEVE: He has opened the door to talking
16 about quality issues. There have been at least 20 notices
17 sent to his company about quality issues. I didn't ask him
18 about any of that. He has now talked about how they are the
19 only this, that or the other of Heparin. I have got all
20 kinds of evidence about how they have gotten warning letters
21 from the FDA, et cetera. I don't want to go into it. But
22 when he opens the door like that, it puts me in a really
23 awkward position.

24 MR. JACOBS: Your Honor, he was tying it all up
25 to the Heparin side, which is APP. That discussion was not

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1 a general claim about Abraxane.

2 THE COURT: I disagree, Mr. Scheve. I am going
3 to deny your request to get into this area. I don't think
4 he has opened the door. I think it has been confined to
5 Heparin. Not even insofar as his conversation about
6 Heparin -- he is talking about AIDS, I think, as I
7 understand it.

8 MR. SCHEVE: The Heparin is the thing that was
9 the subject of a TV thing the other night. Actually, they
10 have been criticized for raising their prices 12 fold. That
11 was the controversy. So now he has stuck his foot into it.
12 I don't want to go there. It is these gratuitous answers
13 that put me in a position --

14 THE COURT: As you know, and I am sure have
15 observed, trying to be as vigilant as I can, without getting
16 too much into both cases to council the witnesses to be more
17 responsive.

18 I am trying to be mindful of the fact that these
19 are scientists and these are difficult questions, all the
20 time not capable of yes-or-no answers. I certainly
21 commiserate with your frustration with the last witness. I
22 don't think that is this witness' tendency; if it proves to
23 be, I will get involved.

24 MR. SCHEVE: That is all I ask. Thank you.

25 (End of sidebar conference.)

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1 BY MR. SCHEVE:

2 Q. Sir, in terms of this lawsuit, are you listed as an
3 inventor on a patent that covers Abraxane?

4 A. Yes, I am.

5 Q. Do you have a single lab notebook that relates to
6 that, sir?

7 A. No, I don't.

8 Q. Not a single one?

9 A. Well, I have lab notebooks. But I don't have lab
10 notebooks until the time I started working with this. I had
11 50 scientists under me, they took notes, I presented the
12 work to them. They took notes and copiously maintained the
13 notes.

14 Q. No lab notebooks were produced for me. And I wanted
15 to confirm, do you have any lab notebooks reflecting your
16 work with the development of Abraxane?

17 A. I think I just answered you, at that time I had 50
18 scientists under me, they kept the notes. I didn't keep my
19 own per se.

20 Q. Just so the jury understands, sir, do you still own 80
21 percent of that entity known as Abraxis?

22 A. Yes, I do.

23 Q. And what is the market cap on that company today?

24 A. I think in excess of 2 billion.

25 Q. The last I looked at it, it was around 2.68 billion.

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1 Would that sound reasonable?

2 A. Yes.

3 Q. Is Abraxane the only product that Abraxis markets?

4 A. Currently, yes.

5 Q. You would own an 80 percent interest in that company
6 that has that capitalization; is that correct?

7 A. That's right.

8 Q. Now, did your company recently market a generic
9 version of a product that's sold by my client Elan?

10 A. It may have. It's launched 70 generic drugs in the
11 seven years that we acquired the company. In 1998, from
12 then to now, we have the largest numbers of FDA approvals in
13 the history of this country. We have ten approvals a year
14 of generic drugs.

15 Q. Generic drugs are drugs that others had developed and
16 they reached a point regulatorily where people could then
17 come in and make a generic version. Is that correct?

18 A. That's correct.

19 Q. Now, your company actually sued the FDA, did it not,
20 sir, to prevent another company from coming onto the market
21 with a generic form of taxol?

22 MR. JACOBS: Objection, Your Honor.

23 THE COURT: Basis?

24 MR. JACOBS: Relevance.

25 THE COURT: Do we need to go to sidebar?

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1 MR. SCHEVE: If you would like, Your Honor.

2 THE COURT: We should probably address the
3 relevance issue out of the presence of the jury.

4 (The following took place at sidebar.)

5 THE COURT: What is the relevance?

6 MR. SCHEVE: It goes to two things, Your Honor,
7 the testimony, I am going to paraphrase, about saving lives,
8 this, that and the other, when they have taken affirmative
9 steps to prevent competition.

10 In opening statement, there was discussion about
11 motivation from my clients bringing this lawsuit. This goes
12 directly to their effort to prevent by seeking to invalidate
13 my patents and trying to keep others off the market from
14 succeeding.

15 So the fact they have sued to prevent
16 competitive taxol products goes to the very heart of his
17 credibility.

18 MR. JACOBS: I don't think so, Your Honor. I
19 actually confined his direct testimony very directly to the
20 development of Abraxane. We did not get off into other
21 topics. This is a complex world. The jury could be very
22 confused by cases brought in other contexts. I don't see
23 the relevance to the basic story about Elan's motivation in
24 bringing this lawsuit.

25 THE COURT: What was the point you made about

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1 the comment in opening?

2 MR. SCHEVE: The whole motivation issue about
3 why this lawsuit was brought, and if they are able to make
4 comment, either through Dr. Desai, talking about how, you
5 know, it bothered him, et cetera, or to suggest in any way
6 that this lawsuit was brought for inappropriate reasons,
7 then the fact that they are out trying to prevent people
8 from coming on the market clearly goes to show that the
9 conduct that I am accused of or my client is no different
10 than the conduct that they are engaged in.

11 THE COURT: How far down this road do you
12 propose to travel?

13 MR. SCHEVE: About three questions. You sued to
14 prevent this from happening? Depending upon whether it's a
15 yes or no answer, if he says yes, we did, I will move on.
16 If I hear about Abraxane --

17 THE COURT: I will give you a very small, small
18 amount of leeway on this, because I don't want to get off
19 into completely collateral material.

20 (End of sidebar conference.)

21 BY MR. SCHEVE:

22 Q. Do you have my question in mind, sir?

23 A. Could you repeat it?

24 Q. I will be happy to. Isn't it true that Abraxis
25 brought a lawsuit against Donna Shalala and the FDA to

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1 prevent a generic form of taxol coming on the market?

2 A. I didn't.

3 Q. Would that generic have been competition to you, sir?

4 A. When you say "competition," at the time of the
5 lawsuit?

6 Q. Generics result in cheaper products for consumers who
7 have cancer. Right?

8 A. We --

9 THE COURT: All right. Pose the question. Was
10 that a question?

11 MR. SCHEVE: Yes, sir. I said "don't they."

12 BY MR. SCHEVE:

13 Q. Isn't it true, sir, that generics provide a cheaper
14 alternative for folks that are suffering from cancer?

15 A. That is true.

16 Q. Now, sir, there has been some discussion in this
17 lawsuit about a presentation that occurred at the Cleveland
18 Clinic.

19 Do you recall that?

20 A. Yes, I do.

21 Q. Was that in 2004?

22 A. Yes, it was.

23 Q. Approximately what month, sir?

24 A. Around October-November. I can't recall. But it was
25 in the last months, just before Abraxane was about to be

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1 approved.

2 Q. October-November of 2004?

3 A. I think so.

4 Q. Thank you.

5 I am making reference here to a slide from Joint
6 Exhibit 079.

7 Doctor, you are lucky, you get a small notebook
8 compared to some other folks.

9 A. Thank you. What number is this, Mr. Scheve?

10 Q. Joint Exhibit 079, if you like to look at it.

11 My question is, is this one of the slides that
12 you presented at that Cleveland Clinic presentation?

13 A. Yes.

14 Q. Is this a sort of montage of different images that
15 related to Abraxane?

16 A. Yes.

17 Q. Is this here, where it says negative charge zave
18 equals 130 nanometers; does that purport to be a cartoon or
19 caricature of Abraxane particles?

20 A. Yes.

21 Q. Is this a bottle of Abraxane?

22 A. Yes.

23 Q. The image here, what is this?

24 A. That's, again, another cartoon we use for
25 demonstrative purposes.

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1 That is, I think it's a sort of touch-up of an
2 electron micrograph as a cartoon.

3 Q. An electron micrograph?

4 A. Yes.

5 Q. Of Abraxane?

6 A. I am not sure whether that itself is Abraxane or not.

7 Again, it is a cartoon representation. All these are
8 cartoon representations.

9 Q. They are all cartoons?

10 A. Yes.

11 Q. But this is supposed to all deal with Abraxane.

12 Correct?

13 A. Yes.

14 Q. Actually, that image that you used there was also used
15 by Abraxis in other presentations. Correct?

16 A. So that's what we used as a representative cartoon,
17 yes.

18 Q. That is a cartoon?

19 A. Well, this is an electric micrograph. The picture
20 before was the touch-up colorization to generate this as a
21 cartoon.

22 Q. You agree, sir, this is a micrograph of that same
23 image or something that looks like that same image in 1997?

24 This is Joint Exhibit 013.

25 A. I am sorry, you confused me, Mr. Scheve.

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1 Q. Right. Maybe I need a pointer.

2 Do you see this image here, sir?

3 A. Yes.

4 Q. That's Joint Exhibit 079.

5 Now I am going to take you forward to this
6 presentation sometime after April of 1997. Do you see this
7 image?

8 A. Yes.

9 Q. If you could look at Page 8 of Joint Exhibit 13 and
10 just confirm for me that that image was contained in that
11 presentation in 1997.

12 A. Can you give me some time just to look at this
13 presentation itself?

14 Q. Sure.

15 A. You are trying to get me to compare two presentations,
16 is that the gist?

17 Q. I just want you to look at the images, is all. You
18 take whatever time you need, with the Judge's permission.

19 (Pause.)

20 A. Yes, I see it.

21 Q. Same image?

22 A. Same image in this presentation?

23 Q. Yes, sir.

24 A. Yes.

25 Q. As this image that is here and that you were using in

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1 2004.

2 A. I presume, it looks like it. That is exactly what is
3 used as the cartoon, yes.

4 Q. Let's go forward. In fact, that image was being used
5 in presentations in 1996 by Abraxis, was it not? If you
6 would look at Joint Exhibit 026.

7 A. Yes.

8 Q. And if we go forward, this product that you wrote up
9 there where you wrote Capxol, C-A-P-X-O-L?

10 A. Right.

11 Q. Was this image here used to describe Capxol
12 encapsulated taxol?

13 A. Again, it's not necessary to describe Capxol. It's a
14 cartoon demonstration of the concept of particles,
15 nanoparticles, microparticles.

16 Q. Cartoon?

17 A. It's -- I don't know how to describe it to you. It's
18 the best way for a visual layperson to understand what we
19 are trying to do. As opposed to a scientific document.
20 This is not a scientific document. This is a visual for a
21 layperson.

22 These brochures are put together for laypeople,
23 for people about to invest in the company and people to
24 make, get an understanding. Sometimes I make these
25 presentations to doctors. Sometimes I make these

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1 presentations to nurses. Sometimes I make these
2 presentations to investors.

3 So we use this generic version, as you can see,
4 we pulled the same picture up all the time. Sometimes you
5 put color on it. Sometimes we make it black and white. I
6 suppose the best way to describe it is, it's merely a
7 cartoon. I don't know how to describe it, other than the
8 fact it is merely a demonstration.

9 Q. When you say you make presentations to investors, you
10 are trying to convince people to buy into your view of this
11 technology. Is that correct?

12 A. Yes. As I said, we had a vision that was so different
13 from the standard dogma of chemotherapy, nobody had ever
14 made a nanoparticle of this type before. A large company
15 like Bristol Myers declined taking the chance.

16 We needed to convince people to follow our
17 vision.

18 Q. Now, sir, actually, this article, written by Kenneth
19 Suslick and Mark Grinstaff, published in 1990 has this image
20 in it, doesn't it, sir?

21 A. Yes.

22 Q. I think you told us that your work didn't begin until
23 around 1991 with taxol?

24 A. With taxol, but you didn't ask me about proteins.

25 Q. But I am talking about paclitaxel nanoparticles.

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1 A. Well, I said, you know, I can't recall when exactly we
2 got the raw material. It was very difficult to get -- there
3 is an organization called Sigma. Sigma is an organization,
4 all scientists understand, that you go buy these poor-grade
5 materials to work with. I can't recall when we got that
6 material. I can recall when we got the material from
7 Bristol Myers. I said, it was between 1990-'91 that I think
8 we got the material from Sigma.

9 Q. Dr. Desai didn't graduate from Texas until sometime in
10 1991. Correct?

11 A. Right. Well, I was doing the work with regard to my
12 nanoparticle and with the albumin and the stem cells and
13 proliferation cells and cross-linking before I met
14 Dr. Desai.

15 Q. Let's make sure the record is clear. We have no lab
16 notebooks from you and the only notebooks, lab notebooks we
17 have are from Dr. Desai -- and he didn't graduate from Texas
18 until 1991. Correct?

19 A. Correct.

20 Q. I have an article here from 1990. Is your name on
21 this article?

22 A. No, it is not.

23 Q. Is this the image that is found in that Suslick
24 article?

25 A. Yes.

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1 Q. Dated 1990?

2 A. Yes. Suslick was a consultant to me. Ken Suslick
3 worked with me. I am not sure whether just before Neil
4 Desai or after Neil Desai. But Ken Suslick and Mark
5 Grinstaff were my two collaborators, scientific
6 collaborators. He was at the University of Chicago Urbana.
7 And I was working with MIT. I was working with jet
8 propulsion lab. I first working with Urbana. I was working
9 with scientists across the country. This is one of these
10 papers. In fact, I recognize this paper. It's a jacks
11 paper that he presented.

12 Q. That Dr. Suslick published in 1990. Correct?

13 A. Correct. And he is a co-inventor of one of our
14 patents.

15 Q. Sir, do you see any similarities between this image
16 here that is used in '96 and '97 all the way up to 2004 in
17 your Abraxis/Abraxane promotional materials? I am talking
18 about the one on the left, and the image that is on the
19 right from Dr. Grinstaff's article?

20 A. They are similar. They are not exactly the same,
21 obviously. You can see the two Mickey Mouses. The two
22 little ones. The answer is, they are similar, yes.

23 Q. So they are similar. They do look similar, don't
24 they, sir?

25 A. Yes. I think, obviously -- sorry.

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1 Q. Who doctored the images to take out the smaller ones
2 here that were aggregating with the larger images? Who
3 doctored that photo?

4 A. This was probably done by the IT department, as I
5 said, to colorize it.

6 Q. IT at what place, sir, which entity?

7 A. I don't remember. You said who doctored it, I don't
8 know. You are trying to connotate a negative -- this is a
9 cartoon. Nobody doctored it. They actually colorized it,
10 as I told you, to make it a cartoon. They may have not
11 liked the fact, to make it clear -- I don't know who -- I
12 can't recall.

13 Q. A cartoon.

14 Let's go back to Dr. Grinstaff's publication.

15 Dr. Grinstaff and Dr. Suslick. Now, sir, isn't
16 it true that this image that they have designed as Figure 1
17 actually is a scanning electron micrograph of a dodecane
18 filled proteinaceous microcapsule with an average particle
19 size of 2.5 microns, and that this microcapsule was using
20 bovine serum albumin?

21 A. That's correct.

22 Q. There isn't even a drug in those microcapsules, is
23 there, sir?

24 A. That's correct.

25 Q. Now --

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1 MR. JACOBS: Your Honor, I object to this whole
2 line of questioning.

3 THE COURT: Okay.

4 (The following took place at sidebar.)

5 THE COURT: What is the basis of the objection?

6 MR. JACOBS: Relevance. Prejudice.

7 THE COURT: Well, relevance first.

8 MR. JACOBS: The question is, in this lawsuit,
9 whether Abraxane is amorphous or --

10 THE COURT: Let me say, before you go forward,
11 you are going to this witness' credibility.

12 MR. SCHEVE: I have heard this story. This was
13 my idea, and we are so different. He lifted this stuff from
14 a fellow one-year doctor before Dr. Desai graduated from
15 school. It is credibility.

16 THE COURT: Your 403 argument -- it is
17 prejudicial. The question is, is it unfair?

18 MR. JACOBS: Yes, I think this is unfair. We
19 got in an exhibit last night at 10:30 p.m.

20 THE COURT: You should have raised that earlier.

21 MR. JACOBS: Your Honor, we should have raised
22 half of the stuff that is going on between the parties.

23 THE COURT: I am sure both of you have not done
24 that, and wisely.

25 MR. JACOBS: Now he is using this exhibit with

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1 this witness, our CEO, and saying he doctored the
2 photograph. This is character assassination.

3 MR. SCHEVE: He said probably his IT department
4 did it.

5 THE COURT: Actually, the last word he said was
6 he didn't know, to be fair.

7 MR. SCHEVE: I am moving on to a new topic.

8 THE COURT: Let's move on.

9 (End of sidebar conference.)

10 BY MR. SCHEVE:

11 Q. Doctor, there has been some testimony about a product
12 that is marketed that utilizes the NanoCrystal technology
13 Rapamune.

14 Are you trying to apply your NAB platform to
15 this product?

16 A. The Rapamune that you are talking about, there is the
17 oral version of Rapamune taken by mouth. To this day, there
18 is no injectable version of Rapamune at all, because of its
19 insoluble. So the answer is yes.

20 So we have actually now encapsulated, in our
21 cross-link, a form of Rapamune. And we are about to -- we
22 actually received FDA approval to initiate Phase 1 trials.

23 Q. If Abraxis is able to somehow challenge these patents
24 and somehow get them declared invalid, then you wouldn't
25 have to confront them as you move forward with your efforts

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1 to develop Rapamune and, indeed, other products, like
2 camptothecin, and others to which the '363 technology has
3 been applied. Correct?

4 A. Well, it's not correct, because we are not confronting
5 them anyway. We don't believe this has anything to do with
6 our technology or our patents.

7 Q. You may believe that, sir, but I am just asking the
8 question about, if the patents aren't there, then you don't
9 have to worry about them at all. Correct?

10 A. Well, if patents aren't there, you don't have worry
11 about them at all, that is correct.

12 Q. Now, sir, does the package insert for Abraxane advise
13 physicians to reconstitute and administer it to patients?

14 A. Yes.

15 Q. And then did Abraxis obtain or rely upon the opinion
16 of qualified patent counsel as to whether the nanoparticles
17 in Abraxane would infringe Elan's '363 patent before making,
18 offering to sell and/or selling Abraxane?

19 A. We were fully aware that we are two different
20 particles. We had collaborations, discussions, in which we
21 knew we had two different particles. One was crystalline,
22 the other one was amorphous. One is cross-linked, one is
23 non-cross-linked. One wanted to stay in the blood, the
24 other one wanted to get out of the blood.

25 When we looked at patents of the '363, it states

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1 within the body of the patents, we are crystalline, not
2 amorphous. In the body of the patents, of the Elan patents,
3 it says we are crystalline, not amorphous. In order for us
4 to become amorphous, you need to do a different method of
5 manufacture, solvent precipitation, which we do. In order
6 to become crystalline, we need to do a different method of
7 manufacture, grinding, which they do.

8 So if they told the Patent Office that they were
9 different, we told the Patent Office we were different. We
10 scientifically knew we were different. We were almost
11 professional colleagues. We were different.

12 So there was no issue from our perspective.

13 MR. SCHEVE: Your Honor, may I move to strike
14 the answer? I asked him whether they obtained an opinion of
15 counsel. As you recall in the pretrial conference, there
16 was an order instructing Mr. Jacobs to --

17 MR. JACOBS: Your Honor, objection. Sidebar.

18 THE COURT: You would like a sidebar, Mr.
19 Jacobs?

20 MR. JACOBS: Please, Your Honor.

21 THE COURT: Let's calm down.

22 (The following took place at sidebar.)

23 MR. JACOBS: Mr. Scheve should not be talking
24 about orders and directions in front of the jury. That is
25 very much not the way Your Honor runs the courtroom.

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1 THE COURT: That is true.

2 MR. JACOBS: Number 2, we were working out a
3 stipulation on this, all of a sudden Elan went silent on us.
4 I asked for the words back in the draft. They went silent.

5 Number 3, we will stipulate to exactly the way
6 Mr. Scheve said it. If that will move us on.

7 MR. SCHEVE: The background on that, Your Honor,
8 we submitted to them three days ago -- we never got the
9 amended interrogatory answers as you ordered Mr. Jacobs to
10 do. So we put together the proposed language, sent it to
11 them three days ago. I can show Your Honor -- I know you
12 don't want to get involved in those details.

13 THE COURT: We don't have time.

14 MR. SCHEVE: I am just asking, did they get an
15 opinion? And he says, we looked at patents, they looked at
16 patents. The patents are different. I want to know, did
17 you get an opinion or not? If they want to stipulate it,
18 I'm able to read it into the record, I am done with this
19 witness.

20 Can I get these two stipulations here that they
21 didn't get an opinion of a qualified patent counsel as to
22 whether the nanoparticles would infringe Elan's '363 before
23 making, offering to sell and/or selling and a separate one
24 that they obtained or relied upon an opinion of qualified
25 patent counsel as to whether the '363 patent was valid

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1 and/or enforceable before making, offering to sale, and/or
2 selling? Will I get those two stipulations?

3 MR. JACOBS: So stipulated.

4 MR. SCHEVE: I am finished with the witness.

5 THE COURT: Do you object to them being
6 announced by Mr. Scheve?

7 MR. JACOBS: No.

8 MR. SCHEVE: Your Honor, would you like me to
9 dismiss the witness and then read the stipulation, or do it
10 while he is on the stand?

11 THE COURT: While he is on the stand or after?

12 MR. JACOBS: After.

13 (End of sidebar conference.)

14 THE COURT: Doctor, I am advised we have come to
15 the end of the cross-examination. You are excused.

16 MR. JACOBS: Your Honor, could we have one
17 minute to confer on redirect?

18 THE COURT: I am sorry.

19 MR. SCHEVE: May I read the stipulation?

20 THE COURT: We will announce it.

21 MR. SCHEVE: Abraxis has stipulated, meaning
22 that they agree, that they did not obtain or rely upon an
23 opinion of qualified patent counsel as to whether the
24 nanoparticles in Abraxane would infringe Elan's '363 patent
25 for making, offering to sell, and/or selling Abraxane.

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1 In addition, they stipulate or agree that
2 Abraxis did not obtain or rely upon an opinion of qualified
3 patent counsel as to whether the '363 patent was valid
4 and/or enforceable before making, offering to sell, and/or
5 selling Abraxane.

6 THE COURT: That is another one of those rare
7 occasions, ladies and gentlemen; there is an agreement
8 there.

9 REDIRECT EXAMINATION

10 BY MR. JACOBS:

11 Q. Dr. Soon-Shiong, I only have one more question for you
12 on what we call redirect. Why not?

13 A. Because we absolutely felt very clear from our
14 perspective, we felt we knew it, we felt they knew it. It
15 wasn't an issue for us, because we were developing two
16 different pathways. We had an amorphous version. They had
17 a crystalline version. We had a cross-linked version. They
18 had a non-cross-linked version.

19 This may be interesting, it's sort of
20 interesting. The same patent examiner was examining both
21 patents at the same time. It's just an interesting, I
22 suppose, coincidence or maybe not, because this is the
23 examiner in this field at the U.S. Patent Office, Thurmond
24 Page, was the same examiner examining our patents, examining
25 their patents. And the Patent Office felt it was different.

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1 MR. JACOBS: Thank you. No further questions.

2 THE COURT: You are excused, Doctor. Thank you.

3 (Witness excused.)

4 MR. JACOBS: Abraxis rests, Your Honor.

5 THE COURT: Let's see counsel for a moment.

6 (The following took place at sidebar.)

7 THE COURT: When will you be ready to start your
8 rebuttal case?

9 MR. SCHEVE: You tell me when.

10 THE COURT: Do you want to break for lunch now?

11 MR. SCHEVE: Yes. We are bringing two
12 witnesses. I think our rebuttal case will last an hour, but
13 to be safe, I will say an hour 20 minutes. I anticipate
14 calling Dr. Manning and Dr. Liversidge.

15 THE COURT: Okay. So, then, moving on to the
16 time when we will be able to meaningfully consider the final
17 proposed jury instructions, and the verdict forms, over the
18 lunch, why don't you confer with your teams. Let's give
19 them when we come back some estimate as to when we will be
20 able to do that.

21 MR. SCHEVE: We had our little conference and
22 urged our associates. And we will make sure that this moves
23 along. I am sorry for any inconvenience, Judge.

24 THE COURT: It is not my inconvenience -- to a
25 degree it is, because we are resource limited. But I don't

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1 want to continue to gripe about that. The system is built
2 the way it is.

3 It is the jury that I have the most concern
4 about and having them just cooling their heels. And we have
5 promised them an eight-day trial.

6 MR. SCHEVE: I do think, Judge, I have to rely
7 on some others, but I talked to John Day, and he says, it
8 may look like there is a lot of disagreements, but it is
9 really just preserving the record. The dispute is down to
10 about 12. But I have to look at it and make sure.

11 MR. JACOBS: Maybe we could excuse the jury and
12 spend a few minutes on the schedule from here through
13 closings. We actually have a fair amount of time to work
14 with. So we can relax.

15 THE COURT: Let's let the jury go.

16 I will announce that Elan will have a rebuttal
17 case upon our return from the normal lunch hour. We will
18 stick around for a few minutes.

19 MR. JACOBS: To lay it out all out, the way we
20 sequenced this, I could have a rebuttal on invalidity. It
21 would be very short.

22 THE COURT: I guess that's right. Do you know
23 at this point?

24 MR. JACOBS: I think it depends on what
25 Mr. Scheve actually does. It would be Dr. Amiji on

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1 invalidity and it would be brief.

2 (End of sidebar conference.)

3 THE COURT: Ladies and gentlemen, as you have
4 just heard, Abraxis has rested. We are going to break to
5 lunch now. You should anticipate upon our return, take an
6 hour, hearing a relatively brief rebuttal case from the Elan
7 plaintiff. And you may hear additional brief, further
8 rebuttal on the invalidity question from Defendant Abraxis.
9 They will react in realtime, depending upon what happens
10 during plaintiff's rebuttal. I will let you know. We will
11 see you back in an hour.

12 (Jury leaves courtroom at 12:40 p.m.)

13 THE COURT: So we are going to stick around for
14 a few minutes here, as Mr. Scheve and other counsel and I
15 agree, we will discuss the schedule. For those of you who
16 need to stay, okay. Those who need to take lunch, go right
17 ahead.

18 I was happy to hear that much of the disputes
19 that have been denominated as such are actually record
20 preservation of disputes. The disputes have been distilled
21 down to about 12. It can be better. I expect it to be.

22 The verdict form. Where are we on that? Trying
23 to meld something together?

24 MR. JACOBS: Here is what I heard before we did
25 the examination, Your Honor. We can tee up one issue at the

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1 threshold of the verdict form, and then, if you decide that
2 issue, it will be over. That's what I heard.

3 THE COURT: That's very helpful.

4 So, then, let's talk about the balance of the
5 schedule.

6 MR. JACOBS: My proposal, Your Honor, is that we
7 do our closing arguments tomorrow morning. You would
8 instruct them first, I believe.

9 THE COURT: Yes.

10 MR. JACOBS: We could probably close, I am
11 speaking at least for our side, we could probably close both
12 cases before lunch.

13 THE COURT: I think that's a little ambitious.
14 Let's just think about that for a moment. We are probably
15 going to come out with somewhere in the neighborhood of a
16 hundred or so pages of instructions. Right?

17 MR. SULLIVAN: Yes, Your Honor.

18 THE COURT: That is going to take me roughly two
19 hours to deliver. Quite frankly, I am thinking about trying
20 something a little different and taking a break midway, just
21 to give my lungs a rest. But really, I do, in all
22 seriousness, think that the jury can use a break.

23 I have watched their eyes glaze over now enough,
24 as I go through these kinds of things, this exercise, that I
25 am not sure is the best way to deliver the instructions in

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1 the first place, but it is what we do right now in this
2 country, and maybe just let them take a quick stretch at
3 some midpoint. You have roughly two hours, an hour 40
4 minutes to two hours I suspect, that is what it will take us
5 to deliver them. If we start at 9:00, that gets us to
6 roughly 11:00 or so. We want to give them another break at
7 the end.

8 Then I expect we may be able to get in the
9 initial opening, perhaps, of Mr. Scheve. What do you think?
10 How long do you plan to run your mouth?

11 I am teasing.

12 MR. SCHEVE: I know the importance of being
13 concise in telling my story. But I do think, Your Honor,
14 even though it's been seven days, it has been fairly complex
15 and drawing the inferences. I was going to suggest maybe we
16 take an early lunch break, do mine, then do theirs, if the
17 jury has time to deliberate -- in other words, instructions,
18 give them the important breaks that you feel are necessary,
19 then take our lunch, and I stand up, they stand up, and we
20 are finished.

21 MR. JACOBS: That would be absolutely fine, Your
22 Honor.

23 THE COURT: Let's -- that sounds like a fair
24 plan to me. That would mean probably a fairly early lunch
25 break, in the neighborhood of roughly 11:30, I think,

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1 probably is where I would anticipate it would be.

2 Let me ask you this, Counsel: Do you plan on
3 discussing the verdict forms during your closing? Some do,
4 some don't.

5 The answer will sort of give me some guidance as
6 to how much I need to say or not about the verdict forms.

7 MR. JACOBS: I would very much like to in mine.

8 MR. SCHEVE: I would fully expect I've got to
9 show them what they need to do.

10 THE COURT: I am going to defer that part of my
11 instructions to you. I will tell them I am not going to go
12 over the verdict, because we will have an instruction in the
13 final instructions I am sure that will tell them. In fact,
14 in the beginning, I will go over this and that and I will go
15 over the verdict form with you. Well, I am not going to go
16 over the verdict form with them, with your agreement.

17 MR. JACOBS: I think that's fine.

18 THE COURT: Okay. That's a plan.

19 See you back in an hour.

20 (Luncheon recess taken.)

21 MR. SCHEVE: Your Honor, I have one item. Now
22 that Abraxis has closed its case on infringement and we are
23 where we are in the case, and they didn't call Dr. Brittain,
24 it seems to me that the predicate facts upon which Your
25 Honor's previous ruling about a negative inference, there is

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1 no evidence now in this record --

2 THE COURT: We can address that later.

3 MR. SCHEVE: The reason I raise that is I do
4 need to confer with my client whether I need to address the
5 issue of calling him. My sense is, without any evidence in
6 this record, there is nothing to draw an inference from.

7 I will need to deal with it. I am just bringing
8 it to Your Honor's attention so you are not blindsided. But
9 it seems to me we have a different set of facts than what
10 was argued at the pretrial conference and, indeed,
11 throughout the trial. They have closed. There is nothing
12 in this record about what Dr. Brittain did or didn't do. No
13 privilege log. Clearly there is no evidence upon which to
14 draw an inference about anything.

15 THE COURT: One other thing about closing -- did
16 you have some additional evidence you wanted? You closed
17 your case in chief conditionally upon --

18 MR. SCHEVE: Yes. That the evidence from
19 Dr. Desai and from Dr. Soon-Shiong would be included in our
20 case.

21 THE COURT: That is already agreed then.

22 MR. SCHEVE: That was agreed by counsel. The
23 only other thing, Your Honor, would be on the JMOL motions,
24 how you would want to deal with that. I assume you don't
25 want us standing up and slowing this thing down today. Will

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1 there been time tomorrow to address that and put it on the
2 record?

3 THE COURT: Well, we can do that. Frankly, I
4 will be surprised and interested to see what the parties
5 have to say about JMOL. This case squarely rests with the
6 jury, to preview from me to you what I am going to be
7 thinking about JMOL, for both sides, quite frankly.

8 MR. SCHEVE: We appreciate that, Your Honor.

9 THE COURT: But you do have to preserve your
10 issues. Yes.

11 It seems to me that an easy way to do that is in
12 some type of abbreviated written submission, so that the
13 Federal Circuit won't have the ability to say you have
14 waived the issue. But I can tell you that it is likely as
15 not that I am not only not going to reserve, I am going to
16 deny motions from both sides on all issues of JMOL. But I
17 will hear you if you want to be heard at some point
18 tomorrow.

19 MR. SCHEVE: If we do, Your Honor, I can assure
20 you from our side it will be brief. Thank you for the
21 guidance.

22 THE COURT: Mr. Jacobs, on the Dr. Brittain
23 issue.

24 MR. JACOBS: On the Dr. Brittain issue, the
25 privilege log is in evidence. That was part of the point of

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1 clarifying what's in evidence. So is his engagement letter,
2 it is in evidence. The negative inference is in a Court
3 order.

4 From my standpoint, we dealt with all that
5 pretrial and I get to argue the negative inference.

6 THE COURT: Your reaction?

7 MR. SCHEVE: Your Honor, there is a privilege
8 log submitted by counsel which is indeed, they have put it
9 on their exhibit list. Our point is, there has been no
10 testimony from Dr. Brittain that was forecast for you on
11 repeated occasions. In fact, this morning, there was a
12 motion by counsel or discussion by opposing counsel about
13 the questions they were trying to ask and trying to limit me
14 on cross-examination. There is no testimony from
15 Dr. Brittain. He has not been asked the question, did you
16 not produce this information, et cetera. So there is no
17 facts in this record -- it's not that they couldn't have
18 tried to develop a record. But the record is now closed on
19 their case.

20 For there to be an inference drawn when the jury
21 has heard none of that, I don't know what the evidentiary
22 basis would be.

23 So we would, again, Your Honor dealt with a set
24 of cards at the time you ruled. That set of cards is far
25 different now that you have a record. We would again urge

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1 that there would be no basis for that. It does affect our
2 decision on how we deal with our rebuttal case, which we
3 hope to be two more witnesses. Depending upon Your Honor's
4 ruling, maybe it has to be three.

5 MR. JACOBS: Your Honor, the order is the order.
6 The order says there would be a negative inference. We were
7 relying on the order. If it now seems we need to develop a
8 record in order to support the order, I would ask that we be
9 able to reopen our case and call Dr. Brittain.

10 THE COURT: I think the order addressed a
11 request, that request that you made to the Court to consider
12 the events that existed at the time, and that I make a
13 ruling based upon certain activities during the course of
14 discovery. I did.

15 I guess Mr. Scheve contends that that is as good
16 only as far as it goes, in that now we have a -- I guess
17 your argument, Mr. Scheve, is that because we have had no
18 live testimony before the jury, or evidence of any type,
19 adduced before this jury, regarding Dr. Brittain and his
20 testing, that there is no basis upon which the Court should
21 draw the jurors' attention to an adverse inference.

22 MR. SCHEVE: That's correct, Your Honor. Your
23 Honor was faced with a set of allegations in the pretrial,
24 just as in the JMOL motion, I may point out to you tomorrow
25 in a very judicious way, that there are a couple of opinions

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1 they needed to offer and which the law required them to
2 offer.

3 THE COURT: I said I will listen to you on JMOL.

4 MR. SCHEVE: But to draw the inference there has
5 got to be some evidence here from Dr. Brittain. There has
6 been nothing established about what he did, what he didn't
7 do, what he withheld. All that has been previewed to you.
8 And they closed.

9 THE COURT: You need to address their point,
10 Mr. Scheve, about reliance on the Court's order, I think.

11 MR. SCHEVE: Well, it was the in limine motion,
12 Your Honor. The law of the Federal Circuit and the Third
13 Circuit is very clear. An in limine motion --

14 THE COURT: I think it's the Third Circuit that
15 will control.

16 MR. SCHEVE: It is the Third Circuit procedural
17 issue. All in limine motions are previewing for the Court
18 so the Court can express its preliminary views in the
19 traditional trial of cases, what I have always understood
20 that atom is before I open my mouth on something subject to
21 a motion in limine I am supposed to approach the Court and
22 get a ruling. This is still my ruling. I am going to
23 exclude it.

24 But at this point the predicate of their request
25 during pretrial was that this witness should be forced to

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1 come and testify. He has been here pursuant to subpoena.
2 And they didn't call him.

3 They have closed their case. So to say that
4 Your Honor should be put in a position -- and I have said
5 this, I hope I have not misinterpreted Your Honor. We
6 really think this is error. I don't want to come back. Our
7 position is, there is nothing here for an inference to be
8 drawn from, because they made the lawyerly -- they used
9 their good judgment, but they didn't put this into the case.
10 And there is no facts before this jury upon which to draw
11 that inference.

12 THE COURT: You say, Mr. Jacobs, in reliance on
13 the Court's order you proceeded from an evidentiary point of
14 view in a certain way?

15 MR. JACOBS: Yes. And I think the larger
16 context of an issue like this is, in a pretrial ruling, one
17 makes certain rulings and one excludes or includes evidence
18 based on what happened in discovery. And that is what
19 happened here. The Court issued an order saying an adverse
20 inference shall be drawn, recounted the necessary facts
21 leading though that adverse inference.

22 I can't remember litigating discovery disputes
23 in front of the jury. Part of the reason I didn't want to
24 put Dr. Brittain on today is, frankly, I just don't want the
25 jury to see that kind of thing. I don't want to have to

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1 cross-examine Dr. Brittain on what Elan produced in
2 discovery.

3 That would have not been seemly. It would not
4 have been attractive to this jury, which thinks these
5 matters proceed in an orderly fashion.

6 THE COURT: So you say there are certain things
7 that did or did not happen, during the course of discovery,
8 and that as a sanction for some things that did not happen,
9 specifically with regard to the testing, the production of
10 that information, that Abraxis is entitled to at least infer
11 that something negative as a result of the failure of Elan
12 to do what you contend it should have.

13 MR. JACOBS: Exactly. An area in which I might
14 add, District Court's have broad discretion in managing the
15 process leading up to trial. I made a strategic call, you
16 are absolutely right, Your Honor, I did not want the
17 Dr. Brittain testimony to spin out in circles on circles as
18 to who did what to whom. I think that was in the interest
19 of the process. I was obviously interested, motivated by
20 the result as well. It shouldn't prejudice the order we
21 have from the Court.

22 THE COURT: Do we have a proposal for the
23 instruction?

24 MR. JACOBS: It's embodied in the jury
25 instructions, Your Honor. There is also this proposed

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1 statement that I referred to before, which was another
2 effort.

3 THE COURT: What about the instruction? Where
4 is it in the instructions?

5 MR. JACOBS: It would be in the infringement
6 section.

7 THE COURT: The folks in the well of the court
8 and everyone can sit for a moment.

9 Mr. Scheve, I am going to give you a chance.

10 MR. SCHEVE: Thank you, Judge.

11 MR. JACOBS: It is in Abraxis's proposed
12 instruction 4.3 on Page 48. I can hand it up.

13 THE COURT: I think I have a copy.

14 Maybe you better hand it up, on Page 48, there
15 is no such instruction. I have parties proposed general
16 instructions, clean version. And I have parties' proposed
17 general instructions.

18 MR. JACOBS: May I hand it up?

19 THE COURT: Yes. Do you have this, Mr. Scheve?

20 MR. SCHEVE: I am sure my team does, Your Honor.

21 THE COURT: Somebody. Yes.

22 You know, it is interesting, Mr. Jacobs's, the
23 title of what you handed me is parties' proposed general
24 instructions. I have a document with the same title, but
25 different Page 48s.

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1 MR. JACOBS: It is perhaps an older version.

2 THE COURT: It may be that I have an older
3 version.

4 MR. JACOBS: Maybe 4.3 has remained. 4.3, for
5 this purpose, Your Honor.

6 It's after Elan's proposed opinion on, proposed
7 instruction on willfulness.

8 THE COURT: It's the same 4.3. This reads, for
9 the record, "You have heard that Elan withheld the documents
10 of Dr. Brittain's test listed in DX-508. You shall infer
11 from Elan's non-production of Dr. Brittain's testing
12 documents that these documents would have been unfavorable
13 to Elan's case on infringement."

14 I have just been handed, in order to refresh my
15 recollection, a copy of my order in regards to Abraxis's
16 motions 1 and 4, which is, I think, the relevant order.

17 MR. JACOBS: Yes, it is, Your Honor.

18 THE COURT: At the very least, just for purposes
19 of talking about this a little bit, I would think that it
20 would be more appropriate to say that you may infer from
21 Elan's non-production, not you shall infer. I don't think I
22 can direct the jury to make an inference. I can council
23 them that they may. They are the fact-finders. Wouldn't
24 you agree with that?

25 MR. JACOBS: It was actually the "shall," the

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1 shall was in your order, Your Honor. And it was the shall
2 that partly led us to not have to put a case on in front of
3 them about the production. It's the last paragraph, I
4 believe, Your Honor.

5 THE COURT: Well, it should have been "may," may
6 infer. I don't think that I can -- if Mr. Scheve is right,
7 he is right. I think he is double right -- I don't think I
8 can instruct the jury that they shall draw a negative
9 inference.

10 Mr. Scheve? Apart from your position on whether
11 I should give this instruction at all.

12 MR. SCHEVE: Yes, sir. I agree with what Your
13 Honor has said. The only other language is "you have heard
14 evidence that." That is my position that they haven't heard
15 it.

16 THE COURT: I was going to get to that. I
17 understand why you write it this way.

18 I don't think I need to compound the error that
19 I think exists in the order part, that is, in Paragraph 3 of
20 the Court's order, where I did write "the Court will
21 instruct the jury that it shall infer." That's incorrect,
22 as a matter of law.

23 MR. JACOBS: Your Honor, if I may, let me give
24 you what I think is the, as one of my math teachers used to
25 say, the lemma for the dilemma.

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1 THE COURT: Okay.

2 MR. JACOBS: Because we did not wish to put on
3 in front of the jury, the saga of what happened and who
4 produced what to whom and what instructions were given.
5 There is a set of facts that Your Honor found in that order
6 that would explain the story to them and with "may" would
7 set the predicate for this. And I gave this to Mr. Scheve
8 yesterday.

9 THE COURT: I will take a look.

10 (Pause.)

11 THE COURT: Okay. You say that my decision on
12 this is going to inform, Mr. Scheve, how many witnesses you
13 put on in your rebuttal case?

14 MR. SCHEVE: Yes, Your Honor. I will need to
15 confer further with my client before I look at Your Honor
16 and say I rest.

17 The language here on 42, Your Honor, where it
18 says "you have heard that Elan withheld." The only thing
19 they have heard is a statement by counsel in opening.

20 Then, there is simply no factual record that all
21 of those items listed in Defendant's Exhibit 508 were tests
22 on Abraxane. I can tell the Court, as an officer of the
23 Court, the overwhelming majority of those did not involve
24 tests on Abraxane.

25 So this record is devoid of evidence that would

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1 allow Your Honor to say, you have heard evidence that that
2 exhibit relates to Abraxane, because it doesn't.

3 THE COURT: I agree that as a matter of
4 precision it would be inaccurate to say you have heard
5 evidence. As to your statements as an officer of the Court,
6 I respect you as such; it is attorney argument. Your
7 representation, I have seen no declaration, evidence one way
8 or the other as to what was in those testing documents, and
9 you know that. While I respect your representation, it is
10 what it is, the record, that is.

11 So my question to you gentlemen is, do you need
12 to give me a few minutes to think further about this? Or
13 are you prepared to get on with your rebuttal case?

14 MR. SCHEVE: I am prepared to go on, Your Honor.
15 I apologize for throwing you this curve ball. I thought it
16 needed to be previewed because I would like the opportunity
17 to confer with my client before we stand up and tell Your
18 Honor we now close on your rebuttal case.

19 THE COURT: Let's start on the rebuttal case and
20 let's see how we go.

21 MR. SCHEVE: Okay.

22 THE COURT: I will tell you, I am going to be
23 perusing this a little. But I am listening to what's going
24 on.

25 Ms. Walker.

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1 (Jury enters courtroom 2:05 p.m.)

2 THE COURT: All right, members of the jury.

3 Please take your seats.

4 Mr. Scheve.

5 MR. SCHEVE: Thank you, Your Honor. In the
6 rebuttal portion of our case we would like to recall to the
7 stand Dr. Mark Manning, please.

8 MARK MANNING, having been previously sworn as a
9 witness, was examined and testified further as follows ...

10 DIRECT EXAMINATION

11 BY MR. SCHEVE:

12 Q. Good afternoon, Doctor.

13 Very briefly, could you remind the jury who you
14 are and where did you come from here today?

15 A. Sure. My name is Mark Manning. I am currently the
16 chief scientific officer at Legacy Bio Design.

17 Q. I want to address in rebuttal some specific testimony
18 that was put into the case by Abraxis during its case. The
19 first is, the testimony of Dr. Desai, wherein he testified
20 in this court that, "There is disulfide cross-linked albumin
21 in our natural blood circulating around all the time."

22 Have you reviewed that testimony?

23 A. I have.

24 Q. Do you agree with that testimony?

25 A. I absolutely do not.

Manning - direct

1 Q. Would you explain to the jury why you believe that
2 that statement is not accurate?

3 A. Sure. Remember, before, I was talking about albumin,
4 albumin being this protein that's found in your bloodstream
5 at fairly high concentrations. That protein is essentially
6 a monomer. All the treatises and descriptions of that in
7 the literature are consistent with that. In fact, there is
8 a well-established textbook called "All About Albumin,"
9 believe it or not, there is such a book. That tells us that
10 in fact that is not the case.

11 It goes to another really important point. When
12 the FDA considers protein-based pharmaceuticals, their
13 overriding concern is always whether or not the protein is
14 what they call aggregated. That means is it stuck together
15 in large pieces or clumps. Because the larger those pieces
16 are, the more likely there is a chance to trigger an adverse
17 response, for the body to say, this is foreign, it shouldn't
18 be here and tries to do something about it.

19 So if this was the case, I think all of us, we
20 would be quite ill if that is in fact the case. The reality
21 is the protein albumin in your body that's used as the
22 starting material for the pharmaceutical products we have
23 talked about is in fact monomeric.

24 Q. Then during the course of questioning of Dr. Amiji,
25 counsel asked him, "Do you recall when Dr. Manning gave

Manning - direct

1 testimony regarding 15 to 20 percent cross-linking?"

2 Dr. Amiji says: "Yes, I do."

3 Did you ever testify to that, sir?

4 A. I never testified to that.

5 Q. Would you explain to the jury what you actually
6 testified to rather than this characterization?

7 A. Sure. And you can certainly check the record.

8 But what I told you is that in my opinion, that
9 the albumin was essentially free of intermolecular
10 cross-linkages, therefore was not cross-linked. So I never
11 gave a number. I never said it was cross-linked to any
12 extent.

13 Q. Now, Dr. Desai, from Abraxis, also testified at Page
14 1221 of the court reporter's transcript of Day 6 of the
15 trial, "The idea of having albumin as a cross-linked shell
16 around it helps to stabilize that structure. And by
17 cross-linked, I mean it's like a mesh or a net. So the
18 individual albumin molecules are linked together to create
19 this net or mesh that holds the structure together. Those
20 are the critical features, sort of, of Abraxane."

21 Did you review that testimony?

22 A. I did.

23 Q. Did you find documents within Abraxis's collection of
24 its own internal documents that you believe shed light on
25 the accuracy of this testimony of Dr. Desai?

Manning - direct

1 A. I found no basis for this sort of statement.

2 Q. Now, with regard to this exhibit here, sir, which is
3 Plaintiff's Exhibit 363, what is its significance in
4 relating to this testimony by Dr. Desai that the albumin is
5 in a net or a mesh around the nanoparticles?

6 A. This is a really important point. Remember, I was
7 talking to you last week about this idea that proteins can
8 be weakly associated, like when I put my hands together, or
9 they can be strongly connected or linked, as I told you when
10 I collapsed my hands to try to make that sort of
11 distinction.

12 What you are hearing here that there is in fact
13 this mesh or network. I think Dr. Soon-Shiong also used
14 this connotation of a tea bag sort of thing. Is that you
15 would have these strong chemical bonds, one protein to the
16 next protein to the next protein. So if that was the case,
17 then you would form this kind of network. But the reality
18 is, as you see on this particular slide, the protein
19 molecules come apart individually very quickly.

20 Over and over it says rapidly dissolves, rapidly
21 dissociates.

22 So the point here is, if these, in fact, were
23 these strong chemical bonds, it would take a great deal of
24 energy and time for those to come apart. And there is just
25 no way to have this entire mesh of network dissociate and

Manning - direct

1 fall apart.

2 The other point of this slide, too, is we have
3 heard over and over about how the albumin binds the
4 paclitaxel and carries it inside the cell. And, in fact,
5 albumin does that. It binds lots of different hydrophobic
6 or poorly water-soluble molecules. Not just paclitaxel.

7 In other words, there is a functionality that
8 has to occur with the albumin. Again, if you start to tie
9 up the albumin with bond to bond to bond, most likely it's
10 also going to limit or compromise its ability to bind the
11 paclitaxel as well.

12 This whole idea of a mesh or a network is
13 inconsistent with this sort of description. I mean,
14 logically, you would say, if it's going to fall apart
15 quickly, I can't tie it altogether. I have got to let them
16 be free to dissociate.

17 Again, in my opinion, it is not cross-linked,
18 based on all the scientific technical evidence we have been
19 talking about, but just simply the way that it actually
20 works in the body, the way we have heard it presented to the
21 FDA, to regulatory authorities, scientific meetings. They
22 all tell us this is how it works. That we can't have these
23 strong bond to bond to bond across an entire network. It's
24 kind of like, again, going back to this whole tea bag
25 notion. Your tea bag doesn't dissolve. This network

Manning - direct

1 doesn't dissolve quickly. Why? Because they are all tied
2 together. Just like a fishing net, interconnected and so
3 on. It has to be free to dissociate, therefore it has to be
4 free of these strong cross-linkages.

5 Q. Did you view the video that Dr. Soon-Shiong showed to
6 the jury today?

7 A. I did.

8 Q. Let's pull up a short clip.

9 (Video played.)

10 THE WITNESS: If we can stop it there. We have
11 this pictorial description, which helps us get a sense of
12 how this drug works. There are some things in here we need
13 to take a close look at, if I may. The first is this
14 particular process. Here we have the description of the
15 paclitaxel nanoparticles surrounded by albumin. As it is
16 shown in this description, it almost looks like it's
17 exploding or fragmenting when it hits the surface or the
18 cell wall or the wall of the blood vessel.

19 The reality is, again, it's not an explosion.
20 It's not a fragmentation. It's dissolution, where the
21 particles come off individually.

22 So you could certainly misinterpret this sort of
23 video to say, oh, gee, this idea if I have a lollipop and I
24 want to dissolve it in water what I should do is throw it
25 against a wall and watch it fragment. It is not the same

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1 process. There is a fragmentation that can occur because of
2 mechanical energy. We are talking about putting something
3 in the body, allowing it to dissolve. For that to happen,
4 the albumin has to be free to move away from each other. If
5 they are not cross-linked, yes, they can come apart very
6 quickly.

7 In this sort of network, these bonds are strong,
8 it takes a great deal of energy to break them up. That
9 would take, as I said, some energy and some time for that to
10 occur.

11 Q. Just to sum this up. If you would rewind that,
12 please. Thank you.

13 Does this video showing this rapid dissociation,
14 does that support the evidence of cross-linking of the
15 albumin adsorbed onto the surface of the particles?

16 A. No, it does not. It's consistent with it not being
17 cross-linked and free to dissociate quickly.

18 Q. Go to the next slide.

19 Now, Dr. Desai confirmed in his testimony that
20 they were unable to discern or find a glass transition
21 temperature from the differential scanning calorimetry, DSC.
22 And then Dr. Desai went on and said, "And because we have
23 albumin complex with the paclitaxel, that property of glass
24 transition of paclitaxel is lost, because it's complexed
25 with albumin molecules and it's not complexed with itself.

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1 And glass transition is a bulk property, so you need bulk
2 material, that is, a lot of paclitaxel molecules, to be
3 associated to each other, to be able to see that. Because
4 we have albumin, and the albumin is complexed to the
5 paclitaxel, you wouldn't expect to see that."

6 Did you hear that testimony by Dr. Desai?

7 A. Yes, I did.

8 Q. Now, do you agree with this testimony, sir?

9 A. I do not.

10 Q. Could you explain to the jury what you believe to be
11 inappropriate about it?

12 A. Sure. The one part here that is, again, it speaks to
13 is this binding event. Certainly when the paclitaxel is
14 bound to the protein floating free in solution, we don't
15 have bulk paclitaxel. In the Abraxane product that was
16 tested, we have these interact nanoparticles. Remember,
17 this is a solid core, entirely consisting of paclitaxel.
18 There is no albumin in the interior of it. There is nothing
19 else in there except paclitaxel.

20 So, therefore, we have material that has bulk
21 properties. It is a bulk. It is a chunk, if you will, of
22 paclitaxel.

23 So we have a situation where it shows those bulk
24 properties. Dr. Desai explained to you that if it's a bulk
25 material, therefore, it should have bulk properties like

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1 scattering x-rays. If that's true, then it should also have
2 the bulk properties of showing glass transition temperature
3 if it is, in fact, amorphous. So this statement tried to
4 confuse the issue about complexation and so on, make sure we
5 are very clear here. When that nanoparticle is intact, it
6 displays bulk properties. Therefore, if it is in fact
7 amorphous, there should be a glass transition temperature
8 that can be measured by differential scanning calorimetry,
9 DSC. That is the transition that was absolutely not
10 observed.

11 Then you heard last week that my opinion about
12 that was, therefore, it cannot be completely amorphous.

13 Q. The next slide, sir, where Dr. Desai also testified at
14 Page 1230 on Day 6, he said, "So this is mixed up under high
15 sheer conditions so you get a very fine droplet size. That
16 will be seen in a second."

17 He was showing a video.

18 A. Yes.

19 Q. "At this stage, you get the cross-linking of albumin.
20 Around the droplets, the albumin accumulates. Then the
21 cross-linking occurs."

22 Did you see that video, sir, and hear his
23 testimony?

24 A. I did.

25 Q. Do you agree with what Dr. Desai described here as

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1 cross-linking occurring when this mixing occurs?

2 A. I do not.

3 Q. Could you explain to the jury why?

4 A. I have spent a lot of time looking at proteins and
5 their stability and their formulation. And in a couple
6 contexts I have encountered these sorts of situations. One,
7 as you saw yesterday, I've written a book chapter that was
8 in a volume that I edited about proteins at surfaces.

9 In addition, for reasons of the fact that I
10 teach classes around the world as far as training people how
11 to do protein-phased formulation. And so, as a result of
12 that I have reviewed, this may sound very strange, I have
13 actually reviewed every paper that has been published on
14 high-shear effects on protein since 1970, because it is a
15 topic that people are very interested in and I want to be
16 able to make sure I express what is exactly correct there.

17 In all those articles, going back now almost 40
18 years, there is only two articles that even talk about the
19 possibility. And in both of those cases, they have to admit
20 that there is no conclusive evidence that ever there is any
21 form of intermolecular covalent disulfide cross-linking
22 during sheer mixing.

23 In other words, there is not enough energy in
24 the sheer process, and we didn't hear anything
25 quantitatively about how much sheer is generated. That is

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1 obviously an important thing to know. So even if you were
2 able to create high sheer, we don't know exactly if there is
3 or there is not in the Abraxane process. We just don't
4 enough energy to start tearing bonds up, start to form new
5 bonds and so on. In other words, the protein will survive
6 chemically. You will not form these new disulfide bonds.

7 Q. Finally, to make sure the jury understands the
8 distinction between the data that you relied upon and that
9 which Dr. Amiji relied upon; again, did you hear the
10 testimony of Dr. Amiji?

11 A. Yes.

12 Q. In terms of the materials that you relied upon as
13 compared to what he relied upon, what differences do you
14 want the jury to understand?

15 A. First of all, they put up that we didn't do any tests,
16 which is true. The reality is, experts on neither side have
17 done any tests. All the testing that was done was done by
18 Abraxis' employees.

19 Then I want you to understand how maybe to think
20 about or evaluate the quality of experiments. I know that's
21 maybe a hard thing. But for me, I always set kind of three
22 standards in my mind. The first is that you have heard
23 about peer review, where other scientists look at the data,
24 comment on it, say good, bad, change this, that sort of
25 thing.

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1 The second standard I would set is, if something
2 has been presented to a regulatory agency, you really have
3 to think there is some validity and truth behind that
4 because you don't want to be making those sorts of claims to
5 the federal government.

6 The third is, is there enough information
7 presented that I myself could go back and do that experiment
8 the same way that they did it, and hopefully get the same
9 result.

10 So if we set those kinds of criteria as about
11 being reasonable scientific approaches to say this is a good
12 experiment, this data is worth considering or relying upon,
13 what I have seen is that the data that I looked at really
14 didn't meet those criteria. In all the cases, the
15 experiments you heard about yesterday, they actually go
16 back, they don't tell you how the samples were handled, how
17 the samples were stored, what sort of manipulations or
18 preparations were done before they did their testing. It
19 was never peer-reviewed. It was never part of regulatory
20 filings.

21 For all those reasons you have to be very
22 skeptical here and say there is not data here that as a
23 scientist I can rely upon; as a result, I didn't.

24 Q. Let's make sure the record is clear. When you said
25 the experts on both sides, you are referring only to the

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1 cross-linking issue, is that correct, as opposed to the
2 crystallinity issue?

3 A. That's correct.

4 Q. The materials that you relied upon, were they all
5 included in regulatory filings to our Food & Drug
6 Administration?

7 A. All the ones that I relied upon, yes, they were all
8 founded in those kinds of documents.

9 Q. The documents that Dr. Amiji relied on, were they sent
10 to the FDA for review and peer-reviewed?

11 A. I am not aware of any of them were, no.

12 Q. And then with regard to the materials that you relied
13 upon, did they include materials that were sent outside of
14 Abraxis for purposes of scientific forums or meetings?

15 A. Yes, and I used some of those slides in my
16 presentation. There were presentations made as you saw,
17 scientific meetings, presentations to doctors and so on.

18 Q. Again, contrasting that with Dr. Amiji, was that data
19 that he looked at and talked about with the jury, had that
20 been subjected to outside peer review?

21 A. No data that I saw yesterday meets that criteria.

22 Q. I want to turn very quickly to the enablement issue,
23 sir.

24 Have you reviewed the patent and claim
25 construction orders of this Court?

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1 A. I have.

2 Q. Have you reviewed all the language about how, the
3 screening process and the various steps that are outlined in
4 the '363 patent for selecting compatible surface modifiers
5 for use with chemotherapy therapeutic agents?

6 A. I have.

7 Q. Do you hold an opinion, sir, to a reasonable degree of
8 scientific certainty, as to whether or not Elan's '363
9 patent provides a disclosure that would enable one of
10 ordinary skill in the art to practice the claimed invention
11 without undue experimentation?

12 A. I have formed an opinion on that.

13 Q. What is that opinion?

14 A. I agree with that statement. There is sufficient
15 description, detail, that allows someone of ordinary skill
16 in the art to teach them to make and to use that invention
17 described in the '363 patent.

18 Q. Do you hold an opinion to a reasonable degree of
19 scientific certainty as to whether Elan's '363 patent
20 provides a sufficient written description of the claimed
21 invention as viewed from the perspective of one of ordinary
22 skill in the art?

23 A. I have formed an opinion.

24 Q. What is that opinion?

25 A. That opinion is that I find the written description to

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1 be clearly communicated, completely described, and certainly
2 would allow anyone again to make and use that invention.

3 Q. Do you hold an opinion, sir, to a reasonable degree of
4 scientific certainty, as to whether or not Elan's '025
5 patent provides a disclosure that would enable one of
6 ordinary skill in the art to practice the claimed invention
7 without undue experimentation?

8 A. I have formed an opinion.

9 Q. What is that opinion?

10 A. That opinion is, like the '363 patent, I find that the
11 description of the patent is more than sufficient to teach a
12 person of ordinary skill in the art to make and to use that
13 invention without any undue experimentation.

14 Q. Do you hold an opinion, to a reasonable degree of
15 scientific certainty, sir, as to whether or not the Elan
16 '025 patent provides a sufficient written description of the
17 claimed invention as viewed from the perspective of one of
18 ordinary skill in the art?

19 A. I have formed an opinion.

20 Q. Now that I have asked the technical question, sir,
21 does that '363 patent provide enough detail to show that the
22 inventors actually achieved the invention claimed therein?

23 A. Yes. In my opinion, because there is such detailed
24 description of the process, because there is a large number
25 of examples, in my opinion, they were clearly in possession

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1 of the entire invention.

2 Q. And do you hold that opinion to a reasonable degree of
3 scientific certainty?

4 A. I do.

5 MR. SCHEVE: Your Honor, I pass this witness.

6 THE COURT: Mr. Jacobs.

7 CROSS-EXAMINATION

8 BY MR. JACOBS:

9 Q. Dr. Manning, let's start where you left off. On
10 enablement. Whether someone could take the description in
11 the '363 patent back in 1992, and without undue
12 experimentation carry out the claimed inventions. That is
13 the issue you were addressing. Correct?

14 A. That's correct.

15 Q. And it's your opinion, to a reasonable degree of
16 scientific certainty, that one could have done so. Is that
17 correct?

18 A. That is my opinion, yes.

19 Q. Did you do any experiments to take the disclosure of
20 the '363 and put yourself back with what was known in 1992
21 and figure out if you could actually make any of those
22 anticancer medicaments?

23 A. The question is did I do any experiments myself?

24 Q. That's correct.

25 A. I did not.

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1 Q. Did you actually study in any detail the documentation
2 that Elan has on the troubles it was having actually making
3 the particles described in the '363 patent?

4 A. I reviewed a large number of documents about what was
5 being done in the context of that, yes.

6 Q. When did you do that, sir?

7 A. When did I do that?

8 Q. Yes.

9 A. During the course of this litigation.

10 Q. When?

11 A. I believe I started that early last year.

12 Q. Do you recall when last year?

13 A. I don't. I apologize.

14 Q. I have some invoices from you that, but I don't think
15 I have the complete set. I want to see if you can shed some
16 light on this. December was a busy month in this
17 litigation, wasn't it?

18 A. Yes, it was.

19 Q. For you?

20 A. Yes.

21 Q. And I have you rendering 2.75 hours for the whole
22 month of December.

23 A. You are saying busy as far as this case. I thought
24 you meant busy in general. No.

25 Q. So when did you do all this work?

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1 A. I believe, if I recall correctly, I started in
2 February of last year.

3 Q. How many hours did you put in?

4 A. I couldn't tell you. The invoices I am sure would
5 show it, because I billed by the hour.

6 Q. What is an end point, Dr. Manning?

7 A. An end point is when you do an experiment, you
8 establish what sort of quality or performance you would like
9 to observe or see. And then you, in most cases you try to
10 identify some quantitative measure of that end point.

11 Q. What is an end point, say, for using a drug in a
12 human?

13 A. End point of using a drug in a human, in the United
14 States, the Food & Drug Administration as of 1962 has
15 established that that should be efficacy and safety.

16 Q. And what's a meaningful end point for preclinical
17 animal studies?

18 A. Preclinical animal studies have really two functions.
19 They are basically to try to provide some information about
20 the toxicity, which means does it have some correlation to
21 the safety aspect. And the second is typically there is
22 also animal models or some surrogate that addresses
23 something about the biological response or activity.

24 Q. So what do you need in order to do that? Do you have
25 to have a composition that you can actually deliver to the

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1 animals and test whether they live or die?

2 A. You have to have a composition. In my experience,
3 that composition may or may not be the same as the final
4 formulation that goes into humans.

5 Q. But it has to be stable enough that you can do some
6 experiments over time. Correct?

7 A. That's correct.

8 Q. You don't want instability in the formulation to
9 interfere -- you don't want it to be, as one of our other
10 witnesses used, you don't want it to create an artifactual
11 result. Correct?

12 A. That's correct.

13 Q. By an "artifactual result," we mean that sort of a
14 result that doesn't really tell you what's going on with the
15 drug in the animal. Isn't that correct?

16 A. Artifact, yes, that's what that means.

17 Q. We don't want artifactual results, we want real,
18 demonstrable, reliable results. Right?

19 A. That's correct.

20 Q. What you need is a formulation of your composition
21 that's actually stable and that you can give to the animals
22 over time and see whether it works or not?

23 A. Right. You want to have stability that is sufficient
24 to allow you to do those animal studies in a timely fashion.

25 Q. What is the end point described in the '363 patent,

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1 Dr. Manning?

2 A. The end point, I mean, are you talking about a
3 clinical or toxicological end point?

4 Q. It seems to me you know a lot about end points. Did
5 you study the '363 patent and come to a conclusion about end
6 points?

7 A. Well, the invention is to allow you to provide, to
8 stabilize nanoparticles by placing surface modifiers into
9 the formulation, with all of the provisos and description
10 that we have in there, yes.

11 Q. You said in your expert report, on this topic,
12 certainly, any screening process involves end points that do
13 not employ the exact same criteria for a commercially usable
14 formulation. However, this does not make the screening end
15 point meaningless.

16 Were you referring to the '363 patent, sir?

17 A. I was.

18 Q. What is the screening end point described in the '363
19 patent?

20 A. The way the screening process is described in the '363
21 patent is that you take a composition, where you have
22 generated nanoparticles, and in this case they did that by
23 grinding, but there is no limitation that you couldn't make
24 them by some other method.

25 You then screen them by adding various surface

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1 modifiers to see if there is some sort of ability of that
2 surface modifier to keep the particles from associating.
3 Agglomeration is the scientific term. And they did that by
4 visual inspection.

5 Q. So some sort of ability by visual inspection. Is that
6 the end point described in the '363 patent, sir?

7 A. It is.

8 Q. And let's take a look at that, just to be clear we are
9 talking about the same thing.

10 This is from JX-81, the '363 patent. This is a
11 description of the screening process. If you go down to the
12 bottom, it states, does it not, sir, by stable, it is meant
13 that the dispersion exhibits no flocculation or particle
14 agglomeration visible to the naked eye, and preferably, when
15 viewed under the optical microscope at a thousand times at
16 least 15 minutes and preferably at least two days or longer
17 after preparation.

18 Do you see that?

19 A. Yes.

20 Q. So there is a preferred end point of under the
21 microscope and two days, but there is an acceptable end
22 point of 15 minutes and under the naked eye. Is that
23 correct?

24 A. That's correct.

25 Q. You wouldn't put a dispersion that had only been

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1 proven to exhibit no flocculation or particle agglomeration
2 visible to the naked eye for at least 15 minutes, you
3 wouldn't put that in your body? Would you, Dr. Manning?

4 A. Well, that actually raised an interesting point, which
5 is visual inspection, certainly, in this case you would see
6 that certainly, you know, in one sense out of convenience,
7 because, obviously, if things are so bad you can see them
8 with the naked eye at a molecular level, that is obviously a
9 bad thing. You want to avoid that.

10 But it turns out visual inspection is actually a
11 really valuable tool in our industry. Every drug that is
12 made for parenteral administration, that is by injection,
13 undergoes visual inspection. And I personally had a number
14 of clients that have lost entire batches because they failed
15 visual inspection.

16 Q. That wasn't quite my question, was it, sir?

17 My question was, would you want to put in a
18 human body a composition that had only been proven to not
19 agglomerate on the basis of visual inspection for 15
20 minutes?

21 A. And that would never happen. If we go back to my
22 statement in my expert report, I said there is a screening
23 process, and that screening process is quite different from
24 what you would ultimately want to use for a commercial
25 product.

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1 Q. Let's just focus on this screening process and exactly
2 what you would get out of it, sir. You get 15 minutes of
3 stability. Right?

4 A. Or longer, it says, yes.

5 Q. And you get visual-inspection-based stability. That's
6 what it promises?

7 A. That's the screening tool, yes.

8 Q. And we are talking about nanoparticles. We have heard
9 in this case testimony after testimony about how tiny
10 nanoparticles are, haven't we?

11 A. We have.

12 Q. By the way, you have never intentionally created
13 nanoparticles, have you?

14 A. That's correct.

15 Q. So you don't have a lot of experience in actually
16 working with intentionally created nanoparticles, somebody
17 like, a accompany like Abraxis or, for that matter, a
18 company like Elan trying to create crystalline nanoparticles
19 and a company like Abraxis trying to create completely
20 different nanoparticles, you don't have that kind of
21 experience?

22 A. Microparticles, but not nanoparticles.

23 Q. So this end point here, 15 minutes under the naked
24 eye, that's just the starting point for lots more
25 experimentation to see whether you have a viable drug

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1 candidate, isn't it, Dr. Manning?

2 A. That's correct.

3 Q. Lots more experimentation. Correct?

4 A. In terms of making a commercial product.

5 Q. Even an animal test product, isn't that true, Dr.

6 Manning? You wouldn't stick a 15-minute-based composition

7 in an animal if you cared about the animals in your

8 laboratory, would you, sir, and using them efficiently and

9 productively?

10 A. You would certainly never intentionally risk an

11 animal, yes.

12 Q. You would never intentionally risk an animal based on

13 testing for 15 minutes of non-agglomeration,

14 non-flocculation?

15 A. Again, it's a screening tool and after which you would

16 certainly, again, if you are going continue commercial

17 development, preclinical or clinical, there certainly, as we

18 have heard a number of other people say, there is years of

19 arduous effort involved.

20 Q. Now, is that your explanation, sir, for all these

21 internal Elan documents that describe the problems they were

22 having, that they were actually trying to do the next step

23 beyond 15 minutes?

24 A. They certainly were engaged in a variety of activities

25 in terms of commercial development, yes.

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1 Q. Let's take a look at what I hope is -- no, let me flip
2 through this.

3 Let's take a look at DX-190, I think. Do you
4 see at the bottom of DX-190, sir, it says there is no
5 surfactant of choice for parenteral products at this time?

6 Do you see that?

7 A. I do see that.

8 Q. Of course, they are actually trying to create
9 something that might be viable and go into animal studies
10 and do something for humankind. Correct? That's what's
11 going on in this memo. Right?

12 A. I don't know what the context of the memo is.

13 Q. Let's take a look at -- let me ask you this: Do you
14 agree with the following statement: Ten years after the
15 1992 '363 patent application, the choice of a surface
16 stabilizer is non-trivial and usually requires extensive
17 experimentation to realize a desirable formulation?

18 A. Could we put that quote up on the screen so I could
19 read through it?

20 Q. Sure.

21 A. Thank you.

22 Q. Do you agree with that, sir?

23 A. If we could go through it.

24 Q. Just the February 2003 statement, the choice of a
25 surface stabilizer is non-trivial and usually requires

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1 extensive experimentation?

2 A. I have opinions about each piece of that. There is
3 actually two independent statements there.

4 Q. I will take both.

5 A. The first one says the choice of a surface stabilizer
6 is non-trivial. That is in fact the case. That is, in my
7 opinion, the value of the '363 patent, that invention, it
8 allows there to be a process to say -- in the formulation
9 business we never know ahead of time which combination of
10 stabilizer and drug will work. We may have, as over time,
11 we will gain a sense of what that should be so we don't have
12 to try everything in the world. But we don't know ahead of
13 time, a priori, as they say, what that means. So in fact it
14 is a non-trivial exercise.

15 The last part of the statement goes on to say,
16 usually requires extensive experimentation to realize a
17 desirable formulation.

18 Again, depending what you mean by desirable
19 formulation, the context in which this was used, again,
20 remember, there is a process to do the initial step, that's
21 the beauty of the '363 patent, getting to that initial
22 point, saying, this looks promising, let's start to do more
23 development work. Or does it talk about the more elaborate
24 lengthy formulation development process?

25 There is parts there, in the context of which

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1 this was taken, I would either say I would agree or we would
2 have to qualify.

3 Q. Let's take a look at DX-238. Page 240.

4 This is an internal Elan document, Technology
5 Development Department. We are -- already, in 1993 -- go
6 back to the opening slide, please -- we are going to
7 introduce new technology for nanocrystals. Do you see that?

8 A. I do see that.

9 Q. Now the next page, they are saying, We have a problem.
10 Few surfactants meet the criteria necessary for a successful
11 drug NanoCrystal formulation.

12 Size, stability, safety and efficacy.

13 Isn't it true, sir, that they had a heck of a
14 time getting past that 15 minutes visually observed
15 non-agglomeration? Isn't that exactly what that slide is
16 saying?

17 A. No, I don't see that slide saying that at all.

18 Q. The issue of contamination, is that the answer, sir,
19 that the contamination is not an issue because all we are
20 talking about is 15 minutes of observation in a beaker by
21 the naked eye?

22 A. Sorry. Can we go over that question again?

23 Q. Contamination matters if you are actually going to put
24 one of these compositions in an animal, doesn't it, sir?

25 A. It certainly could, yes.

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1 Q. And contamination would certainly matter if you were
2 going to put one in a human being, wouldn't it?

3 A. That is certainly true.

4 Q. If there were contamination issues that underpinned
5 the very technology disclosed in the '363 patent, that would
6 be important for people to know, wouldn't it?

7 A. It's important to know that the invention works the
8 way it is intended, yes.

9 Q. That's my whole point, I guess. What is the intent,
10 sir? Is the intent of this patent to create particles that
11 subsist for 15 minutes under visual inspection? Or is the
12 intent of this patent to create something that would be
13 useful?

14 A. The intent of the patent is what's captured in the
15 claim language.

16 Q. Let's go there. Thank you for leading me along.
17 Let's take a look at some of the claims.

18 Let's take a look at Claim 10, one of the claims
19 in the lawsuit.

20 A. All right.

21 Q. In a method of treating a mammal. We had some
22 testimony about this. A mammal includes everything from
23 mice to humans. Right?

24 A. That's correct.

25 Q. We are claiming that we have invented a method of

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1 treating a mammal comprising administering to the mammal an
2 effective amount of an anticancer agent, the improvement
3 wherein the efficacy of said anticancer agent is increased
4 by administering said anticancer agent in the form of the
5 particles of Claim 1.

6 Do you see that?

7 A. I do.

8 Q. The end point here is efficacy in mammals, isn't it?

9 A. Yes. They claim a method for treating a mammal.

10 Q. Improved efficacy in mammals, that is the end point?

11 A. The efficacy is, yes.

12 Q. Then in Claim 11, in a method of treating a mammal
13 comprising administering to the mammal an effective amount
14 of an anticancer agent, the improvement wherein the toxicity
15 is reduced by using the particles disclosed in this patent
16 application.

17 Do you see that?

18 A. I do see that.

19 Q. So in this case the end point is reduced toxicity,
20 isn't it?

21 A. Yes.

22 Q. Would 15 minutes under visual inspection give you any
23 insight whatsoever into whether that composition would
24 ultimately exhibit reduced toxicity?

25 A. No. That would allow you to choose which agents would

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1 be worth moving forward with.

2 Q. With all that extensive experimentation that you
3 acknowledged a few minutes ago you would still have to do?

4 A. Whatever experimentation would be required, yes.

5 Q. But it would typically be a lot, from 15 minutes to
6 actually knowing that you have got in a mammal reduced
7 toxicity, wouldn't it, sir?

8 A. Well, it would be less for commercialization as
9 opposed to preclinical testing.

10 Q. But it would still be a lot?

11 A. It would be whatever is necessary.

12 Q. Well, typically, it's going to be a lot, isn't it? We
13 saw boxes and boxes of work for paclitaxel, didn't we?

14 A. For their NDA, absolutely.

15 Q. And, by the way, mammal does include humans, doesn't
16 it?

17 A. It does.

18 Q. So they didn't limit the claims to mice?

19 A. That's right, they did not.

20 Q. They claimed they had invented nanoparticulate
21 anticancer agents, many of them in Claim 1, eight or so of
22 them in Claim 5, with all these surface modifiers, and they
23 said, we have invented a way to introduce them into mammals,
24 didn't they, sir?

25 A. That's what they claimed, yes.

|Manning - cross

1 Q. And they claimed that they could do it with increased
2 efficacy?

3 A. Yes, in Claim 10.

4 Q. And they claimed they could do it with reduced
5 toxicity?

6 A. That's what they say in Claim 11.

7 Q. In the case of toxicity, sir, while this application
8 was pending in the United States Patent Office, they never
9 disclosed to the Patent Office all the problems with
10 contamination that we have seen in the course of this trial,
11 did they?

12 A. I am not exactly sure exactly which data was provided
13 on that topic.

14 Q. By the way, what's the end point in Claim 1?

15 A. The end point is to -- if you put it up on the screen.
16 It is to have particles containing medicaments useful in
17 treating cancer. And it goes on to say that there is going
18 to be a certain amount of surface modifier. And as we go
19 down here, it is basically a composition patent. There is a
20 composition of useful nanoparticles that fit the screening
21 methodology.

22 Q. Where the medicament used for treating cancer is
23 susceptible to treatment.

24 Do you see that?

25 A. Yes.

|Manning - cross

1 Q. Is the end point here 15 minutes under visual
2 inspection?

3 A. No. It is particles that have a composition that
4 meets this language.

5 Q. What kind of stability do they have to exhibit, sir?

6 A. According to the screening process, the step is to
7 identify which are useful versus not useful, is the visual
8 inspection screening process we described.

9 Q. For 15 minutes?

10 A. Or longer.

11 Q. So, in your view, the end point here is anything from
12 15 minutes to it works in the human body?

13 A. No. My point is this is a composition claim. It's
14 just talking about the particles and what they need to have.

15 Q. Let's go at it a slightly different way.

16 A. Sure.

17 Q. Does the '363 patent teach you how to create
18 compositions that you would have some reasonable degree of
19 confidence would be useful, compositions according to Claim
20 1 that would be useful in humans?

21 A. They teach you how to make particles, how to screen
22 for them, they also provide guidance in terms of what
23 surface modifiers would have reasonable success of being
24 useful, yes.

25 Q. Reasonable success of being useful, sir?

|Manning - cross

1 A. Yes.

2 Q. What do you mean by reasonable?

3 A. That in their description they say, here is a variety
4 of surface modifiers. They go on to qualify and say that
5 the ones that we would prefer to choose or you should choose
6 would be those that are listed in the Handbook of
7 Pharmaceutical Excipients, those that are commercially
8 available or easily synthesized. So there is additional
9 guides of what surface modifiers would be useful.

10 Q. Put yourself back in 1992. And somebody hands you the
11 '363 patent. And they say, Dr. Manning, you are really
12 smart. Go make a useful drug composition out of this. Tell
13 me exactly what you would have to do in order to achieve
14 that.

15 A. Sure.

16 Q. You have done that before. Right? You have made
17 drugs?

18 A. I have.

19 Q. So you know what it takes to get from start to finish?

20 A. Yeah. I was actually doing it in 1992 as well.

21 Q. You know what it takes to get to preclinicals in
22 animals, don't you?

23 A. I do.

24 Q. But you don't know for nanoparticles?

25 A. I have not made nanoparticle preparations.

|Manning - cross

1 Q. Leave that out and tell us the steps that you would
2 have to do from the '363 patent disclosure, 15 minutes under
3 visual inspection, before you had something that you would
4 put in animals?

5 A. Again, the point is, first of all, we need to pick
6 some modifiers that are going to meet the criteria. The
7 inventors were quite clear. We are not going to try
8 everything on the shelf. We are not going to go to a
9 chemical catalog and buy everything that they have.

10 We are going to pick ones that have certain sets
11 of properties. And that's why, also, remember, this is
12 written for someone skilled in the art. They would have a
13 sense of, in my business, you are going to go ahead and try
14 things, for example, that are already found in approved
15 products.

16 That list was certainly shorter in '92 than it
17 is now. But it's still a reasonably short list. So you
18 have some constraints on you in terms of what you are going
19 to choose.

20 Once you go through the screening process and
21 find which of those things that actually keep those
22 nanoparticles pure, that will allow you to proceed, because
23 before you go on and to there, you want to be careful and
24 proceed with caution before you use that.

25 Q. That's okay. I think we got a sense that this is a

|Manning - cross

1 first step on a multi-step process, isn't it, sir?

2 A. For commercialization, absolutely.

3 Q. Even for preclinical studies?

4 A. Yes.

5 Q. Now, let's talk about the question of whether there
6 are disulfide bonds. I want to switch away from enablement,
7 put on your cross-linking hat and we will talk about that
8 for a minute. Let's put up PX-165.

9 Do you recognize what PX-165 is, sir?

10 A. Not off the top of my head. Orient me, please?

11 Q. This is a certificate of analysis of human albumin
12 from a company called Grifols that is certifying -- it was
13 testified to, I believe, in the course of the trial.

14 A. All right.

15 Q. Do you have it?

16 A. Yes.

17 Q. Can we highlight the polymers and aggregates. This
18 certification, if you were here for the testimony, this is
19 about whether this human albumin is sufficiently comparable
20 to the albumin in the bloodstream that it can be
21 administered. Is that your understanding? Why don't you
22 assume with me, I will ask you a hypothetical question.
23 Assume with me that's what this certification is.

24 A. All right.

25 Q. Isn't it true, sir -- let's go back a little bit. You

|Manning - cross

1 say polymers and aggregates?

2 A. I see that, yes.

3 Q. Do you see the specification, less than five percent?

4 A. I do see that.

5 Q. So the specification for albumin with polymers and
6 aggregates is less than five percent?

7 A. That's right.

8 Q. For this. But there is a ton of albumin in the blood,
9 isn't there? Not a ton literally, but there is lots of
10 albumin in the blood?

11 A. Yes, there is.

12 Q. In fact, in this case, in this Grifols, there was 4.16
13 percent of polymers and aggregates, wasn't there?

14 A. As measured by their certificate of analysis, yes.

15 Q. So contrary to what you said in response to Mr.
16 Scheve's questions, polymers and aggregates are present in
17 human serum albumin, aren't they, sir?

18 A. And in my previous testimony, when I talked about the
19 fact that Abraxis uses USP albumin, they also set a similar
20 sort of limit saying it is less than five percent polymers
21 and aggregates.

22 Q. Let's see if we can connect on this. In the
23 bloodstream, is there albumin that is represented by
24 polymers and aggregates?

25 A. In the bloodstream? I don't believe there is.

|Manning - cross

1 Q. So this is not sufficiently similar to human
2 bloodstream albumin, in your view?

3 A. Yes. Maybe I need to clarify how we get from the body
4 to this sort of product.

5 All the albumin that is used in commercial
6 products is obtained by plasma fractionation. Remember, I
7 described for you last week something called the Cohen
8 fractionation process. This group at Harvard in the 1940s
9 identified a way to extract proteins from human plasma.
10 Plasma is the part that doesn't contain your red blood
11 cells.

12 When they do that, they are able to selectively
13 precipitate or remove albumin, gamma globulin and other
14 things that turn out to be very useful in medicinal agents.
15 Albumin is one of those, because, as we talked about, it is
16 present in very high concentrations.

17 So in the process of doing that, purifying it,
18 isolating it and so on, there is formulation of these
19 aggregates, these weakly associated things that form.
20 Because that happens, to some degree, they have to set what
21 is called a specification, saying we are going to put an
22 upper limit and we will not sell a product that exceeds that
23 limit. So every batch has to meet that specification.

24 Q. And this batch is suitable for administration to
25 people, isn't it?

|Manning - cross

1 A. Yes, it is.

2 Q. So you could administer human serum albumin in
3 substantial quantities with up to five percent aggregation,
4 couldn't you?

5 A. That's right, because, again, we are talking about
6 these things that are weakly associated and can come apart
7 quite easily. So as soon as they get in your bloodstream it
8 dilutes out and you have monomeric albumin again.

9 Q. Isn't that what the video showed, it broke apart and
10 diluted and all of a sudden the paclitaxel is out?

11 A. What the video showed --

12 Q. Leaving aside the impact -- I think you misunderstood
13 a little bit -- leaving aside the impact, didn't it show the
14 particle breaking apart?

15 A. It showed the albumin coming across in individual
16 pieces.

17 Q. So, sir, now let's just clarify this whole point about
18 your testimony versus Dr. Amiji's testimony.

19 Let's have JX-5. Let's go to 401A.

20 This is the INDA. You talked about how you
21 reviewed this document. Do you recall that?

22 A. Yes.

23 Q. Abraxis reported the level of polymers, et cetera,
24 non-monomeric content, to the FDA in this document. Right?

25 A. That's right.

|Manning - cross

1 Q. So if we go to 401, it's Bates 401, 547 in the
2 document. Can we highlight the albumin isomer issues.

3 Dr. Manning, when you reviewed this document and
4 when you have heard the back-and-forth, you agree with me
5 that this is the isomer ratio in the entire Abraxane
6 composition. Correct?

7 A. I believe that to be the case. There is parts of it
8 that aren't absolutely clear. But I believe that to be the
9 case.

10 Q. In this particular document, Abraxis is doing
11 precisely what you said drug companies do, they are
12 reporting to the FDA in this case the isomer composition of
13 all of the albumin. Right?

14 A. By a particular analytical method, that's correct.

15 Q. And it's showing that even looking at all of the
16 albumin, about 20 percent of it is not a monomer. Do you
17 see that?

18 A. Yes. By their analytical method, they find that the
19 monomer content is 79.8 and 79.6.

20 Q. You weren't critiquing this analytical method?

21 A. In what context? I am sorry.

22 Q. In any context. Did you have any problem with this
23 experiment? I don't remember any testimony to that effect?

24 A. I did not testify on this particular table, that's
25 correct.

|Manning - cross

1 Q. You testified about it but you didn't critique it.
2 Right?

3 A. Well, in my testimony I showed a different table of
4 results.

5 Q. But the same data. Right? Very similar data?

6 A. No. In the table that I showed, after formulation,
7 you may recall that the monomer content was reported as
8 84.68 percent.

9 Q. Let's go with that. When you looked at that one, you
10 were looking at all the albumin. Right?

11 A. I believe that's how they did the experiment, yes.

12 Q. And you didn't -- that doesn't really tell you
13 anything about the level of cross-linking on the albumin
14 that's adsorbed to the amorphous paclitaxel, does it?

15 A. As I stated in my testimony, the analytical method of
16 size exclusion chromatography does not tell you anything
17 about whether or not there is an existence of a chemical
18 strong interaction between them. Simply that there is a
19 distribution of sizes, that's correct.

20 Q. This figure is not the relevant figure, or the 84
21 percent is not the relevant figure for the analysis
22 underpinning this lawsuit, is it, sir?

23 A. I am not sure what you mean, underpinning the lawsuit.

24 Q. The question this jury needs to decide is whether the
25 albumin that is adsorbed to the paclitaxel in Abraxane, that

|Manning - cross

1 albumin, has any kind of cross-link, isn't it?

2 MR. SCHEVE: Excuse me, Your Honor. May we have
3 a sidebar?

4 THE COURT: You can rephrase.

5 BY MR. JACOBS:

6 Q. The technical question that needs to be asked in order
7 to answer the question here is whether the human serum
8 albumin that is adsorbed to the surface of the paclitaxel in
9 Abraxane has any kind of cross-linkages between it, isn't
10 it?

11 A. Yes. If I may go to the claim and the claim
12 construction. This says that the individually adsorbed
13 molecules had to be essentially free of intermolecular
14 cross-linkages. That is the definition the Court has
15 construed for non-cross-linking.

16 MR. JACOBS: Thank you, Doctor.

17 MR. SCHEVE: Nothing, Your Honor.

18 THE COURT: Thank you, Doctor.

19 (Witness excused.)

20 (The following took place at sidebar.)

21 THE COURT: Mr. Scheve is right, there is no
22 evidence in the record. On the other hand, I would expect
23 you would be willing to stipulate that, if recalled, he
24 would say that he did testing on Abraxane, even though there
25 is no evidence, you are correct.

1 MR. SCHEVE: Some testing on Abraxane. But I
2 can't waive the privilege, Judge.

3 THE COURT: I am not asking you to do that.

4 MR. SCHEVE: If I say what he did or what he
5 didn't do for Mr. Sipio, what I have told you is he didn't
6 do any x-ray powder diffraction on Abraxane. He didn't
7 separate any particles in doing any x-ray powder
8 diffraction.

9 MR. JACOBS: That is a new fact. Now we are
10 going further than we were.

11 MR. SCHEVE: The stuff he did for Mr. Sipio, I
12 represented for you and know for a fact, that is not all on
13 Abraxane. A lawyer goes to a Ph.D. and says help me
14 understand some concepts. And that's what happened here.
15 So the inference that you are being asked to draw is look at
16 all these tests on Abraxane. And I am saying, there is no
17 evidence in this record to support that.

18 THE COURT: When you hold your hands apart and
19 you say all these tests --

20 MR. SCHEVE: 440-some references, that I did my
21 duty --

22 THE COURT: I am not expecting to permit the use
23 of that exhibit, number one.

24 Just -- let me go to the end. This may help
25 inform your views as to how we can get through this. Here

1 is the instruction I am going to give: Doctor hear Britain
2 was retained as an expert by Elan in this case. Dr.
3 Brittain performed tests on Abraxane for Elan. Prior to
4 trial, Abraxis requested Elan provide it with the documents
5 related to this testing. Elan failed to produce these
6 documents. I have been asked to decide whether this
7 activity by Elan was proper. I have determined that under
8 the Federal Rules of Civil Procedure it was not. As a
9 result, I will instruct that you may infer that the contents
10 of these documents would have been favorable to Elan's case
11 on infringement.

12 That is the instruction I am going to give.

13 MR. SCHEVE: I will register my objection. But
14 I understand where we are going.

15 THE COURT: I need to know -- Mr. Scheve is
16 right, we don't have any evidence in the record on this
17 issue. In other words, for me to say, as was proposed here,
18 you have heard that Elan withheld documents -- no, the jury
19 hasn't.

20 MR. JACOBS: So I think that meets, I think we
21 he would prefer shall, under the circumstances. But I
22 understand the Court's view. I think that is adequate. I
23 think that would be sufficient. I don't think we need to do
24 any kind of voir dire of Dr. Brittain. I have thought about
25 that. But I don't think we need to do that. I think we

1 have the record and we can proceed.

2 MR. SCHEVE: Thank you, Your Honor. Could I
3 please take a biological break. Dr. Liversidge will be our
4 last witness in rebuttal.

5 (End of sidebar conference.)

6 THE COURT: We are going to take a short break,
7 ladies and gentlemen. We have one more rebuttal witness
8 from Elan, and then I should be able to tell you whether
9 there is going to be any more rebuttal from Abraxis.

10 (Jury leaves courtroom at 3:00 p.m.)

11 THE COURT: All right. Let's bring in the jury.
12 We are going to need to end at 4:15. I have a criminal
13 matter.

14 MR. JACOBS: We will be done by then.

15 (Jury enters courtroom at 3:13 p.m.)

16 We will resume, thank you. Please take your
17 seats.

18 Mr. Scheve.

19 MR. SCHEVE: Thank you, Your Honor. With the
20 Court's permission, Your Honor, we would recall Dr. Gary
21 Liversidge.

22 THE COURT: Okay.

23 ... GARY LIVERSIDGE, having been previously
24 sworn as a witness, was examined and testified further as
25 follows ...

G. Liversidge - direc

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DIRECT EXAMINATION

BY MR. SCHEVE:

Q. Dr. Liversidge, I hope to be quick with you. But I want to address a few items that were raised during the trial. Dr. Amiji testified, I am going to quote, he said, "It would take a lifetime to screen the compounds identified in the '363 patent," end quote.

Do you recall hearing that testimony?

A. Yes, I do.

Q. Would it take a lifetime for one of ordinary skill in the art to screen compounds identified in the '363 patent?

A. No, it wouldn't.

MR. JACOBS: Objection.

THE COURT: What is the basis?

MR. JACOBS: Asking for an expert opinion, Your Honor. We just went through that.

THE COURT: Sustained.

BY MR. SCHEVE:

Q. Does your laboratory routinely screen potential compounds for use with the surface modifiers identified in the '363 patent?

A. Yes, we do.

Q. How many compounds does your lab screen in an average week?

A. It kind of goes up and down. On average, I would say

G. Liversidge - direct

1 we screen about ten new compounds a week. Some weeks, you
2 know, it may be. Some weeks, it may be 15. So I am giving
3 you an average.

4 Q. Now, this screening process about which Dr. Amiji
5 testified, sir, does the determination of whether or not you
6 have got a compound that could move forward into
7 development, does it end with the screen?

8 A. No. That's just the first step to identify suitable
9 combinations of the drug and surface modifiers.

10 Q. What is communicated in the patent to those skilled in
11 the art about the steps after using the screening process to
12 identify potentially compatible drugs and surface modifiers?

13 MR. JACOBS: Same objection.

14 THE COURT: Sustained.

15 BY MR. SCHEVE:

16 Q. Are there companies that contain within their four
17 walls persons of ordinary skill in the art who have a
18 license and actually practice the '363 invention?

19 A. Yes, there are.

20 Q. What companies are they?

21 A. There are five. There is BMS -- I am sorry, Bristol
22 Myers Squibb. Sanofi-Aventis. Merck. Johnson & Johnson.
23 And I blanked on the fifth one. Let me go through that
24 again. BMS, J&J, Sanofi-Aventis, Merck.

25 Q. Might it be Roche?

G. Liversidge - direct

1 A. Roche, sorry.

2 Q. Has anyone from Bristol Myers Squibb, Roche, Merck,
3 J&J or Sanofi-Aventis ever complained to Elan that the '363
4 patent does not provide adequate description of the
5 invention?

6 A. No, nobody has.

7 Q. Has anyone from those companies who have licensed the
8 '363 and nanoparticulate technology ever complained to Elan
9 about how to practice the invention described in the '363?

10 A. No. They are all doing it.

11 Q. Sir, Dr. Soon-Shiong testified in the case that the
12 invention that's disclosed in the '363 patent was designed
13 to stay in the blood. Do you agree with that?

14 A. No.

15 Q. Could you explain to the jury why?

16 A. Well, you want to get the drug, as Dr. Sion -- maybe I
17 pronounced his name wrong -- you want to get the drug to the
18 site of action, in this particular case, the tumor. So if
19 you kept it in the blood, it wouldn't have any efficacy.
20 So, you know, why would you want to give an anticancer agent
21 that doesn't get to the cancer?

22 We show in the patent examples of efficacy of
23 our invention when given to preclinical models and we
24 compare that to the commercial product and show substantial
25 improvements in the efficacy.

G. Liversidge - direct

1 Q. Through what kinds of models was that be established?

2 A. The murine and the xenograft models that my wife
3 explained. I can explain them again if people want. But I
4 thought she explained them pretty good.

5 Q. Are the claims of the '363 patent limited to the
6 creation of nanoparticles using ball milling?

7 A. No.

8 Q. So if the jury goes to the claims of the '363 patent,
9 is it only limited to nanoparticles that are created through
10 a ball mill?

11 THE COURT: I think you could rephrase that.

12 BY MR. SCHEVE:

13 Q. Does the language of the '363 claims -- is it limited
14 to nanoparticles created through a wet ball mill?

15 A. No, it isn't.

16 MR. SCHEVE: Pass the witness, Your Honor.

17 THE COURT: All right. Mr. Jacobs.

18 CROSS-EXAMINATION

19 BY MR. JACOBS:

20 Q. Let me see if we can clear up a little bit of
21 confusion.

22 BMS, do you have a relationship with them?

23 A. Yes. I thought that was a statement. Sorry.

24 Q. It was a kind of question. If it confuses you, I will
25 do the other kind. I don't mean to try and confuse you.

G. Liversidge - cross

1 A. No, that's okay.

2 Q. Did you go to BMS and say, BMS, here is the '363
3 patent, nothing else, we want X percent of the royalties on
4 the drugs that you create?

5 A. Could you just rephrase that, counselor?

6 Q. I will rephrase it. Does your relationship with BMS
7 consist of Elan providing BMS with the '363 patent, nothing
8 else, and saying, go forth and prosper and give us a
9 percentage of your revenues?

10 A. The '363 and other patents are included in the
11 license.

12 Q. Many other patents. Correct?

13 A. There are. But don't ask me the number. I just can't
14 remember off the top of my head.

15 Q. If the jury takes a look at that license agreement,
16 they will see a long list of patents. Right, sir?

17 A. You are definitely going to see a list of patents. I
18 just can't tell you exactly the number in there.

19 Q. But the fact is that Elan has improved on the
20 technology in the '363 patent over time, hasn't it?

21 A. Yes. I mean, everyone strives for continual
22 improvement.

23 Q. In fact, you have made, in your corporate view,
24 substantial improvements over what you disclosed in the '363
25 patent. Correct?

G. Liversidge - cross

1 A. Well, we have other patents which were issued after
2 that one that covers the NanoCrystal technology.

3 Q. And whether or not it is in a patent, you have just
4 developed the technology you spent 15 years working on, that
5 technology. Correct?

6 A. I think maybe a little longer than that. Yes, round
7 about that much time.

8 Q. You have be invested lots and lots of money to try and
9 take the '363 disclosure and make it something that would be
10 actually useful to drug companies. Correct?

11 A. I am not following you. Ask me a slightly different
12 way, please.

13 Q. The questions Mr. Scheve was asking you were, did
14 anyone complain to you that the '363 patent doesn't provide
15 enough disclosure. Do you recall those questions?

16 A. Yes.

17 Q. Nobody is -- in fact, literally no one has just taken
18 a license to the '363 and not gotten anything else from
19 Elan. Correct?

20 A. I think you are right.

21 Q. So no one has just been given a little package of
22 however many columns and pictures in it, where Elan says to
23 them, take the '363, go develop drugs, by the way, if you
24 have any problems, give us a call? You haven't done that
25 with anybody. Right?

G. Liversidge - cross

1 A. No, we haven't.

2 Q. You have always given them a complete package
3 representing lots and lots of development work beyond the
4 '363 patent disclosure. Correct?

5 A. Beyond the invention, we have shared with them
6 additional know-how and development aspects, yes.

7 Q. Including manufacturing methods?

8 A. I am trying to think.

9 Q. Including much later on in time, you developed some
10 techniques to reduce contamination. Right?

11 A. We had techniques at the time as well.

12 Q. But later on you developed techniques to reduce
13 contamination, didn't you?

14 A. In addition to the ones we already had, yes.

15 Q. And the '363 patent doesn't actually tell you how to
16 take the contamination out of the particles that you have
17 developed, does it?

18 A. It teaches you through carbon 5 through 7 how to
19 optimize the formulation, and the embodiment there is the
20 milling process, and it teaches you all the conditions in
21 there in which to be employed.

22 Q. So while I was sitting there, trying to get up here
23 very quickly to ask you questions, I did the math, let's see
24 if we can compare notes.

25 I believe you said that you screen on average

G. Liversidge - cross

1 ten or 15 compounds per week. Is that right?

2 A. Ten. Some weeks it may be 15, maybe some weeks it may
3 be five. On average, I would say about ten.

4 Q. That's about 520 per year. Right?

5 A. Yes.

6 Q. Let's just take a low-end estimate of what Dr. Amiji
7 was saying, how many compounds there are.

8 Let's say there were 52,000 combinations of
9 compounds in the '363 patent. By my calculation that would
10 take a hundred years. Does that match your math?

11 A. It obviously didn't. I don't want to seem facetious,
12 but, you know, we get the compounds and they go out in that
13 same week.

14 Q. The ten compounds a week?

15 A. Yes.

16 Q. On this issue of prolonged circulation in the
17 bloodstream, are you suggesting that it was not Elan's
18 intent that the NanoCrystal anticancer medicaments you were
19 thinking about in the early nineties exhibit prolonged
20 circulation in the bloodstream?

21 A. Some will, depending on the stabilizer system, some
22 won't.

23 Q. I asked you about Elan's intent around the time of the
24 '363 patent. Isn't it true that it was Elan's intent that
25 the NanoCrystal compositions exhibit prolonged circulation

G. Liversidge - cross

1 in the bloodstream?

2 A. I am trying to think what our intent was back then.

3 Q. Can I help you a little bit by showing you a document?

4 A. Sure. That would help. Thank you.

5 Q. So this is the -- these are the slides you sent to
6 Abraxis. Do you recall that exhibit?

7 A. Yes, I have seen these before.

8 Q. JX-20. Did you actually write these slides,
9 Dr. Liversidge? I don't remember if we covered that.

10 A. Some of them I definitely did. Some of them I am not
11 sure about.

12 Q. How about the ones we have highlighted here on the
13 screen, the page is indicated Parenteral NanoCrystal
14 Applications. The drawing of the Y with the NanoCrystals
15 and Application of NanoCrystal Technology to Parenterals?

16 A. I definitely know that middle one, like the blood
17 vessel, I definitely did that. The other two I am not -- I
18 just can't recall. But I definitely know that middle one.

19 Q. You sent this in 1996 to Abraxis. Correct?

20 A. Yes.

21 Q. And the slides themselves were created a few years
22 before?

23 A. I just, honestly -- some of them may, some of them may
24 not. I just can't tell you.

25 Q. It is true, is it not, Dr. Liversidge, that these

G. Liversidge - cross

1 slides exhibit a design idea of restricting compounds to the
2 bloodstream? Correct?

3 A. I think that top one you have got there, that A, says
4 platform to restrict compounds to the vasculature.

5 Now, we have to take that in light of the major
6 therapeutic focuses that were there for Sterling.

7 We had a major diagnostic imaging program.

8 People may not be familiar with diagnostic
9 imaging. What you do is, say, you have a blockage in the
10 heart, and you want to see how bad the blockage is. What
11 you take is an imaging agent, which has iodine molecules on
12 it, so they are radio dense, when you shine the x-rays
13 through, you don't go through those. What we have is a lot
14 of these water-soluble agents.

15 So if we wanted to, God forbid if this ever has
16 to happen to you, but if you had a heart attack, what we
17 would do with the state of the art at the time is, we would
18 get into your artery, cut you in the groin, then we would
19 thread up this tube to just above your heart, and then we
20 would squirt in the imaging agent. And what happens to that
21 imaging agent is it diffused that rapidly so we only got one
22 shot of you. If we mucked it up, you have to come back a
23 month later, because the imaging agent had to clear.

24 So one of our focuses was to try and restrict
25 these diagnostic imaging agents to the vasculature so we

G. Liversidge - cross

1 could just have these nanoparticles, a simple peripheral
2 injection that would fly all around the body and we could
3 image your heart. And if we didn't get a good picture, we
4 could image it again.

5 That is the genesis on this top yellow thing
6 that you have highlighted.

7 Q. The same is true for the bottom that I have
8 highlighted, Application of NanoCrystal Technology to
9 Parenterals, Focus: Poorly water soluble diagnostic imaging
10 agents and oncologics that may benefit from prolonged
11 vascular circulation?

12 A. No doubt about it, that's what we say. Could I just
13 give you a little bit of explanation?

14 Q. I think I got the answer I wanted, which was yes?

15 A. It's always but. All right. Since the Court's wants
16 us to move along, I won't give you the explanation.

17 Q. Thank you, Doctor.

18 MR. JACOBS: No further questions, thank you.

19 THE COURT: Mr. Scheve.

20 REDIRECT EXAMINATION

21 BY MR. SCHEVE:

22 Q. Just quickly, Doctor. Do you have an explanation that
23 you wanted to offer in response to the last question?

24 A. Yes. It was just that many particulates, when they
25 are given an IV, they get taken up by what is called the

|Manning - redirect

1 reticuloendothelial system. And there is a special type of
2 cell that literally comes out and grabs these particles.
3 And these fibrositic cells are located in the liver and
4 spleen.

5 So what happens is a major problem for
6 particulate or nanoparticles and delivery systems in our
7 art is people would inject them. And the body is designed
8 to naturally take up these foreign particles into the liver
9 and spleen.

10 What we were trying to avoid here, we were
11 trying to communicate, albeit poorly and I can see the
12 confusion, we were trying to say, we don't want this to
13 happen because they clear very fast from the blood system.
14 But they don't go to the tumor. They clear to the liver and
15 the spleen. And so you don't want that. You want to keep
16 them in the blood system, so they have sufficient time to go
17 out and accumulate in the tumor.

18 MR. SCHEVE: That's all I have, Your Honor.

19 THE COURT: All right. Thank you, Doctor.

20 (Witness excused.)

21 THE COURT: Mr. Scheve.

22 MR. SCHEVE: Your Honor, I get to utter the
23 words, we rest.

24 THE COURT: All right. Mr. Jacobs.

25 MR. JACOBS: We rest, Your Honor.

1 THE COURT: All right. For planning purposes,
2 let me see counsel.

3 (The following took place at sidebar.)

4 THE COURT: I am trying to decide what time to
5 have the jury hear, because we are not going to be ready
6 with these instructions tonight. That is clear. The
7 logistics of this will be somewhat of a challenge. I don't
8 know if you have a more recent iteration for me.

9 MR. SCHEVE: I think they have been banging
10 heads on the sixth floor.

11 THE COURT: We will be able to talk about that
12 tonight?

13 MR. SCHEVE: If I told you I would be speaking
14 from a position of lack of knowledge.

15 THE COURT: If we can talk about them tonight,
16 that's going to advance the issue, the time that the jury
17 can come in.

18 But if we can't, we are going to need to spend,
19 I would imagine, a little bit of time, beginning at maybe
20 8:30, talking about them. I am thinking about having the
21 jury report at 10:00. What do you think?

22 MR. SCHEVE: I think it is a good idea.

23 MR. JACOBS: That sounds fine.

24 THE COURT: Do the physical collating and get
25 the instructions.

1 MR. JACOBS: Can I raise one thing, responsive
2 to your comment about the length of reading of the
3 instructions.

4 Is there some way the parties could stipulate to
5 some other procedure? We wouldn't have to talk to them to
6 two full hours --

7 THE COURT: I am open.

8 MR. SCHEVE: I think the law requires it, Judge.
9 I am sorry, I know it's miserable, I think it's required.

10 THE COURT: Over the evening, I will take
11 another look at that.

12 MR. SCHEVE: We will look, too.

13 MR. JACOBS: There are obviously some key
14 instructions that go to the issues. But I think they kind
15 of got the point of this exercise.

16 THE COURT: I agree with the spirit of what you
17 are saying.

18 My thinking is that Mr. Scheve is probably
19 correct.

20 I only injected what I did because of the
21 reality that it does become a rather exhausting process for
22 them listening. I wouldn't mind taking a break, either.
23 Delivering patent instructions, you have been in complex
24 cases --

25 MR. SCHEVE: Yes, Your Honor, but not this kind

1 of stuff.

2 THE COURT: Any complex civil stuff can get
3 rather dense.

4 Let's tell them, we will resume at 8:30 but the
5 jury will be here at 10:00.

6 (End of sidebar conference.)

7 THE COURT: All right, ladies and gentlemen. We
8 have now come to the close of the evidence from both
9 parties. And it is going to be my job to next give you
10 final instructions. That won't happen today. We were just
11 talking about trying to plan the logistics of this and what
12 time you should come back, because there is still some
13 discussion that I must have with the lawyers about some
14 differences they have over how the final instructions should
15 look, not in terms of physical appearance, but the contents
16 of the instructions.

17 So other lawyers you don't see here for both
18 sides are in the process now of having a discussion with a
19 view toward trying to narrow down those disputes.

20 Eventually, to bring to me for resolution with
21 regards to those they can't resolve on their own. With that
22 in mind, we will take our best guesstimate. And I am going
23 to tell you to be back here at 10:00 o'clock in the morning,
24 with the earnest hope that we will all be ready for you. We
25 will start well before you get here, but by the time you get

1 here, it is our hope that we will be prepared to have you
2 come in, have me instruct you, probably take a lunch break
3 at that point, and then come back and hear the closing
4 speeches of counsel. Then we will give you the case.

5 Now that all the evidence is in, it is critical
6 for you to recall my earlier instructions: Keep an open
7 mind. You will have time to discuss the evidence and come
8 to a conclusion after you have listened to one another,
9 considered all the evidence that you deem it appropriate to
10 consider.

11 Don't do any research. Don't listen to anything
12 touching on this subject of cancer research drug development
13 at all. I would suggest, just leave alone any drug
14 development things that you might run across in the popular
15 literature over the evening and on TV or the radio. Don't
16 talk about these events with anyone. We will see you back
17 here tomorrow at 10:00 o'clock. Take care. Travel safely.

18 (Jury leaves courtroom at 3:37 p.m.)

19 THE COURT: Mr. Scheve, is there anyone here
20 that you can ask that question?

21 MR. WALTERS: The status of the jury
22 instructions?

23 THE COURT: Yes.

24 MR. WALTERS: We took Your Honor's words to
25 heart and met this afternoon, Mr. Sullivan and I. And

1 narrowed them down significantly. I think we are at the
2 point where we need to get, to talk to Mr. Jacobs and
3 Mr. Scheve about a few issues, and one of our associates is
4 back turning around what we had agreed upon. And there is
5 about, I don't know the exact number, but around, around ten
6 issues that are still teed up that we need to have a
7 discussion among lead counsel.

8 THE COURT: You have teed up these issues for
9 discussion with lead counsel?

10 MR. SULLIVAN: And eliminated others, Your
11 Honor.

12 MR. WALTERS: They are in trial, so we knew that
13 wasn't going to happen this afternoon.

14 THE COURT: It would be helpful, if possible, if
15 you can get just those that remain at issue after lead
16 counsel get a chance to consider your positions, and just
17 provide me with a copy of those before we leave for the end
18 of the day. I could take those home with me.

19 MR. SCHEVE: Your Honor, may I suggest that in
20 light of the instruction that you read to Mr. Jacobs and I,
21 that we may go from ten to nine, I suspect that's one of
22 them, about which there is some controversy. They wouldn't
23 be aware that Your Honor has advised us of what the
24 instruction would be.

25 THE COURT: Okay. Perhaps I will just give you

1 this piece of paper with my handwriting on it. I think it's
2 legible enough. Mr. Maurer has transcribed it verbatim.

3 MR. WALTERS: I assume for the rest of the
4 package, just a clean copy of the entire set of
5 instructions.

6 THE COURT: Yes.

7 What I need to have, as to the disputed
8 instructions, is the reasons for the disputes. And the
9 authority that each of you cite in support of your
10 positions, so that's I can consider that authority and come
11 to some conclusion.

12 Again, if you are able to get that to me
13 tonight, that would be a great thing. I will be here until
14 around -- well, probably at least until 6:00. And maybe
15 after that, depending, if you give a call and want me to
16 wait, because I may go downstairs. We will make a couple of
17 copies of this. This is the instruction regarding
18 Dr. Brittain, that I have jotted an instruction down.

19 Ms. Walker will make a copy for each side, so
20 you will have it, particularly for Mr. Scheve's side.

21 MR. JACOBS: We have a Rule 50 motion, Your
22 Honor.

23 THE COURT: Yes.

24 We could do that now, if you are ready. Or we
25 could do it as part of our exercise in the morning.

1 MR. SCHEVE: I think it would be helpful for us,
2 Your Honor, to be able to get it in the written format you
3 described, more of a bullet point sort of approach.

4 THE COURT: Okay. Ms. Walker, Mr. Jacobs is
5 approaching with something.

6 You are Bench-filing this.

7 MR. JACOBS: Yes, we will also e-file, Your
8 Honor.

9 THE COURT: Mr. Scheve has his side's copy.
10 These are all the same?

11 MR. JACOBS: Yes, they are.

12 THE COURT: Anything else, counsel, before we
13 recess?

14 Just give a call over to chambers.

15 (Court recessed at 3:40 p.m.)

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17 Reporter: Kevin Maurer

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