IN THE UNITED STATES DISTRICT COURT

IN AND FOR THE DISTRICT OF DELAWARE

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

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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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APPEARANCES CONTINUED:

ELENA C. NORMAN, ESQ., and
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Young Conaway Stargatt & Taylor, LLP
-and-
MICHAEL A. JACOBS, ESQ.,
EMILY A. EVANS, ESQ.,
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LISA CHIARINI, ESQ.,
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Counsel for Defendant

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THE COURT: Good morning.

(Counsel respond "Good morning.")

THE COURT: I understand we have an issue.

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

THE COURT: I hope they are short.

MR. JACOBS: Two are short and one may take a few minutes. No. 1, we have reached a stipulation on a person of ordinary skill in the art.

THE COURT: Good. I was wondering whether we were going to hear about that mystic person.

MR. JACOBS: Procedurally, Your Honor, would you like Ms. Kruze to read it? It would have come up in Dr. Amiji's testimony. Ms. Kruze could just read the stipulation into the record, if that would be appropriate.

MR. SCHEVE: Fine.

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

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

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

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

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

THE COURT: For your record, they are in.

MR. JACOBS: For closing --

THE COURT: That's evidence.

MR. JACOBS: Terrific.

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

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

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

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

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

THE COURT: I got it yesterday, you say?

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

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

MR. SCHEVE: Yes.

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

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

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

Mr. Jacobs.

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

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

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

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

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

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

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

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

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

Ms. Walker, bring in this jury.

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

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

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

THE COURT: I just rejected --

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

wrongfully --

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

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

THE COURT: That is where it will be.

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

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

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

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

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

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

MS. KRUZE: Yes.

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

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

Dr. Amiji, please.

Doctor, you are still under oath. Good morning.

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

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

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

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

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

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

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

Alternatively, the person of ordinary skill in

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

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

(Sidebar conference not reported.)

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

DIRECT EXAMINATION CONTINUED

BY MS. KRUZE:

Q. Good morning, Dr. Amiji.

A. Good morning, Ms. Kruze.

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

A. Yes.

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

A. No, they did not.
Q. Let's take a quick look at what the patentees did tell the Patent Office. That's JX-81 at Columns 3 through 4. I believe it's in Column 4, in the second paragraph.
Did the patentees tell the Patent Office that Tween 80 was a particularly preferred surface modifier?
A. Yes, they did.
Q. But internally, that surface modifier had failed?
A. That's correct, yes.
Q. Let's switch to DD106.
Did you review any other documents regarding Elan's efforts to make a nano-piposulfan product?
A. Yes, I reviewed several other documents.
Q. Could you read some of the statements that you found in those documents? This, for the record, is JX-47, JX-55, JX-81, DX-258 and DX-286.
MR. SCHEVE: Your Honor, I object to just reading documents. It's inappropriate form.
THE COURT: I will sustain the objection.
BY MS. KRUZE:
Q. Did you review any other documents regarding Elan's efforts to make a piposulfan project?
A. Yes, I did.
Q. What did those documents say to you?
A. So here we can see from the different time points, we

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

In '96, formulation does have its problems.

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

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

A. Yes.

Q. Did you review laboratory notebooks regarding those experiments?

A. Yes, I reviewed several different laboratory notebooks.

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

A. No, they were not.

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

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

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

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

A. Yes, I have.

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

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

A. Yes, I am.

Q. What did Abraxis ask Elan?

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

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

A. Yes.

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

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

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

Q. And we have --

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

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

THE COURT: Let me see counsel for a moment.

(The following took place at sidebar.)

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

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

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

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

MS. KRUZE: We have the documents.

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

But why don't you react to this.

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

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

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

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

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

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

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

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

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

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

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

Why don't you go ahead.

(End of sidebar conference.)

BY MS. KRUZE:

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

THE COURT: We are going to take this down.

BY MS. KRUZE:

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

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

(Banker's box held up.)

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

BY MS. KRUZE:

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

A. Yes. There were a lot of failures.

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

A. No, they did not.

Q. Why is this important?

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

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

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

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

A. No, they cannot.

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

A. Yes, they will.
Q. Do you have an opinion today that is relevant to the requirement that the '363 patent be enabled like we saw in the patent video?
A. Yes.
Q. And do you hold that opinion to a reasonable degree of scientific certainty?
A. Yes, I do.
Q. At the time the patent was filed, did the '363 patent enable ordinary scientists to make and use the claimed inventions without undue experimentation?
A. No, they wouldn't.
Q. Do you have an opinion today that is relevant to the requirement that the '363 patent have an adequate written description?
A. Yes, I do.
Q. Do you hold that opinion to a reasonable degree of scientific certainty?
A. Yes, I do.
Q. Could you tell the jury what your opinion is?
A. That it wouldn't enable.
Q. At the time the patent was filed, did the patent convey that Elan was actually in possession of the full scope of the patent claims?
A. Yes.

Q. In other words, at the time the patent was filed, was Elan in possession of all the drug and surface modifier combinations?
A. No, they were not.
Q. And while the patent application was pending, did Elan tell the Patent Office about these bad tests that we reviewed or all the failures that you were speaking of?
A. No, they did not.
Q. And did these bad tests or failures contradict statements that Elan was making to the Patent Office?
A. Yes.
Q. Dr. Amiji, let's talk about contamination.

Mr. Broyles, if you could bring up JX-81 on the screen, Column 6. Do you have testimony today relevant to the enablement requirement in terms of contamination?
A. Yes, I do.
Q. What is the method for making nanoparticles that's disclosed in the '363 patent?
A. So the '363 patent mentions this grinding process, the wet grinding process, which uses the grinding media, and reduces the particle size from larger crystals into smaller crystals.
Q. Could you bring up DD107, which is from Elan's website.

Is this a depiction of how the large crystals

become smaller?
A. Yes, it is.
Q. And if you could go to JX-81 again at Column 6. What types of instruments does the patent tell one to use to make these crystals go from smaller to -- or bigger to smaller?
A. So it uses the milling equipment, which is a ball mill, and then there is the grinding media. The grinding media or these beads are made from zirconium oxide, zirconium silicate, and glass.
Q. And let's turn to Column 7. How long does the patent teach one to grind?
A. In the simple screening method, for instance, it says up to 120 hours, which is more than five days.
Q. Just to clarify for the jury, what is zirconium oxide?
A. Zirconium oxide is a metal, a heavy-metal oxide. It has this oxygen and a heavy metal.
Q. Silicate, what is that?
A. Silicate is, again, a compound from silica. Silica is one of the major constituents of sand.
Q. Do you have an animation that illustrates the manufacturing process of the '363 patent that would help the jury's understanding?
A. Yes, I do.
Q. Let's play that animation.
Can you narrate what's happening?

A. **This is Abraxane.**

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

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

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

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

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

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

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

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

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

A. Zirconium oxide, zirconium silicate, or glass.

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

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

Q. How does this contamination occur exactly?

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

Q. Let's play that.

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

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

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

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

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

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

A. Contamination is a big problem in pharmaceuticals because you clearly want this product to be safe and effective. And safety, not only from the drug point of view, but from the purity and from the quality control point of view. You want to make sure that the product will not have any contamination, any type of contamination. Pharmaceutical products, especially those are intended for administration into the bloodstream you really have to be very careful about making sure that the quality is as pure

and as best as possible.

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

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

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

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

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

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

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

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

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

A. Yes, it does.

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

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

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

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

A. Yes, I was.

Q. What was he referring to?

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

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

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

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

Q. Is this sufficient to avoid contamination?

A. No, it is not.

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

A. Yes, I did.

Q. And what did these documents show?

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

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

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

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

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

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

acceptable.

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

A. That's correct, yes.

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

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

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

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

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

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

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

A. Right. This is June 16, 1993.
Q. So that was while the Patent Office was working on the patent?
A. That's correct, yes.
Q. And let's pull up DD-100. Could you please tell the jury what this is?
A. This is a presentation in Elan from November of '93. And again, the highlighted statement is that roller and media milling using zirconium and glass beads generates unacceptable contamination.
Q. The source of this document -- there is actually two -- is DX-238 and DX-607.
Can you see when the document was dated?
A. Yes. November of '93.
Q. And did Elan tell the Patent Office about this problem?
A. No, they did not.
Q. Let's turn to DX-238 at 85245.
Were you in the courtroom when Dr. Liversidge testified about polymeric milling media and things like microfluidization?
A. Yes, I was.
Q. Are those things relevant to solving the problem in the '363 patent?
A. Right. So in order to -- in the '363 patent it is

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

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

A. That's correct, yes.

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

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

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

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

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

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

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

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

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

particles are spun down and collected as a pellet.

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

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

Q. The contamination sticks on the particles?

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

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

A. Yes, I was.

Q. Do you agree with him?

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

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

A. Yes, I was here.

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

patent.
Q. To the best of your knowledge, do any of these products that they refer to use the zirconium media that's disclosed in the '363 patent?
A. No. The technology that Elan has now moved away from or is now using are these polymeric media, the grinding media. And they are not using the zirconia or glass beads.
Q. Did Elan ever disclose the contamination problems it was having to the Patent Office?
A. No, they have not.
Q. Let's bring up DD98.
Are the internal documents that you reviewed consistent with what Elan told the Patent Office?
A. No, they are not. Here is an example. For instance, we see that in the patent, it says the level of contamination which are believed to be acceptable. Whereas internal documents contradict that and say the levels are unacceptable.
Q. Let me ask you to consider the '363 patent technology in the context of a scientific publication.
Would scientists consider the internal Elan documents you reviewed concerning contamination something that was important to disclose?
A. Yes, absolutely.
Q. And do you have an opinion today that is relevant to

enablement?
A. Yes, I have.
Q. Do you hold this opinion to a reasonable degree of scientific certainty?
A. Yes, I do.
Q. To summarize, does the '363 patent teach, at the time it was filed, how to make drug particles or compositions that are essentially free of contamination?
A. No, they do not.
Q. And did some of the internal documents you reviewed about contamination problems contradict what Elan told the Patent Office?
A. Yes.
Q. And with these problems in mind, what real-world usefulness does the patent have?
A. In my opinion, not a lot, because these are some of the serious problems with having a pharmaceutical product that actually can have such high degree of contamination.
Q. Let's back up just for a quick moment and talk about the '363 patent and mention, just because I think it's easy to get confused. DD-86.

Did Elan invent crystalline paclitaxel?

A. No. Crystalline paclitaxel has been around for a long time.
Q. And did Elan invent nanoparticles?

A. No. Again, nanoparticles, nanoformulations or nanoparticles have been around for a long time.
Q. Did Elan invent nano-sized drugs?
A. No. Again, there have been many others that have preceded Elan in that.
Q. So what, exactly, does Elan say it invented?
A. Well, it claims to have invented this huge list of anticancer drugs, very, very large list of surface modifiers, and ratios of the two, going from having .1 of surface modifier to 90 percent and 10 percent drug up to 99.9 percent drug. In reality, in my opinion, it is not really enabled.
Q. Dr. Amiji, if Elan had invented all those combinations of drugs and surface modifiers, would that be a significant breakthrough?
A. Absolutely. Cancer is one of those areas where we direly need newer drugs, newer methods of treatment. Even a few of those, that were in the clinic and really helping the patient, it would be a huge breakthrough and huge significance in cancer treatment.
Q. Did Elan, in fact, invent that?
A. No, they did not.
MS. KRUZE: Thank you.
THE COURT: You are done, Ms. Kruze?
MS. KRUZE: Yes. No more questions.

THE COURT: Mr. Scheve.

MR. SCHEVE: Thank you, Your Honor.

CROSS-EXAMINATION

BY MR. SCHEVE:

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

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

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

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

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

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

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

and we are talking to various parties.

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

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

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

BY MR. SCHEVE:

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

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

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

A. No, I have not.

Q. Would you please dial up the video.

Do you know Dr. Desai?

A. I have met Dr. Desai in 2007.

Q. Would you play it, please.

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

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

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

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

"Question: Was he trying to market that technology?

"Answer: I suppose you could use that word.

"Question: And what was the technology?

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

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

"Answer: No, not at that point."

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

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

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

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

A. Yes. Many of these presidents of institutions

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

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

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

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

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

A. Yes, there are.

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

A. Not true, Mr. Scheve. Actually, it's climbing up. We are going up in the ranking, even within the Boston area.
Q. During your deposition that was taken here three months ago, didn't you tell me it was ranked 11th out of the 13 in the Boston area?
A. I don't believe I said it was ranked 11th. I said -- in terms of the institutions that are in the Boston area, like Harvard and MIT, certainly they are ranked higher than us. But Northeastern right now is around the same ranking as Tufts. It's a little below BU, but it's right near Brandeis and others.
Q. Let's make sure the jury understands.

Does your pharmacy school which you are a part of, does it own any equipment?
A. Yes, we do. We do own a lot of equipment.
Q. The pharmacy school does?
A. No. The way, in academia, what we have is, we have equipment that is owned by investigators themselves. For instance, my lab, if there is equipment that I need for research that is routinely used in my lab, I would have them.

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

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

Q. Does the pharmacy school own equipment, sir?

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

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

MS. KRUZE: Asked and answered.

THE COURT: Overruled.

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

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

Q. Right.
A. I don't -- again, I would say that, you know, there are equipments within our purview and what we can use. I am not sure who owns them, because, you know, it's part of our -- we use these equipments. It is in our daily use.
Q. Is there a solid-state NMR capabilities anywhere in your program, sir
A. We have liquid NMR. We don't have solid-state NMR, because, again, our research does not, at least current research does not use solid-state NMR. But we do have liquid NMR. We actually have three very state-of-the-art NMR equipments now at Northeastern that does various types of characterization.
Q. So the answer is you don't have solid-state NMR?
A. No, we don't have solid-state NMR.
Q. Does your lab even have an x-ray diffraction machine?
A. No. Again, there is an x-ray diffraction in one of these user facilities that I mentioned.
Q. Your lab doesn't even have an diffraction machine. Correct, sir?
A. Yes. As I said, we have equipment within our usage on a daily basis. Sometimes this equipment is very expensive. So you don't want to have these in your lab if there is going to be equipment that is going to be used on campus, and it is not routinely used, especially in our case. We

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

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

Then we would take those results and use them.

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

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

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

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

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

then that persuaded me to go to Purdue.
Q. Was that a yes or a no?
A. The answer to your question, did I use surface modifier to --
Q. While an undergraduate, sir, isn't it true that none of your research involved applying or utilizing a surface modifier adsorbed onto the surface of a molecule?
A. Not as an undergraduate. But subsequent to that I have done a lot of work in this area. Nanotechnology, I have done work in surface modification of materials. My Ph.D. thesis was on surface modification of materials, which is, you know, a four-year work on various types of modifiers, various types of surfaces. And I have subsequently published extensively in the area of nanotechnology. Including the book that you saw.
Q. Actually, your dissertation dealt with glass.
A. Not necessarily, Mr. Scheve. Actually, you know, what happened in my dissertation was that we looked at surfaces. We looked at surfaces that were hydrophobic. You, members of the jury, have heard about hydrophobic surfaces. These are surfaces that do not like water.
So we are interested in looking at surface modification of these hydrophobic, model hydrophobic surfaces with the intent that these will be able to resist blood interactions, will resist platelets. These are cells

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

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

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

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

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

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

A. Yes, I was.

Q. You weren't in the medicinal chemistry department at Purdue. Correct?
A. No, the pharmaceutics program at Purdue is in the industrial and physical pharmacy program.
Q. Do you agree with me, sir, or not, did you or did you not go through the medicinal chemistry department or curriculum at Purdue?
A. No. I went through the industrial and physical pharmacy program, which trains students to get degree in formulation development.
Q. Did you go through any curriculum in medicinal chemistry while at Purdue?
A. No, I did not. My training is in the physical pharmacy. It's on formulation development, biomaterials, which is in the area of my thesis. And that's what my training was.
Q. You don't hold any degree in medicinal chemistry. Correct?
A. No. My degree from Purdue is a Doctor of Philosophy degree. Purdue designates that as purely a Doctor of Philosophy degree. Then my thesis, which is what defines me based on my work that I did at Purdue, is in the area of surface modification of biomaterials.
Q. Those biomaterials being modified plastic, plastic --
THE COURT: We have done that, Mr. Scheve.

MR. SCHEVE: All right.

BY MR. SCHEVE:

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

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

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

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

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

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

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

Is it correct or not that you did not formulate

any anticancer drugs while at Purdue?
A. Yes, I did not formulate anticancer drug. But my thesis was in the area of biomaterials.
Q. After you left Purdue, you went to a company called Columbia Research Laboratories?
A. Yes. This was a small company that was in Madison, Wisconsin. It was a great opportunity, because it was a startup company by a faculty member that I admired a lot, the late Professor Joseph Robinson. He is my academic grandfather. My advisor graduated from his lab. And he started this company. It was my first opportunity to go and work in a private company.
Q. Now, while at this Columbia Research Laboratories, is it not true, sir, or is it true, sir, that you had no involvement with anticancer agents, no involvement with paclitaxel, no involvement with efforts to utilize surface modifiers on nanoparticulate anticancer drugs, and, in fact, had no involvement in any nanoparticulate technology while there?
A. Again, you know, when you work for a company, you are obviously going to focus on a specific product. Our product was not in the nano area. We were interested in other types of products when I was at Columbia.
But the training that I had and work that I have done subsequent to that shows that once you develop as a

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

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

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

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

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

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

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

Q. You joined Northeastern in 1993?

A. Yes, I did.
Q. Isn't it true, sir, that Northeastern didn't offer its first what's called Pharma D or pharmacy doctorate degree until the year 2002?
A. Well, let me clarify that for the jury.
So --
MR. SCHEVE: Your Honor, I have to object. Can I ask him to answer the question.
THE COURT: Doctor, please, endeavor to respond directly to the question posed.
Ms. Kruze will have an opportunity to ask you additional questions. We will get through this a lot quicker if you do that.
THE WITNESS: Thank you, Your Honor.
So pharmacy schools in the time that I joined were offering a Bachelor of Science degree.
Subsequent to that, in the year 2000, around that time frame, the American Association of Pharmacy, which is an organization that has membership of all the colleges of pharmacy, as well as the American Council of Pharmaceutical Education, which is the accrediting agency of all pharmacy schools, mandated that every school of pharmacy move to this Doctor of Pharmacy program.
So before then, there were very few Doctor of Pharmacy programs in the nation. Only in California mostly.

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

BY MR. SCHEVE:

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

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

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

A. Yes, they do.

Q. They rank yours 46th?

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

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

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

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

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

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

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

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

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

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

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

mentioned.
Q. U.S. News and World Report, you would call that pretty arbitrary. Is that correct?
A. Well, I mean, you know, it's a subjective ranking. That's what it is. It is based on somebody at U.S. News and World Report making --
THE COURT: We are never going to agree on this particular point. It's probably time to move on.
BY MR. SCHEVE:
Q. Now, this Center for Pharmaceutical Biotechnology Nanomedicine that you told the jury about, that didn't come into existence until 2006. Correct?
A. Yes. There are two things. One is the Center for Pharmaceutical Biotechnology and Nanomedicine, which the director of that center is our department chair. The other that I am a member of is actually called the Nanomedicine Education and Research Consortium. It's different from the two.
Q. That's what I want to establish. You don't even belong to Northeastern's Center of Pharmaceutical Biotechnology and Nanomedicine program. Correct?
A. No. I am an affiliate of that center, because it was started by a faculty, my chair, his name is Professor Vladimir Torchilin. He has his own program, and he has his own students, his own postdoctoral associates. He does his

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

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

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

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

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

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

Q. The answer is yes?

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

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

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

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

MR. SCHEVE: May I approach, Your Honor?

THE COURT: Counsel, you may.

BY MR. SCHEVE:

Q. Sir, did you give your deposition in this case?
A. Yes, I did.
Q. At that deposition, sir, were you asked this question, beginning at Page 173, Line 14?
A. Yes, I did give this.
Q. Did you give the answer that follows it?
A. Yes. So let me clarify for the jury.
MR. SCHEVE: May I ask the question, Your Honor.
THE COURT: Yes.
BY MR. SCHEVE:
Q. Were you asked the following:
"Question: So the actual funding for this Nanomedicine Consortium program now known as the Nanomedicine Education Research Consortium came in to existence in 2005?"
Did you give the following answer, sir:
"No. Let me clarify. The nanomedicine, the consortium is a group of faculty members who had individually had their own research funding. And we formed this consortium in order to collaborate within the department. The consortium itself did not have and still does not have its own funding. We never got funding specifically for the consortium. We have obtained funding through various collaborative efforts."
Did you give that answer or not give that answer

under oath, sir?
A. Yes, I did.
Again, I think it requires a little bit of clarification for the jury, Your Honor.
THE COURT: You will get a chance to respond to questions from Ms. Kruze.
MS. KRUZE: I was going to object. I will let --
THE COURT: Object to what?
MS. KRUZE: I don't believe it's contradictory.
THE COURT: I disagree, as to whether it is an appropriate question. As to whether it is contradictory, that is up to the jury to decide.
The jury will disregard Counsel's comment as to what she believes as to whether it is contradictory or not. You will have to make that determination.
BY MR. SCHEVE:
Q. Now, with regard to its Ph.D. program, sir, when did Northeastern first start offering a Ph.D. program in nanotechnology?
A. The nanotechnology program -- we have Ph.D. programs in various departments. We have Ph.D. program in pharmaceutical science. We have a Ph.D. program in chemistry. Ph.D. in physics. Ph.D. in biology and other engineering disciplines. Nanotechnology is a new field. So

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

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

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

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

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

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

A. Yes, I heard the testimony.

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

October 2005?

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

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

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

Q. Is that yes?

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

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

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

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

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

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

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

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

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

Could you re-put the question.

BY MR. SCHEVE:

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

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

THE COURT: Is that a yes, Doctor?

THE WITNESS: Yes.

MR. SCHEVE: Thank you.

BY MR. SCHEVE:

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

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

where the medicinal chemistry research is done.
Q. Sir, when I asked you isn't that correct? And you say no, are you agreeing with me or not agreeing with me?
A. Yes. We don't have a designated medicinal chemistry program. But we do have a center for drug discovery where medicinal chemistry is done.
Q. Now, sir, did you sign an agreement when you became involved in this case, where you agreed that you wouldn't take on a case or take on any work or perform any services that, if it were adverse to the attorneys, called Morrison & Forester?
A. Yes, I did. This is the letter of agreement that I signed.
Q. So if, hypothetically, one of my clients wanted to hire you, you would have to go to these lawyers first and find out whether they are on the other side, and then if you found out that they are on the other side, then you would have to get their permission, no matter how meritorious my client's position is, no matter how correct the science, you would have to go to their lawyers and get permission before you could take it on? Is that what you contractually obligated yourself to?
A. Yes. But as you look at the line just below where you have highlighted, the agreement can be terminated at the discretion of either party within ten days of notice. So I

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

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

A. Right, yeah.

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

A. Yes. I am paid.

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

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

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

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

So I have gone to various meetings and met with

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

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

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

Q. Well, that begs several questions, sir.

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

A. Again, I am --

Q. Yes or no, sir.

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

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

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

Baxter and other types of products.

This is not something to take very trivially.

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

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

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

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

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

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

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

A. Right.

Q. What are those drugs?

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

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

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

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

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

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

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

A. Yes, it does.

Q. Does CMC stand for chemistry, manufacturing, and

control?
A. That's correct.
Q. Now, that chemistry, manufacturing and control segment of the IND submitted for each one of these injectables, does it have to communicate in very precise detail any sorts of information about contamination to the FDA?
A. It does. And again, you know, we are looking at this purely from the '363 patent. The technology that's adopted may involve more than one patent, may involve other secret methods that may be present within the company. But in the context of the '363 patent, there is contamination. In zirconia, glass, in zirconium silicate that is in the '363 that is causing contamination.
Q. Have you seen the contamination levels or any part of the CMC for those three injectable drugs that we have just talked about?
MS. KRUZE: Your Honor, objection. Sidebar.
THE COURT: Yes.
(The following took place at sidebar.)
MS. KRUZE: Your Honor, there is no foundation for any of these questions. We have no documents supporting -- the misleading part of his --
THE COURT: Sustained.
(End of sidebar conference.)
BY MR. SCHEVE:

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

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

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

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

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

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

MS. KRUZE: Same objection. There is no foundation.

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

BY MR. SCHEVE:

Q. What pharmaceutical companies do you consult with?

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

companies, smaller companies in the Boston area.
Q. Those smaller companies, sir, you told me their names during the deposition. Who are they?
A. There is one called, Cequent Pharmaceutical. Maybe I can pull up my CV. Do you have my CV in one of these binders?
Q. I do not, sir, sorry.
Maybe I do. Let me see if I can find the companies. It was Novavax, Zydus and Biocure?
A. Biocure, I do consult. Novavax, I used to consult. It's in Pennsylvania, Malvern, Pennsylvania. I do not anymore. And Zydus is an Indian company. They asked me to be on their scientific advisory board, but I do not have any consulting with they mean.
Q. Sir, do you consult with Merck?
A. No, I do not consult with Merck.
Q. Abbott Labs?
A. No, I do not consult with them.
Q. Roche?
A. No.
Q. AstraZeneca?
A. No.
Q. Sanofi-Aventis?
A. No, I do not have consulting.
Q. BMS or Glaxo?

A. No, none of those.
Q. You heard the testimony that all of those companies have licensed the nanocrystalline technology?
A. Yes.
Q. Do you think their lawyers and their scientists internally are licensing invalid patent technology?
A. Again, you know, I can't speak for, what I can speak for is really what I saw as the exhibits that were submitted to me. And based on the exhibits, I feel that the '363 patent is invalid.
Q. Do you have my question in mind, sir? Do you think they got it wrong?
A. Again, I can't speak for the lawyers in these different companies.
Q. In your experience, sir, are the scientists within each one of those companies going to do due diligence before they sign a license agreement to license that kind of technology?
A. Again, you know, many of them may do. I don't know exactly how each company operates. I don't have any information related to their process and procedure.
Q. All right, sir.
Let's go to a new topic then.
Isn't it true, sir, that up through the year 2000 you had not published any paper specifically on

nanoparticle formulations?

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

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

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

A. Yes, as I mentioned before.

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

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

Q. Was it an anticancer agent in your thesis, sir?
A. No. Again, hydrophobic surfaces that become implantable devices. We were interested in studying how these interact with blood.
Q. Isn't it true, sir, that you have not used any anti-tumor agent or attempted to modify the surface of any anti-tumor agents with a protein?
A. Again, you know, we have worked on area of drug delivery and we have used polymeric drug delivery. We have used a number of different types of other nanoparticulate concepts.

But not specifically in the protein drug -- no.

Q. Is it true you have never used human serum albumin in any research on a nanoparticle?
A. No. My work on human serum albumin has been on modification of surfaces in my Ph.D. thesis. And then we have used human serum albumin for other types of applications. We have also used obal human, which is a derivative of albumin, recently in studying some of the properties as a vaccine model.
Q. To boil this down, sir, isn't it true that none of your research involves proteins adsorbed under the surface of an anticancer nanoparticulate formulation?
A. Yes. Mr. Scheve, that is a very specific area. As I said before, scientists are focused on problem solving.

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

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

I have done all that.

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

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

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

Abraxane has submitted all the documents for --

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

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

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

THE COURT: Doctor, was it submitted?

THE WITNESS: No, it wasn't.

BY MR. SCHEVE:

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

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

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

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

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

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

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

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

THE COURT: Doctor....

Would you repeat the question.

BY MR. SCHEVE:

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

A. Yes.

MR. SCHEVE: Pass the witness.

THE COURT: Ms. Kruze, you may redirect.

REDIRECT EXAMINATION

BY MS. KRUZE:

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

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

Q. And are you a representative for the USP?

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

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

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

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

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

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

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

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

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

implying in his questions?
A. No. I have not seen a single documentary support.
MR. SCHEVE: Objection. Foundation.
THE COURT: Sustained.
BY MS. KRUZE:
Q. Based on the documents you have seen, Dr. Amiji, was contamination a significant problem with the '363 patent?
A. Yes, it is.
Q. And were any of the products that Elan's counsel referred to, were any of them around at the time that the patent was filed?
A. No, I don't believe they were.
Q. And the issue of enablement, that's determined at the time the patent was filed. Correct?
A. Yes, that's correct.
Q. For cross-linking, did Elan's counsel ask you any substantive questions about your opinion that Abraxane is substantially cross-linked?
MR. SCHEVE: Objection. Form.
THE COURT: Sustained.
BY MS. KRUZE:
Q. Did Elan's counsel ask you any questions --
THE COURT: Same ruling.
MS. KRUZE: All right. No further questions.
THE COURT: You are excused, Doctor. Thank you.

THE WITNESS: Thank you very much, Your Honor.

THE COURT: You are excused.

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

THE COURT: I would like to speak with counsel.

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

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

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

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

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

some reasonable agreements.

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

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

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

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

appeal to the Federal Circuit.

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

We are in recess.

(Recess taken.)

THE COURT: All right. Ms. Walker.

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

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

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

THE COURT: All right.

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

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

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

"Answer: Yes.

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

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

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

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

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

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

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

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

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

"Answer: You want me to split the question?

"Question: Sure.

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

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

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

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

"Question: Why not?

"Answer: I simply don't know.

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

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

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

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

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

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

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

"(Record read.)

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

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

"Answer: Okay.

"Have you seen this document before?

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

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

"Answer: Yes.

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

"Answer: Yes.

"Question: Could you turn to page 96 of

Sarpotdar Exhibit 3, which is Bates numbered ELANP0007588. Have you found that page, Doctor?

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

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

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

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

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

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

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

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

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

"Question: Dr. Sarpotdar, you have been handed

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

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

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

"Answer: Because my name is on it.

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

"Answer: Yes, I do.

"Question: Why is shelf stability a problem?

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

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

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

"Question: Yes.

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

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

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

"Question: Yes.

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

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

Defendants now call Dr. Patrick Soon-Shiong.

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

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

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

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

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

A. Twenty-three years old.

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

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

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

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

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

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

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

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

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

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

Q. Did you work with the pancreas, Dr. Soon-Shiong?
A. Yes.
Q. Could you tell the jury a little bit about that work?
A. From my residency days or intern days, I had a fascination with the organ called the pancreas. While a surgical resident, there was a patient with pancreatitis. We performed the country's first total pancreatectomy and transplantation of that organ into the patients leg so the patient could be relieved of the pain.

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

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

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

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

Could you tell the jury about a few of these?
A. Well, the recognition was really for a multitude of

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

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

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

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

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

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

Then, as you said, I did islet and pancreas

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

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

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

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

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

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

A. About 50 patents.

Q. How many publications are you an author on?

A. I have about a hundred, over a hundred publications.
Q. You mentioned your islet cell work, Dr. Soon-Shiong. Can you describe for the jury how the islet cell work that you did ultimately translated into the initial development efforts for Abraxane?
A. It's a span of a decade.
Your Honor, may I go up to the board?
THE COURT: Yes, sir.
(Witness steps down from stand.)
A. So I think the issue is how did it connect, the work involving pancreas transplants, how did that get to Abraxane. What is exciting about science, there is always a continuum of thought. The area, I will draw a diagram, this is the pancreas.
THE COURT: Doctor, hold on just a second. We are going to mike you up.
THE WITNESS: Sorry.
THE COURT: That's okay.
THE WITNESS: So the area of pancreas transplant and pancreatic cancer is where I started my work. As I said, within the pancreas there is a cell called the islet cell, which secretes insulin. The idea is diabetic patients, unfortunately, have destruction of the cell and the opportunity to transplant this whole organ.
Q. Let's break that down. What cell is destroyed?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Thank you, sir.

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

We were excited to say that together with Dr.

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

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

So to me this was a --

BY MR. JACOBS:

Q. I think the battery may be going.

(Pause.)

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

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

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

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

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

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

A. That's correct, sir.

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

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

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

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

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

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

understand the chemical structure of albumin.

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

So --

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

A. Insulin.

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

It dawned upon me, that is what was happening

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

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

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

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

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

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

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

Q. Th CIS is?

A. The National Cancer Institute.

Q. A government funded, or government organization?

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

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

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

prototype that we handed to Bristol Myers in 1995.

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

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

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

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

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

Q. Thank you, Dr. Soon-Shiong.

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

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

THE COURT: You may.

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

THE COURT: I assume that this was all --

MR. JACOBS: Absolutely, Your Honor.

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

THE COURT: All right.

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

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

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

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

BY MR. JACOBS:

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

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

believe Abraxane works.

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

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

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

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

Then the albumin gets into the tumor and feeds

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Now the question is, how does it get out?

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

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

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

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

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

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

And you want it here rapidly.

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

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

is what we had approved first in breast cancer.

BY MR. JACOBS:

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

(Witness resumes stand.)

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

Do you believe that Abraxane infringes the '363 patent?

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

THE COURT: Please, Mr. Jacobs.

BY MR. JACOBS:

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

MR. SCHEVE: Same objection, Your Honor.

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

BY MR. SCHEVE:

Q. Did you see the '363 patent?

A. Yes.
Q. Did you form a judgment about whether Abraxane and whether Abraxis would be infringing it?
A. Yes.
Q. What was that judgment?
A. I was very clear, not at all.
Q. Why is that? What was the basis for that belief?
A. Well, firstly, our design was totally opposite, clearly, I think, as I tried to express. Maybe it would be easier if I may just go to two pictures on that to express that, if I may.

(Witness steps down from stand.)

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

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

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

then, show it.

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

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

BY MR. JACOBS:

Q. Thank you.

(Witness resumes stand.)

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

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

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

ever done this on a commercial scale. And they declined.
Q. How did that affect your plans or thinking about the development of Abraxane?
A. It was a very, very difficult time for us, because we now had 50 people. And the choice to us was, do we drop this drug? And we did not have expertise in scale-up or large scale-up as a pharmaceutical company.

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

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

So we went ahead and, this is what became APP.
Q. And APP was a predecessor company to Abraxis?
A. Well, it was the other way around. Abraxis owned the technology. We created within Abraxis a subsidiary called

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

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

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

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

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

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

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

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

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

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

Q. Then what was the next step?

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

Q. Anaphylaxis is?

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

steroid medication, the patients may die from aphylactic reaction. To me, that was a tragic. You would survive your cancer and die from an allergic reaction to a chemical that is added. So we decided, we should first go after breast cancer.

So we went after breast cancer first, where we would take patients first that were in what we call first and second lines of chemotherapy with 300 milligrams, as we described.

Q. That was the Phase 2 study?

A. That was the Phase 2 study. It's a memorable moment for me, because the first patient was actually our employee. And this was the 300 milligram per meter squared, never been done before. As you recall, I acquired this company with 500 employees. And my top marketing person came to me and said, I have breast cancer throughout my body. Please, put me on your trials as your first patient.

She had failed chemotherapy. We put her on our trial as our first patient, 300 milligrams, and she had a complete response. She lived seven years from that.

Q. Could you describe the Phase 3 study, please?

A. We then went on to do, now that we knew that we could do it not only safely, we actually showed we had a 64 percent response rate in our Phase 2, a remarkable response rate. So to actually scientifically prove that, we then

needed to take taxol and Abraxane and do head-to-head studies in breast cancer and compare them.

So we did taxol and Abraxane head-to-head studies. Not only did we prove what we proved in Stage 2, that we actually doubled the response rate when compared to taxol. We had no adverse reactions in terms of anaphylaxis, despite not having to give any steroids. And more excitingly, we actually statistically improved survival with the same drug. So that to us was the Phase 3, which allowed us to get approval.

Q. You got approval in January 2005?

A. Correct.

Q. Then once you have approval, you can actually market and sell the drug on the market, as it were?

A. That's correct.

Q. Have clinical trials continued for Abraxane since then?

A. Yes. As I said, the opportunity for this drug now is not limited to any one cancer, because all cancers need to feed or die.

So we went then after lung cancer, we went after all the cancers. We believe that there are huge unmet needs, meaning that we have not yet been able to, as physicians and oncologists, attack these diseases, lung cancer, melanoma, pancreatic cancer.

As some of you may know, these are cancers for which, unfortunately, we have made very little progress. Lung cancer, the response rate is only like 16, 15 to 16 percent, no matter what drug you give.

Q. For existing drugs?

A. Correct. For existing drugs.

So we did this first in lung cancer and presented it in ASCO, we got 50 percent rate.

Q. ASCO, what is that?

A. ASCO is the largest collection of doctors, oncologists, in a meeting together every year. They just had one in Chicago, 30,000 oncologists come together, where we share scientific, clinical information. And I think around 2004, '5, I forget, '6, that time frame, we presented our lung cancer data.

We also then did trials in patients who were actually growing their tumor in breast cancer while on taxol and while on paclitaxel, and then gave them Abraxane, and they responded.

We then also did trials in patients with melanoma, where there is no treatment, unfortunately. And we doubled the progression-free survival, the time before they got a recurrence when compared to other drugs.

Now most excitingly, we have done this in pancreatic cancer. Now we have patients with pancreatic

cancer with a 70-percent response rate. Some of the work was done at Johns Hopkins and University of Arizona, and I think 14 to 15 consecutive patients now had a response rate with pancreatic cancer.

Q. Where do you see this for the future? What is the future for Abraxis in your view, Dr. Soon-Shiong?

MR. SCHEVE: Objection. Foundation.

THE COURT: Overruled.

THE WITNESS: I got to tell you, I just came back from ASCO last week. I was in ASCO, and the investigators met with me privately in the room to share with me the results on pancreatic cancer. They were so overwhelmed by the findings of 77 percent. They feel that by adding one more drug, and we designed their protocol now, in combination with Abraxane, we could eradicate pancreatic cancer. To me, that would be the most exciting thing we could have contributed to.

But I think what is truly exciting is that not just paclitaxel, this is other drugs that we can put into, and more importantly, it's available not just for one cancer but a broad range of cancers, whether it be breast, lung, melanoma, head and neck cancer, pancreatic cancer.

MR. JACOBS: Thank you very much. No further questions.

THE COURT: Mr. Scheve.

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?

A. That was my insight into working with jet propulsion lab working with monodispersion, knowing particle size matters is important with regard to nanoparticles, working with that. And also working on albumin and working on the proliferation stems cells.

Q. Stem cells?

A. Correct.

Q. 1992, what was that?

A. Same. I am sorry. I have repeated myself. That was all in that same time frame, working on albumin, understanding the concept that albumin actually will maybe feed the proliferating cells.

Q. Here you wrote 1992 taxol, is this when you began your work with paclitaxel, in'92?

A. We began our work before that. That's when I went to the NCI conference. I was first invited to the NCI conference because we were working on taxol.

Q. When did your work with taxol begin?

A. I think, as I said, probably around 1990, 1991.

Q. 1991?

A. In that time frame. I know it was before the '92 conference because, obviously, we were invited because we were working on taxol. I would say roughly 1990 to 1991.

Q. Now --

A. When I say working, we didn't have the raw material.

We may have got some from some -- you can buy chemical grade, non-pharmaceutical grade material. In 1992, the importance of the NCI is they introduced me to Bristol Myers so I could get the material as being used in man.

Q. This islet research, actually, those people that got the implants, there were deaths that occurred. Correct?

A. No.

Q. Where is this today? Has it gone anywhere?

A. No -- well, gone anywhere? There were two reasons. One, the limitation -- islet cell transplant, the NIH actually then stepped forward and said islet cell transplant is now an established procedure and actually created seven centers in the country. However, because of this capsule and the ability to get enough cells -- patients now have been cured of diabetes with islet cells.

Q. My question was, in terms of your research today, did you get rid of that part of your business?

A. No, I did not.

Q. What was that business called? You formed a company called VivaRex. Correct?

A. Correct.

Q. Did VivaRex only deal with cancer?

A. There were two organizations, one was VivaRex Diabetes and one was VivaRex Pharmaceuticals.

Q. Did VivaRex Diabetes have this islet specimen

research?

A. Correct.

Q. Where is VivaRex Diabetes today?

A. That is now disbanded because the problem was developing stem cells. But the other problem, the most important problem, was the alternative other than stem cells, but to actually put pig cells.

Unfortunately, in 1998, there was a discovery made that within pigs there is a virus equivalent to the AIDS virus called the perv virus.

We had the country's first FDA approval to go from using pig cells into man. But I worked with the FDA to say we should ethically shut this down because there is no way for us being able to prevent the transmission of pig viruses into man. As you may know, about the issue of SARS. In 1998, I participated on the FDA biological board to actually establish new standards for safety of pigs to man, and they shut down in vivo transplants in the United States as a result of that. Correctly so.

The irony of that is, because of that work, we now as a company, APP, are the only supplier of Heparin to the United States, this blood thinner, because it comes from pigs. And we've established with the FDA a safe supply chain starting in 2000, 2005. As a consequence, the irony of all of this is that science prevails, we now have the

only safe supply of Heparin through APP in the United States as a result.

Q. So this VivaRex Diabetes is no longer in the picture. Correct?

A. I will personally continue this work on the stem cell. But --

MR. SCHEVE: Your Honor, may I ask that he answer my question.

THE COURT: He is answering the question.

THE WITNESS: The answer is correct. VivaRex Diabetes company, that is no longer here.

MR. SCHEVE: Your Honor, may I approach?

THE COURT: Yes, sir.

(The following took place at sidebar.)

MR. SCHEVE: He has opened the door to talking about quality issues. There have been at least 20 notices sent to his company about quality issues. I didn't ask him about any of that. He has now talked about how they are the only this, that or the other of Heparin. I have got all kinds of evidence about how they have gotten warning letters from the FDA, et cetera. I don't want to go into it. But when he opens the door like that, it puts me in a really awkward position.

MR. JACOBS: Your Honor, he was tying it all up to the Heparin side, which is APP. That discussion was not

a general claim about Abraxane.

THE COURT: I disagree, Mr. Scheve. I am going to deny your request to get into this area. I don't think he has opened the door. I think it has been confined to Heparin. Not even insofar as his conversation about Heparin -- he is talking about AIDS, I think, as I understand it.

MR. SCHEVE: The Heparin is the thing that was the subject of a TV thing the other night. Actually, they have been criticized for raising their prices 12 fold. That was the controversy. So now he has stuck his foot into it. I don't want to go there. It is these gratuitous answers that put me in a position --

THE COURT: As you know, and I am sure have observed, trying to be as vigilant as I can, without getting too much into both cases to council the witnesses to be more responsive.

I am trying to be mindful of the fact that these are scientists and these are difficult questions, all the time not capable of yes-or-no answers. I certainly commiserate with your frustration with the last witness. I don't think that is this witness' tendency; if it proves to be, I will get involved.

MR. SCHEVE: That is all I ask. Thank you.

(End of sidebar conference.)

BY MR. SCHEVE:

Q. Sir, in terms of this lawsuit, are you listed as an inventor on a patent that covers Abraxane?

A. Yes, I am.

Q. Do you have a single lab notebook that relates to that, sir?

A. No, I don't.

Q. Not a single one?

A. Well, I have lab notebooks. But I don't have lab notebooks until the time I started working with this. I had 50 scientists under me, they took notes, I presented the work to them. They took notes and copiously maintained the notes.

Q. No lab notebooks were produced for me. And I wanted to confirm, do you have any lab notebooks reflecting your work with the development of Abraxane?

A. I think I just answered you, at that time I had 50 scientists under me, they kept the notes. I didn't keep my own per se.

Q. Just so the jury understands, sir, do you still own 80 percent of that entity known as Abraxis?

A. Yes, I do.

Q. And what is the market cap on that company today?

A. I think in excess of 2 billion.

Q. The last I looked at it, it was around 2.68 billion.

Would that sound reasonable?
A. Yes.
Q. Is Abraxane the only product that Abraxis markets?
A. Currently, yes.
Q. You would own an 80 percent interest in that company that has that capitalization; is that correct?
A. That's right.
Q. Now, did your company recently market a generic version of a product that's sold by my client Elan?
A. It may have. It's launched 70 generic drugs in the seven years that we acquired the company. In 1998, from then to now, we have the largest numbers of FDA approvals in the history of this country. We have ten approvals a year of generic drugs.
Q. Generic drugs are drugs that others had developed and they reached a point regulatorily where people could then come in and make a generic version. Is that correct?
A. That's correct.
Q. Now, your company actually sued the FDA, did it not, sir, to prevent another company from coming onto the market with a generic form of taxol?
MR. JACOBS: Objection, Your Honor.
THE COURT: Basis?
MR. JACOBS: Relevance.
THE COURT: Do we need to go to sidebar?

MR. SCHEVE: If you would like, Your Honor.

THE COURT: We should probably address the relevance issue out of the presence of the jury.

(The following took place at sidebar.)

THE COURT: What is the relevance?

MR. SCHEVE: It goes to two things, Your Honor, the testimony, I am going to paraphrase, about saving lives, this, that and the other, when they have taken affirmative steps to prevent competition.

In opening statement, there was discussion about motivation from my clients bringing this lawsuit. This goes directly to their effort to prevent by seeking to invalidate my patents and trying to keep others off the market from succeeding.

So the fact they have sued to prevent competitive taxol products goes to the very heart of his credibility.

MR. JACOBS: I don't think so, Your Honor. I actually confined his direct testimony very directly to the development of Abraxane. We did not get off into other topics. This is a complex world. The jury could be very confused by cases brought in other contexts. I don't see the relevance to the basic story about Elan's motivation in bringing this lawsuit.

THE COURT: What was the point you made about

the comment in opening?

MR. SCHEVE: The whole motivation issue about why this lawsuit was brought, and if they are able to make comment, either through Dr. Desai, talking about how, you know, it bothered him, et cetera, or to suggest in any way that this lawsuit was brought for inappropriate reasons, then the fact that they are out trying to prevent people from coming on the market clearly goes to show that the conduct that I am accused of or my client is no different than the conduct that they are engaged in.

THE COURT: How far down this road do you propose to travel?

MR. SCHEVE: About three questions. You sued to prevent this from happening? Depending upon whether it's a yes or no answer, if he says yes, we did, I will move on. If I hear about Abraxane --

THE COURT: I will give you a very small, small amount of leeway on this, because I don't want to get off into completely collateral material.

(End of sidebar conference.)

BY MR. SCHEVE:

Q. Do you have my question in mind, sir?

A. Could you repeat it?

Q. I will be happy to. Isn't it true that Abraxis brought a lawsuit against Donna Shalala and the FDA to

prevent a generic form of taxol coming on the market?
A. I didn't.
Q. Would that generic have been competition to you, sir?
A. When you say "competition," at the time of the lawsuit?
Q. Generics result in cheaper products for consumers who have cancer. Right?
A. We --
THE COURT: All right. Pose the question. Was that a question?
MR. SCHEVE: Yes, sir. I said "don't they."
BY MR. SCHEVE:
Q. Isn't it true, sir, that generics provide a cheaper alternative for folks that are suffering from cancer?
A. That is true.
Q. Now, sir, there has been some discussion in this lawsuit about a presentation that occurred at the Cleveland Clinic.
Do you recall that?
A. Yes, I do.
Q. Was that in 2004?
A. Yes, it was.
Q. Approximately what month, sir?
A. Around October-November. I can't recall. But it was in the last months, just before Abraxane was about to be

approved.

Q. October-November of 2004?

A. I think so.

Q. Thank you.

I am making reference here to a slide from Joint Exhibit 079.

Doctor, you are lucky, you get a small notebook compared to some other folks.

A. Thank you. What number is this, Mr. Scheve?

Q. Joint Exhibit 079, if you like to look at it.

My question is, is this one of the slides that you presented at that Cleveland Clinic presentation?

A. Yes.

Q. Is this a sort of montage of different images that related to Abraxane?

A. Yes.

Q. Is this here, where it says negative charge zave equals 130 nanometers; does that purport to be a cartoon or caricature of Abraxane particles?

A. Yes.

Q. Is this a bottle of Abraxane?

A. Yes.

Q. The image here, what is this?

A. That's, again, another cartoon we use for demonstrative purposes.

That is, I think it's a sort of touch-up of an electron micrograph as a cartoon.

Q. An electron micrograph?

A. Yes.

Q. Of Abraxane?

A. I am not sure whether that itself is Abraxane or not. Again, it is a cartoon representation. All these are cartoon representations.

Q. They are all cartoons?

A. Yes.

Q. But this is supposed to all deal with Abraxane. Correct?

A. Yes.

Q. Actually, that image that you used there was also used by Abraxis in other presentations. Correct?

A. So that's what we used as a representative cartoon, yes.

Q. That is a cartoon?

A. Well, this is an electric micrograph. The picture before was the touch-up colorization to generate this as a cartoon.

Q. You agree, sir, this is a micrograph of that same image or something that looks like that same image in 1997? This is Joint Exhibit 013.

A. I am sorry, you confused me, Mr. Scheve.

Q. Right. Maybe I need a pointer.

Do you see this image here, sir?

A. Yes.

Q. That's Joint Exhibit 079.

Now I am going to take you forward to this presentation sometime after April of 1997. Do you see this image?

A. Yes.

Q. If you could look at Page 8 of Joint Exhibit 13 and just confirm for me that that image was contained in that presentation in 1997.

A. Can you give me some time just to look at this presentation itself?

Q. Sure.

A. You are trying to get me to compare two presentations, is that the gist?

Q. I just want you to look at the images, is all. You take whatever time you need, with the Judge's permission.

(Pause.)

A. Yes, I see it.

Q. Same image?

A. Same image in this presentation?

Q. Yes, sir.

A. Yes.

Q. As this image that is here and that you were using in

2004.

A. I presume, it looks like it. That is exactly what is used as the cartoon, yes.

Q. Let's go forward. In fact, that image was being used in presentations in 1996 by Abraxis, was it not? If you would look at Joint Exhibit 026.

A. Yes.

Q. And if we go forward, this product that you wrote up there where you wrote Capxol, C-A-P-X-O-L?

A. Right.

Q. Was this image here used to describe Capxol encapsulated taxol?

A. Again, it's not necessary to describe Capxol. It's a cartoon demonstration of the concept of particles, nanoparticles, microparticles.

Q. Cartoon?

A. It's -- I don't know how to describe it to you. It's the best way for a visual layperson to understand what we are trying to do. As opposed to a scientific document. This is not a scientific document. This is a visual for a layperson.

These brochures are put together for laypeople, for people about to invest in the company and people to make, get an understanding. Sometimes I make these presentations to doctors. Sometimes I make these

presentations to nurses. Sometimes I make these presentations to investors.

So we use this generic version, as you can see, we pulled the same picture up all the time. Sometimes you put color on it. Sometimes we make it black and white. I suppose the best way to describe it is, it's merely a cartoon. I don't know how to describe it, other than the fact it is merely a demonstration.

Q. When you say you make presentations to investors, you are trying to convince people to buy into your view of this technology. Is that correct?

A. Yes. As I said, we had a vision that was so different from the standard dogma of chemotherapy, nobody had ever made a nanoparticle of this type before. A large company like Bristol Myers declined taking the chance.

We needed to convince people to follow our vision.

Q. Now, sir, actually, this article, written by Kenneth Suslick and Mark Grinstaff, published in 1990 has this image in it, doesn't it, sir?

A. Yes.

Q. I think you told us that your work didn't begin until around 1991 with taxol?

A. With taxol, but you didn't ask me about proteins.

Q. But I am talking about paclitaxel nanoparticles.

A. Well, I said, you know, I can't recall when exactly we got the raw material. It was very difficult to get -- there is an organization called Sigma. Sigma is an organization, all scientists understand, that you go buy these poor-grade materials to work with. I can't recall when we got that material. I can recall when we got the material from Bristol Myers. I said, it was between 1990-'91 that I think we got the material from Sigma.

Q. Dr. Desai didn't graduate from Texas until sometime in 1991. Correct?

A. Right. Well, I was doing the work with regard to my nanoparticle and with the albumin and the stem cells and proliferation cells and cross-linking before I met Dr. Desai.

Q. Let's make sure the record is clear. We have no lab notebooks from you and the only notebooks, lab notebooks we have are from Dr. Desai -- and he didn't graduate from Texas until 1991. Correct?

A. Correct.

Q. I have an article here from 1990. Is your name on this article?

A. No, it is not.

Q. Is this the image that is found in that Suslick article?

A. Yes.

Q. Dated 1990?
A. Yes. Suslick was a consultant to me. Ken Suslick worked with me. I am not sure whether just before Neil Desai or after Neil Desai. But Ken Suslick and Mark Grinstaff were my two collaborators, scientific collaborators. He was at the University of Chicago Urbana. And I was working with MIT. I was working with jet propulsion lab. I first working with Urbana. I was working with scientists across the country. This is one of these papers. In fact, I recognize this paper. It's a jacks paper that he presented.
Q. That Dr. Suslick published in 1990. Correct?
A. Correct. And he is a co-inventor of one of our patents.
Q. Sir, do you see any similarities between this image here that is used in '96 and '97 all the way up to 2004 in your Abraxis/Abraxane promotional materials? I am talking about the one on the left, and the image that is on the right from Dr. Grinstaff's article?
A. They are similar. They are not exactly the same, obviously. You can see the two Mickey Mouses. The two little ones. The answer is, they are similar, yes.
Q. So they are similar. They do look similar, don't they, sir?
A. Yes. I think, obviously -- sorry.

Q. Who doctored the images to take out the smaller ones here that were aggregating with the larger images? Who doctored that photo?

A. This was probably done by the IT department, as I said, to colorize it.

Q. IT at what place, sir, which entity?

A. I don't remember. You said who doctored it, I don't know. You are trying to connotate a negative -- this is a cartoon. Nobody doctored it. They actually colorized it, as I told you, to make it a cartoon. They may have not liked the fact, to make it clear -- I don't know who -- I can't recall.

Q. A cartoon.

Let's go back to Dr. Grinstaff's publication.

Dr. Grinstaff and Dr. Suslick. Now, sir, isn't it true that this image that they have designed as Figure 1 actually is a scanning electron micrograph of a dodecane filled proteinaceous microcapsule with an average particle size of 2.5 microns, and that this microcapsule was using bovine serum albumin?

A. That's correct.

Q. There isn't even a drug in those microcapsules, is there, sir?

A. That's correct.

Q. Now --

MR. JACOBS: Your Honor, I object to this whole line of questioning.

THE COURT: Okay.

(The following took place at sidebar.)

THE COURT: What is the basis of the objection?

MR. JACOBS: Relevance. Prejudice.

THE COURT: Well, relevance first.

MR. JACOBS: The question is, in this lawsuit, whether Abraxane is amorphous or --

THE COURT: Let me say, before you go forward, you are going to this witness' credibility.

MR. SCHEVE: I have heard this story. This was my idea, and we are so different. He lifted this stuff from a fellow one-year doctor before Dr. Desai graduated from school. It is credibility.

THE COURT: Your 403 argument -- it is prejudicial. The question is, is it unfair?

MR. JACOBS: Yes, I think this is unfair. We got in an exhibit last night at 10:30 p.m.

THE COURT: You should have raised that earlier.

MR. JACOBS: Your Honor, we should have raised half of the stuff that is going on between the parties.

THE COURT: I am sure both of you have not done that, and wisely.

MR. JACOBS: Now he is using this exhibit with

this witness, our CEO, and saying he doctored the photograph. This is character assassination.

MR. SCHEVE: He said probably his IT department did it.

THE COURT: Actually, the last word he said was he didn't know, to be fair.

MR. SCHEVE: I am moving on to a new topic.

THE COURT: Let's move on.

(End of sidebar conference.)

BY MR. SCHEVE:

Q. Doctor, there has been some testimony about a product that is marketed that utilizes the NanoCrystal technology Rapamune.

Are you trying to apply your NAB platform to this product?

A. The Rapamune that you are talking about, there is the oral version of Rapamune taken by mouth. To this day, there is no injectable version of Rapamune at all, because of its insoluble. So the answer is yes.

So we have actually now encapsulated, in our cross-link, a form of Rapamune. And we are about to -- we actually received FDA approval to initiate Phase 1 trials.

Q. If Abraxis is able to somehow challenge these patents and somehow get them declared invalid, then you wouldn't have to confront them as you move forward with your efforts

to develop Rapamune and, indeed, other products, like camptothecin, and others to which the '363 technology has been applied. Correct?

A. Well, it's not correct, because we are not confronting them anyway. We don't believe this has anything to do with our technology or our patents.

Q. You may believe that, sir, but I am just asking the question about, if the patents aren't there, then you don't have to worry about them at all. Correct?

A. Well, if patents aren't there, you don't have worry about them at all, that is correct.

Q. Now, sir, does the package insert for Abraxane advise physicians to reconstitute and administer it to patients?

A. Yes.

Q. And then did Abraxis obtain or rely upon the opinion of qualified patent counsel as to whether the nanoparticles in Abraxane would infringe Elan's '363 patent before making, offering to sell and/or selling Abraxane?

A. We were fully aware that we are two different particles. We had collaborations, discussions, in which we knew we had two different particles. One was crystalline, the other one was amorphous. One is cross-linked, one is non-cross-linked. One wanted to stay in the blood, the other one wanted to get out of the blood.

When we looked at patents of the '363, it states

within the body of the patents, we are crystalline, not amorphous. In the body of the patents, of the Elan patents, it says we are crystalline, not amorphous. In order for us to become amorphous, you need to do a different method of manufacture, solvent precipitation, which we do. In order to become crystalline, we need to do a different method of manufacture, grinding, which they do.

So if they told the Patent Office that they were different, we told the Patent Office we were different. We scientifically knew we were different. We were almost professional colleagues. We were different.

So there was no issue from our perspective.

MR. SCHEVE: Your Honor, may I move to strike the answer? I asked him whether they obtained an opinion of counsel. As you recall in the pretrial conference, there was an order instructing Mr. Jacobs to --

MR. JACOBS: Your Honor, objection. Sidebar.

THE COURT: You would like a sidebar, Mr. Jacobs?

MR. JACOBS: Please, Your Honor.

THE COURT: Let's calm down.

(The following took place at sidebar.)

MR. JACOBS: Mr. Scheve should not be talking about orders and directions in front of the jury. That is very much not the way Your Honor runs the courtroom.

THE COURT: That is true.

MR. JACOBS: Number 2, we were working out a stipulation on this, all of a sudden Elan went silent on us. I asked for the words back in the draft. They went silent.

Number 3, we will stipulate to exactly the way Mr. Scheve said it. If that will move us on.

MR. SCHEVE: The background on that, Your Honor, we submitted to them three days ago -- we never got the amended interrogatory answers as you ordered Mr. Jacobs to do. So we put together the proposed language, sent it to them three days ago. I can show Your Honor -- I know you don't want to get involved in those details.

THE COURT: We don't have time.

MR. SCHEVE: I am just asking, did they get an opinion? And he says, we looked at patents, they looked at patents. The patents are different. I want to know, did you get an opinion or not? If they want to stipulate it, I'm able to read it into the record, I am done with this witness.

Can I get these two stipulations here that they didn't get an opinion of a qualified patent counsel as to whether the nanoparticles would infringe Elan's '363 before making, offering to sell and/or selling and a separate one that they obtained or relied upon an opinion of qualified patent counsel as to whether the '363 patent was valid

and/or enforceable before making, offering to sale, and/or selling? Will I get those two stipulations?

MR. JACOBS: So stipulated.

MR. SCHEVE: I am finished with the witness.

THE COURT: Do you object to them being announced by Mr. Scheve?

MR. JACOBS: No.

MR. SCHEVE: Your Honor, would you like me to dismiss the witness and then read the stipulation, or do it while he is on the stand?

THE COURT: While he is on the stand or after?

MR. JACOBS: After.

(End of sidebar conference.)

THE COURT: Doctor, I am advised we have come to the end of the cross-examination. You are excused.

MR. JACOBS: Your Honor, could we have one minute to confer on redirect?

THE COURT: I am sorry.

MR. SCHEVE: May I read the stipulation?

THE COURT: We will announce it.

MR. SCHEVE: Abraxis has stipulated, meaning that they agree, that they did not obtain or rely upon an opinion of qualified patent counsel as to whether the nanoparticles in Abraxane would infringe Elan's '363 patent for making, offering to sell, and/or selling Abraxane.

In addition, they stipulate or agree that Abraxis did not obtain or rely upon an opinion of qualified patent counsel as to whether the '363 patent was valid and/or enforceable before making, offering to sell, and/or selling Abraxane.

THE COURT: That is another one of those rare occasions, ladies and gentlemen; there is an agreement there.

REDIRECT EXAMINATION

BY MR. JACOBS:

Q. Dr. Soon-Shiong, I only have one more question for you on what we call redirect. Why not?

A. Because we absolutely felt very clear from our perspective, we felt we knew it, we felt they knew it. It wasn't an issue for us, because we were developing two different pathways. We had an amorphous version. They had a crystalline version. We had a cross-linked version. They had a non-cross-linked version.

This may be interesting, it's sort of interesting. The same patent examiner was examining both patents at the same time. It's just an interesting, I suppose, coincidence or maybe not, because this is the examiner in this field at the U.S. Patent Office, Thurmond Page, was the same examiner examining our patents, examining their patents. And the Patent Office felt it was different.

MR. JACOBS: Thank you. No further questions.

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

(Witness excused.)

MR. JACOBS: Abraxis rests, Your Honor.

THE COURT: Let's see counsel for a moment.

(The following took place at sidebar.)

THE COURT: When will you be ready to start your rebuttal case?

MR. SCHEVE: You tell me when.

THE COURT: Do you want to break for lunch now?

MR. SCHEVE: Yes. We are bringing two witnesses. I think our rebuttal case will last an hour, but to be safe, I will say an hour 20 minutes. I anticipate calling Dr. Manning and Dr. Liversidge.

THE COURT: Okay. So, then, moving on to the time when we will be able to meaningfully consider the final proposed jury instructions, and the verdict forms, over the lunch, why don't you confer with your teams. Let's give them when we come back some estimate as to when we will be able to do that.

MR. SCHEVE: We had our little conference and urged our associates. And we will make sure that this moves along. I am sorry for any inconvenience, Judge.

THE COURT: It is not my inconvenience -- to a degree it is, because we are resource limited. But I don't

want to continue to gripe about that. The system is built the way it is.

It is the jury that I have the most concern about and having them just cooling their heels. And we have promised them an eight-day trial.

MR. SCHEVE: I do think, Judge, I have to rely on some others, but I talked to John Day, and he says, it may look like there is a lot of disagreements, but it is really just preserving the record. The dispute is down to about 12. But I have to look at it and make sure.

MR. JACOBS: Maybe we could excuse the jury and spend a few minutes on the schedule from here through closings. We actually have a fair amount of time to work with. So we can relax.

THE COURT: Let's let the jury go.

I will announce that Elan will have a rebuttal case upon our return from the normal lunch hour. We will stick around for a few minutes.

MR. JACOBS: To lay it out all out, the way we sequenced this, I could have a rebuttal on invalidity. It would be very short.

THE COURT: I guess that's right. Do you know at this point?

MR. JACOBS: I think it depends on what Mr. Scheve actually does. It would be Dr. Amiji on

invalidity and it would be brief.

(End of sidebar conference.)

THE COURT: Ladies and gentlemen, as you have just heard, Abraxis has rested. We are going to break to lunch now. You should anticipate upon our return, take an hour, hearing a relatively brief rebuttal case from the Elan plaintiff. And you may hear additional brief, further rebuttal on the invalidity question from Defendant Abraxis. They will react in realtime, depending upon what happens during plaintiff's rebuttal. I will let you know. We will see you back in an hour.

(Jury leaves courtroom at 12:40 p.m.)

THE COURT: So we are going to stick around for a few minutes here, as Mr. Scheve and other counsel and I agree, we will discuss the schedule. For those of you who need to stay, okay. Those who need to take lunch, go right ahead.

I was happy to hear that much of the disputes that have been denominated as such are actually record preservation of disputes. The disputes have been distilled down to about 12. It can be better. I expect it to be.

The verdict form. Where are we on that? Trying to meld something together?

MR. JACOBS: Here is what I heard before we did the examination, Your Honor. We can tee up one issue at the

threshold of the verdict form, and then, if you decide that issue, it will be over. That's what I heard.

THE COURT: That's very helpful.

So, then, let's talk about the balance of the schedule.

MR. JACOBS: My proposal, Your Honor, is that we do our closing arguments tomorrow morning. You would instruct them first, I believe.

THE COURT: Yes.

MR. JACOBS: We could probably close, I am speaking at least for our side, we could probably close both cases before lunch.

THE COURT: I think that's a little ambitious. Let's just think about that for a moment. We are probably going to come out with somewhere in the neighborhood of a hundred or so pages of instructions. Right?

MR. SULLIVAN: Yes, Your Honor.

THE COURT: That is going to take me roughly two hours to deliver. Quite frankly, I am thinking about trying something a little different and taking a break midway, just to give my lungs a rest. But really, I do, in all seriousness, think that the jury can use a break.

I have watched their eyes glaze over now enough, as I go through these kinds of things, this exercise, that I am not sure is the best way to deliver the instructions in

the first place, but it is what we do right now in this country, and maybe just let them take a quick stretch at some midpoint. You have roughly two hours, an hour 40 minutes to two hours I suspect, that is what it will take us to deliver them. If we start at 9:00, that gets us to roughly 11:00 or so. We want to give them another break at the end.

Then I expect we may be able to get in the initial opening, perhaps, of Mr. Scheve. What do you think? How long do you plan to run your mouth?

I am teasing.

MR. SCHEVE: I know the importance of being concise in telling my story. But I do think, Your Honor, even though it's been seven days, it has been fairly complex and drawing the inferences. I was going to suggest maybe we take an early lunch break, do mine, then do theirs, if the jury has time to deliberate -- in other words, instructions, give them the important breaks that you feel are necessary, then take our lunch, and I stand up, they stand up, and we are finished.

MR. JACOBS: That would be absolutely fine, Your Honor.

THE COURT: Let's -- that sounds like a fair plan to me. That would mean probably a fairly early lunch break, in the neighborhood of roughly 11:30, I think,

probably is where I would anticipate it would be.

Let me ask you this, Counsel: Do you plan on discussing the verdict forms during your closing? Some do, some don't.

The answer will sort of give me some guidance as to how much I need to say or not about the verdict forms.

MR. JACOBS: I would very much like to in mine.

MR. SCHEVE: I would fully expect I've got to show them what they need to do.

THE COURT: I am going to defer that part of my instructions to you. I will tell them I am not going to go over the verdict, because we will have an instruction in the final instructions I am sure that will tell them. In fact, in the beginning, I will go over this and that and I will go over the verdict form with you. Well, I am not going to go over the verdict form with them, with your agreement.

MR. JACOBS: I think that's fine.

THE COURT: Okay. That's a plan.

See you back in an hour.

(Luncheon recess taken.)

MR. SCHEVE: Your Honor, I have one item. Now that Abraxis has closed its case on infringement and we are where we are in the case, and they didn't call Dr. Brittain, it seems to me that the predicate facts upon which Your Honor's previous ruling about a negative inference, there is

no evidence now in this record --

THE COURT: We can address that later.

MR. SCHEVE: The reason I raise that is I do need to confer with my client whether I need to address the issue of calling him. My sense is, without any evidence in this record, there is nothing to draw an inference from.

I will need to deal with it. I am just bringing it to Your Honor's attention so you are not blindsided. But it seems to me we have a different set of facts than what was argued at the pretrial conference and, indeed, throughout the trial. They have closed. There is nothing in this record about what Dr. Brittain did or didn't do. No privilege log. Clearly there is no evidence upon which to draw an inference about anything.

THE COURT: One other thing about closing -- did you have some additional evidence you wanted? You closed your case in chief conditionally upon --

MR. SCHEVE: Yes. That the evidence from Dr. Desai and from Dr. Soon-Shiong would be included in our case.

THE COURT: That is already agreed then.

MR. SCHEVE: That was agreed by counsel. The only other thing, Your Honor, would be on the JMOL motions, how you would want to deal with that. I assume you don't want us standing up and slowing this thing down today. Will

there been time tomorrow to address that and put it on the record?

THE COURT: Well, we can do that. Frankly, I will be surprised and interested to see what the parties have to say about JMOL. This case squarely rests with the jury, to preview from me to you what I am going to be thinking about JMOL, for both sides, quite frankly.

MR. SCHEVE: We appreciate that, Your Honor.

THE COURT: But you do have to preserve your issues. Yes.

It seems to me that an easy way to do that is in some type of abbreviated written submission, so that the Federal Circuit won't have the ability to say you have waived the issue. But I can tell you that it is likely as not that I am not only not going to reserve, I am going to deny motions from both sides on all issues of JMOL. But I will hear you if you want to be heard at some point tomorrow.

MR. SCHEVE: If we do, Your Honor, I can assure you from our side it will be brief. Thank you for the guidance.

THE COURT: Mr. Jacobs, on the Dr. Brittain issue.

MR. JACOBS: On the Dr. Brittain issue, the privilege log is in evidence. That was part of the point of

clarifying what's in evidence. So is his engagement letter, it is in evidence. The negative inference is in a Court order.

From my standpoint, we dealt with all that pretrial and I get to argue the negative inference.

THE COURT: Your reaction?

MR. SCHEVE: Your Honor, there is a privilege log submitted by counsel which is indeed, they have put it on their exhibit list. Our point is, there has been no testimony from Dr. Brittain that was forecast for you on repeated occasions. In fact, this morning, there was a motion by counsel or discussion by opposing counsel about the questions they were trying to ask and trying to limit me on cross-examination. There is no testimony from Dr. Brittain. He has not been asked the question, did you not produce this information, et cetera. So there is no facts in this record -- it's not that they couldn't have tried to develop a record. But the record is now closed on their case.

For there to be an inference drawn when the jury has heard none of that, I don't know what the evidentiary basis would be.

So we would, again, Your Honor dealt with a set of cards at the time you ruled. That set of cards is far different now that you have a record. We would again urge

that there would be no basis for that. It does affect our decision on how we deal with our rebuttal case, which we hope to be two more witnesses. Depending upon Your Honor's ruling, maybe it has to be three.

MR. JACOBS: Your Honor, the order is the order. The order says there would be a negative inference. We were relying on the order. If it now seems we need to develop a record in order to support the order, I would ask that we be able to reopen our case and call Dr. Brittain.

THE COURT: I think the order addressed a request, that request that you made to the Court to consider the events that existed at the time, and that I make a ruling based upon certain activities during the course of discovery. I did.

I guess Mr. Scheve contends that that is as good only as far as it goes, in that now we have a -- I guess your argument, Mr. Scheve, is that because we have had no live testimony before the jury, or evidence of any type, adduced before this jury, regarding Dr. Brittain and his testing, that there is no basis upon which the Court should draw the jurors' attention to an adverse inference.

MR. SCHEVE: That's correct, Your Honor. Your Honor was faced with a set of allegations in the pretrial, just as in the JMOL motion, I may point out to you tomorrow in a very judicious way, that there are a couple of opinions

they needed to offer and which the law required them to offer.

THE COURT: I said I will listen to you on JMOL.

MR. SCHEVE: But to draw the inference there has got to be some evidence here from Dr. Brittain. There has been nothing established about what he did, what he didn't do, what he withheld. All that has been previewed to you. And they closed.

THE COURT: You need to address their point, Mr. Scheve, about reliance on the Court's order, I think.

MR. SCHEVE: Well, it was the in limine motion, Your Honor. The law of the Federal Circuit and the Third Circuit is very clear. An in limine motion --

THE COURT: I think it's the Third Circuit that will control.

MR. SCHEVE: It is the Third Circuit procedural issue. All in limine motions are previewing for the Court so the Court can express its preliminary views in the traditional trial of cases, what I have always understood that atom is before I open my mouth on something subject to a motion in limine I am supposed to approach the Court and get a ruling. This is still my ruling. I am going to exclude it.

But at this point the predicate of their request during pretrial was that this witness should be forced to

come and testify. He has been here pursuant to subpoena. And they didn't call him.

They have closed their case. So to say that Your Honor should be put in a position -- and I have said this, I hope I have not misinterpreted Your Honor. We really think this is error. I don't want to come back. Our position is, there is nothing here for an inference to be drawn from, because they made the lawyerly -- they used their good judgment, but they didn't put this into the case. And there is no facts before this jury upon which to draw that inference.

THE COURT: You say, Mr. Jacobs, in reliance on the Court's order you proceeded from an evidentiary point of view in a certain way?

MR. JACOBS: Yes. And I think the larger context of an issue like this is, in a pretrial ruling, one makes certain rulings and one excludes or includes evidence based on what happened in discovery. And that is what happened here. The Court issued an order saying an adverse inference shall be drawn, recounted the necessary facts leading though that adverse inference.

I can't remember litigating discovery disputes in front of the jury. Part of the reason I didn't want to put Dr. Brittain on today is, frankly, I just don't want the jury to see that kind of thing. I don't want to have to

cross-examine Dr. Brittain on what Elan produced in discovery.

That would have not been seemly. It would not have been attractive to this jury, which thinks these matters proceed in an orderly fashion.

THE COURT: So you say there are certain things that did or did not happen, during the course of discovery, and that as a sanction for some things that did not happen, specifically with regard to the testing, the production of that information, that Abraxis is entitled to at least infer that something negative as a result of the failure of Elan to do what you contend it should have.

MR. JACOBS: Exactly. An area in which I might add, District Court's have broad discretion in managing the process leading up to trial. I made a strategic call, you are absolutely right, Your Honor, I did not want the Dr. Brittain testimony to spin out in circles on circles as to who did what to whom. I think that was in the interest of the process. I was obviously interested, motivated by the result as well. It shouldn't prejudice the order we have from the Court.

THE COURT: Do we have a proposal for the instruction?

MR. JACOBS: It's embodied in the jury instructions, Your Honor. There is also this proposed

statement that I referred to before, which was another effort.

THE COURT: What about the instruction? Where is it in the instructions?

MR. JACOBS: It would be in the infringement section.

THE COURT: The folks in the well of the court and everyone can sit for a moment.

Mr. Scheve, I am going to give you a chance.

MR. SCHEVE: Thank you, Judge.

MR. JACOBS: It is in Abraxis's proposed instruction 4.3 on Page 48. I can hand it up.

THE COURT: I think I have a copy.

Maybe you better hand it up, on Page 48, there is no such instruction. I have parties proposed general instructions, clean version. And I have parties' proposed general instructions.

MR. JACOBS: May I hand it up?

THE COURT: Yes. Do you have this, Mr. Scheve?

MR. SCHEVE: I am sure my team does, Your Honor.

THE COURT: Somebody. Yes.

You know, it is interesting, Mr. Jacobs's, the title of what you handed me is parties' proposed general instructions. I have a document with the same title, but different Page 48s.

MR. JACOBS: It is perhaps an older version.

THE COURT: It may be that I have an older version.

MR. JACOBS: Maybe 4.3 has remained. 4.3, for this purpose, Your Honor.

It's after Elan's proposed opinion on, proposed instruction on willfulness.

THE COURT: It's the same 4.3. This reads, for the record, "You have heard that Elan withheld the documents of Dr. Brittain's test listed in DX-508. You shall infer from Elan's non-production of Dr. Brittain's testing documents that these documents would have been unfavorable to Elan's case on infringement."

I have just been handed, in order to refresh my recollection, a copy of my order in regards to Abraxis's motions 1 and 4, which is, I think, the relevant order.

MR. JACOBS: Yes, it is, Your Honor.

THE COURT: At the very least, just for purposes of talking about this a little bit, I would think that it would be more appropriate to say that you may infer from Elan's non-production, not you shall infer. I don't think I can direct the jury to make an inference. I can council them that they may. They are the fact-finders. Wouldn't you agree with that?

MR. JACOBS: It was actually the "shall," the

shall was in your order, Your Honor. And it was the shall that partly led us to not have to put a case on in front of them about the production. It's the last paragraph, I believe, Your Honor.

THE COURT: Well, it should have been "may," may infer. I don't think that I can -- if Mr. Scheve is right, he is right. I think he is double right -- I don't think I can instruct the jury that they shall draw a negative inference.

Mr. Scheve? Apart from your position on whether I should give this instruction at all.

MR. SCHEVE: Yes, sir. I agree with what Your Honor has said. The only other language is "you have heard evidence that." That is my position that they haven't heard it.

THE COURT: I was going to get to that. I understand why you write it this way.

I don't think I need to compound the error that I think exists in the order part, that is, in Paragraph 3 of the Court's order, where I did write "the Court will instruct the jury that it shall infer." That's incorrect, as a matter of law.

MR. JACOBS: Your Honor, if I may, let me give you what I think is the, as one of my math teachers used to say, the lemma for the dilemma.

THE COURT: Okay.

MR. JACOBS: Because we did not wish to put on in front of the jury, the saga of what happened and who produced what to whom and what instructions were given. There is a set of facts that Your Honor found in that order that would explain the story to them and with "may" would set the predicate for this. And I gave this to Mr. Scheve yesterday.

THE COURT: I will take a look.

(Pause.)

THE COURT: Okay. You say that my decision on this is going to inform, Mr. Scheve, how many witnesses you put on in your rebuttal case?

MR. SCHEVE: Yes, Your Honor. I will need to confer further with my client before I look at Your Honor and say I rest.

The language here on 42, Your Honor, where it says "you have heard that Elan withheld." The only thing they have heard is a statement by counsel in opening.

Then, there is simply no factual record that all of those items listed in Defendant's Exhibit 508 were tests on Abraxane. I can tell the Court, as an officer of the Court, the overwhelming majority of those did not involve tests on Abraxane.

So this record is devoid of evidence that would

allow Your Honor to say, you have heard evidence that that exhibit relates to Abraxane, because it doesn't.

THE COURT: I agree that as a matter of precision it would be inaccurate to say you have heard evidence. As to your statements as an officer of the Court, I respect you as such; it is attorney argument. Your representation, I have seen no declaration, evidence one way or the other as to what was in those testing documents, and you know that. While I respect your representation, it is what it is, the record, that is.

So my question to you gentlemen is, do you need to give me a few minutes to think further about this? Or are you prepared to get on with your rebuttal case?

MR. SCHEVE: I am prepared to go on, Your Honor. I apologize for throwing you this curve ball. I thought it needed to be previewed because I would like the opportunity to confer with my client before we stand up and tell Your Honor we now close on your rebuttal case.

THE COURT: Let's start on the rebuttal case and let's see how we go.

MR. SCHEVE: Okay.

THE COURT: I will tell you, I am going to be perusing this a little. But I am listening to what's going on.

Ms. Walker.

(Jury enters courtroom 2:05 p.m.)

THE COURT: All right, members of the jury. Please take your seats.

Mr. Scheve.

MR. SCHEVE: Thank you, Your Honor. In the rebuttal portion of our case we would like to recall to the stand Dr. Mark Manning, please.

MARK MANNING, having been previously sworn as a witness, was examined and testified further as follows ...

DIRECT EXAMINATION

BY MR. SCHEVE:

Q. Good afternoon, Doctor.

Very briefly, could you remind the jury who you are and where did you come from here today?

A. Sure. My name is Mark Manning. I am currently the chief scientific officer at Legacy Bio Design.

Q. I want to address in rebuttal some specific testimony that was put into the case by Abraxis during its case. The first is, the testimony of Dr. Desai, wherein he testified in this court that, "There is disulfide cross-linked albumin in our natural blood circulating around all the time."

Have you reviewed that testimony?

A. I have.

Q. Do you agree with that testimony?

A. I absolutely do not.

Q. Would you explain to the jury why you believe that that statement is not accurate?

A. Sure. Remember, before, I was talking about albumin, albumin being this protein that's found in your bloodstream at fairly high concentrations. That protein is essentially a monomer. All the treatises and descriptions of that in the literature are consistent with that. In fact, there is a well-established textbook called "All About Albumin," believe it or not, there is such a book. That tells us that in fact that is not the case.

It goes to another really important point. When the FDA considers protein-based pharmaceuticals, their overriding concern is always whether or not the protein is what they call aggregated. That means is it stuck together in large pieces or clumps. Because the larger those pieces are, the more likely there is a chance to trigger an adverse response, for the body to say, this is foreign, it shouldn't be here and tries to do something about it.

So if this was the case, I think all of us, we would be quite ill if that is in fact the case. The reality is the protein albumin in your body that's used as the starting material for the pharmaceutical products we have talked about is in fact monomeric.

Q. Then during the course of questioning of Dr. Amiji, counsel asked him, "Do you recall when Dr. Manning gave

testimony regarding 15 to 20 percent cross-linking?"
Dr. Amiji says: "Yes, I do."
Did you ever testify to that, sir?
A. I never testified to that.
Q. Would you explain to the jury what you actually testified to rather than this characterization?
A. Sure. And you can certainly check the record.
But what I told you is that in my opinion, that the albumin was essentially free of intermolecular cross-linkages, therefore was not cross-linked. So I never gave a number. I never said it was cross-linked to any extent.
Q. Now, Dr. Desai, from Abraxis, also testified at Page 1221 of the court reporter's transcript of Day 6 of the trial, "The idea of having albumin as a cross-linked shell around it helps to stabilize that structure. And by cross-linked, I mean it's like a mesh or a net. So the individual albumin molecules are linked together to create this net or mesh that holds the structure together. Those are the critical features, sort of, of Abraxane."
Did you review that testimony?
A. I did.
Q. Did you find documents within Abraxis's collection of its own internal documents that you believe shed light on the accuracy of this testimony of Dr. Desai?

A. I found no basis for this sort of statement.

Q. Now, with regard to this exhibit here, sir, which is Plaintiff's Exhibit 363, what is its significance in relating to this testimony by Dr. Desai that the albumin is in a net or a mesh around the nanoparticles?

A. This is a really important point. Remember, I was talking to you last week about this idea that proteins can be weakly associated, like when I put my hands together, or they can be strongly connected or linked, as I told you when I collapsed my hands to try to make that sort of distinction.

What you are hearing here that there is in fact this mesh or network. I think Dr. Soon-Shiong also used this connotation of a tea bag sort of thing. Is that you would have these strong chemical bonds, one protein to the next protein to the next protein. So if that was the case, then you would form this kind of network. But the reality is, as you see on this particular slide, the protein molecules come apart individually very quickly.

Over and over it says rapidly dissolves, rapidly dissociates.

So the point here is, if these, in fact, were these strong chemical bonds, it would take a great deal of energy and time for those to come apart. And there is just no way to have this entire mesh of network dissociate and

fall apart.

The other point of this slide, too, is we have heard over and over about how the albumin binds the paclitaxel and carries it inside the cell. And, in fact, albumin does that. It binds lots of different hydrophobic or poorly water-soluble molecules. Not just paclitaxel.

In other words, there is a functionality that has to occur with the albumin. Again, if you start to tie up the albumin with bond to bond to bond, most likely it's also going to limit or compromise its ability to bind the paclitaxel as well.

This whole idea of a mesh or a network is inconsistent with this sort of description. I mean, logically, you would say, if it's going to fall apart quickly, I can't tie it altogether. I have got to let them be free to dissociate.

Again, in my opinion, it is not cross-linked, based on all the scientific technical evidence we have been talking about, but just simply the way that it actually works in the body, the way we have heard it presented to the FDA, to regulatory authorities, scientific meetings. They all tell us this is how it works. That we can't have these strong bond to bond to bond across an entire network. It's kind of like, again, going back to this whole tea bag notion. Your tea bag doesn't dissolve. This network

doesn't dissolve quickly. Why? Because they are all tied together. Just like a fishing net, interconnected and so on. It has to be free to dissociate, therefore it has to be free of these strong cross-linkages.

Q. Did you view the video that Dr. Soon-Shiong showed to the jury today?

A. I did.

Q. Let's pull up a short clip.

(Video played.)

THE WITNESS: If we can stop it there. We have this pictorial description, which helps us get a sense of how this drug works. There are some things in here we need to take a close look at, if I may. The first is this particular process. Here we have the description of the paclitaxel nanoparticles surrounded by albumin. As it is shown in this description, it almost looks like it's exploding or fragmenting when it hits the surface or the cell wall or the wall of the blood vessel.

The reality is, again, it's not an explosion. It's not a fragmentation. It's dissolution, where the particles come off individually.

So you could certainly misinterpret this sort of video to say, oh, gee, this idea if I have a lollipop and I want to dissolve it in water what I should do is throw it against a wall and watch it fragment. It is not the same

process. There is a fragmentation that can occur because of mechanical energy. We are talking about putting something in the body, allowing it to dissolve. For that to happen, the albumin has to be free to move away from each other. If they are not cross-linked, yes, they can come apart very quickly.

In this sort of network, these bonds are strong, it takes a great deal of energy to break them up. That would take, as I said, some energy and some time for that to occur.

Q. Just to sum this up. If you would rewind that, please. Thank you.

Does this video showing this rapid dissociation, does that support the evidence of cross-linking of the albumin adsorbed onto the surface of the particles?

A. No, it does not. It's consistent with it not being cross-linked and free to dissociate quickly.

Q. Go to the next slide.

Now, Dr. Desai confirmed in his testimony that they were unable to discern or find a glass transition temperature from the differential scanning calorimetry, DSC. And then Dr. Desai went on and said, "And because we have albumin complex with the paclitaxel, that property of glass transition of paclitaxel is lost, because it's complexed with albumin molecules and it's not complexed with itself.

And glass transition is a bulk property, so you need bulk material, that is, a lot of paclitaxel molecules, to be associated to each other, to be able to see that. Because we have albumin, and the albumin is complexed to the paclitaxel, you wouldn't expect to see that."

Did you hear that testimony by Dr. Desai?

A. Yes, I did.

Q. Now, do you agree with this testimony, sir?

A. I do not.

Q. Could you explain to the jury what you believe to be inappropriate about it?

A. Sure. The one part here that is, again, it speaks to is this binding event. Certainly when the paclitaxel is bound to the protein floating free in solution, we don't have bulk paclitaxel. In the Abraxane product that was tested, we have these interact nanoparticles. Remember, this is a solid core, entirely consisting of paclitaxel. There is no albumin in the interior of it. There is nothing else in there except paclitaxel.

So, therefore, we have material that has bulk properties. It is a bulk. It is a chunk, if you will, of paclitaxel.

So we have a situation where it shows those bulk properties. Dr. Desai explained to you that if it's a bulk material, therefore, it should have bulk properties like

scattering x-rays. If that's true, then it should also have the bulk properties of showing glass transition temperature if it is, in fact, amorphous. So this statement tried to confuse the issue about complexation and so on, make sure we are very clear here. When that nanoparticle is intact, it displays bulk properties. Therefore, if it is in fact amorphous, there should be a glass transition temperature that can be measured by differential scanning calorimetry, DSC. That is the transition that was absolutely not observed.

Then you heard last week that my opinion about that was, therefore, it cannot be completely amorphous.

Q. The next slide, sir, where Dr. Desai also testified at Page 1230 on Day 6, he said, "So this is mixed up under high sheer conditions so you get a very fine droplet size. That will be seen in a second."

He was showing a video.

A. Yes.

Q. "At this stage, you get the cross-linking of albumin. Around the droplets, the albumin accumulates. Then the cross-linking occurs."

Did you see that video, sir, and hear his testimony?

A. I did.

Q. Do you agree with what Dr. Desai described here as

cross-linking occurring when this mixing occurs?

A. I do not.

Q. Could you explain to the jury why?

A. I have spent a lot of time looking at proteins and their stability and their formulation. And in a couple contexts I have encountered these sorts of situations. One, as you saw yesterday, I've written a book chapter that was in a volume that I edited about proteins at surfaces.

In addition, for reasons of the fact that I teach classes around the world as far as training people how to do protein-phased formulation. And so, as a result of that I have reviewed, this may sound very strange, I have actually reviewed every paper that has been published on high-sheer effects on protein since 1970, because it is a topic that people are very interested in and I want to be able to make sure I express what is exactly correct there.

In all those articles, going back now almost 40 years, there is only two articles that even talk about the possibility. And in both of those cases, they have to admit that there is no conclusive evidence that ever there is any form of intermolecular covalent disulfide cross-linking during sheer mixing.

In other words, there is not enough energy in the sheer process, and we didn't hear anything quantitatively about how much sheer is generated. That is

obviously an important thing to know. So even if you were able to create high sheer, we don't know exactly if there is or there is not in the Abraxane process. We just don't enough energy to start tearing bonds up, start to form new bonds and so on. In other words, the protein will survive chemically. You will not form these new disulfide bonds.

Q. Finally, to make sure the jury understands the distinction between the data that you relied upon and that which Dr. Amiji relied upon; again, did you hear the testimony of Dr. Amiji?

A. Yes.

Q. In terms of the materials that you relied upon as compared to what he relied upon, what differences do you want the jury to understand?

A. First of all, they put up that we didn't do any tests, which is true. The reality is, experts on neither side have done any tests. All the testing that was done was done by Abraxis' employees.

Then I want you to understand how maybe to think about or evaluate the quality of experiments. I know that's maybe a hard thing. But for me, I always set kind of three standards in my mind. The first is that you have heard about peer review, where other scientists look at the data, comment on it, say good, bad, change this, that sort of thing.

The second standard I would set is, if something has been presented to a regulatory agency, you really have to think there is some validity and truth behind that because you don't want to be making those sorts of claims to the federal government.

The third is, is there enough information presented that I myself could go back and do that experiment the same way that they did it, and hopefully get the same result.

So if we set those kinds of criteria as about being reasonable scientific approaches to say this is a good experiment, this data is worth considering or relying upon, what I have seen is that the data that I looked at really didn't meet those criteria. In all the cases, the experiments you heard about yesterday, they actually go back, they don't tell you how the samples were handled, how the samples were stored, what sort of manipulations or preparations were done before they did their testing. It was never peer-reviewed. It was never part of regulatory filings.

For all those reasons you have to be very skeptical here and say there is not data here that as a scientist I can rely upon; as a result, I didn't.

Q. Let's make sure the record is clear. When you said the experts on both sides, you are referring only to the

cross-linking issue, is that correct, as opposed to the crystallinity issue?

A. That's correct.

Q. The materials that you relied upon, were they all included in regulatory filings to our Food & Drug Administration?

A. All the ones that I relied upon, yes, they were all founded in those kinds of documents.

Q. The documents that Dr. Amiji relied on, were they sent to the FDA for review and peer-reviewed?

A. I am not aware of any of them were, no.

Q. And then with regard to the materials that you relied upon, did they include materials that were sent outside of Abraxis for purposes of scientific forums or meetings?

A. Yes, and I used some of those slides in my presentation. There were presentations made as you saw, scientific meetings, presentations to doctors and so on.

Q. Again, contrasting that with Dr. Amiji, was that data that he looked at and talked about with the jury, had that been subjected to outside peer review?

A. No data that I saw yesterday meets that criteria.

Q. I want to turn very quickly to the enablement issue, sir.

Have you reviewed the patent and claim construction orders of this Court?

A. I have.
Q. Have you reviewed all the language about how, the screening process and the various steps that are outlined in the '363 patent for selecting compatible surface modifiers for use with chemotherapy therapeutic agents?
A. I have.
Q. Do you hold an opinion, sir, to a reasonable degree of scientific certainty, as to whether or not Elan's '363 patent provides a disclosure that would enable one of ordinary skill in the art to practice the claimed invention without undue experimentation?
A. I have formed an opinion on that.
Q. What is that opinion?
A. I agree with that statement. There is sufficient description, detail, that allows someone of ordinary skill in the art to teach them to make and to use that invention described in the '363 patent.
Q. Do you hold an opinion to a reasonable degree of scientific certainty as to whether Elan's '363 patent provides a sufficient written description of the claimed invention as viewed from the perspective of one of ordinary skill in the art?
A. I have formed an opinion.
Q. What is that opinion?
A. That opinion is that I find the written description to

be clearly communicated, completely described, and certainly would allow anyone again to make and use that invention.

Q. Do you hold an opinion, sir, to a reasonable degree of scientific certainty, as to whether or not Elan's '025 patent provides a disclosure that would enable one of ordinary skill in the art to practice the claimed invention without undue experimentation?

A. I have formed an opinion.

Q. What is that opinion?

A. That opinion is, like the '363 patent, I find that the description of the patent is more than sufficient to teach a person of ordinary skill in the art to make and to use that invention without any undue experimentation.

Q. Do you hold an opinion, to a reasonable degree of scientific certainty, sir, as to whether or not the Elan '025 patent provides a sufficient written description of the claimed invention as viewed from the perspective of one of ordinary skill in the art?

A. I have formed an opinion.

Q. Now that I have asked the technical question, sir, does that '363 patent provide enough detail to show that the inventors actually achieved the invention claimed therein?

A. Yes. In my opinion, because there is such detailed description of the process, because there is a large number of examples, in my opinion, they were clearly in possession

of the entire invention.

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

A. I do.

MR. SCHEVE: Your Honor, I pass this witness.

THE COURT: Mr. Jacobs.

CROSS-EXAMINATION

BY MR. JACOBS:

Q. Dr. Manning, let's start where you left off. On enablement. Whether someone could take the description in the '363 patent back in 1992, and without undue experimentation carry out the claimed inventions. That is the issue you were addressing. Correct?

A. That's correct.

Q. And it's your opinion, to a reasonable degree of scientific certainty, that one could have done so. Is that correct?

A. That is my opinion, yes.

Q. Did you do any experiments to take the disclosure of the '363 and put yourself back with what was known in 1992 and figure out if you could actually make any of those anticancer medicaments?

A. The question is did I do any experiments myself?

Q. That's correct.

A. I did not.

Q. Did you actually study in any detail the documentation that Elan has on the troubles it was having actually making the particles described in the '363 patent?
A. I reviewed a large number of documents about what was being done in the context of that, yes.
Q. When did you do that, sir?
A. When did I do that?
Q. Yes.
A. During the course of this litigation.
Q. When?
A. I believe I started that early last year.
Q. Do you recall when last year?
A. I don't. I apologize.
Q. I have some invoices from you that, but I don't think I have the complete set. I want to see if you can shed some light on this. December was a busy month in this litigation, wasn't it?
A. Yes, it was.
Q. For you?
A. Yes.
Q. And I have you rendering 2.75 hours for the whole month of December.
A. You are saying busy as far as this case. I thought you meant busy in general. No.
Q. So when did you do all this work?

A. I believe, if I recall correctly, I started in February of last year.
Q. How many hours did you put in?
A. I couldn't tell you. The invoices I am sure would show it, because I billed by the hour.
Q. What is an end point, Dr. Manning?
A. An end point is when you do an experiment, you establish what sort of quality or performance you would like to observe or see. And then you, in most cases you try to identify some quantitative measure of that end point.
Q. What is an end point, say, for using a drug in a human?
A. End point of using a drug in a human, in the United States, the Food & Drug Administration as of 1962 has established that that should be efficacy and safety.
Q. And what's a meaningful end point for preclinical animal studies?
A. Preclinical animal studies have really two functions. They are basically to try to provide some information about the toxicity, which means does it have some correlation to the safety aspect. And the second is typically there is also animal models or some surrogate that addresses something about the biological response or activity.
Q. So what do you need in order to do that? Do you have to have a composition that you can actually deliver to the

animals and test whether they live or die?
A. You have to have a composition. In my experience, that composition may or may not be the same as the final formulation that goes into humans.
Q. But it has to be stable enough that you can do some experiments over time. Correct?
A. That's correct.
Q. You don't want instability in the formulation to interfere -- you don't want it to be, as one of our other witnesses used, you don't want it to create an artifactual result. Correct?
A. That's correct.
Q. By an "artifactual result," we mean that sort of a result that doesn't really tell you what's going on with the drug in the animal. Isn't that correct?
A. Artifact, yes, that's what that means.
Q. We don't want artifactual results, we want real, demonstrable, reliable results. Right?
A. That's correct.
Q. What you need is a formulation of your composition that's actually stable and that you can give to the animals over time and see whether it works or not?
A. Right. You want to have stability that is sufficient to allow you to do those animal studies in a timely fashion.
Q. What is the end point described in the '363 patent,

Dr. Manning?

A. The end point, I mean, are you talking about a clinical or toxicological end point?

Q. It seems to me you know a lot about end points. Did you study the '363 patent and come to a conclusion about end points?

A. Well, the invention is to allow you to provide, to stabilize nanoparticles by placing surface modifiers into the formulation, with all of the provisos and description that we have in there, yes.

Q. You said in your expert report, on this topic, certainly, any screening process involves end points that do not employ the exact same criteria for a commercially usable formulation. However, this does not make the screening end point meaningless.

Were you referring to the '363 patent, sir?

A. I was.

Q. What is the screening end point described in the '363 patent?

A. The way the screening process is described in the '363 patent is that you take a composition, where you have generated nanoparticles, and in this case they did that by grinding, but there is no limitation that you couldn't make them by some other method.

You then screen them by adding various surface

modifiers to see if there is some sort of ability of that surface modifier to keep the particles from associating. Agglomeration is the scientific term. And they did that by visual inspection.

Q. So some sort of ability by visual inspection. Is that the end point described in the '363 patent, sir?

A. It is.

Q. And let's take a look at that, just to be clear we are talking about the same thing.

This is from JX-81, the '363 patent. This is a description of the screening process. If you go down to the bottom, it states, does it not, sir, by stable, it is meant that the dispersion exhibits no flocculation or particle agglomeration visible to the naked eye, and preferably, when viewed under the optical microscope at a thousand times at least 15 minutes and preferably at least two days or longer after preparation.

Do you see that?

A. Yes.

Q. So there is a preferred end point of under the microscope and two days, but there is an acceptable end point of 15 minutes and under the naked eye. Is that correct?

A. That's correct.

Q. You wouldn't put a dispersion that had only been

proven to exhibit no flocculation or particle agglomeration visible to the naked eye for at least 15 minutes, you wouldn't put that in your body? Would you, Dr. Manning?

A. Well, that actually raised an interesting point, which is visual inspection, certainly, in this case you would see that certainly, you know, in one sense out of convenience, because, obviously, if things are so bad you can see them with the naked eye at a molecular level, that is obviously a bad thing. You want to avoid that.

But it turns out visual inspection is actually a really valuable tool in our industry. Every drug that is made for parenteral administration, that is by injection, undergoes visual inspection. And I personally had a number of clients that have lost entire batches because they failed visual inspection.

Q. That wasn't quite my question, was it, sir?

My question was, would you want to put in a human body a composition that had only been proven to not agglomerate on the basis of visual inspection for 15 minutes?

A. And that would never happen. If we go back to my statement in my expert report, I said there is a screening process, and that screening process is quite different from what you would ultimately want to use for a commercial product.

Q. Let's just focus on this screening process and exactly what you would get out of it, sir. You get 15 minutes of stability. Right?
A. Or longer, it says, yes.
Q. And you get visual-inspection-based stability. That's what it promises?
A. That's the screening tool, yes.
Q. And we are talking about nanoparticles. We have heard in this case testimony after testimony about how tiny nanoparticles are, haven't we?
A. We have.
Q. By the way, you have never intentionally created nanoparticles, have you?
A. That's correct.
Q. So you don't have a lot of experience in actually working with intentionally created nanoparticles, somebody like, a accompany like Abraxis or, for that matter, a company like Elan trying to create crystalline nanoparticles and a company like Abraxis trying to create completely different nanoparticles, you don't have that kind of experience?
A. Microparticles, but not nanoparticles.
Q. So this end point here, 15 minutes under the naked eye, that's just the starting point for lots more experimentation to see whether you have a viable drug

candidate, isn't it, Dr. Manning?
A. That's correct.
Q. Lots more experimentation. Correct?
A. In terms of making a commercial product.
Q. Even an animal test product, isn't that true, Dr. Manning? You wouldn't stick a 15-minute-based composition in an animal if you cared about the animals in your laboratory, would you, sir, and using them efficiently and productively?
A. You would certainly never intentionally risk an animal, yes.
Q. You would never intentionally risk an animal based on testing for 15 minutes of non-agglomeration, non-flocculation?
A. Again, it's a screening tool and after which you would certainly, again, if you are going continue commercial development, preclinical or clinical, there certainly, as we have heard a number of other people say, there is years of arduous effort involved.
Q. Now, is that your explanation, sir, for all these internal Elan documents that describe the problems they were having, that they were actually trying to do the next step beyond 15 minutes?
A. They certainly were engaged in a variety of activities in terms of commercial development, yes.

Q. Let's take a look at what I hope is -- no, let me flip through this.

Let's take a look at DX-190, I think. Do you see at the bottom of DX-190, sir, it says there is no surfactant of choice for parenteral products at this time?

Do you see that?

A. I do see that.

Q. Of course, they are actually trying to create something that might be viable and go into animal studies and do something for humankind. Correct? That's what's going on in this memo. Right?

A. I don't know what the context of the memo is.

Q. Let's take a look at -- let me ask you this: Do you agree with the following statement: Ten years after the 1992 '363 patent application, the choice of a surface stabilizer is non-trivial and usually requires extensive experimentation to realize a desirable formulation?

A. Could we put that quote up on the screen so I could read through it?

Q. Sure.

A. Thank you.

Q. Do you agree with that, sir?

A. If we could go through it.

Q. Just the February 2003 statement, the choice of a surface stabilizer is non-trivial and usually requires

extensive experimentation?

A. I have opinions about each piece of that. There is actually two independent statements there.

Q. I will take both.

A. The first one says the choice of a surface stabilizer is non-trivial. That is in fact the case. That is, in my opinion, the value of the '363 patent, that invention, it allows there to be a process to say -- in the formulation business we never know ahead of time which combination of stabilizer and drug will work. We may have, as over time, we will gain a sense of what that should be so we don't have to try everything in the world. But we don't know ahead of time, a priori, as they say, what that means. So in fact it is a non-trivial exercise.

The last part of the statement goes on to say, usually requires extensive experimentation to realize a desirable formulation.

Again, depending what you mean by desirable formulation, the context in which this was used, again, remember, there is a process to do the initial step, that's the beauty of the '363 patent, getting to that initial point, saying, this looks promising, let's start to do more development work. Or does it talk about the more elaborate lengthy formulation development process?

There is parts there, in the context of which

this was taken, I would either say I would agree or we would have to qualify.

Q. Let's take a look at DX-238. Page 240.

This is an internal Elan document, Technology Development Department. We are -- already, in 1993 -- go back to the opening slide, please -- we are going to introduce new technology for nanocrystals. Do you see that?

A. I do see that.

Q. Now the next page, they are saying, We have a problem. Few surfactants meet the criteria necessary for a successful drug NanoCrystal formulation.

Size, stability, safety and efficacy.

Isn't it true, sir, that they had a heck of a time getting past that 15 minutes visually observed non-agglomeration? Isn't that exactly what that slide is saying?

A. No, I don't see that slide saying that at all.

Q. The issue of contamination, is that the answer, sir, that the contamination is not an issue because all we are talking about is 15 minutes of observation in a beaker by the naked eye?

A. Sorry. Can we go over that question again?

Q. Contamination matters if you are actually going to put one of these compositions in an animal, doesn't it, sir?

A. It certainly could, yes.

Q. And contamination would certainly matter if you were going to put one in a human being, wouldn't it?
A. That is certainly true.
Q. If there were contamination issues that underpinned the very technology disclosed in the '363 patent, that would be important for people to know, wouldn't it?
A. It's important to know that the invention works the way it is intended, yes.
Q. That's my whole point, I guess. What is the intent, sir? Is the intent of this patent to create particles that subsist for 15 minutes under visual inspection? Or is the intent of this patent to create something that would be useful?
A. The intent of the patent is what's captured in the claim language.
Q. Let's go there. Thank you for leading me along. Let's take a look at some of the claims.
Let's take a look at Claim 10, one of the claims in the lawsuit.
A. All right.
Q. In a method of treating a mammal. We had some testimony about this. A mammal includes everything from mice to humans. Right?
A. That's correct.
Q. We are claiming that we have invented a method of

treating a mammal comprising administering to the mammal an effective amount of an anticancer agent, the improvement wherein the efficacy of said anticancer agent is increased by administering said anticancer agent in the form of the particles of Claim 1.

Do you see that?

A. I do.

Q. The end point here is efficacy in mammals, isn't it?

A. Yes. They claim a method for treating a mammal.

Q. Improved efficacy in mammals, that is the end point?

A. The efficacy is, yes.

Q. Then in Claim 11, in a method of treating a mammal comprising administering to the mammal an effective amount of an anticancer agent, the improvement wherein the toxicity is reduced by using the particles disclosed in this patent application.

Do you see that?

A. I do see that.

Q. So in this case the end point is reduced toxicity, isn't it?

A. Yes.

Q. Would 15 minutes under visual inspection give you any insight whatsoever into whether that composition would ultimately exhibit reduced toxicity?

A. No. That would allow you to choose which agents would

be worth moving forward with.
Q. With all that extensive experimentation that you acknowledged a few minutes ago you would still have to do?
A. Whatever experimentation would be required, yes.
Q. But it would typically be a lot, from 15 minutes to actually knowing that you have got in a mammal reduced toxicity, wouldn't it, sir?
A. Well, it would be less for commercialization as opposed to preclinical testing.
Q. But it would still be a lot?
A. It would be whatever is necessary.
Q. Well, typically, it's going to be a lot, isn't it? We saw boxes and boxes of work for paclitaxel, didn't we?
A. For their NDA, absolutely.
Q. And, by the way, mammal does include humans, doesn't it?
A. It does.
Q. So they didn't limit the claims to mice?
A. That's right, they did not.
Q. They claimed they had invented nanoparticulate anticancer agents, many of them in Claim 1, eight or so of them in Claim 5, with all these surface modifiers, and they said, we have invented a way to introduce them into mammals, didn't they, sir?
A. That's what they claimed, yes.

Q. And they claimed that they could do it with increased efficacy?
A. Yes, in Claim 10.
Q. And they claimed they could do it with reduced toxicity?
A. That's what they say in Claim 11.
Q. In the case of toxicity, sir, while this application was pending in the United States Patent Office, they never disclosed to the Patent Office all the problems with contamination that we have seen in the course of this trial, did they?
A. I am not exactly sure exactly which data was provided on that topic.
Q. By the way, what's the end point in Claim 1?
A. The end point is to -- if you put it up on the screen. It is to have particles containing medicaments useful in treating cancer. And it goes on to say that there is going to be a certain amount of surface modifier. And as we go down here, it is basically a composition patent. There is a composition of useful nanoparticles that fit the screening methodology.
Q. Where the medicament used for treating cancer is susceptible to treatment.
Do you see that?
A. Yes.

Q. **Is the end point here 15 minutes under visual inspection?**

A. **No. It is particles that have a composition that meets this language.**

Q. **What kind of stability do they have to exhibit, sir?**

A. **According to the screening process, the step is to identify which are useful versus not useful, is the visual inspection screening process we described.**

Q. **For 15 minutes?**

A. **Or longer.**

Q. **So, in your view, the end point here is anything from 15 minutes to it works in the human body?**

A. **No. My point is this is a composition claim. It's just talking about the particles and what they need to have.**

Q. **Let's go at it a slightly different way.**

A. **Sure.**

Q. **Does the '363 patent teach you how to create compositions that you would have some reasonable degree of confidence would be useful, compositions according to Claim 1 that would be useful in humans?**

A. **They teach you how to make particles, how to screen for them, they also provide guidance in terms of what surface modifiers would have reasonable success of being useful, yes.**

Q. **Reasonable success of being useful, sir?**

A. Yes.
Q. What do you mean by reasonable?
A. That in their description they say, here is a variety of surface modifiers. They go on to qualify and say that the ones that we would prefer to choose or you should choose would be those that are listed in the Handbook of Pharmaceutical Excipients, those that are commercially available or easily synthesized. So there is additional guides of what surface modifiers would be useful.
Q. Put yourself back in 1992. And somebody hands you the '363 patent. And they say, Dr. Manning, you are really smart. Go make a useful drug composition out of this. Tell me exactly what you would have to do in order to achieve that.
A. Sure.
Q. You have done that before. Right? You have made drugs?
A. I have.
Q. So you know what it takes to get from start to finish?
A. Yeah. I was actually doing it in 1992 as well.
Q. You know what it takes to get to preclinicals in animals, don't you?
A. I do.
Q. But you don't know for nanoparticles?
A. I have not made nanoparticle preparations.

Q. Leave that out and tell us the steps that you would have to do from the '363 patent disclosure, 15 minutes under visual inspection, before you had something that you would put in animals?

A. Again, the point is, first of all, we need to pick some modifiers that are going to meet the criteria. The inventors were quite clear. We are not going to try everything on the shelf. We are not going to go to a chemical catalog and buy everything that they have.

We are going to pick ones that have certain sets of properties. And that's why, also, remember, this is written for someone skilled in the art. They would have a sense of, in my business, you are going to go ahead and try things, for example, that are already found in approved products.

That list was certainly shorter in '92 than it is now. But it's still a reasonably short list. So you have some constraints on you in terms of what you are going to choose.

Once you go through the screening process and find which of those things that actually keep those nanoparticles pure, that will allow you to proceed, because before you go on and to there, you want to be careful and proceed with caution before you use that.

Q. That's okay. I think we got a sense that this is a

first step on a multi-step process, isn't it, sir?
A. For commercialization, absolutely.
Q. Even for preclinical studies?
A. Yes.
Q. Now, let's talk about the question of whether there are disulfide bonds. I want to switch away from enablement, put on your cross-linking hat and we will talk about that for a minute. Let's put up PX-165.
Do you recognize what PX-165 is, sir?
A. Not off the top of my head. Orient me, please?
Q. This is a certificate of analysis of human albumin from a company called Grifols that is certifying -- it was testified to, I believe, in the course of the trial.
A. All right.
Q. Do you have it?
A. Yes.
Q. Can we highlight the polymers and aggregates. This certification, if you were here for the testimony, this is about whether this human albumin is sufficiently comparable to the albumin in the bloodstream that it can be administered. Is that your understanding? Why don't you assume with me, I will ask you a hypothetical question. Assume with me that's what this certification is.
A. All right.
Q. Isn't it true, sir -- let's go back a little bit. You

say polymers and aggregates?
A. I see that, yes.
Q. Do you see the specification, less than five percent?
A. I do see that.
Q. So the specification for albumin with polymers and aggregates is less than five percent?
A. That's right.
Q. For this. But there is a ton of albumin in the blood, isn't there? Not a ton literally, but there is lots of albumin in the blood?
A. Yes, there is.
Q. In fact, in this case, in this Grifols, there was 4.16 percent of polymers and aggregates, wasn't there?
A. As measured by their certificate of analysis, yes.
Q. So contrary to what you said in response to Mr. Scheve's questions, polymers and aggregates are present in human serum albumin, aren't they, sir?
A. And in my previous testimony, when I talked about the fact that Abraxis uses USP albumin, they also set a similar sort of limit saying it is less than five percent polymers and aggregates.
Q. Let's see if we can connect on this. In the bloodstream, is there albumin that is represented by polymers and aggregates?
A. In the bloodstream? I don't believe there is.

Q. So this is not sufficiently similar to human bloodstream albumin, in your view?

A. Yes. Maybe I need to clarify how we get from the body to this sort of product.

All the albumin that is used in commercial products is obtained by plasma fractionation. Remember, I described for you last week something called the Cohen fractionation process. This group at Harvard in the 1940s identified a way to extract proteins from human plasma. Plasma is the part that doesn't contain your red blood cells.

When they do that, they are able to selectively precipitate or remove albumin, gamma globulin and other things that turn out to be very useful in medicinal agents. Albumin is one of those, because, as we talked about, it is present in very high concentrations.

So in the process of doing that, purifying it, isolating it and so on, there is formulation of these aggregates, these weakly associated things that form. Because that happens, to some degree, they have to set what is called a specification, saying we are going to put an upper limit and we will not sell a product that exceeds that limit. So every batch has to meet that specification.

Q. And this batch is suitable for administration to people, isn't it?

A. Yes, it is.
Q. So you could administer human serum albumin in substantial quantities with up to five percent aggregation, couldn't you?
A. That's right, because, again, we are talking about these things that are weakly associated and can come apart quite easily. So as soon as they get in your bloodstream it dilutes out and you have monomeric albumin again.
Q. Isn't that what the video showed, it broke apart and diluted and all of a sudden the paclitaxel is out?
A. What the video showed --
Q. Leaving aside the impact -- I think you misunderstood a little bit -- leaving aside the impact, didn't it show the particle breaking apart?
A. It showed the albumin coming across in individual pieces.
Q. So, sir, now let's just clarify this whole point about your testimony versus Dr. Amiji's testimony.
Let's have JX-5. Let's go to 401A.
This is the INDA. You talked about how you reviewed this document. Do you recall that?
A. Yes.
Q. Abraxis reported the level of polymers, et cetera, non-monomeric content, to the FDA in this document. Right?
A. That's right.

Q. So if we go to 401, it's Bates 401, 547 in the document. Can we highlight the albumin isomer issues.

Dr. Manning, when you reviewed this document and when you have heard the back-and-forth, you agree with me that this is the isomer ratio in the entire Abraxane composition. Correct?

A. I believe that to be the case. There is parts of it that aren't absolutely clear. But I believe that to be the case.

Q. In this particular document, Abraxis is doing precisely what you said drug companies do, they are reporting to the FDA in this case the isomer composition of all of the albumin. Right?

A. By a particular analytical method, that's correct.

Q. And it's showing that even looking at all of the albumin, about 20 percent of it is not a monomer. Do you see that?

A. Yes. By their analytical method, they find that the monomer content is 79.8 and 79.6.

Q. You weren't critiquing this analytical method?

A. In what context? I am sorry.

Q. In any context. Did you have any problem with this experiment? I don't remember any testimony to that effect?

A. I did not testify on this particular table, that's correct.

Q. You testified about it but you didn't critique it. Right?
A. Well, in my testimony I showed a different table of results.
Q. But the same data. Right? Very similar data?
A. No. In the table that I showed, after formulation, you may recall that the monomer content was reported as 84.68 percent.
Q. Let's go with that. When you looked at that one, you were looking at all the albumin. Right?
A. I believe that's how they did the experiment, yes.
Q. And you didn't -- that doesn't really tell you anything about the level of cross-linking on the albumin that's adsorbed to the amorphous paclitaxel, does it?
A. As I stated in my testimony, the analytical method of size exclusion chromatography does not tell you anything about whether or not there is an existence of a chemical strong interaction between them. Simply that there is a distribution of sizes, that's correct.
Q. This figure is not the relevant figure, or the 84 percent is not the relevant figure for the analysis underpinning this lawsuit, is it, sir?
A. I am not sure what you mean, underpinning the lawsuit.
Q. The question this jury needs to decide is whether the albumin that is adsorbed to the paclitaxel in Abraxane, that

albumin, has any kind of cross-link, isn't it?

MR. SCHEVE: Excuse me, Your Honor. May we have a sidebar?

THE COURT: You can rephrase.

BY MR. JACOBS:

Q. The technical question that needs to be asked in order to answer the question here is whether the human serum albumin that is adsorbed to the surface of the paclitaxel in Abraxane has any kind of cross-linkages between it, isn't it?

A. Yes. If I may go to the claim and the claim construction. This says that the individually adsorbed molecules had to be essentially free of intermolecular cross-linkages. That is the definition the Court has construed for non-cross-linking.

MR. JACOBS: Thank you, Doctor.

MR. SCHEVE: Nothing, Your Honor.

THE COURT: Thank you, Doctor.

(Witness excused.)

(The following took place at sidebar.)

THE COURT: Mr. Scheve is right, there is no evidence in the record. On the other hand, I would expect you would be willing to stipulate that, if recalled, he would say that he did testing on Abraxane, even though there is no evidence, you are correct.

MR. SCHEVE: Some testing on Abraxane. But I can't waive the privilege, Judge.

THE COURT: I am not asking you to do that.

MR. SCHEVE: If I say what he did or what he didn't do for Mr. Sipio, what I have told you is he didn't do any x-ray powder diffraction on Abraxane. He didn't separate any particles in doing any x-ray powder diffraction.

MR. JACOBS: That is a new fact. Now we are going further than we were.

MR. SCHEVE: The stuff he did for Mr. Sipio, I represented for you and know for a fact, that is not all on Abraxane. A lawyer goes to a Ph.D. and says help me understand some concepts. And that's what happened here. So the inference that you are being asked to draw is look at all these tests on Abraxane. And I am saying, there is no evidence in this record to support that.

THE COURT: When you hold your hands apart and you say all these tests --

MR. SCHEVE: 440-some references, that I did my duty --

THE COURT: I am not expecting to permit the use of that exhibit, number one.

Just -- let me go to the end. This may help inform your views as to how we can get through this. Here

is the instruction I am going to give: Doctor hear Britain was retained as an expert by Elan in this case. Dr. Brittain performed tests on Abraxane for Elan. Prior to trial, Abraxis requested Elan provide it with the documents related to this testing. Elan failed to produce these documents. I have been asked to decide whether this activity by Elan was proper. I have determined that under the Federal Rules of Civil Procedure it was not. As a result, I will instruct that you may infer that the contents of these documents would have been favorable to Elan's case on infringement.

That is the instruction I am going to give.

MR. SCHEVE: I will register my objection. But I understand where we are going.

THE COURT: I need to know -- Mr. Scheve is right, we don't have any evidence in the record on this issue. In other words, for me to say, as was proposed here, you have heard that Elan withheld documents -- no, the jury hasn't.

MR. JACOBS: So I think that meets, I think we he would prefer shall, under the circumstances. But I understand the Court's view. I think that is adequate. I think that would be sufficient. I don't think we need to do any kind of voir dire of Dr. Brittain. I have thought about that. But I don't think we need to do that. I think we

have the record and we can proceed.

MR. SCHEVE: Thank you, Your Honor. Could I please take a biological break. Dr. Liversidge will be our last witness in rebuttal.

(End of sidebar conference.)

THE COURT: We are going to take a short break, ladies and gentlemen. We have one more rebuttal witness from Elan, and then I should be able to tell you whether there is going to be any more rebuttal from Abraxis.

(Jury leaves courtroom at 3:00 p.m.)

THE COURT: All right. Let's bring in the jury. We are going to need to end at 4:15. I have a criminal matter.

MR. JACOBS: We will be done by then.

(Jury enters courtroom at 3:13 p.m.)

We will resume, thank you. Please take your seats.

Mr. Scheve.

MR. SCHEVE: Thank you, Your Honor. With the Court's permission, Your Honor, we would recall Dr. Gary Liversidge.

THE COURT: Okay.

... GARY LIVERSIDGE, having been previously sworn as a witness, was examined and testified further as follows ...

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

we screen about ten new compounds a week. Some weeks, you know, it may be. Some weeks, it may be 15. So I am giving you an average.

Q. Now, this screening process about which Dr. Amiji testified, sir, does the determination of whether or not you have got a compound that could move forward into development, does it end with the screen?

A. No. That's just the first step to identify suitable combinations of the drug and surface modifiers.

Q. What is communicated in the patent to those skilled in the art about the steps after using the screening process to identify potentially compatible drugs and surface modifiers?

MR. JACOBS: Same objection.

THE COURT: Sustained.

BY MR. SCHEVE:

Q. Are there companies that contain within their four walls persons of ordinary skill in the art who have a license and actually practice the '363 invention?

A. Yes, there are.

Q. What companies are they?

A. There are five. There is BMS -- I am sorry, Bristol Myers Squibb. Sanofi-Aventis. Merck. Johnson & Johnson. And I blanked on the fifth one. Let me go through that again. BMS, J&J, Sanofi-Aventis, Merck.

Q. Might it be Roche?

A. Roche, sorry.
Q. Has anyone from Bristol Myers Squibb, Roche, Merck, J&J or Sanofi-Aventis ever complained to Elan that the '363 patent does not provide adequate description of the invention?
A. No, nobody has.
Q. Has anyone from those companies who have licensed the '363 and nanoparticulate technology ever complained to Elan about how to practice the invention described in the '363?
A. No. They are all doing it.
Q. Sir, Dr. Soon-Shiong testified in the case that the invention that's disclosed in the '363 patent was designed to stay in the blood. Do you agree with that?
A. No.
Q. Could you explain to the jury why?
A. Well, you want to get the drug, as Dr. Sion -- maybe I pronounced his name wrong -- you want to get the drug to the site of action, in this particular case, the tumor. So if you kept it in the blood, it wouldn't have any efficacy. So, you know, why would you want to give an anticancer agent that doesn't get to the cancer?
We show in the patent examples of efficacy of our invention when given to preclinical models and we compare that to the commercial product and show substantial improvements in the efficacy.

Q. Through what kinds of models was that be established?
A. The murine and the xenograft models that my wife explained. I can explain them again if people want. But I thought she explained them pretty good.
Q. Are the claims of the '363 patent limited to the creation of nanoparticles using ball milling?
A. No.
Q. So if the jury goes to the claims of the '363 patent, is it only limited to nanoparticles that are created through a ball mill?
THE COURT: I think you could rephrase that.
BY MR. SCHEVE:
Q. Does the language of the '363 claims -- is it limited to nanoparticles created through a wet ball mill?
A. No, it isn't.
MR. SCHEVE: Pass the witness, Your Honor.
THE COURT: All right. Mr. Jacobs.

CROSS-EXAMINATION

BY MR. JACOBS:
Q. Let me see if we can clear up a little bit of confusion.
BMS, do you have a relationship with them?
A. Yes. I thought that was a statement. Sorry.
Q. It was a kind of question. If it confuses you, I will do the other kind. I don't mean to try and confuse you.

A. No, that's okay.
Q. Did you go to BMS and say, BMS, here is the '363 patent, nothing else, we want X percent of the royalties on the drugs that you create?
A. Could you just rephrase that, counselor?
Q. I will rephrase it. Does your relationship with BMS consist of Elan providing BMS with the '363 patent, nothing else, and saying, go forth and prosper and give us a percentage of your revenues?
A. The '363 and other patents are included in the license.
Q. Many other patents. Correct?
A. There are. But don't ask me the number. I just can't remember off the top of my head.
Q. If the jury takes a look at that license agreement, they will see a long list of patents. Right, sir?
A. You are definitely going to see a list of patents. I just can't tell you exactly the number in there.
Q. But the fact is that Elan has improved on the technology in the '363 patent over time, hasn't it?
A. Yes. I mean, everyone strives for continual improvement.
Q. In fact, you have made, in your corporate view, substantial improvements over what you disclosed in the '363 patent. Correct?

A. Well, we have other patents which were issued after that one that covers the NanoCrystal technology.
Q. And whether or not it is in a patent, you have just developed the technology you spent 15 years working on, that technology. Correct?
A. I think maybe a little longer than that. Yes, round about that much time.
Q. You have be invested lots and lots of money to try and take the '363 disclosure and make it something that would be actually useful to drug companies. Correct?
A. I am not following you. Ask me a slightly different way, please.
Q. The questions Mr. Scheve was asking you were, did anyone complain to you that the '363 patent doesn't provide enough disclosure. Do you recall those questions?
A. Yes.
Q. Nobody is -- in fact, literally no one has just taken a license to the '363 and not gotten anything else from Elan. Correct?
A. I think you are right.
Q. So no one has just been given a little package of however many columns and pictures in it, where Elan says to them, take the '363, go develop drugs, by the way, if you have any problems, give us a call? You haven't done that with anybody. Right?

A. No, we haven't.
Q. You have always given them a complete package representing lots and lots of development work beyond the '363 patent disclosure. Correct?
A. Beyond the invention, we have shared with them additional know-how and development aspects, yes.
Q. Including manufacturing methods?
A. I am trying to think.
Q. Including much later on in time, you developed some techniques to reduce contamination. Right?
A. We had techniques at the time as well.
Q. But later on you developed techniques to reduce contamination, didn't you?
A. In addition to the ones we already had, yes.
Q. And the '363 patent doesn't actually tell you how to take the contamination out of the particles that you have developed, does it?
A. It teaches you through carbon 5 through 7 how to optimize the formulation, and the embodiment there is the milling process, and it teaches you all the conditions in there in which to be employed.
Q. So while I was sitting there, trying to get up here very quickly to ask you questions, I did the math, let's see if we can compare notes.
I believe you said that you screen on average

ten or 15 compounds per week. Is that right?
A. Ten. Some weeks it may be 15, maybe some weeks it may be five. On average, I would say about ten.
Q. That's about 520 per year. Right?
A. Yes.
Q. Let's just take a low-end estimate of what Dr. Amiji was saying, how many compounds there are.
Let's say there were 52,000 combinations of compounds in the '363 patent. By my calculation that would take a hundred years. Does that match your math?
A. It obviously didn't. I don't want to seem facetious, but, you know, we get the compounds and they go out in that same week.
Q. The ten compounds a week?
A. Yes.
Q. On this issue of prolonged circulation in the bloodstream, are you suggesting that it was not Elan's intent that the NanoCrystal anticancer medicaments you were thinking about in the early nineties exhibit prolonged circulation in the bloodstream?
A. Some will, depending on the stabilizer system, some won't.
Q. I asked you about Elan's intent around the time of the '363 patent. Isn't it true that it was Elan's intent that the NanoCrystal compositions exhibit prolonged circulation

in the bloodstream?
A. I am trying to think what our intent was back then.
Q. Can I help you a little bit by showing you a document?
A. Sure. That would help. Thank you.
Q. So this is the -- these are the slides you sent to Abraxis. Do you recall that exhibit?
A. Yes, I have seen these before.
Q. JX-20. Did you actually write these slides, Dr. Liversidge? I don't remember if we covered that.
A. Some of them I definitely did. Some of them I am not sure about.
Q. How about the ones we have highlighted here on the screen, the page is indicated Parenteral NanoCrystal Applications. The drawing of the Y with the NanoCrystals and Application of NanoCrystal Technology to Parenterals?
A. I definitely know that middle one, like the blood vessel, I definitely did that. The other two I am not -- I just can't recall. But I definitely know that middle one.
Q. You sent this in 1996 to Abraxis. Correct?
A. Yes.
Q. And the slides themselves were created a few years before?
A. I just, honestly -- some of them may, some of them may not. I just can't tell you.
Q. It is true, is it not, Dr. Liversidge, that these

slides exhibit a design idea of restricting compounds to the bloodstream? Correct?

A. I think that top one you have got there, that A, says platform to restrict compounds to the vasculature.

Now, we have to take that in light of the major therapeutic focuses that were there for Sterling.

We had a major diagnostic imaging program.

People may not be familiar with diagnostic imaging. What you do is, say, you have a blockage in the heart, and you want to see how bad the blockage is. What you take is an imaging agent, which has iodine molecules on it, so they are radio dense, when you shine the x-rays through, you don't go through those. What we have is a lot of these water-soluble agents.

So if we wanted to, God forbid if this ever has to happen to you, but if you had a heart attack, what we would do with the state of the art at the time is, we would get into your artery, cut you in the groin, then we would thread up this tube to just above your heart, and then we would squirt in the imaging agent. And what happens to that imaging agent is it diffused that rapidly so we only got one shot of you. If we mucked it up, you have to come back a month later, because the imaging agent had to clear.

So one of our focuses was to try and restrict these diagnostic imaging agents to the vasculature so we

could just have these nanoparticles, a simple peripheral injection that would fly all around the body and we could image your heart. And if we didn't get a good picture, we could image it again.

That is the genesis on this top yellow thing that you have highlighted.

Q. The same is true for the bottom that I have highlighted, Application of NanoCrystal Technology to Parenterals, Focus: Poorly water soluble diagnostic imaging agents and oncologics that may benefit from prolonged vascular circulation?

A. No doubt about it, that's what we say. Could I just give you a little bit of explanation?

Q. I think I got the answer I wanted, which was yes?

A. It's always but. All right. Since the Court's wants us to move along, I won't give you the explanation.

Q. Thank you, Doctor.

MR. JACOBS: No further questions, thank you.

THE COURT: Mr. Scheve.

REDIRECT EXAMINATION

BY MR. SCHEVE:

Q. Just quickly, Doctor. Do you have an explanation that you wanted to offer in response to the last question?

A. Yes. It was just that many particulates, when they are given an IV, they get taken up by what is called the

reticuloendothelial system. And there is a special type of cell that literally comes out and grabs these particles. And these fibrositic cells are located in the liver and spleen.

So what happens is a major problem for particulate or nanoparticulates and delivery systems in our art is people would inject them. And the body is designed to naturally take up these foreign particles into the liver and spleen.

What we were trying to avoid here, we were trying to communicate, albeit poorly and I can see the confusion, we were trying to say, we don't want this to happen because they clear very fast from the blood system. But they don't go to the tumor. They clear to the liver and the spleen. And so you don't want that. You want to keep them in the blood system, so they have sufficient time to go out and accumulate in the tumor.

MR. SCHEVE: That's all I have, Your Honor.

THE COURT: All right. Thank you, Doctor.

(Witness excused.)

THE COURT: Mr. Scheve.

MR. SCHEVE: Your Honor, I get to utter the words, we rest.

THE COURT: All right. Mr. Jacobs.

MR. JACOBS: We rest, Your Honor.

THE COURT: All right. For planning purposes, let me see counsel.

(The following took place at sidebar.)

THE COURT: I am trying to decide what time to have the jury hear, because we are not going to be ready with these instructions tonight. That is clear. The logistics of this will be somewhat of a challenge. I don't know if you have a more recent iteration for me.

MR. SCHEVE: I think they have been banging heads on the sixth floor.

THE COURT: We will be able to talk about that tonight?

MR. SCHEVE: If I told you I would be speaking from a position of lack of knowledge.

THE COURT: If we can talk about them tonight, that's going to advance the issue, the time that the jury can come in.

But if we can't, we are going to need to spend, I would imagine, a little bit of time, beginning at maybe 8:30, talking about them. I am thinking about having the jury report at 10:00. What do you think?

MR. SCHEVE: I think it is a good idea.

MR. JACOBS: That sounds fine.

THE COURT: Do the physical collating and get the instructions.

MR. JACOBS: Can I raise one thing, responsive to your comment about the length of reading of the instructions.

Is there some way the parties could stipulate to some other procedure? We wouldn't have to talk to them to two full hours --

THE COURT: I am open.

MR. SCHEVE: I think the law requires it, Judge. I am sorry, I know it's miserable, I think it's required.

THE COURT: Over the evening, I will take another look at that.

MR. SCHEVE: We will look, too.

MR. JACOBS: There are obviously some key instructions that go to the issues. But I think they kind of got the point of this exercise.

THE COURT: I agree with the spirit of what you are saying.

My thinking is that Mr. Scheve is probably correct.

I only injected what I did because of the reality that it does become a rather exhausting process for them listening. I wouldn't mind taking a break, either. Delivering patent instructions, you have been in complex cases --

MR. SCHEVE: Yes, Your Honor, but not this kind

of stuff.

THE COURT: Any complex civil stuff can get rather dense.

Let's tell them, we will resume at 8:30 but the jury will be here at 10:00.

(End of sidebar conference.)

THE COURT: All right, ladies and gentlemen. We have now come to the close of the evidence from both parties. And it is going to be my job to next give you final instructions. That won't happen today. We were just talking about trying to plan the logistics of this and what time you should come back, because there is still some discussion that I must have with the lawyers about some differences they have over how the final instructions should look, not in terms of physical appearance, but the contents of the instructions.

So other lawyers you don't see here for both sides are in the process now of having a discussion with a view toward trying to narrow down those disputes.

Eventually, to bring to me for resolution with regards to those they can't resolve on their own. With that in mind, we will take our best guesstimate. And I am going to tell you to be back here at 10:00 o'clock in the morning, with the earnest hope that we will all be ready for you. We will start well before you get here, but by the time you get

here, it is our hope that we will be prepared to have you come in, have me instruct you, probably take a lunch break at that point, and then come back and hear the closing speeches of counsel. Then we will give you the case.

Now that all the evidence is in, it is critical for you to recall my earlier instructions: Keep an open mind. You will have time to discuss the evidence and come to a conclusion after you have listened to one another, considered all the evidence that you deem it appropriate to consider.

Don't do any research. Don't listen to anything touching on this subject of cancer research drug development at all. I would suggest, just leave alone any drug development things that you might run across in the popular literature over the evening and on TV or the radio. Don't talk about these events with anyone. We will see you back here tomorrow at 10:00 o'clock. Take care. Travel safely.

(Jury leaves courtroom at 3:37 p.m.)

THE COURT: Mr. Scheve, is there anyone here that you can ask that question?

MR. WALTERS: The status of the jury instructions?

THE COURT: Yes.

MR. WALTERS: We took Your Honor's words to heart and met this afternoon, Mr. Sullivan and I. And

narrowed them down significantly. I think we are at the point where we need to get, to talk to Mr. Jacobs and Mr. Scheve about a few issues, and one of our associates is back turning around what we had agreed upon. And there is about, I don't know the exact number, but around, around ten issues that are still teed up that we need to have a discussion among lead counsel.

THE COURT: You have teed up these issues for discussion with lead counsel?

MR. SULLIVAN: And eliminated others, Your Honor.

MR. WALTERS: They are in trial, so we knew that wasn't going to happen this afternoon.

THE COURT: It would be helpful, if possible, if you can get just those that remain at issue after lead counsel get a chance to consider your positions, and just provide me with a copy of those before we leave for the end of the day. I could take those home with me.

MR. SCHEVE: Your Honor, may I suggest that in light of the instruction that you read to Mr. Jacobs and I, that we may go from ten to nine, I suspect that's one of them, about which there is some controversy. They wouldn't be aware that Your Honor has advised us of what the instruction would be.

THE COURT: Okay. Perhaps I will just give you

this piece of paper with my handwriting on it. I think it's legible enough. Mr. Maurer has transcribed it verbatim.

MR. WALTERS: I assume for the rest of the package, just a clean copy of the entire set of instructions.

THE COURT: Yes.

What I need to have, as to the disputed instructions, is the reasons for the disputes. And the authority that each of you cite in support of your positions, so that's I can consider that authority and come to some conclusion.

Again, if you are able to get that to me tonight, that would be a great thing. I will be here until around -- well, probably at least until 6:00. And maybe after that, depending, if you give a call and want me to wait, because I may go downstairs. We will make a couple of copies of this. This is the instruction regarding Dr. Brittain, that I have jotted an instruction down.

Ms. Walker will make a copy for each side, so you will have it, particularly for Mr. Scheve's side.

MR. JACOBS: We have a Rule 50 motion, Your Honor.

THE COURT: Yes.

We could do that now, if you are ready. Or we could do it as part of our exercise in the morning.

MR. SCHEVE: I think it would be helpful for us, Your Honor, to be able to get it in the written format you described, more of a bullet point sort of approach.

THE COURT: Okay. Ms. Walker, Mr. Jacobs is approaching with something.

You are Bench-filing this.

MR. JACOBS: Yes, we will also e-file, Your Honor.

THE COURT: Mr. Scheve has his side's copy.

These are all the same?

MR. JACOBS: Yes, they are.

THE COURT: Anything else, counsel, before we recess?

Just give a call over to chambers.

(Court recessed at 3:40 p.m.)

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Reporter: Kevin Maurer